Trachomatous Trichiasis:
Surgical Management and Impact

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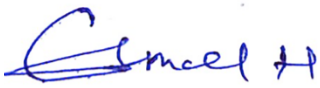
Declaration

I, Esmael Habtamu Ali, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature: 

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Abstract

Background

Trachomatous trichiasis (TT), is the in-turning of eyelashes from long-term, progressive conjunctival scarring initiated by *chlamydia trachomatis*. It is the painful blinding stage of trachoma. We aimed to measure impact of TT on Quality of Life (QoL) and household poverty; identify the most effective of two commonly used surgical TT procedures; and measure impact of TT surgery on QoL and daily living.

Methods

A randomized, controlled, single-masked clinical trial was conducted in Ethiopia comparing the bilamellar tarsal rotation (BLTR) and posterior lamellar tarsal rotation (PLTR) procedures (1000-participants). A case-control study was nested within the trial to measure QoL using standard quantitative tools, and household poverty using three economic measures (asset-based analysis, self-rated and peer-rated wealth) among TT cases and compared to healthy neighborhood controls (200-participants). These participants were followed-up after one year to measure impact of TT surgery on QoL and daily living using the same tools.

Results

PLTR was the superior surgical procedure, with only 13% recurrent TT by 12-months compared to 22% in the BLTR (OR=1.96; 95%CI:1.40–2.75; p=0.0001). At baseline, TT cases were more likely to belong to poorer households with substantially lower QoL, less likely to participate in, more likely to report difficulty and assistance in performing productive and leisure activities regardless of visual impairment than controls. Twelve months after surgery, QoL scores of TT cases and their ability to perform daily activities without difficulty and assistance improved substantially, independent of the presence of visual acuity improvement.

Conclusions

PLTR surgery appears to be superior in terms of reduced recurrence and complications for the programmatic management of TT. TT is associated with household poverty and is disabling and substantially reduces QOL. Corrective surgery improves QoL and functional capabilities of affected individuals even without vision gains and may contribute to improved household income and wealth.

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Glossary of Abbreviations

ANOVA	Analysis of Variance
ARHB	Amhara Regional Health Bureau
AT	Active Trachoma
BLTR	Bilamellar Tarsal Rotation Surgery
CI	Confidence Interval
CO	Corneal Opacity
Ct	Chlamydia trachomatis
DSMB	Data Safety Monitoring Board
EB	Elementary Body
ECA	Eyelid Contour Abnormality
ELQ	Economic Ladder Question
FDR	False Discovery Rate
FMHACA	Food, Medicine and Healthcare Administration and Control Authority of Ethiopia
FPC	Follicles Papillae Cicatricae
GAR	(Education) Gross Attendance Ratio
GET2020	Global Elimination of Trachoma by the year 2020
GDP	Gross Domestic Product
HEAD START	Human Eyelid Analogue Device for Surgical Training And skills Reinforcement in Trachoma
HRQoL	Health Related Quality of Life
ICEH	International Centre for Eye Health
IECW	Integrated Eye Care Worker
LGV	Lympho Granuloma Venereum
IL	Interleukin
LMICs	Low and Middle Income Countries
LogMAR	Logarithm of the Minimum Angle Resolution
LSHTM	London School of Hygiene & Tropical Medicine
LSMS	Living Standard Measurement Survey
MMP	Matrix Metalloproteinases
MPI	Multidimensional Poverty Index
NGO	Non-governmental Organisation
NRERC	National Research Ethics Review Committee
OR	Odds Ratio
PBD	Prevention of Blindness and Deafness
PBL	Prevention of Blindness
PEEK	Portable Eye Examination Kit

PIQ	Pain Impact Questionnaire
PCA	Principal Component Analysis
PTT	Postoperative Trachomatous Trichiasis
PLTR	Posterior Lamellar Tarsal Rotation Surgery
PPP	Purchasing Power Parity
QoL	Quality of Life
RB	Reticular Body
RCT	Randomised Controlled Trial
SAFE	Surgery, Antibiotic, Facial Cleanliness, Environmental improvements
SD	Standard Deviation
SES	Socioeconomic Status
SOP	Standard Operating Procedure
TCC	The Carter Center
TF	Trachomatous Follicle
TIMPs	Tissue inhibitor of Matrix Metalloproteinases
T_H1	Type 1 T-helper cell
T_H2	Type 2 T-helper cell
TS	Trachomatous Scarring
TSC	Trial Steering Committee
TT	Trachomatous Trichiasis
TNF-α	Tumour Necrosis Factor-α
USD	United States Dollar
VF	Visual Function
VI	Visual Impairment
VRQoL	Vision Related Quality of Life
WHO	World Health Organization
WHOQOL-BREF	World Health Organization Quality of Life – Brief version of QoL measure

Acknowledgment

The work presented in this thesis has been a team effort. It would not have been possible without the contributions of many individuals both in the UK and Ethiopia to whom I am extremely grateful. The specific contributions of these individuals are highlighted in Table I.

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I dedicate this thesis to Escholarez, Zebiba, Abatie and Abba.

An excellent and hard working research team

Table I: List of people contributed to the work presented in this thesis

Person	*Position*	*Contribution*
Abusent Admas	Trichiasis Surgeon, ARHB	Conducted the TT surgeries in the trial
Addisu Yayeh	Examination Assistant, LSHTM/TCCE	Assisted ocular clinical examination at baseline and follow-up, participant tracking
Aderajew Mohammed	Deputy Country Representative, TCCE	Coordinated project work, and reviewed manuscripts
Alemnesh Tewabe	Trichiasis Surgeon, ARHB	Conducted the TT surgeries in the trial
Amir Bedri	Medical Advisor, Light for the World	Trial steering committee, study design and review of manuscripts
Animaw Andualem	Trichiasis Surgeon, ARHB	Conducted the TT surgeries in the trial
Asmamaw Taddele	Head, Mecha Woreda Administration	Coordinated participant recruitment and follow-up
Bayelign Getinet	Research Data Collector, LSHTM/TCCE	Conducted visual function tests
Befkru Liyew	Research Data Collector, LSHTM/TCCE	Randomisation and intraoperative data collection, and follow-up visual function test
Belayneh Molla	Research Data Collector, LSHTM/TCCE	Randomisation and intraoperative data collection
Berhanu Getie	Mecha Woreda Administration Team Member	Coordinated participant recruitment and follow-up
Berhanu Melak	Amhara Region Trachoma Project Deputy Manager, TCCE	Coordinated field work, and reviewed manuscripts
Bezawit Atinafu	Ophthalmic Nurse, Felegehiwot Hospital	Conducted the TT surgeries in the trial
Binyam Lakew	Field Coordinator, LSHTM/TCC	Coordinated field work, took informed consent
Biruk Zerihun	Research Data Collector	Informed consent and patient interview (QoL& asset data) at baseline and follow-up
Bizuayehu Gashaw	Deputy, Amhara Regional Health Bureau	Coordinated project work, and reviewed manuscripts
David Mabey	Professor, LSHTM	Trial steering committee, study design and review of manuscripts
David Macleod	Statistician, LSHTM	Data analysis and review of manuscript
Desalegn Amsalu	Driver Logistician, LSHTM/TCCE	Drove the research team and trial participants at baseline and follow-up
Gedefaw Bazie	Field Co-ordinator	Coordinated filed work and visual function test
Guadie Sharew	Ophthalmologist, Bahirdar University	Trained and standardised TT surgeons, reviewed manuscripts

Friew Demeke	Logistic Officer, TCCE	Facilitated logistics
Haile Tegegn	Senior Accountant, TCCE Bahirdar	Managed finances
Hannah Kuper	Professor, LSHTM	Study design, data analysis and review of manuscripts
Helen Weiss	Professor, LSHTM	Trial steering committee, study design, data analysis and review of manuscripts
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Kefale Tewodie	Research Data Collector, LSHTM/TCCE	Informed consent and patient interview (QoL data) at baseline and follow-up
Kelly Callahan	Director, TCC Trachoma Control Programme	Trial steering committee, study design and review of manuscripts
Matthew Burton	Professor, LSHTM	PhD supervisor, project funding, study design, analysis, write-up and review of manuscripts
Mekides Samuel	Data Manager, LSHTM/TCCE	Data entry, cleaning and management
Metages G/Michael	Research Data Collector, LSHTM/TCCE	Conducted 10 day follow-up, suture removal, intraoperative data collection, and randomisation
Mezene Getnet	Research Data Collector, LSHTM/TCCE	Informed consent and patient interview (QoL data) at baseline and follow-up
Mulat Zerihun	Amhara Region Project Manager, TCCE	Coordinated field work, and reviewed manuscripts
Paul Emerson	Director, International Trachoma Initiative	Trial steering committee, study design and review of manuscripts
Robin Bailey	Professor, LSHTM	Trial steering committee, study design and review of manuscripts
Sarah Polack	Senior Lecturer, LSHTM	Study design, data analysis and review of manuscripts
Saul Rajak	Honorary Lecturer, LSHTM	Trial steering committee, study design and review of manuscripts
Seble Aliye	Finance and Administration Manager, TCCE	Facilitated project work
Sintayheu Aweke	Field Coordinator, LSHTM/TCCE	Conducted clinical examination at 6-month FU and coordinated recruitment campaigns
Sitotaw Essa	Trichiasis Surgeon, ARHB	Conducted the TT surgeries in the trial
Solomon Berhanu	Operations Manager, TCCE	Facilitated logistics
Tadesse Asrade	Pharmacist, LSHTM/TCCE	Randomisation
Tariku Wondie	Field Coordinator, LSHTM/TCCE	Coordinated recruitment campaigns, follow-ups and research team, managed finances

Tebkew Tilahun	Photographer, LSHTM/TCCE	Taken thousands of eyelid and cornea pictures
Tekalign Mamo	Driver Logistician, TCCE	Facilitated logistics
Temsegen Gelaw	Driver Logistician, LSHTM/TCCE	Drove the research team and trial participants at baseline and follow-up for thousands of kilometers
Tewodros Mekuriyaw	Photographer, LSHTM/TCCE	Taken thousands of eyelid and cornea pictures
Wondimu Gebeyehu	Head, Regional Health Research Laboratory Center	Coordinated project work, and reviewed manuscripts
Yohannis Muche	Trichiasis Surgeon, ARHB	Conducted the TT surgeries in the trial
Yossef Adane	Research Data Collector, LSHTM/TCCE	Informed consent and patient interview (QoL& asset data) at baseline and follow-up
Zebideru Zewudie	Deputy, Amhara Regional Health Bureau	Trial steering committee, and reviewed manuscripts
Zerihun Tadesse	Country Representative, TCCE	Trial steering committee, study design and reviewed manuscripts

Executive Summary

Trachomatous trichiasis (TT) is the in-turning of the eyelashes towards the eye, which results from progressive conjunctival scarring caused by recurrent infection with *Chlamydia trachomatis.* Trichiasis causes painful abrasion of the cornea, leading to corneal opacification and usually irreversible visual impairment. Approximately 3.2 million people have un-treated TT, and 2.4 million people are visually impaired from trachoma of whom 1.2 million are irreversibly blind, making trachoma the leading infectious cause of blindness worldwide.

Trachoma has been long considered a disease of the poor. However, surprisingly there are no adequate quantitative data that formally evaluate and demonstrate this association. It is possible that the people vulnerable to developing TT are the poorest members of the poorest communities. Moreover, TT is thought to have significant social and economic consequences for effected families and communities. It causes significant morbidity due to pain, photophobia and visual impairment, which may greatly hamper quality of life (QoL). The disability caused by TT could lead to reduced productivity, unemployment and loss of income, putting additional financial pressure on an already strained household. These issues have not been adequately investigated before.

The WHO recommends surgery for trichiasis to reduce the risk of blindness using two commonly used procedures: Bilamellar Tarsal Rotation (BLTR) and Posterior Tarsal Rotation (PLTR). There is currently an unprecedented effort to scale up global TT surgery output and improve outcomes, to clear the huge TT backlog. However, recurrence and other unfavourable outcomes following TT surgery are frequent and are undermining these efforts. Despite being a WHO priority research question the relative effectiveness of these two surgical procedures under operational conditions has not been adequately studied.

The effect of TT surgery may go beyond reducing the risk of blindness. It may restore overall wellbeing and capacity to engage in productive household and agricultural activities by effectively treating the pain and photophobia from TT. However, detailed empirical data on the impact of surgery on QoL and functioning are lacking. This project aimed to measure the impact of TT on QoL and household poverty; identify the best surgical procedure for the management of TT; and measure the impact of TT surgery on QoL and daily living.

The project was conducted in Ethiopia and was structured in three interrelated study designs.

The first was a randomized controlled single masked clinical trial to compare the relative effectiveness of the BLTR and PLTR procedures. In this 1000 TT cases with tarsal conjunctival scarring were enrolled, randomized in a 1:1 ratio, operated and followed for one year. The second was a case-control study nested within the trial to measure QoL using standard WHO quantitative tools; and household poverty using three economic measures (asset-based analysis, self- rated wealth and peer-rated wealth) among the TT cases and then compared this with 200 neighborhood healthy controls matched to every fifth trichiasis cases enrolled into the trial. The third was a longitudinal study, in which participants in the case-control study were followed at one year to measure the impact of trichiasis surgery on QoL and daily living using the same tools as the baseline.

PLTR was superior to the BLTR; with only 13% recurrent TT by 12-months compared to 22% in the BLTR (OR, 1.96; 95% CI, 1.40 – 2.75; p=0.0001). Performing more peripheral dissections using scissors reduced postoperative TT in both surgical procedures (PLTR: OR, 0.70; 95% CI; 0.54–0.91; p=0.008; and BLTR: OR, 0.83; 95% CI, 0.72–0.96; p=0.01); while suture distance asymmetry of >2mm (OR, 3.18; 95% CI, 1.31–7.70; p=0.01) and irregular posterior lamellar incision (OR, 6.72; 95% CI, 1.55–29.04; p=0.01) predicted eyelid contour abnormality and granuloma respectively in PLTR surgery.

The case-control studies showed that, trichiasis cases at baseline were more likely to belong to poorer households by all economic measures employed: asset-based analysis (OR, 2.79; 95%CI: 2.06–3.78; p<0.0001), self- rated wealth (OR, 4.41, 95%CI, 2.75–7.07; p<0.0001) and peer-rated wealth (OR, 8.22, 95% CI, 4.59–14.72; p<0.0001); and have substantially lower vision and health related QoL (p<0.0001), be less likely to participate in productive and leisure activities, be more likely to report difficulty and need more assistance in performing productive and leisure activities regardless of visual impairment or postoperative TT than the controls.

The longitudinal studies showed that, twelve months after surgery, vision and health related QoL scores of trichiasis cases improved substantially by 19.1–42.0 points (p<0.0001) and 4.7–17.2 points (p<0.0001), respectively independent of the presence of vision improvement or postoperative TT. In addition, their ability to perform daily productive and leisure activities without difficulty and assistance improved substantially, regardless of the presence of vision improvement or postoperative TT. In contrast these remained largely unchanged among the comparison participants.

The results provided strong evidence that PLTR surgery could be the preferred procedure for the programmatic management of TT. Addressing specific surgical factors during surgery would improve outcomes. TT is associated with household poverty and is disabling and substantially reduces vision and health related quality of life. Corrective surgery improves overall wellbeing and functional capabilities of affected individuals regardless of vision gains and may contribute to improved household income and wealth. These data lend strong support to the view that TT surgery improves function and contributes to improved household income and wealth. Prompt trichiasis intervention using the PLTR is needed both to prevent vision loss and to alleviate physical and psychological suffering, social exclusion and improve productivity and wellbeing.

1 Background

1.1. Overview

Trachoma is the leading infectious cause of blindness worldwide.[1] It is a chronic kerato-conjunctivitis caused by *Chlamydia trachomatis* (*Ct*). Trachoma begins in childhood with recurrent episodes of follicular/papillary conjunctivitis (active trachoma). Chronic inflammation results in immuno-pathologically mediated conjunctival scarring (TS), which causes eyelid in-turning (entropion) with eyelashes scratching the eye, which is known as trichiasis (TT). Eventually sight is lost as irreversible corneal opacification develops (CO).

The infection commonly affects the poorest communities, where there are crowded living conditions and poor water supply and sanitation. Currently, more than 200 million people live in trachoma endemic areas worldwide, of which more than half are found in Africa. The Global Trachoma Mapping Project (GTMP) estimated 3.2 million people have trachomatous trichiasis and are at immediate risk of irreversible blindness.

The impact of blinding trachoma on the individual is devastating. The blindness (unlike that of cataract) is not treatable. Trachoma has major personal, social and economic consequences for effected individuals, families and communities.[2] TT results in significant morbidity due to the visual impairment and pain that it causes and visual impairment from the TT is likely to hamper quality of life and lead to a loss of income at the individual and family level. However, there is currently very limited data on the impact this condition has on the lives of people with TT and their families.

The WHO Alliance for the Global Elimination of Blinding Trachoma by 2020 (GET2020) recommends the use of the ***SAFE Strategy*** for trachoma control.[3] This involves **S**urgery for trichiasis, together with **A**ntibiotics (azithromycin or tetracycline), **F**acial cleanliness and **E**nvironmental improvements to suppress chlamydial infection and transmission. Surgery reduces the risk of blindness from TT by correcting the position of the in-turning lashes through lid margin rotation.[4-6] However, TT frequently recurs after surgery for reasons that are poorly understood.[7] One determinant for recurrence is type of surgical procedure. However, the two most commonly used surgical procedures have not been compared adequately.

This chapter discusses trachoma, its clinical features, pathophysiology, distribution, impact on quality of life and household socioeconomic status, factors influencing recurrence after surgery, and the impact of TT surgery on affected people lives.

1.2. History of Trachoma

Trachoma is an ancient disease. It is believed that the disease first started in ancient Mesopotamia, subsequently spreading towards the west into the wider Middle East region and towards the East into China along ancient trade routes.[8] The earliest references to trachoma are associated with its management. One of the earliest Chinese Emperors in the 2700 BC had trichiasis surgery.[8,9] The Chinese also used different treatments for trachoma, which included copper compounds and rubbing of the eyelid with garlic.[8] Trachoma was traditionally referred by the Chinese as "pepper-seed-like lesions" and "millet-like granules", names that clearly resemble the clinical manifestations of the active infectious stage of the disease.[8] Epilation forceps were found in the site of the ancient city of Ur (Iraq), dating from around 2600BC, suggesting that trachoma existed as a major problem during the times of ancient civilisation.[8]

Trachoma was probably common problem in ancient Egypt in the 15th Century BC. The Egyptians mostly used topical application of substances to treat eye disease, which included onions, myrrh and gazelle juices, and mineral components such as lead sulphate and lead acetate.[8] Ancient writings in India from around 1000 BC described "roughening and thickening in the inner surface of the eyelid", suggestive of conjunctival scarring.[10] These were treated with traditional topical substances such as ginger, rock salt, honey, sulpharsenic acid and ferrous sulphate.

Trachoma was also troubling condition in ancient Greece during the 4th century BC.[8,11] Plato described "Ophthalmia" as a contagious eye disease that can be prevented by improved life styles. Later, Hippocrates provided a trachoma resembling description of "Ophthalmia" and "Lippitudo" which means "bleary or dripping eye". Hippocrates was also the first physician, to use the term "trichosis" for "in-turned eye lashes".[8] Celsus (25 BC – 50 AD) a Greco-Roman physician described trachoma using the Latin word "Aspritudo" for "Rough", which he explained is the result of inflammation.[8] Celsus also suggested the roughness might be short lived or persistent which would result in excessive tearing.[10] The word "Trachoma", a Greek term for "rough eyelid", was first described by the Greek physician Dioscorides (40-90 AD).[8] Later, Galenus a Turkish physician was the first to describe the term "trichiasis" along with the four stages of trachoma which are "Psorophthalmia" for itch, "Choma" for rough, "Sycosis" for scarred, and "Tylosis" for trichiasis.[8,10]

It is believed that trachoma first spread from the Middle East to Europe during the crusades by the returning crusaders in the 13th century.[12] In the 16th century, there was a thought that frequent eye infections in children are the result of flies, while others think the inflammation is seasonal and more common in the summers.[13]

Later during the Napoleonic Wars (1798 – 1815), Egypt was considered to be a source of infectious blindness.[12] Thousands of soldiers were affected with "inflammation of the eyes" characterised by marked swelling and discharge, which led to many French soldiers to be blind from the complications involving the cornea.[12] Following the end of the Battle of the Nile, the "Egyptian Ophthalmia" hugely affected the British soldiers. Then between 1810s and 1860s major outbreak of ophthalmia occurred all over Europe.[8,12] It was the British military surgeons that initially suspected that the "ophthalmia" affecting their soldiers might be contagious. Soldiers from the same barracks or room were infected quickly.[12] However, this relatively acute blinding condition is likely to be different from the chronic cicatricial blinding trachoma – and may have been overshadowed by the epidemic of the acute blinding disease.[14]

The infection then spread into the civil population of Britain through the returning soldiers. In response to the extensive effect of the ophthalmia separate hospitals such as the London Eye Infirmary (later called Moorfield's Eye Hospital) formed mainly to treat the returning soldiers with ophthalmia.[8] Later Trachoma spread into North America mainly through the migrating community from Europe. This led to an extensive programme of screening of all immigrants entering the US.

There is no data on whether trachoma was prevalent in other parts of Africa other than North Africa or on how it spread into other parts of Africa. However, the assumption is, it probably was highly prevalent in most parts of the continent. The disease has disappeared in Europe and North America probably because of major socio-economic development changes during the 19th and early 20th Centuries.

1.3. Anatomy of The Eyelid

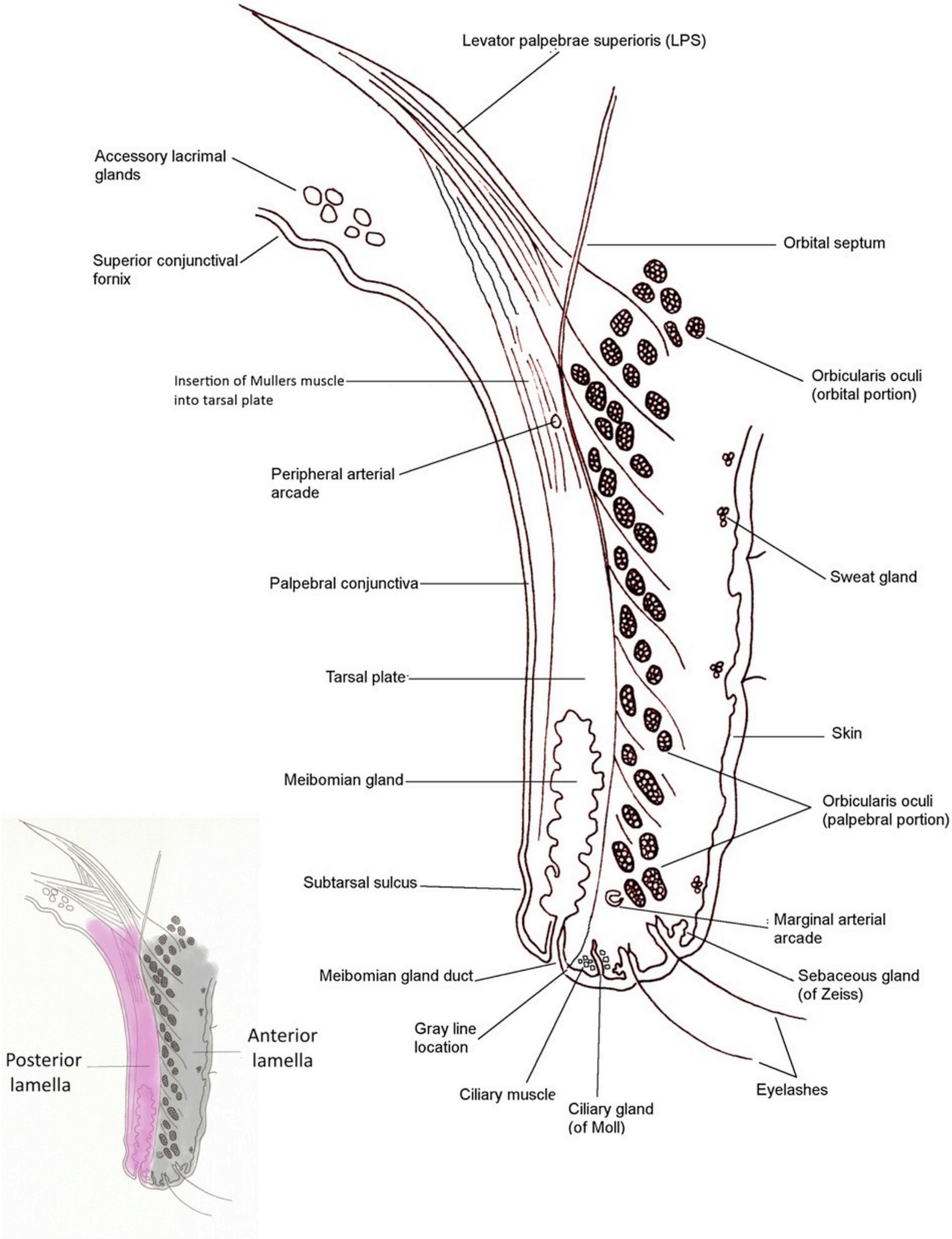
The eyelid is mainly formed from four layers: skin, orbicularis oculi muscle, tarsal plate and tarsal conjunctiva (Figure 1.1). The skin and orbicularis oculi muscle together are known as the anterior lamellae. The tarsal plate and tarsal conjunctiva are known as the posterior lamellae. The conjunctiva and the skin join at the eyelid margin, to form the "grey line". The eyelashes emerge just in front of the eyelid margin. The meibomian gland orifices are located just behind the grey line.

The eyelid is elevated mainly by the levator palpebral superioris along with Muller's muscle. Muller's muscle is superiorly attached to the levator aponeurosis and inferiorly to the superior tarsus. The eyelid crease is usually found 5mm – 10 mm from the lid margin; this is a fold created by the attachment of the orbicularis oculi to the tarsus and the levator aponeurosis to the pretarsal skin.

The tarsal plate is fibrous connective tissue, which is about 29mm in length with about 10mm central height. It provides the eyelid with its structural integrity. The tarsal conjunctiva is a transparent layer covering the inner eyelid surface. It is firmly attached to the tarsal plate so that chronic inflammation affecting the tarsal conjunctiva leads to scarring and distortion of the whole posterior lamella.[15]

The eyelid is one of the most vascularised body parts. The upper eyelid receives its blood supply from the branches of the ophthalmic artery both medially and laterally. The blood vessels are bedded between the orbicularis muscle and the tarsal plate. The upper eyelid gets its nerve supply from the ophthalmic division of the trigeminal nerve.

Figure 1.1: Eyelid anatomy[7]



1.4. Clinical Phenotype of Trachoma

The clinical phenotypes of trachoma can be classified as early stage (active) trachoma and late stage (cicatricial) trachoma. In active trachoma tarsal conjunctival inflammation occurs from recurrent episodes of conjunctival epithelial infection with *Chlamydia trachomatis*. If left untreated, the repeated infection and inflammation leads to cicatricial trachoma at later age, which is characterised by scarring of the tarsal conjunctiva and entropion, which in turn leads to trichiasis. The trichiasis causes painful corneal abrasion, introduces infection and alters the ocular surface eventually leading to irreversible blindness from corneal opacification (CO), (Figure 1.2). These phenotypes are discussed below in detail.

Figure 1.2: Natural history of trachoma [16]

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1.4.1. Active Trachoma

Active trachoma is an inflammatory response characterized by follicular conjunctivitis, which most commonly affects children, with a maximal cross-sectional prevalence in pre-school children.[2,17] It is caused by infection with *Chlamydia trachomatis (Ct*). It is characterised by trachomatous follicles (TF) which are a small white or yellow elevations and accumulations of inflammatory cells measuring about 0.5mm in diameter (Figure 1.3b); and intense inflammation and thickening of the tarsal conjunctiva obscuring the deep tarsal blood vessels (TI) (Figure 1.3c). Severe itching, readiness, photophobia, excessive lacrimation and ocular discharge are the symptoms that accompany active trachoma.

1.4.2. Cicatricial Trachoma

Cicatricial trachoma is characterised by structural changes that occur following repeated episodes of active trachoma.[18] These structural changes are, trachomatous scarring (Figure

1.3d), entropion, trachomatous trichiasis (Figure 1.3e) and corneal opacity (Figure 1.3f), which eventually lead to blindness. In cicatricial trachoma, conjunctival inflammation is less common and less intense and chlamydial infection is rarely detected.[19]

1.4.2.1. Trachomatous Scarring (TS)

Chronic inflammation and recurrent and severe infection of the tarsal conjunctiva eventually lead to scarring. White bands of scar tissue appear on the tarsal conjunctiva. The severity might vary from a few dispersed white spots of scars to a severe horizontal scar known as Arlt's lines. This fibrosis distorts and shortens the eyelid. Scarring trachoma develops and progresses in severity later in life. A study from Tanzania reported that 50% of trachomatous scarring cases had worsened within 5 years.[20] However, the age at which the signs of TS become visible tends to be younger in regions with the highest burden of active trachoma and *Ct* infection, suggesting that this process is largely driven by the cumulative damage of repeated exposure to this infectious agent.[21] Women are more frequently affected by the scarring complications of trachoma, accounting for ¾ of trichiasis cases.[22] This is attributed to their greater lifetime exposure to *Ct* through childcare activities. Studies of the immunopathogenesis of scarring disease suggest that there are genetically determining factors which influence the susceptibility of an individual to developing scarring disease.[21,23]

1.4.2.2. Cicatricial Entropion

The tarsal conjunctiva leads to contracture of the eyelid, resulting in inward rotation of the eyelid margin, called Entropion. Based on its severity, entropion may be mild with only a few in-turned lashes, or severe leading to inward rotation of the whole eyelid margin and the lashes towards the eyeball. This might be associated with lid retraction or shortening due to severe contracture of the posterior lamella.

Data on the rate of entropion is not often collected in population based studies. However, it is likely that Entropion may exist with or without trichiatic lashes and vice versa. In a recent clinical study in Ethiopia we showed that about a quarter of the trichiasis cases recruited into two clinical trials did not have entropion, while about 30% had only mild trichiasis.[24] The rate of severe entropion in such trachoma hyper endemic areas was 16%–18%.[5,24] Mild entropion was also found in 1% of non-trachomatous controls.[24] Degree of entropion has been an important factor for the choice of type of surgical procedure used to treat entropic trichiasis.[25] It has been suggested that severe entropion cases with gross lid retraction require surgical management concentrating on the posterior lamella, while mild to moderate cases could be treated with lid margin and anterior lamellar procedures (discussed in detail in section 1.12.3).[25,26]

1.4.2.3. Trachomatous Trichiasis (TT)

Trachomatous trichiasis (TT), is the in-turning of eyelashes scratching the eyeball and the cornea. It is mainly the result of cicatricial entropion caused by chronic conjunctival scarring. In cohort studies conducted in Tanzania and The Gambia, 10% and 6% of trachomatous conjunctival scarring cases progressed into having TT within 7 and 12 years respectively.[22,27] TT is diagnosed based on the presences of one or more lashes touching the eye or evidence of epilation. There is currently a debate about whether the definition should also include the presence of TS, to help delineate it from other causes of trichiasis.[28] Epilation, the repeated plucking of lashes, is a common traditional practice in most trachoma endemic societies.[29,30]

Trachomatous trichiasis has diverse phenotypes varying with degree of entropion and location.[24] Based on lash type, it ranges from a single metaplastic or misdirected eyelash touching the eyeball without entropion to all eyelashes touching the eyeball secondary to full eyelid entropion. Metaplastic lashes are lashes originating posterior to the normal lash line, in unusual locations.[24] Misdirected lashes are lashes deviating from their normal position and pointing towards the eyeball.[24] A recent study conducted in areas of Ethiopia where there is a huge backlog of TT showed that, about 80% of the trichiatic lashes were aberrant (misdirected or metaplastic).[24] Based on the number of eyelashes touching the eye, trichiasis can be grouped into minor TT (1-5 lashes) and major TT (>5 lashes).[4,31-33]

There is evidence that minor TT cases progress into major trichiasis after a few years. In studies from The Gambia, 33% and 37% of minor TT cases progressed into major TT within one and 4 years respectively.[18,32,34] Patients with evidence of epilation in more than one third of the eyelid are considered as having major TT. In trachoma, the risk of sight loss is directly correlated with the severity and type of trichiasis. In addition, the diverse trichiasis phenotypes have particular relevance to treatment choice and recurrence.[4,31,32]

1.4.2.4. Corneal Opacity

If the TT is left untreated, it causes stabbing pain and photophobia from continuous contact with the ocular surface. Long term contact and abrasion of the eyelashes on the cornea will create ulceration and predisposes the cornea to secondary bacterial or fungal infections. When the ulcer heals it leaves a white opaque scar (CO), which prevents light from interring into the eye, eventually leading to blindness. In cohort studies in The Gambia, 8% of TT cases developed corneal scarring within 4 years, while corneal opacity worsening was reported in 34% of TT cases within 1 year.[32,34] In another long-term cohort study in the Gambia, 20% corneal opacity incidence was reported among TT cases.[22] In a population-based study in Southern Sudan, among TT cases identified about 50% had TT related corneal opacity at least in one eye, and 35% had bilateral corneal opacity.[35]

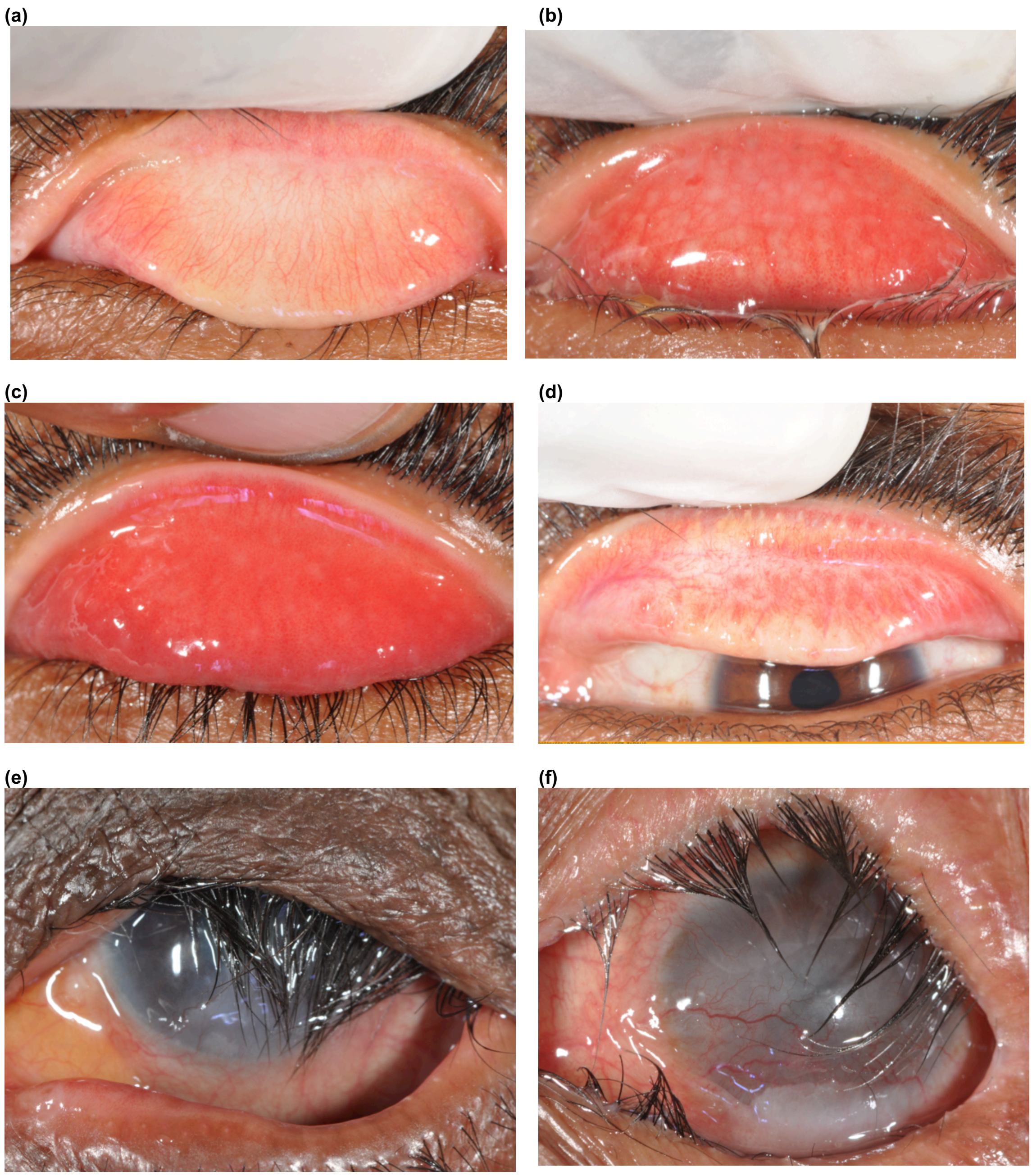
1.4.2.5. Visual Impairment

The continuous rubbing of the eyelashes will eventually lead to irreversible visual impairment and blindness. A population study reported that among 35% and 11% of the TT cases identified had visual impairment and blindness, respectively.[35] Assessing the contribution that TT makes to visual impairment can be difficult as there can be visual impairment due to other conditions such as cataract. Few longitudinal studies have estimated the risk of visual impairment from TT alone. A 12-year cohort study of trachomatous scarring cases in The Gambia demonstrated an association between incidence of visual impairment/blindness and incidence of corneal opacity (OR, 4.5; 95%CI, 1.6–12.6; p=0.0006).[22] In this cohort, 2.5% and 7.7% of the cases with TS and TT, respectively, developed visual impairment related to corneal opacity in 12 years. In another longitudinal study, the incidence of visual impairment and blindness during a 1 year period was 9%.[34] However, it was not clear how much of this was attributable with TT. Similarly, in another cohort study, there was greater visual loss in trichiatic eyes that developed new corneal opacity during the 4 years.[32] At four years, an additional 13.5% (29/214) of the trichiasis eyes had progressed to blindness; corneal opacity was associated very strongly with blindness (OR, 60.4; 95% CI, 2.64–13.8; p<0.001). However, among those that progressed to blindness at 4 years (29 eyes), only 6 (20.7%) had corneal opacity, indicating that other causes contributed to most of the incident blindness in this cohort of TT cases.[32,35]

Trachoma accounts for 3% of the global blindness in 2010.[1] There are 2.4 million people visually impaired from trachoma worldwide of whom 1.2 million are estimated to be irreversibly blind, making trachoma the leading infectious cause of blindness.[1]

Figure 1.3: Clinical features of trachoma

Normal upper tarsal conjunctiva. (b) Trachomatous inflammation - follicular (TF). (c) Trachomatous inflammation – intense (TI). (d) Conjunctival scarring (TS). (e) Trachomatous trichiasis (TT) with entropion. (f) Corneal opacity (CO)



1.5. Clinical Grading of Trachoma

The WHO has developed two grading systems for trachoma: The Follicles Papillae Cicatricae (FPC) grading system and the simplified trachoma grading system.[36,37] The FPC grading system was initially developed about 35 years ago with the aim of identifying cases with the blinding stage of the disease. It was developed to grade severity of trachomatous follicles, papillary inflammation, conjunctival scaring/ trachomatous trichiasis and/or entropion and corneal scarring, Table 1.1. This grading system has been useful for assessing more subtle degrees of variation in clinical phenotype in research, however, it is probably too complex for programmatic activities, where examinations are usually performed by mid and lower level cadres. As a result, the simplified WHO trachoma grading system was primarily developed for programmatic use. This categorises the presence/absence of clinical features, and is perhaps less useful in research where degree of severity is also of interest, Table 1.2.

The WHO FPC grading system has also another limitation. The corneal scaring grading has limited scope in picking subtle changes or progressions of corneal scars. The corneal scar grading is based on the pupil margin, which is subject to change under different light levels. Therefore, we previously developed an extension grading to the FPC corneal opacity (CO) score to provide more objective definitions for subtle corneal scarring changes, Table 1.3.[33]

Figure 1.4: Un everted upper eyelid, showing the tarsal conjunctiva.

The numbered zones refer to those in the FPC Grading System. Zone 3 and 2 are examined when using the WHO simplified system.[38]

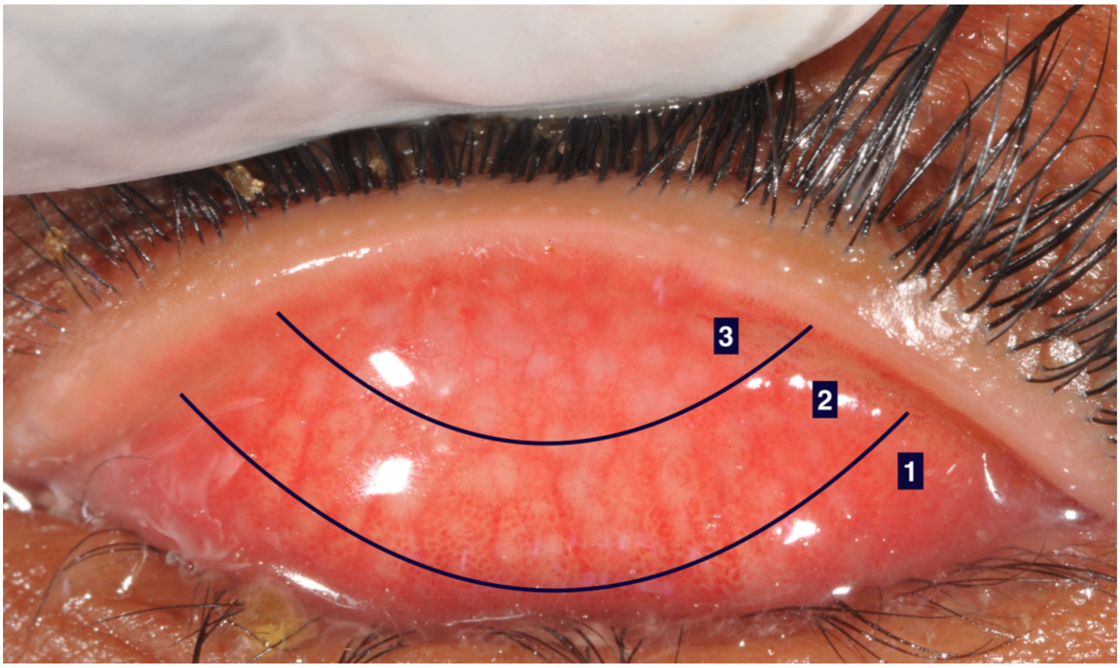


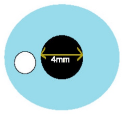
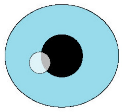
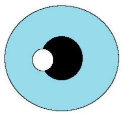
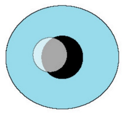
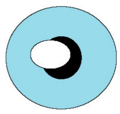
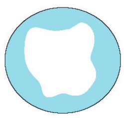
Table 1.1 WHO FPC grading system [36,37]

Grade	Description
Upper Tarsal Follicles (F)	
F 0	No follicles.
F 1	Follicles present, but no more than 5 in zones 2 and 3 together (see Figure 1.4)
F 2	More than 5 follicles in zones 2 and 3 together, but less than 5 in zone 3.
F 3	Five or more follicles in each of the three zones.
Upper tarsal papillary hypertrophy and diffuse inflammation (P)	
P 0	Absent: normal appearance
P 1	Minimal: individual vascular tufts (papillae) prominent, but deep subconjunctival vessels on the tarsus not obscured.
P 2	Moderate: more prominent papillae, and normal vessels appear hazy, even when seen by the naked eye.
P 3	Pronounced: conjunctiva thickened and opaque, normal vessels on the tarsus are hidden over more than half of the surface.
Conjunctival scaring (C)	
C 0	No scarring on the conjunctiva
C 1	Mild: fine scattered scars on the upper tarsal conjunctiva, or scars on other parts of the conjunctiva.
C 2	Moderate: more severe scarring but without shortening or distortion of the upper tarsus.
C 3	Severe: scarring with distortion of the upper tarsus.
Trichiasis and/or entropion (T/E)	
T/E 0	No trichiasis and/or entropion.
T/E 1	Lashes deviated towards the eye, but not touching the globe.
T/E 2	Lashes touching the globe but not rubbing the cornea.
T/E 3	Lashes constantly rubbing the cornea.
Corneal scarring (CC)	
CC 0	Absent
CC 1	Minimal scarring or opacity but not involving the visual axis, and with clear central cornea.
CC 2	Moderate scarring or opacity involving the visual axis, with the papillary margin visible through the opacity.
CC 3	Severe central scarring or opacity with the papillary margin not visible through the opacity.

Table 1.2: WHO simplified grading system for assessment of trachoma [36]

Grade		Description
Trachomatous Inflammation – Follicular	TF	The presence of 5 or more follicles (>0.5mm) in the upper tarsal conjunctiva
Trachomatous Inflammation – Intense	TI	Pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the deep normal vessels
Trachomatous Scarring	TS	The presence of scarring in the tarsal conjunctiva
Trachomatous Trichiasis	TT	At least one lash rubs on the eyeball or evidence of epilation
Corneal Opacity	CO	Easily visible corneal opacity over the pupil

Table 1.3: Expanded corneal scaring grading system [33,39,40]

Grade	Description		WHO equivalent grade
C 0	Absent		CC0
C 1	Opacity not entering central 4mm.		CC1
C 2a	Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is visible through the opacity.		CC2
C 2b	Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity.		
C 2c	Opacity within central 4mm and entering the central 1mm of the cornea. The pupil margin is visible through the opacity.		
C 2d	Opacity within central 4mm and entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity.		
C 3	Opacity large enough and dense enough to make whole pupil margin invisible.		CC3
C 4	Phthisis		

1.6. Trachomatous Trichiasis Symptoms

The rubbing of the eyelashes on the cornea and the conjunctiva leads to considerable pain and discomfort. Patients have described the pain from trichiasis as being like a thorn pricking, itching and burning. The pain and symptoms reported by patients are usually severe or multiple. Excessive tearing and photophobia often accompany the pain. Some patients have also reported headache and insomnia.[41] The effect that this might have on daily living is discussed in sections, 1.6 and 1.7.

1.7. Differential Diagnosis of TT

There are different conditions that resemble the clinical stages of trachoma. Conjunctival scarring occurs in autoimmune diseases (such as ocular mucus membrane pemphigoid, Steven-Johnson syndrome, graft versus host disease and atopic keratoconjunctivitis), sarcoidosis and ocular rosacea.[7] Injuries from chemicals and traditional medicines are also known to cause conjunctival scarring. Non-entropic trichiasis can occur in chronic inflammatory conditions of the lid margin such as blepharitis and ocular rosacea.[7]

1.8. Epidemiology of Trachoma

1.8.1. Global Prevalence and Distribution

The first Trachoma Map showing the global distribution – Mappa Mundi Trachomae, was developed by Wibaut and was presented in the International Congress of Ophthalmology in 1929 (Figure 1.5). The Map and subsequent summary indicated that trachoma affects all races but more commonly poor people and women than men; the infection transmits within families and commonly affects younger children.[8,14]

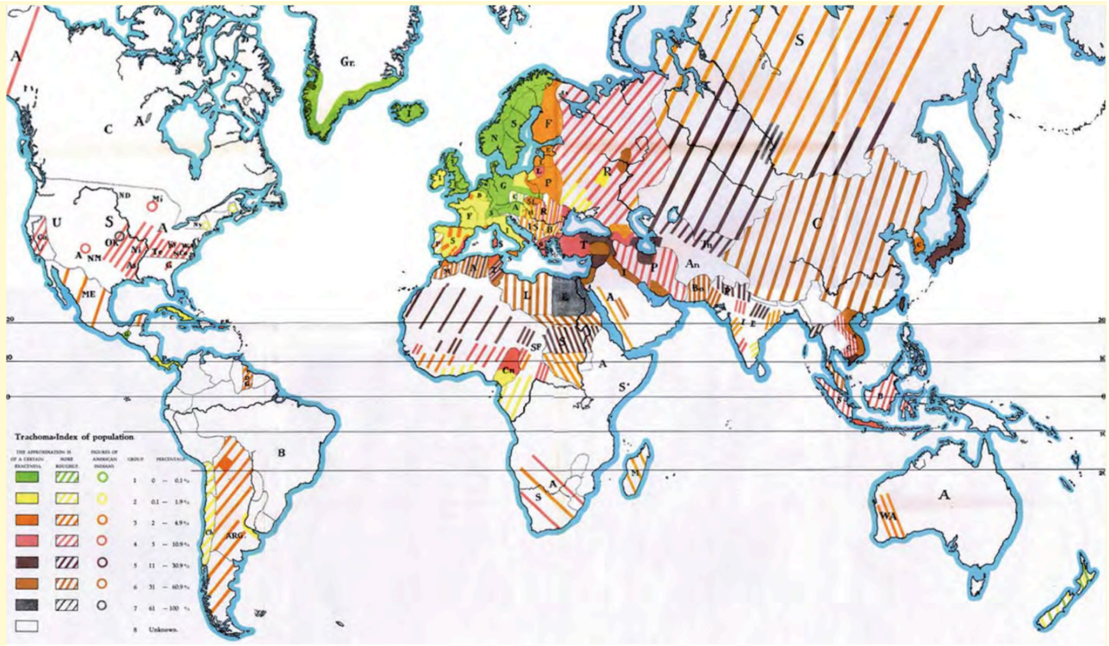
A significant reduction has been seen in the burden of trachoma in the last few decades. In 1996, it was reported that 590 million people were at risk of trachoma, 146 million children had active disease and 10.6 million people were at immediate risk of visual impairment from trachomatous trichiasis; while 5.9 million were estimated to be already blind from trachoma.[3] Then active trachoma cases declined to 21.4 million in 2011.[42] Between 2011 and 2016, the number of people estimated to be living in trachoma endemic districts reduced from 314 million to 200 million; and Trachomatous Trichiasis cases dramatically decreased from about 7 million to 3.2 million.[42-44] Among the initial 58 countries considered to be trachoma endemic, only 42 are currently requiring intervention (Figure 1.6).[43,44] This reduction could be attributed both to the global effort to tackle trachoma in the last few decades and the availability of more reliable global data on burden of the disease from the Global Trachoma Mapping Project

(GTMP) which has considerably less extrapolation unlike the previous estimates. In the GTMP, 2.6 million people were screened in 1546 districts from 29 countries within three years.[43]

The clinical features of trachoma are strongly related to age. The active stage of the disease predominantly affects children, while the late and blinding stage is more common in adults.[45-47] The highest burden and incidence of active trachoma infection is found in pre-school children, with prevalence dropping with increasing age.[48] On the other hand, the burden of TT is generally 4 times higher in people >40 than those <40 years of age population.[49] The peak TT prevalence age is the 50–70 years population, constituting for more than 40% of the TT burden.[49]

Women are more affected by trachoma, probably due to their frequent contact with affected children.[50] A meta-analysis of 24 studies from 12 countries showed that the odds of TT in women is approximately twice that of males (OR, 1.82; 95% CI, 1.61—2.07), with the highest estimate coming from Ethiopia showing nearly 4 times higher burden of TT among women than men (80% vs 20%).[51,52]

Figure 1.5: Mappa Mundi Trachomae[8]



Key for Figure 1.5

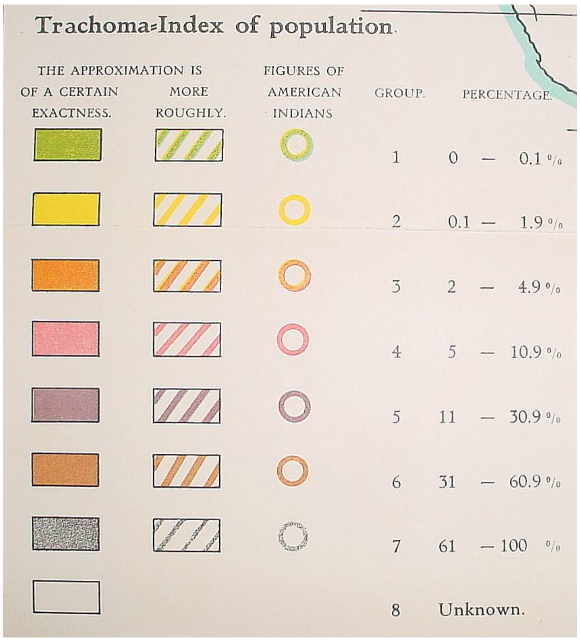
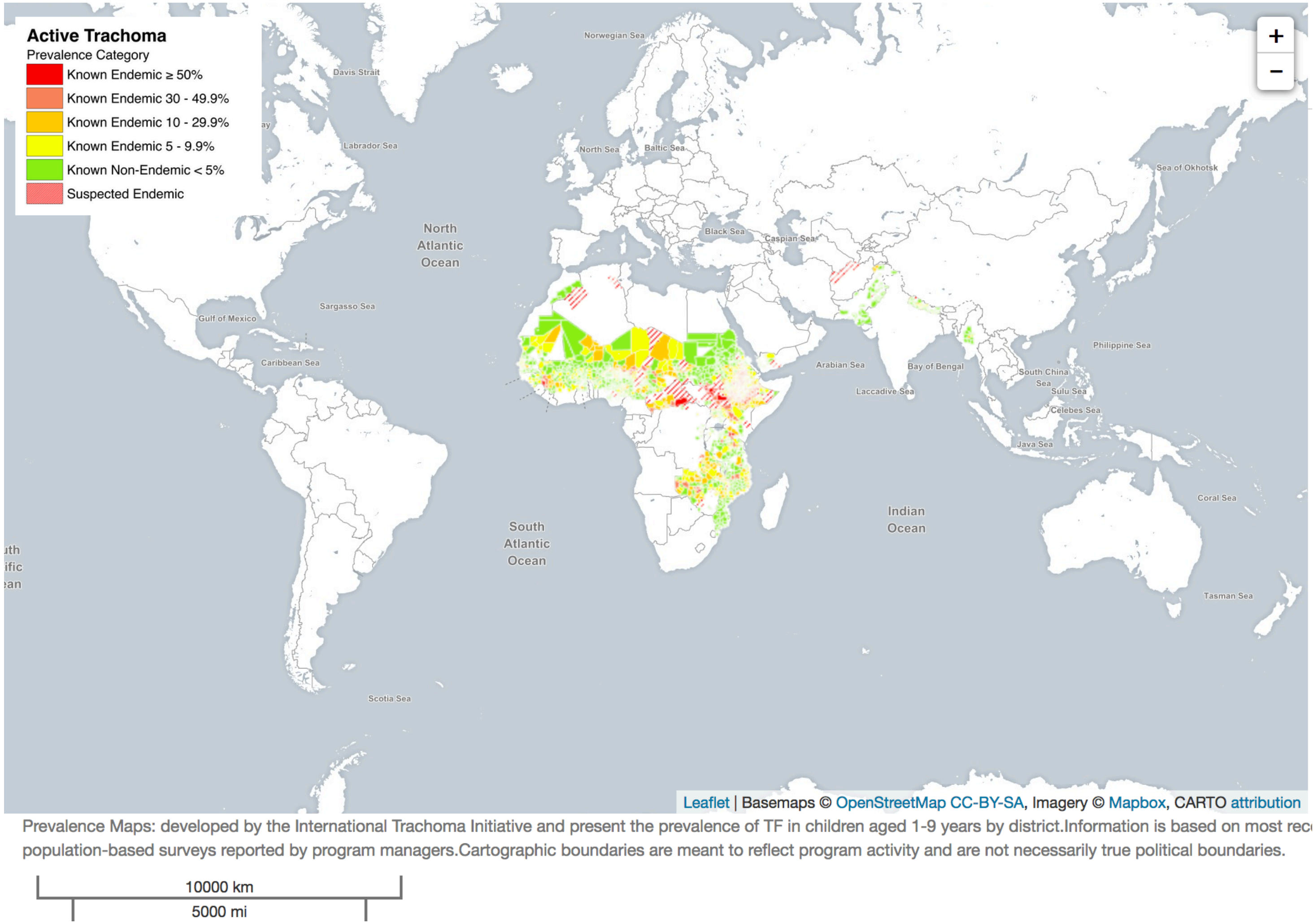


Figure 1.6: Global distribution of trachoma, 2015



(http://www.trachomaatlas.org/global-trachoma-atlas)

1.8.2. Trachoma in Africa

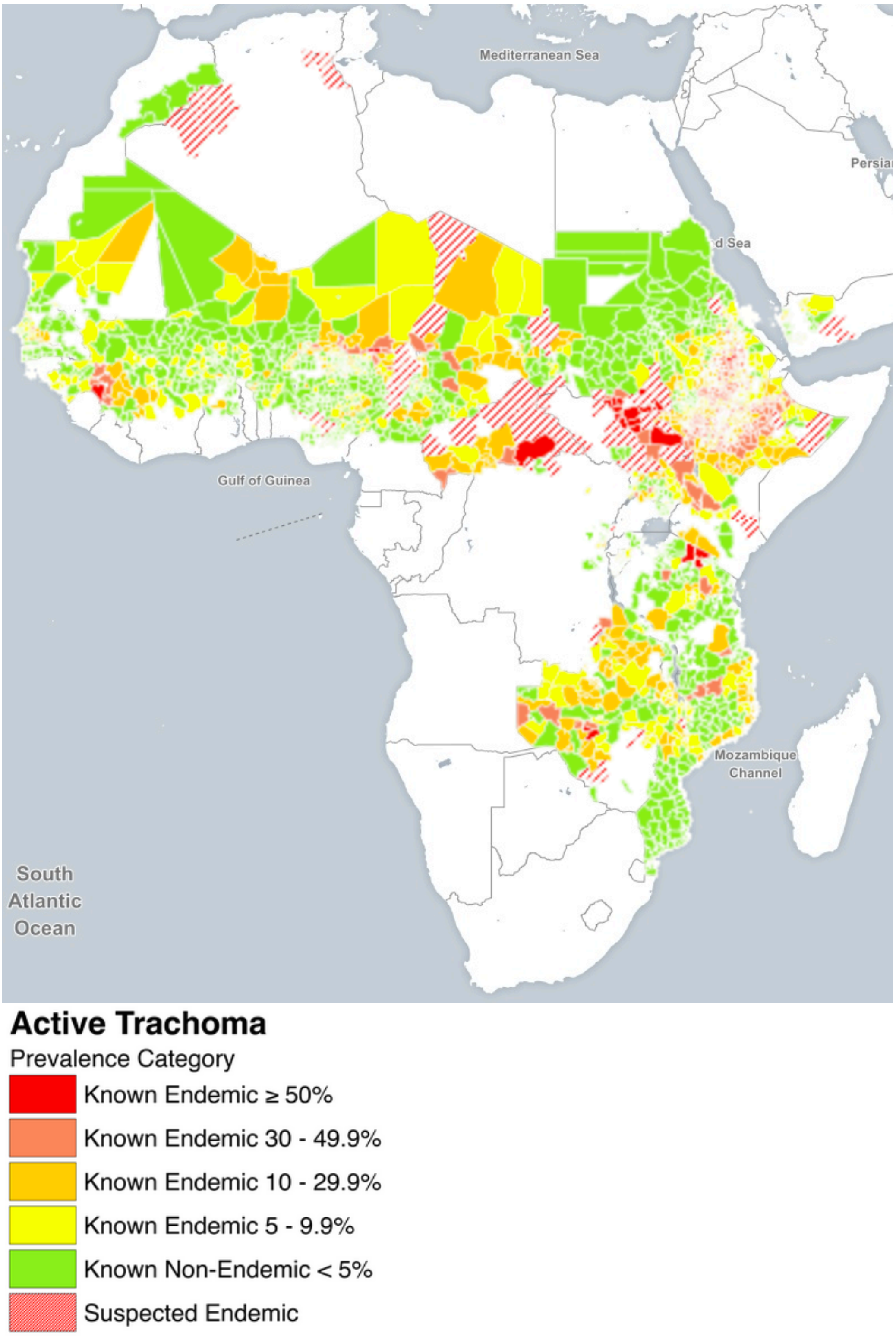
Trachoma affects the poorest communities predominantly in Africa and Asia. Africa is the most affected continent from trachoma (Figure 1.7). Among the 46 WHO Africa region countries, 29 have been endemic to trachoma and about 71% of the population is estimated to be living in trachoma endemic areas.[42] About 18.3 million active trachoma cases and 2.24 million TT cases are found in Africa.[42] This accounts for 85.3% and 70.9% of the active trachoma and TT cases worldwide. Three African countries (Ethiopia, Malawi and Nigeria) account for the 50% of trachoma at risk population worldwide. Four African countries (Ethiopia, Nigeria, Egypt and Uganda) account for more than 43% of the global TT surgical backlog. [43]

1.8.3. Trachoma in Ethiopia

Ethiopia is the most trachoma affected country worldwide.[43] About 76% of its population, which is more than 75 million people, live in trachoma endemic areas. Active trachoma prevalence in under 10 year of age children is more than 30% in most parts of the country (Figure 1.8a). More than 0.69 million people are in urgent need of corrective eyelid surgery to prevent irreversible blindness from TT, accounting for 22% of the global TT backlog (Figure 1.8b).[43] The 2006 National blindness survey showed that trachoma (11.5%) is the second most common cause of blindness, after cataract (49.9%); and the third most common cause of visual impairment at 7.7% after cataract (42.3%) and refractive error (33.4%).[53]

The prevalence of trachoma is fourfold higher in rural areas than in urban areas. This probably is related to the poor water supply and sanitation coverage in the rural areas. In 2005, safe water was available to only 25.2% of the rural population compared to 92% for the urban population; and sanitation coverage was 22% in rural communities compared to 91% in urban communities. (Health Status Indicators by the Federal Ministry of Health of Ethiopia for the year 2004/5). Although there was positive improvement, this gap persisted in 2016 with only 5.7% of the rural population using improved latrine facilities, compared to 50.5% urban; and only 56.5% rural population having access to safe drinking water compared to 97.3% urban.[54,55]

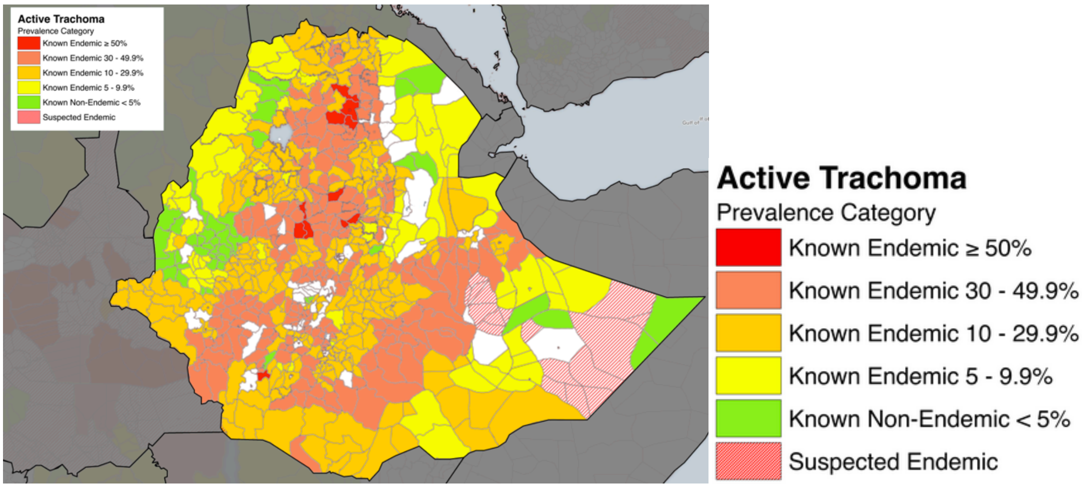
Figure 1.7: Trachoma distribution in Africa



(http://www.trachomaatlas.org/global-trachoma-atlas)

Figure 1.8: Trachoma distribution in Ethiopia, 2015: a) active trachoma, b) trachomatous trichiasis[43]

a)



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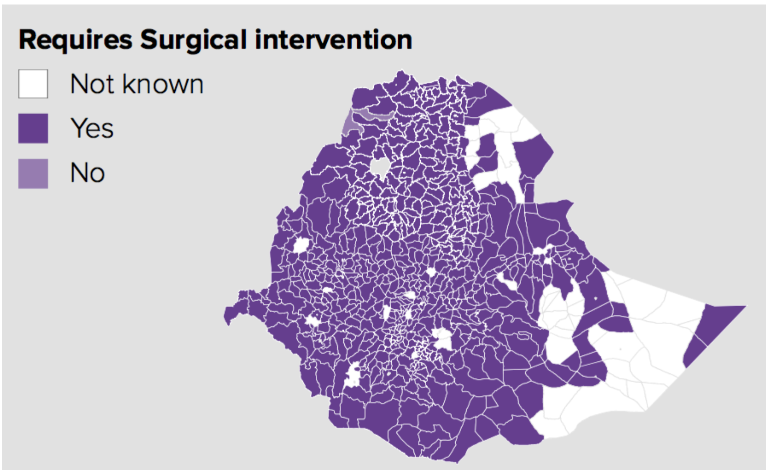
b)

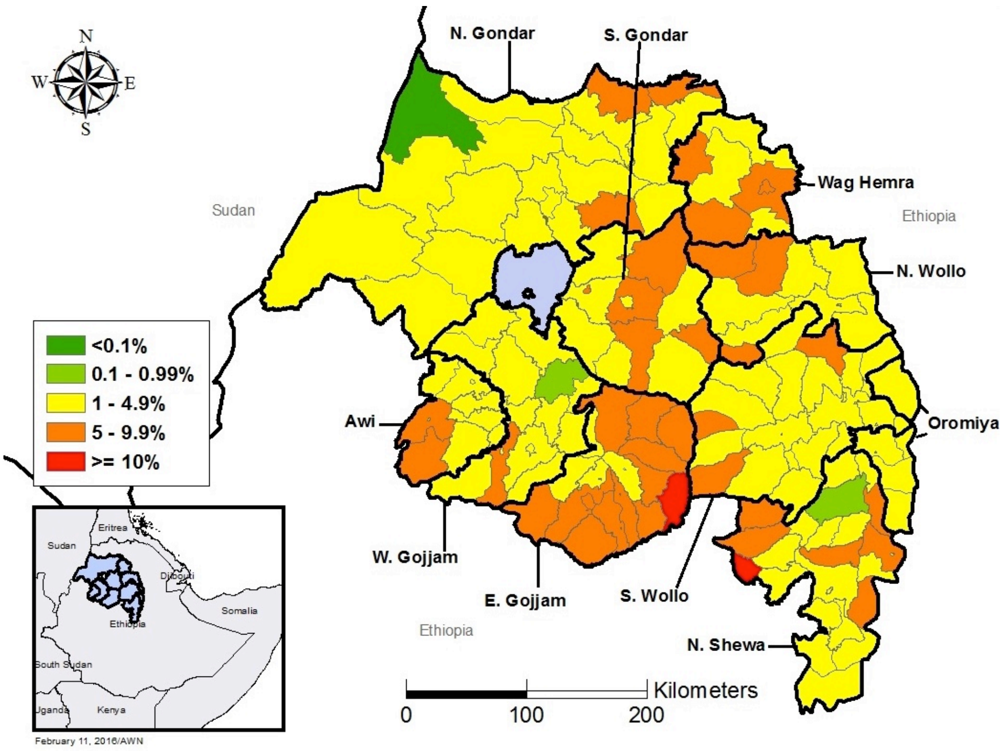


1.8.3.1. Trachoma in Amhara Region, Ethiopia

Amhara Region has a disproportionately large burden of Ethiopia's Trachoma. A population based prevalence survey conducted in 127 randomly selected woredas in each of the ten zones in 2014, showed the prevalence of active trachoma ranged from 16.4% to 50.7% (in children under 10 years), with a regional average of 25.9%. In 2015, among the 167 woredas of the region, 65 (39%) had active trachoma prevalence of ≥30%, while another 75 (45%) of the districts had prevalence of active trachoma between 10% and 30%.

Amhara Region contains about half of Ethiopia's TT backlog at 341,101 in 2015 (Amhara regional Health Bureau – Carter Center Report). In 2015, 27% of the districts had a TT prevalence rate of between 5% and 10%, while another 68% had a TT prevalence between 1% and 5% (Figure 1.9).

Figure 1.9: TT prevalence in Amhara Region, 2015 (Courtesy of the Carter Center)



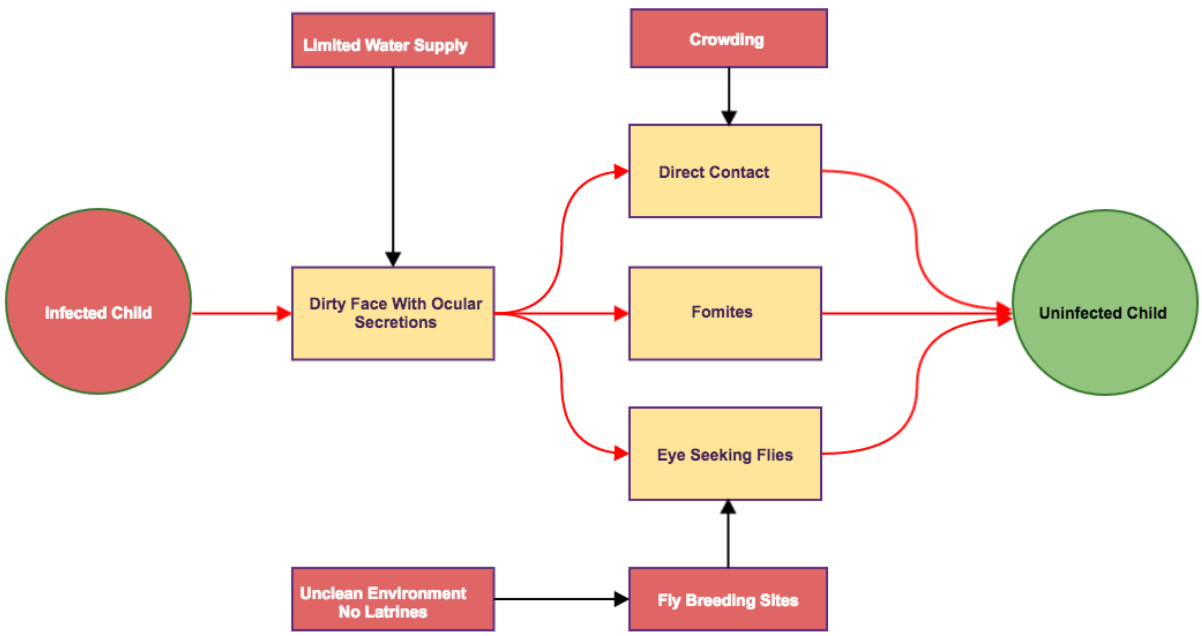
1.8.4. Trachoma Transmission and Risk Factors

Many studies have investigated risk factors for active trachoma in different locations.[56] These have largely identified a fairly consistent group of risk factors associated with the presence of active trachoma, which probably reflect things that promote the underlying transmission of *Ct* and maintain the infection prevalence in the community (Figure 1.10).

Infection is probably transmitted between people through various personal and environmental routes, although direct evidence of how this happens is limited.[56] Among the personal factors, poor personal hygiene is probably important in trachoma transmission.[57,58] Initially *Ct* organisms leave an infected eye in ocular secretions, which are associated with active disease and infection.[59] The organism is probably then passed onto others through direct contact, fomites or the behaviour of eye seeking flies.[58,60,61] There is an indication that frequent facial cleanliness and improved living conditions reduce transmission of the disease.[57]

Many studies have found active trachoma to be associated with crowded living conditions, dirty environment (promoting fly breeding) and a limited water supply (difficult to keep faces clean).[56] Overcrowded living conditions contributes to the transmission of trachoma infection though direct contact, flies and sharing of clothing.[58,61] Dirty environment, human faeces animal dung provide breeding space to flies. Studies have shown association between presence of latrine and reduced risk of trachoma.[46,57,61] It is assumed that the presence of latrine would reduce the flies breading sites. Eye seeking flies are probably attracted to ocular secretions of infected children.[62] *Musca sorbens* species were found to make more frequent eye contact than the other species of flies, suggesting that controlling the density of these types of flies through different mechanisms would contribute to trachoma infection reduction.[63] There is evidence that fly control interventions can reduce the rate of trachoma infection.[63,64] Trachoma is more prevalent in areas with poor water supplies.[46] Presence of adequate water supply and latrine increases the likelihood of personal hygiene and sanitation.[46,57,58] However, accessibility to water sources and latrines alone might not contribute to trachoma infection reduction.[65] Utilisation practices are probably more important in active trachoma control.[65,66]

Figure 1.10 Trachoma risk factors



1.9. Pathophysiology of Trachoma

1.9.1. Chlamydia Trachomatis

Chlamydia trachomatis is one of the three species within the genus *Chlamydia,* which infects only humans. The other two species being, *C. Muridarum (infects only mice), and C. Suis (endemic in pigs).*[8] *Chlamydiae* are gram-negative obligate intracellular bacteria, which are even smaller than many viruses.[67] *Chlamydia trachomatis* was first identified by Halberstaedter and von Prowazek in 1907 from conjunctival epithelial cells of people with trachoma.[68] Later, a series of experiments demonstrated the transmission of this pathogen causing follicular conjunctivitis in both humans and animals.[69-71] There are nineteen serovars of C. trachomatis, which are in turn subdivided into two biovars: the trachoma biovar and the lymphogranuloma venereum (LGV) biovar. The trachoma biovar consists serovars A to K, while the LGV biovar consists of servoars L1, L2 and L3. Various studies showed that trachoma is commonly caused by serovars A, B, Ba and C, while the serovars D to K are associated with genital chlamydial infection. [72]

Chlamydia trachomatis has a unique two form developmental cycle: Elementary Bodies (EB) and Reticulate Bodies (RB). The EB are extracellular infectious but metabolically inactive forms which measure only up to 0.6µ. These attach to epithelial cells and then induce endocytosis. Once in the cell they transform into RB, which are larger (up to 1.5µ) intracellular metabolically active forms that replicate within the inclusion body through binary division. Within a couple of days the RB transform back to EB, which will then be released from the host cell through lysis.[8]

Eyes of preschool children are the major reservoirs of chlamydial infection, which have also the highest rate of active disease.[73] C. trachomatis can also be found in mucosal surfaces and naso-pharyngeal secretions.[74] Although chlamydial infection is common in cattle and pigs, there is no known animal reservoir to the *C. trachomatis* serovars.

1.9.2. Pathophysiology: the pathway to blindness

Trachoma begins in childhood with recurrent episodes of conjunctival epithelial infection with *Chlamydia trachomatis*. The peak age of infection is between 1 and 5 years. In response to the infection, the immune system produces inflammatory reaction characterised by inflammatory cell infiltrates in the sub-epithelial stroma and pro-inflammatory cytokine response.[75,76] The inflammatory infiltrates in active trachoma largely contain T and B-lymphocytes, macrophages, plasma cells and neutrophils, which form follicular/papillary conjunctivitis.[76] This condition might persist for many weeks even after the infection is cleared. Why this exactly happens is poorly understood, but indicates that the persistent inflammatory process and subsequent tissue damage are largely driven by the immune response.

Various studies demonstrated that the initial response to *C. trachomatis* infection is mediated by the innate immune system, which leads to the production of various pro-inflammatory cytokines such as Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interleukin-8 (IL-8) and Tumour Necrosis Factor-α (TNF-α).[77] These cytokines stimulate the rapid recruitment of neutrophils and macrophages into the infected tissue.[78] Then this initial immune response is proceeded by the adaptive immune response, which in turn can involve an antibody mediated response (humoral) and cell mediated immune response. Following an infection the T helper cells differentiate either into Type 1 T-helper cell (T_H1) or Type 2 T-helper cell (T_H2). The T_H1 initiates cell-mediated response characterised by the activation of macrophages, release of cytokines and promote B-cells to produce antibodies. The T_H2 cells initiate a humoral response and activate B-cells to produce antibodies. It is believed that clinical outcomes in trachoma could be influenced by these two adaptive immune responses.

Recurrent and persistent infections are critical in the development of inflammatory response to the organism that leads to immuno-pathologically mediated progressive conjunctival scarring.[79-81] The increased expression of pro-inflammatory cytokines and chemokines such as Interleukin-1β, Interleukin-17A (IL17A) and TNF-α from repeated infection would activate matrix metalloproteinases (MMP), which are enzymes that degrade the extracellular matrix, promote inflammatory cell infiltration and facilitate tissue remodelling and scar formation.[75,82,83] Increased expression (in the conjunctiva) of several MMPs (MMP7, MMP9, MMP12), as well as increased pro-inflammatory factors were found in adults with conjunctival scarring (TS).[6]

Conjunctival scaring is characterised by marked atrophy of the conjunctival epithelium and loss of goblet cells.[84] The normally loose vascular stroma found beneath the epithelium and composed of Type I and III collagen is changed into thick scar mainly composed of vertically orientated densely packed Type V and Type IV collagen. These thick fibres are firmly attached to the posterior surface of the tarsal plate causing distortion for the tarsal plate leading to the inward rotation of the eyelid margin (entropion) with eyelashes scratching the eye (trachomatous trichiasis [TT].[84]

1.10. Trachoma Control

1.10.1. History

Ocular diseases treatments date back to ancient times. The Egyptians prescribed topical treatments using animal, mineral and plant products; while bathing and cautery were among the treatment modalities for ocular diseases advocated by ancient Greek physicians.[8,85] Probably, the first trachoma control measures were taken in the 1810s by the British army following blindness of thousands of British soldiers from the Egyptian ophthalmia during the Battle of the Nile. These included identification and isolation of cases, face cleaning under running water and use of individual towel, pillowcase and bed sheets that should be washed regularly and avoiding overcrowding. In subsequent years, separate eye hospitals were formed mainly to treat soldiers with ophthalmia.

The first international congress of ophthalmology was held in 1857 in Brussels. One of the aims of this meeting was on how to halt the ophthalmia. Le Ligue Contre le Trachome was founded in 1923 in Paris, this later founded the International Organisation Against Trachoma (IOAT) in 1930 in Geneva.[13] In the 1929 International Ophthalmology congress control of national frontiers, compulsory notification of cases and examination and treatment of schoolchildren and army personnel were recommended as trachoma control measures.[86] The first report on Trachoma was published in 1935.[8,87]

Trachoma cases were mainly treated with copper sulphate and silver nitrate. In the late 1930s, oral sulphonamides were the first antimicrobial agents used for the treatment of trachoma infection. These were used concomitantly with the newly invented tetracycline between the 1940s and 60s until their use has been eventually replaced by topical tetracycline through time, which is found to be effective against chlamydia.[8]

The WHO was formed in 1948, then in 1952, it recommended the use of topical tetracycline for two months four times per day, which was later reduced to twice a day in 1956.[8] During the same time the WHO also recommended that trachoma control activities should involve identifying and treating cases, health education and fly destruction and environmental sanitation. In 1973, the WHO published a manual on "Field methods for the control of trachoma".[88] This manual described the importance of antibiotic distribution, trichiasis surgery, health professional training and health education for trachoma control. This gave way for the 1981 "Guide to Trachoma Control", which detailed the following seven strategies for trachoma control: Assessment of the problem and establishment of priorities, allocation of resources, chemotherapeutic intervention mainly using topical tetracycline, surgical intervention to correct lid deformities, training and utilisation of local health aids and other non-specialised health workers, health education and community participation, and evaluation of intervention programmes.[37]

1.10.2. The SAFE Strategy

In 1993, the **SAFE Strategy** was proposed as an intervention strategy for trachoma control in the WHO field guide "Achieving community support for trachoma control, a guide for district health work".[16] This involves **S**urgery for trichiasis for those at immediate risk of developing visual impairment from TT, together with **A**ntibiotics treatment of cases with active trachoma, Clean **F**aces to prevent disease from spreading from one child to another and **E**nvironmental improvement (water and sanitation) to suppress chlamydial infection and transmission.

The first global scientific meeting on trachoma was held in 1996, which identified 47, 13 and 16 countries as having blinding trachoma, blinding trachoma suspects and non-blinding trachoma suspects respectively, most of which were from Sub-Saharan Africa, the Middle East, Latin America and Asia.[3] The meeting recommended the implementation of the ***SAFE Strategy*** in trachoma endemic countries for trachoma control. In 1997, The WHO in collaboration with member states national eye care programs and non-governmental organisation founded the Alliance for the Global Elimination of Trachoma by the year 2020 (GET2020).[89]

The research question and the studies presented in this thesis mainly relate to the Surgery component of the SAFE strategy. Trachomatous trichiasis surgical management and outcomes, and the impact of TT and TT surgery are reviewed in-depth in the following sections.

1.11. A Brief History of Trichiasis Management

Ancient Chinese, Egyptians and Greeks used different methods for treating trichiasis. Surprisingly little has changed with modern day management; the most commonly described ancient treatments for trichiasis were Epilation and Surgery. The surgery mostly involved scarification followed by application of mineral components and excision of granular tissue from the inner conjunctiva followed by cauterisation.

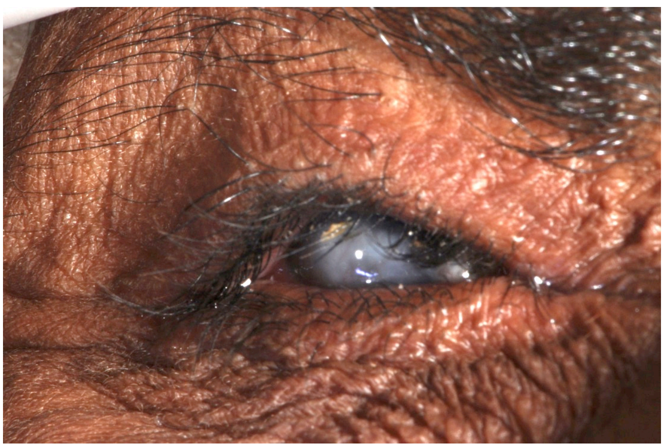
Surgical management of trichiasis dates back to the 2700 BC, during which Chinese Emperor Huang Ti Nei Ching had surgical management of his trichiasis.[8,9] Ancient Indian treatment of trichiasis in the 10th century BC included "surgical incision of the lid, with everting sutures made of human hair or cauterisation of the lash follicles.[10] Hippocrates described three different surgical managements for trichiasis: (1) scarification of the everted conjunctiva using a wool rapped wooden stick followed by application of copper powder; (2) Surgical excision of granular conjunctiva for cases with marked thickening, followed by iron cauterisation; and (3) surgical eversion and suturing of the eyelid using two hair sutures which should be tightened to evert the eyelid to correct entropic trichiasis.[8] The procedure described by Hippocrates on suturing is probably the basis for modern day trichiasis surgery.

From the 6th century AD, removal of a fold of skin from the entropic eyelid using two tightly tied sticks was practised to treat trichiasis.[13] This procedure has been used until recently as a traditional management of trichiasis in the Middle East. From personal observation of some deformed eyelids following traditional "surgery", (Figure 1.11) a similar procedure might have been practiced until recently in some parts of Ethiopia.

Epilation was also described for trichiasis management in the Ebers' Papyrus in ancient Egypt.[85] Epilation forceps were also found in tombs dating back to the 15th to 11th century BC.[13] The first ancient focal lash root treatment to treat trichiasis was described by Celsus, as "cautery of the lashes with a hot iron needle".[10] He also suggested various other management options ranging from scarification in cases with advanced rough eyelid, to bathing and hot compresses of the eyelid. He also recommended surgical correction of the eyelid using "women's hair for suture".[10]

Figure 1.11: Deformed eyelid from traditional TT surgery.

Note the short eyelid height with no eyelid crease, because much of the upper lid has been excised. The lady cannot close her eyes completely (lid closure defect/lagophthalmos) as a result of the deformity caused by traditional surgery, Amhara Region, Ethiopia, 2014.



1.12. Trachomatous Trichiasis Management in Trachoma Endemic Settings

Generally, trichiasis management options are broadly divided into lash management procedures, lash follicle destruction procedures, and corrective lid surgery. Lash treatment strategies are those that remove the trichiatic lashes, such as epilation. The lash follicle destruction procedures vary from simple electrolysis to cryotherapy and even laser photocoagulation or X-ray radiation. The commonest trichiasis management strategies are discussed below. Please also see Appendix I for a Cochrane Review we recently conducted on "Interventions for trachoma trichiasis".

1.12.1. Lash Management Procedures

1.12.1.1. Epilation

Epilation is the repeated plucking of lashes. It has been practised since ancient times for treating trachomatous trichiasis, and is still a very common traditional practice in many trachoma endemic settings.[7,32,39] People use either homemade metal forceps to remove the lashes from their roots or scissors to shorten lashes that scratch the eye, or burn the trichiatic lashes with a firewood or hot metal, or even use their fingers to pull them away. Various studies conducted in areas with reliable trichiasis surgical services suggest that more than 70% of people with TT epilate predominantly with homemade forceps regardless of surgical service availability.[29-31,39] Significant number of patients who declined surgical treatment believe epilation is a good enough treatment.[29] In a couple of studies, among patients epilating, using homemade forceps, about a quarter have successfully epilated with no lashes touching the eye. [30,39]

Until recently the WHO recommended, "All patients should be offered surgery for entropion TT".[90] However, detailed clinical phenotyping studies have found that up to half of the individuals with trachomatous trichiasis do not have significant entropion.[24] Therefore it was not clear how programmes should manage patients with non-entropic trichiasis which constitute about half of their backlog. Furthermore, many individuals with trichiasis, particularly those with mild disease, decline surgery, even when this is provided free and close to home. Lack of time and fear of surgery are frequently reported as one of the major reasons for poor surgical uptake among trichiasis patients, signifying the need for non-invasive alternative management for those refusing surgery. [29,32,91]

Despite considerable efforts by control programmes in endemic countries to scale-up the amount of surgical provision, the most recent information from the WHO suggests that for the last five years only around 200,000 people/year have received TT surgery, indicating that at this rate of surgical intervention the current 3.2 million backlog (ignoring incident cases) of TT would not be dealt with until 2032, twelve years after the 2020 target year for controlling trachoma.[43] Even if the surgeries are conducted in higher volume, the quality of outcomes both in terms of recurrence (up to 60% at 3 years) and the cosmetic appearance of the lid can be unsatisfactory (up to 24%) creating additional challenges to the prevention of trachomatous blindness.[4,92-94] Cases with few trichiatic lashes may still have recurrence after surgical management. A 16% surgical recurrence at 2 years has been reported in patients with minor trichiasis at baseline.[33]

Many clinicians and researchers believed that epilation could be an alternative treatment for patients with a few trichiatic lashes and performing tarsal rotation surgery probably is unnecessary for a people with a few non-entropic lashes.[33] These lashes probably carry a lower risk of corneal opacity and visual impairment compared to the entropic lashes. However, until recently there was no trial data to support the use of epilation. One longitudinal study found that among patients who refused surgery at baseline and reported epilation, 37% progressed from minor to major trichiasis over a four years period.[32] A couple of cross-sectional studies have found that epilation is associated with a reduced risk of corneal disease in patients with advanced entropion, who decline surgery.[31,39] In another study, corneal opacification was less common in epilated eyes with recurrent trichiasis.[92] [32,92]

In view of the problems in delivering the necessary volume of surgery, high rate of refusals and concerns about the quality of outcomes, our research team recently conducted a randomized controlled trial of epilation verses surgery for the management of minor TT in Ethiopia.[33] The two years follow-up results found no difference in the change in visual acuity or change in corneal disease (on photographic comparison) between the two groups. At the two-year time-point all individuals who had been randomised to epilation were offered free surgery, however, the majority declined. This group of people was reassessed four years after their initial of enrolment.[95] This study is attached in this thesis as Appendix II. In summary, during the four-year period only 33% of minor TT cases initially randomised to epilation had undergone surgery despite the presence of free community-based surgery. Among those who declined surgery and continued epilating (383, 67%) more than half (54.1%) fully controlled their trichiasis, 43.3% had minor trichiasis and only 2.6% had progressed to major trichiasis (>5 lashes). In addition, 92% of these did not seek trichiasis surgery, 85% reported that they were happy epilating and 92% had retained at least one pair of epilation forceps from the two pairs, which were given to them at baseline. More importantly, there was no difference between the epilation and surgery groups in terms of change in vision (p=0.89) and corneal opacity (p=0.38) between baseline and four years.[95]

The evidence from this clinical trial led the WHO to accept epilation as a reasonable second line alternative to surgery for minor trichiasis (five or fewer lashes touching the eyeball), or for cases in which the patient declines surgery or has no immediate access to surgery, or patients with postoperative trichiasis, or patients with lower lid trichiasis.[28]

Patients who choose epilation should be regularly followed up by a service that can provide trichiasis surgery.[28] To reduce the risk of blindness from trichiasis, epilation needs to be repeated when eyelashes re-grow and should be conducted by a trained person (Figure 1.12), using good quality epilation forceps that have durable frames and rounded tips with non-cutting opposing edges, in a size that enables the instrument to be used comfortably by individuals with fingers of different sizes.

Figure 1.12: Epilation training

1.12.1.2. Sticking Plaster

Sticking the trichiatic lashes outside the eye with plaster has been proposed for temporary management of trichiasis. One randomised trial in china compared the relative effectiveness of sticking plaster (with median application of 7 days) with epilation, both conducted by health professionals in health facilities.[96] This reported that 32/39 (82.0%) of the sticking plaster group had "good clinical status", defined as "no lashes touching the eyeball, complete lid closure, no conjunctival hyperaemia, and no unplanned treatment", compared to 3/18 (16.6%)% in the epilation group (p<0.001), after 4 weeks of treatment.[96] However, the practicality of such intervention in trachoma endemic settings is questionable both in relation to tolerance of the sticking plaster for long period as well as the application of both interventions at health facility level which requires frequent follow-up.

1.12.2. Lash Follicle Destruction Procedures

These treatment strategies are usually used in areas with established ophthalmic facilities and are rarely used in trachoma endemic countries for the following reasons. Firstly, although there are very limited studies on their effectiveness, they are generally considered as a treatment choice to treat few aberrant lashes in absence of entropion, which is not the case for trichiasis patients in trachoma endemic countries where at least 50% of the case have moderate to severe entropion. Secondly, electrolysis is done to each and every lash, which is tedious and time consuming. This is a major drawback given that millions of the trichiasis cases have major trichiasis. Thirdly, these procedures require expensive and specialised equipment and skilled manpower, which makes them unsuitable for most trachoma control programmes. This thesis focuses on the management of trichiasis in trachoma endemic settings and therefore only two of the commonly used lash follicle destruction treatment strategies are discussed briefly below.

1.12.2.1. Electrolysis

In low-income countries such as Ethiopia, electrolysis is performed in some tertiary hospitals. These are mostly done for cases with few metaplastic or misdirected lashes usually caused by non-trachomatous conditions with no or very little entropion. The aim of this procedure is to destroy the lash follicles of the aberrant lashes. The procedure involves passing a fine needle along the eyelashes up to the lash root with the help of magnification. The needle should be inserted up to a depth of 2.5mm to completely contact 95% of the follicles. A low power alternating current is passed through a metallic resistor to produce heat, which then should be followed by removing the eyelashes.[7] Electrolysis is often used in conjunction with other surgical procedures or to treat a few recurrent lashes following a particular surgical procedure.[97]

The only clinical trial that explored the relative effectiveness of electrolysis with tarsal rotation surgery and cryoablation in minor TT cases was conducted in Oman.[98] In that trial, electrolysis had a very low success rate (29%) in terms of absence of recurrent trichiasis after about 1 year, compared to tarsal rotation surgery (80%). This might be related to the fact that the minor TT cases randomised in both the electrolysis and surgery arm had entropion (25.4%) and even 43.7% had previous eyelid surgery. Another non-concurrent study of trichiasis patients who received electro-epilation and tarsal rotation surgery was conducted in Oman.[93] After three years, this found a lower rate of recurrence rate among the electro-epilation (51%) cases than in the tarsal rotation cases (62%). Why this difference might have happened is unclear, but may be related to differences in preoperative disease severity between the cases treated with these two surgical procedures. Electrolysis may cause scarring and contraction on the eyelid margin.[99]

1.12.2.2. Cryotherapy

Cryotherapy is a procedure used to destroy trichiatic lash follicles through freezing. It was tried for the treatment of trichiasis after an observation of lash destruction in a therapy for cutaneous malignancy.[100,101] A nitrous oxide probe is applied to the base of the trichiatic lashes to freeze and destroy the lash follicles. The procedure is done in two cycles with a temperature of -20^{0}C to -30^{0}C, each taking about 20 seconds, under local anaesthesia and shielding the globe. The local anaesthesia should contain epinephrine to facilitate greater depth of freezing and prolonged thawing, thereby enhancing success rate.[99] This is followed by removing the offending lashes, topical antibiotic and application of a firm pad on the eye. In the Oman trial, the success rate of cryotherapy was the lowest (18%) of the procedures compared (electrolysis and surgery).[98] However, this study probably used a single treatment. Other studies, which used an improved cyoprobe showed that the success of cryotherapy could be as high as 84% with two-cycle treatment.[102]

Cryotherapy is known to cause several relatively frequent complications, particularly excessive swelling, recurrence and damage to adjacent tissues resulting in depigmentation, tissue necrosis, notching, conjunctival psuedomembrane and worsening of entropion.[99,100,102-104] Both lower rate of complications and treatment success could be achieved with using appropriate size of cryoprobe and applying cryotherapy to the lid margin or the tarsal conjunctiva instead of the skin.[101,102] Use of standard retinal cryoprobe is reported to cause a higher rate of complications, suggesting that a high-flow large-surface probe improves the success rate.[99,101]

Another variation of cryotherapy is the cryosurgery procedure. This involves a full thickness incision or a posterior lamella only half thickness incision and usually also an incision through the grey line of the lid margin. This is followed by application of cryotherapy. This 'internal' application to the posterior lamella is thought to have a higher success rate and lower rate of complications including loss of non-trichiatic lashes and depigmentation.[99] In general, cryotherapy is more likely to be successful in non-trachomatous trichiasis cases with more than a few trichiatic lashes in clusters and with minimal conjunctival scarring and tarsal distortion.[99,101]

1.12.3. Surgical Management

Surgical management is the mainstay of treatment for trachomatous trichiasis. It is a widely-used treatment strategy by trachoma control programmes in trachoma endemic countries. Surgical correction of trichiasis is performed mainly to reduce the risk of blindness by limiting the abrasive damage of the eyelashes rubbing on the cornea. Patients also benefit from a marked reduction in the pain they experience and may have some improvement in vision.[92]

Many different surgical procedures have been tried in the past to correct TT suggesting that no "ideal" solution exists (Table 1.4).[7,105-107] These ranged from eyelid margin splinting to excision of the tarsus. Some surgical procedures are focused on the lid margin and the anterior lamella while others are focused on lengthening or rotating the tarso-conjunctiva. The main principle behind all the surgical procedure is repositioning of the deformed and in-rolled eyelid by surgical incision and suturing to stop the eyelashes from scratching the cornea. The later section describes each of the surgical procedures tried for the management of trachomatous trichiasis. Based on which part of the eyelid they are seeking to correct, trichiasis surgeries can be broadly categorised as follows:

1) Tarsal Rotation
2) Tarsal Advance
3) Posterior Lamellar Lengthening
4) Lid Margin Eversion
5) Anterior Lamellar Repositioning
6) Tarsal Grooving
7) Tarsal Excision

1.12.3.1. Tarsal Rotation Surgical Procedures

In 1895, Lagleyze's description of the mechanical outward rotation of the eyelid margin and the lashes through surgery initiated the development of the current tarsal rotation surgeries.[99]

The tarsal rotation surgeries mainly involve cutting through the scarred eyelid, followed by rotation of the tarsus and suturing of the eyelid in the corrected position.[108] There are two type of commonly used tarsal rotation procedures: Bilamellar Tarsal Rotation (BLTR), and Posterior Lamellar Tarsal Rotation (PLTR) or "Trabut" operation. These are the most commonly used surgical procedures for the treatment of entropic trichiasis in the trachoma endemic countries.

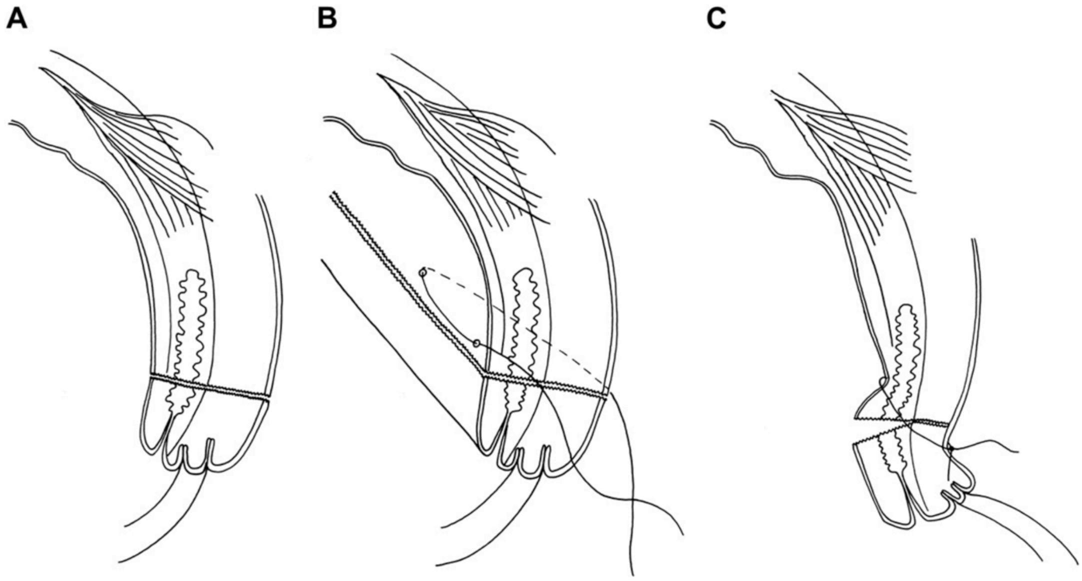
1.12.3.1.1. Bilamellar Tarsal Rotation (BLTR) Surgery

Ballen, first adapted the BLTR in 1963 for the treatment of upper lid entropion trichiasis, from the Wies surgical procedure developed to treat lower lid non-cicatricial entropion.[109,110] Wies indicated making an incision at around 4mm from the eyelid margin.[111] However, in Ballen's paper on the surgical procedure "an incision of 2 mm above the root of the lashes" was described.[109] This was probably to avoid overcorrection, which was considered the commonest draw back of the Wies surgical procedure. However, this was subsequently changed to an incision made at 3 mm from the lid margin, as slight overcorrection is deemed necessary for adequate long-term correction. [108,112]

In BLTR surgery, a full thickness horizontal incision is made through the upper eyelid and sutures are inserted to evert the distal part of the incised eyelid (Figure 1.13). Below is the summary of the standard BLTR surgical procedure being used currently.

Figure 1.13: Sketch of BLTR procedure.[7]

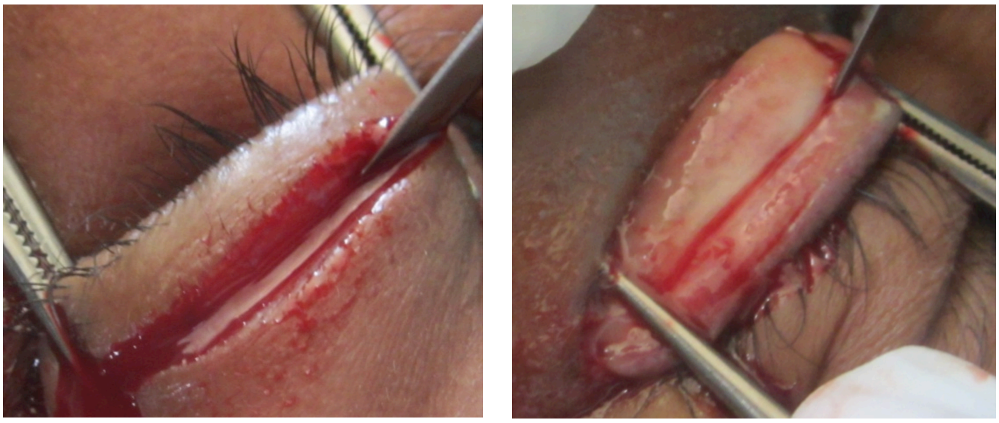
A, Full thickness incision; B, Inserting mattress sutures; C, Everted eyelid with tightened sutures



Following infiltration of local anaesthesia between the eyelid skin and the muscle, a full thickness incision parallel and at 3mm distance to the lid margin is made, starting at 1mm lateral to the puncutm and extending up to the lateral canthus. There are two methods of making the surgical incision. In the first method, two haemostats are used to fix the eyelid laterally and medially (Figure 1.14). Great care is taken not to damage the punctum and the canaliculus while placing the haemostats and they should be located within 5mm distance of the lid margin to avoid damage to the eyelid during eversion. Once the haemostats are positioned correctly, a horizontal half thickness incision is made through the skin and the orbicularis muscle (Figure 1.14a). Then the eyelid is everted with the help of the two haemostats. The anterior incision is connected to a posterior incision made in the tarsal conjunctiva and through the tarsus, again at 3mm from the lid margin (Figure 1.14b). This procedure uses a lid guard to protect the eyeball from accidental trauma during both incisions.

Figure 1.14: BLTR procedure using haemostats to fix the eyelid

a) The first half thickens incision through the skin   b) The second half thickens incision after everting eyelid



In the second method, a specifically designed TT clamp or Waddell clamp is used to fix the eyelid (instead of the two haemostats) and simultaneously to protect the eyeball (Figure 1.15a).[113] In this, the eyelid margin should be placed against the vertical portion of the clamp. The clamp allows a single full thickness incision to be created through the skin and the tarsal conjunctiva, parallel and at 3 mm distance to the lid margin without the need to evert the eyelid (Figure 1.15b & c).[108] The relative effectiveness of using these two instruments in reducing the rate of unfavourable outcomes (Postoperative TT, Granuloma and Eyelid Contour Abnormality (ECA)) has been studied recently in a clinical trial.[94] This found that the combined rate of unfavourable outcomes are comparable between the two instruments, but using the TT clamp provided lower rate of granuloma and mild ECA.[94]

After completing the incision, three mattress sutures are inserted through the skin of the marginal fragment 1 mm above the lash line emerging through the cut edge of the muscle layer of the eyelid (Figure 1.15d). These are inserted half thickness through the tarsal plate and 1mm from the cut edge of the tarsal conjunctiva, which should be repeated from the opposite direction of the last bite (if using single armed suture), by inserting the sutures at 5mm apart from the last bite through 1mm distance from the edge of the tarsal conjunctiva and exiting through the cut edge of the marginal fragment tarsus. The next step is returning to the marginal fragment to complete the sutures. This is done by passing the suture through the muscle layer (aligning with the exit site of the suture in the larger fragment) to emerge into the skin at 1mm above the eyelashes. The sutures are tied firmly to create slight over correction and achieve adequate outward rotation of the entropic eyelid margin (Figure 1.15e & f).[108]

There are variations of the BLTR from the current WHO recommended procedure.[114-116] One is making a surgical incision through the skin and the orbicularis muscle at around 4mm distance from the lid margin or even higher at around the eyelid crease.[114,117] After dissecting the marginal orbicularis fibres, an oblique incision is made on the tarsal plate anteriorly at about 2.5mm from the lid margin. This is followed by piercing the conjunctiva at about 1.5mm from the lid margin.[114] It is believed that making a tarsal incision nearer to the lid margin would minimize eyelid deformity and provides adequate eversion due to which the sutures should only be tied with moderate tension.[114]

Another variation is making a "bipedicled tarsoconjunctival advancement flap" with a second horizontal incision on the anterior tarsus.[115] Recently, Cruz et al described a bilamellar tarsal rotation procedure combining both the Wies and Trabut approaches with internal sutures to avoid external sutures.[116] In this technique an external incision is first made on the lid crease followed by exposing the tarsus through a dissection extending up to the root of the lashes to create an anterior lamellar flap. Then the eyelid is everted and a second full thickness incision is made at the tarso-conjunctiva at 3mm from the lid margin. Three double armed sutures are inserted at the edge of the distal tarsus and through the orbicularis muscle behind the lash line.[116]

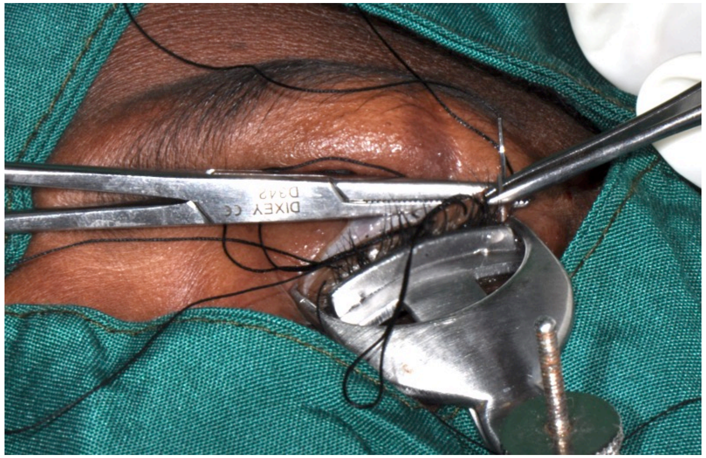
Figure 1.15: Pictures showing main steps of the BLTR procedure

a) Fixing eyelid

b) Full thickness incision

c) Completing the incision

d) Inserting sutures



e) Tying sutures

f) Immediate postop appearance of a corrected eyelid

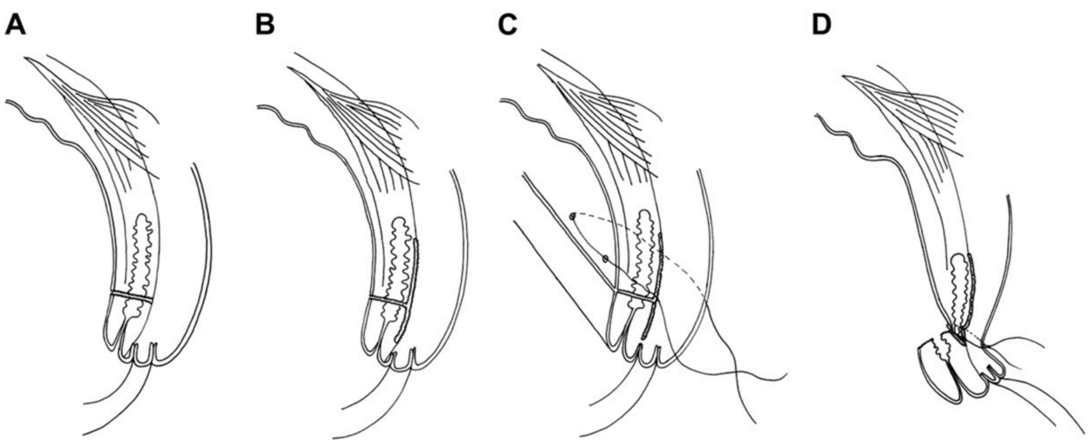
1.12.3.1.2. Posterior Lamellar Tarsal Rotation Surgery (Trabut Operation)

The PLTR procedure is probably one of the earliest practised surgical procedures for the management of trachomatous trichiasis in endemic settings.[118,119] It was first described by Lagleyze.[99] However, it is believed that the procedure descended from Celsus (a Greco-Roman Physician), and was later developed in the 1870s. In 1903 Ewing showed its use for the management of lower lid cicatricial entropion.[114,120] In 1948, Kettesy modified the Lagleyze procedure, which was in turn modified by Trabut in 1949.[105] In 1950, Torgersruud, an expatriate ophthalmologist working in Addis Ababa, Ethiopia, used the PLTR surgery in hundreds of patients successfully and found good results with only few showing sign of recurrence.[118]

In PLTR surgery, a half thickness horizontal incision is made on the tarsal conjunctiva and the tarsus (posterior lamella) separating the posterior lamella from the anterior lamella, and sutures are inserted to evert the distal part of the incised eyelid (Figure 1.16). Below is the summary of the standard PLTR surgical procedure being used currently.

Figure 1.16: Sketch of the PLTR procedure.[7]

A, Half thickness incision on the posterior lamella; B, Dissecting the posterior lamella form the anterior; C, Inserting mattress sutures; D, Everted eyelid with tightened sutures



The PLTR surgery is performed with the eyelid fixed in an everted position using a lid everter (Trabut Plate) with the help of a traction suture inserted at 3mm above the lashes through the skin and the orbicularis of the eyelid (Figure 1.17a). The traction sutures should be removed immediately after suturing is completed. Earlier practices used clamps to evert the eyelid and in the absence of this even spatulas and eversion plates made out of horn have been used.[118,119,121] Once the eyelid is everted, a horizontal half thickness incision at 3mm from and parallel to the lid margin is made on the tarsal conjunctiva through the tarsal plate (posterior lamella) stopping at the orbicularis muscle (Figure 1.17b). This is followed by completing the incision at the medial and lateral edge of the eyelid using scissors. The next step is dissection of the orbicularis oculi muscle away from the tarsal plate, in both the proximal (5mm depth) and distal (3mm depth) fragments of the eyelid (Figure 1.17c).

Three mattress sutures are inserted through the skin of the distal fragment 1 mm above the lash line emerging through the pocket behind the tarsus created during the dissection (Figure 1.17d). This is followed by leading the suture into the cut edge of the proximal fragment tarsal plate (half thickness) and emerging at 1.5mm from the cut edge of the tarsal conjunctiva; which should be repeated from the opposite direction of the last bite (if using single armed suture), by inserting the sutures at 5mm distance from the last bite through the inside of the proximal tarsus at half thickness through the cut edge. The suture is guided through the pocket behind the distal tarsus to exit at the eyelid margin above the lash line. Then all three mattress sutures are pulled together so that the proximal tarsus would be drawn into the pocket of the distal fragment eyelid (Figure 1.17e). The sutures should be tied firmly enough to create a slight over correction and rotation of the eyelid margin in outward and upward position (Figure 1.17f).

There have been various methods described of performing the posterior tarsal rotation surgery. The variations of most of these procedures are on the location of incision, amount of dissection performed on the posterior lamella, and in the insertion of the everting sutures; which are probably the three most important factors for the outcome of the surgery.

In terms of incision there has been a suggestion to perform the incision at 1.5–2mm from the lid margin.[119,122] In addition, incising along the Arlt's scar line in cases with severe trachomatous trichiasis cases has been practiced.[121,123] In the modified Trabut procedure, two relieving lid margin incisions, one on the lateral canthus and another lateral to the upper punctum are done to achieve adequate 180^0 rotation.[26]

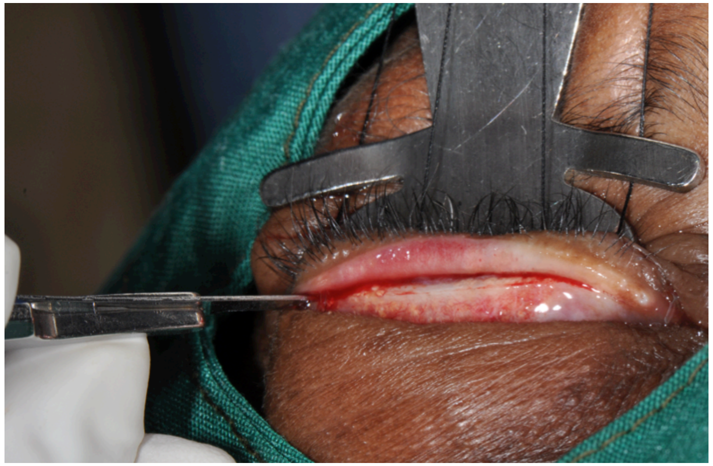
In terms of dissection of the tarsus from the orbicularis tissue, the earlier Lagleyze posterior tarsal rotation technique used no dissection of tarsus from the orbicularis in either the proximal or the distal portions of the incised eyelid. Later the importance of dissection of the tarsus from the orbicularis was better understood, but this was again performed with variation. Some dissected only the proximal portion of the eyelid while others dissected the distal portion alone.[119,123] In 1949, Trabut, first described the need to dissect the tarsus from the orbicularis muscle on both the proximal and distal portion of the incised eyelid.[105] In addition, another variation was dissection of the levator aponeurosis from the anterior surface of the proximal tarsal fragment.[122]

There has been also variation in the insertion and location of the sutures.[105,121] One practice has been the proximal section sutures involving the tarsal conjunctiva and partial thickness of the tarsus, while the sutures at the distal portion appear through the orbicularis muscle anterior to the distal tarsal fragment exiting through the skin at 2mm distance above the lash line.[119,121,122] In a second practice, the sutures pass through the orbicularis and exit exactly at the lash line.[124] In another practice, the sutures pass perpendicular through the distal tarsal fragment and emerge through the lid margin to create a 90^0 rotation.[123]

Figure 1.17: Pictures showing main steps of the PLTR procedure

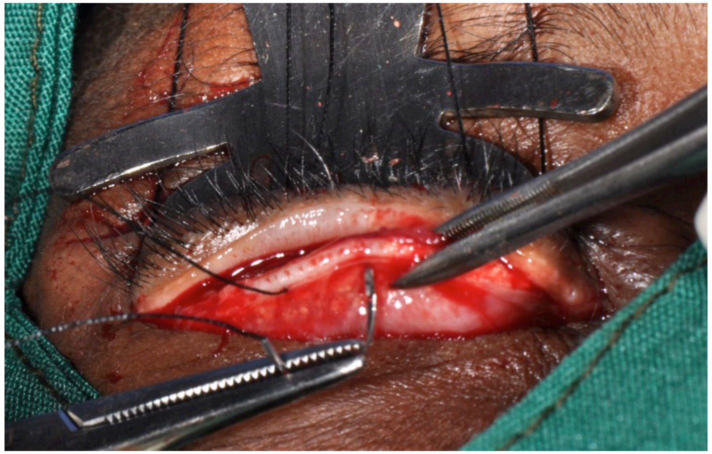
a) Eyelid everted

b) Half thickness incision on the posterior lamella

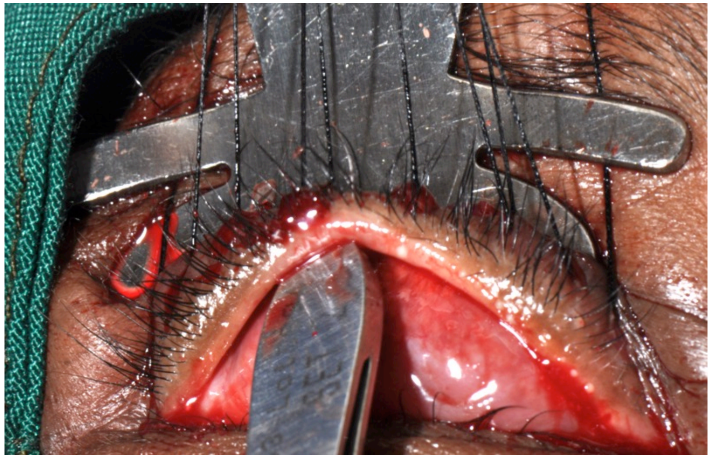


c) Dissecting the posterior lamella from the anterior

d) Inserting sutures



e) Pulling sutures to tuck the proximal edge into the distal fragment pocket



f) Immediate postop appearance of a corrected eyelid

1.12.3.2. Tarsal Advance Procedures

The tarsal advance surgical procedures are characterized by a vertical division of the eyelid into two layers: the anterior lamella and the posterior lamella.[125] This is done by an incision made through the grey line of the lid margin between the tarsus and the orbicularis-levator aponeurosis to the full height of the tarsal plate from near the lacrimal canaliculus medially extending up to the lateral canthus.[125] The main principle behind this surgical procedure is that, in cictricial trachoma there is excessive fibrosis and thickening of the tarso-conjunctiva which is followed by contracture and shortening of the eyelid leading the eyelash to rub the eyeball. Therefore, this surgical procedure is aimed at releasing and advancing the tarsus to anterior position to compensate for the shortened tarsal conjunctiva.[125] There are three variations of the tarsal advance surgical procedure: the tarsal advance, the tarsal advance with mucosal graft application and the tarsal advance and rotation.

1.12.3.2.1. Tarsal advance

In the tarsal advance version, the posterior lamella is advanced forward and the anterior lamella is retracted, so that the posterior lamella rests between the trichiatic lashes and the cornea.[125] In the method described by Welsh, in addition to the splitting of the lamellae as described above, an external 10 mm length vertical incision through the skin and the muscle is done at the lateral canthus followed by dissection of the muscle away from the tarsus up to the upper boarder of the tarsus.[125] In a modified procedure 2mm - 7mm long radial anterior lamellar incisions are made laterally and medially.[126] This anterior lamellar incisions, would facilitate advancement of the posterior lamella, which when pulled down, its edge would advance by 4mm-6mm from the anterior lamella, the position that the two layers should be sutured together. Three horizontal mattress sutures are inserted through the anterior lamella at 3mm from the lid margin and then at about 9mm through the posterior lamella, which then should return back through the posterior lamella and then to the anterior lamella through the skin. When these are tightened, they will produce an opposing effect to the lamellae: lengthening/advancing the posterior lamella, and shortening/retracting the anterior lamella. This would create a 4mm - 6mm raw area of the anterior surface of the posterior lamella at the lid margin. In the Welsh procedure, this should be left to heal by itself within two weeks without the need for interposition of mucous membrane.[125,126] The vertical/radial anterior lamellar incision should be stitched to the tarsal plate and the adjacent skin.[125] Later, Jones et al described the need to mobilize the tarsus by dissecting the fibrosed levator complex and Muller's muscle to treat retraction of the tarsal plate that occurs due to fibrosis of the levator aponeurosis in cicatricial trachoma.[127] A case series on 177 patients with advanced trachoma treated using the tarsal advance procedure found 100% success, while later a clinical trial comparing this with other surgical procedures reported low (27%) success rate in major trichiasis cases.[125,128]

1.12.3.2.2. Tarsal advance with mucous membrane graft

In this variation, following the application of the three-mattress suture a bucccal mucous membrane graft is applied on the exposed anterior surface of the tarso-conjunctiva.[129,130] This is mainly to cover the “over correction” look of the tarsus resulted from the advancement of the posterior lamella, and to facilitate healing.

1.12.3.2.3. Tarsal advance and rotation

The tarsal advance and rotation procedure is a tarsal advance procedure followed by posterior lamellar rotation, which is basically a combination of the tarsal advance and the posterior lamellar tarsal rotation.[26,131] The variation with the tarsal advance is that, the surgical incision to separate the two lamellae is made on the posterior lamella after the eyelid is everted, not through the grey line of the lid margin.[26,98,131] Then two medial and lateral incisions are made to relieving the tarsus: vertical incision at 1mm distance from the punctum, and horizontally at the lateral canthus. As in both tarsal advance and posterior lamellar tarsal rotation procedures, the proximal tarsal fragment should be dissected off from the orbicularis tissue up to the superior fornix to allow a 180^0 rotation.[26,131] Then the proximal tarsus gets 3mm advancement by horizontal mattress sutures “placed across the lid running from the upper fornix diagonally downwards to emerge slightly below the skin crease”.[7,98] Mattress sutures are inserted through the posterior lamella and exiting through the skin to secure the repositioned margin with the proximal tarsus.[98]

Two clinical trials reported a success rate of 41% and 46% at one year for the tarsal advance and rotation procedure for patients with major trichiasis.[98,128] Another trial reported about 8% recurrence rate in six months.[132] The tarsal advance and rotation has also variations and can be combined with a series of modifications, such us adding incision of Muller’s muscle or incision of the Muller’s muscle followed by an inlay graft.[25,105]

1.12.3.3. Posterior Lamellar Lengthening

This procedure is performed to elongate the posterior lamella using a graft in cases with severely atrophied, contracted or shortened posterior lamella such as in cicatricial trachoma.[133-136] The procedure involves harvesting a mucus membrane such as buccal mucosa. The eyelid is everted using traction sutures and a lid everter. A horizontal incision is made through the posterior lamella at about 2mm to 3mm from the lid margin and a vertical incision at both ends of the tarsus to release the distal portion of the eyelid. Then the posterior lamella is separated from the orbicularis muscle. The mucus membrane graft is placed across the incised space between the proximal and distal fragment of the posterior lamella and sutured in place.[134] In a slight variation to this, a canthotomy can be performed so that the mucous membrane graft can be inserted from the lateral end of the canthotomy extending medially.[134] In addition rubber bolsters can be placed and tied under the traction suture at the end of the operation and left in situ for five days to help provide sustained rotation and evertion of the distal portion of the posterior lamella.[134] A prospective cohort in Egypt reported a 10% failure rate few days after posterior lamellar lengthening procedure, but this did not report the long term outcomes.[134]

1.12.3.4. Lid Margin Splinting (Eversion Splitting)

In lid margin splinting procedures, the eyelid margin is divided vertically into the "lash bearing section" (skin and muscle) and "non-lash bearing section" (tarso-conjuctival layer). This is done with a vertical incision just posterior to the lash line (through the grey line) up to a depth of 3mm-5mm, based on the severity of entropion trichiasis.[137,138] The lash bearing section of the eyelid is rotated upward and externally away from the eyeball through three sutures tied over a roll of petroleum jelly gauze (30 x 5 mm) serving as an eversion splint.[105,137] One arm of a double armed suture is passed through the conjunctiva of the upper fornix and through the tarsal plate exiting through the skin 6mm from the lid margin, while the other end of the suture is inserted adjacent to the first and passes through anterior to the tarsal plate and exits through the skin 1mm distance from the lid margin.[137] The petroleum jelly gauze is placed horizontally between the two suture arms, then when the sutures are tightened it will force the incised eyelid margin to gape which create 90^0 of outward rotation of the lash bearing section of the eyelid margin.[137] In a study in Burma, this procedure was found to be successful in trichiasis cases. Although it reports recurrence of 0.3% in cases with "soft and pliable eyelids" and 6% with "hard eyelid on palpation" at one year after surgery, the 28% (528/1861) follow up rate is inadequate to draw conclusions.[137] Other authors have suggested that a more conservative estimate of 28% success should be inferred from this study, assuming that those only seen at follow-up are considered to have successful outcomes.[105] Another clinical trial, which compared the relative effectiveness of this surgical procedure with others, showed a very low success rate (29%), which is comparable with the above conservative estimate of success for the Burma study. [128]

Other variations of the lid margin splinting procedure insert grafts such as buccal mucous membrane, a skin flap of the eyelid or sclera into the incised lid margin.[138,139] Granuloma occurred in 10% of the cases with scleral homograft inlay.[138] In one of these variations a polyethylene tube has been used to stabilise the eversion and the skin graft.[139] A report from Nigeria, showed 94% and 92% success rates for lid margin splinting procedures which used eyelid skin graft and scleral homograft inlay respectively.[138,139] Another study from Nigeria, which compared the relative effectiveness of lid margin splinting and scleral marginal graft with the bilamellar tarsal rotation surgery in retrospective case review reported a 74% and 77% success rate respectively.[140]

1.12.3.5. Anterior Lamellar Repositioning / Anterior Lid Shortening

In anterior lamellar repositioning, the tarsal plate is exposed through a horizontal skin incision at about 6mm distance from the lid margin. This is followed by dissection of the anterior lamella from the tarsus starting from the incision line down to around 2mm from the lash roots. Then to rotate the lash bearing edge of the eyelid, 3 to 4 mattress sutures are inserted just behind the lash line, and guided at 6mm distance through the tarsal plate to exit back the skin near the lid margin. On tying sutures tightly the anterior lamella is repositioned and the trichiatic lashes everted.[25] This procedure is usually recommended for cases with mild entropic trichiasis and without metaplastic lashes emanating from the posterior lamella.[25]

The anterior lamellar repositioning could be combined with a series of other trichiatic correction procedures, particularly when further eversion is sought. Firstly, for cases with moderate entropion trichiasis, anterior lamellar repositioning could be combined with lid margin splinting, by making a grey line incision to a depth of 2mm.[25,97] In a recent study using this procedure in trachomatous trichiasis or entropion cases with thin and short tarsus, a 66% success rate at six month was reported.[97] Secondly, in a markedly thickened tarsus, the anterior lamellar repositioning could be combined with lid margin splinting and then tarsal wedge resection.[25,132] Thirdly, anterior lamellar repositioning can be combined with excision of the orbicularis muscle, which should be followed by sutures passing from the inferior edge of the eyelid margin through the levator aponeurosis and exiting at the superior edge of the skin. Fourthly, anterior lamellar repositioning can be combined with lash follicle excision in cases with mild trichiasis.[141]

Another variation of this procedure is anterior lamellar recession with blepharoplasty and supratarsal fixation.[142] In this procedure, unlike the above anterior lamellar repositioning procedures, a division of the anterior lamella from the tarsus is done through a grey line incision up to a depth of 5mm. Then the anterior lamella is recessed with absorbable sutures. This is followed by removing excess anterior lamella (blepharoplasty) and fixing the anterior lamella with the supratarsal region using sutures. This is mainly to avoid sliding of the anterior lamella to the lid margin which may result in recurrent entropion.[142]

1.12.3.6. Tarsal Grooving /Tarsal Wedge Resection

The tarsal grooving procedure, which is also known as tarsal wedge resection was first described by Streatfield in 1857.[105] The procedure involves making anterior lamellar incisions, exposing the tarsus and making two angled incisions on the tarsus and then excising a tarsal wedge.[105,143-145] Firstly, two horizontal anterior lamellar incisions are made to remove excessive skin fold. The first skin incision is made at around the lid crease (about 5mm-6mm from the lid margin) extending above the punctum and the lateral margin of the eyelid. The location for the second incision is determined by the amount of skin to be removed, but usually would not be lower than 4mm from the lid margin.[145] The two ends of this incision should be joined to the ends of the first incision. Secondly, the tarsus is exposed through blunt dissection both up to the lid margin and the upper end of the tarsus, which is then followed by two angled incisions on the tarsal plate at around 4mm and 6mm above the lid margin at the length of the tarsus and at 1mm-1.5mm depth.[144] This creates a wedge of a tarsus, which is removed.[145] Three mattress sutures are inserted through the lid margin, anterior lamella through the distal groove of the tarsal plate and then through the proximal tarsus and back to the distal tarsus emerging at the skin. Before tightening these sutures, skin sutures are inserted to close the skin incisions. When the tarsal sutures are pulled and tightened, they force the groove to close and evert the eyelid margin.

The tarsal grooving procedure was considered time consuming and would provide unsatisfactory results when performed in a short and heavily scarred tarsus.[125] A study that compared the relative effectiveness of 5 surgical procedures found that the tarsal grooving procedure had the lowest success rate (11%) at around six month. However, patients randomised to this surgical procedure had more severe disease than the patients randomised to three of the other surgical procedures.[128] A slightly advanced tarsal grooving procedure that might reduce the recurrence rate in severe entropion trichiasis cases has been suggested.[146] This included combining the tarsal wedge resection with separation of the orbital septum through a horizontal incision, then suturing the edge of the orbital septum with the aponeurosis of the levator muscle. This provided a 90% success rate among 35 eyelids.[146] Another recent variation is combining wedge resection of thickened tarsus with "Anterior Lamellar Marginal Z-plasty".[147] This procedure starts with making three anterior lamellar incisions: the first at the grey line and separating the two lamellae to 4mm–5mm depth; and the second at 4mm–5mm distance above the lid margin through the anterior lamella. This leaves a rectangular anterior lamellar flap. The third incision passes diagonally from the medial edge to the lateral edge creating two triangular anterior lamellar sections that should be transposed using suture.[147]

1.12.3.6.1. Cuenod Nataf Procedure

The Cuenod Nataf surgical procedure, which is predominantly practiced in Vietnam, is a modification of the tarsal grooving procedure. The Cuenod Nataf procedure includes a grey line incision up to the depth of the lash follicles.[143,148,149] In addition this procedure involves the removal of a half thickness wedge of tarsus without buttonholing the tarsal conjunctiva.[145] However, in a further modification to the Cuenod Nataf procedure itself, the removal of a wedge of tarsus is being omitted in current practices in Vietnam, limiting the procedure to just anterior tarsotomy with grey line incision.[148,149] This modified procedure is reported to give satisfactory results in two cohort studies with about 90% success rate one year after surgery.[148,149]

1.12.3.7. Tarsectomy

The other surgical procedure, which has been tried for the treatment of entropic trichiasis from severe scarring and retraction of the tarsus, is excision of the tarsal plate.[150] Another variation to this is tarsal excision followed by levator recession, which is reported to give 80% success rate at 12 months.[127] However, excision of the tarsal plate is not regularly performed for the treatment of entropic trichiasis as it may result in a floppy eyelid which might lead to keratitis.[151] In addition, it has been reported surgical failures that may occur after loss of tarsus are difficult to correct.[129]

Table 1.4: Summary of surgical procedures used for the management of trichiasis and entropion

Category & Type of Surgical Procedures	Indication	Principle	Common Complications
Tarsal Rotation procedures			
Bilamellar Tarsal Rotation [108,109,113-117]	All type of entropion trichiasis, more effective for cases with mild and moderate entropion	Full thickness horizontal incision is made through the skin and muscle of the upper eyelid and three mattress sutures are inserted to evert the distal part of the incised eyelid	Bleeding Over correction Under correction Division of the eyelid margin Granuloma Eyelid contour abnormality Infection Eyelid margin retraction
Posterior Lamellar Tarsal Rotation/Trabut [25,118,119,121,123]	All type of entropion trichiasis, effective for cases with severe scarring and entropion, keratinisation of the tarso conjunctiva and metaplastic lashes	The eyelid is everted and then half thickness horizontal incision is made on the posterior lamella of the upper eyelid, dissection made to separate the anterior and posterior lamella to enable 180^0 rotation, the proximal tarsus is drawn into the pocket of the distal fragment eyelid by three mattress sutures, which when pulled evert the distal part of the incised eyelid	Over correction Under correction Granuloma Eyelid contour abnormality Lid closure defect Infection
Tarsal advance procedures			
Tarsal Advance [125,126]	Entropion trichiasis with shortened tarsal conjunctiva	Vertical division of the two lamellae through the grey line, followed by forward advancement of the posterior lamella and retraction of the anterior lamella, so that the posterior lamella rests between the trichiatic lashes and the cornea	Overcorrection
Tarsal advance with interposition of mucous membrane [129,130]	Entropion trichiasis with shortened tarsal conjunctiva	Same as tarsal advance with bucccal mucous membrane graft application on the exposed anterior surface of the tarso- conjunctiva due to the posterior lamellar advancement	

Category & Type of Surgical Procedures	Indication	Principle	Common Complications
Tarsal advance and rotation [26,131]	Entropion trichiasis with shortened tarsal conjunctiva	Combination of the tarsal advance and the posterior lamellar tarsal rotation; the surgical incision to separate the two lamellae is made on the posterior lamella after the eyelid is everted, not through the grey line of the lid margin. Vertical medial and lateral relieving incisions are made in the tarsus. Proximal tarsal fragment should be dissected off the orbicularis tissue up to the superior fornix to allow 180^0 rotation	Overcorrection Pyogenic granuloma
Tarsal advance and rotation with division of Muller's muscle [25,127]	Entropion trichiasis with advanced retraction of the tarsal plate and lid closure defect that occurs due to fibrosis of the levator aponeurosis from cicatricial trachoma or previous eyelid surgery	Same as tarsal advance and rotation, but additional dissection of the fibrosed levator complex and Muller's muscle	
Posterior Lamellar Lengthening			
Posterior lamellar lengthening [134-136,145]	Entropion trichiasis with severely atrophied, contracted or shortened posterior lamella	Posterior lamellar incision and division, with suturing of a graft material between distal and proximal tarsal fragments.	Corneal irritation from the graft Heaviness of the eyelid margin
Lid Margin Eversion/ Eversion Splinting			
Lid margin splitting [137]	Mild to moderate disease without tarsoconjunctiva thickening (when thin tarso conjuncutiva)	The eyelid margin is divided vertically into the "lash bearing section" (skin and muscle) and "non-lash bearing section" (tarso conjuctival layer). This is done with a vertical incision just posterior to the lash line or thorough the grey line up to a depth of 3mm. The lash bearing section of the eyelid is rotated upward and externally away from the eyeball through three sutures tied over a roll of petroleum jelly gauze serving as an eversion splint	Surgical failure Under correction
Lid margin splitting with scleral or mucosal membrane inlay [138,139]	Mild to moderate disease without tarsoconjunctival thickening (when thin tarsoconjunctiva)	Same as lid margin splinting with grafts such as buccal mucous membrane, a skin flap of the eyelid or sclera are inserted in the incised lid margin	High rate of granuloma formation Graft rejection Infection

Category & Type of Surgical Procedures	Indication	Principle	Common Complications
Anterior Lamellar Repositioning			
Anterior Lamellar Repositioning /Anterior lid shortening [25]	Mild entropion (early stage entropion trichiasis)	Separation of the anterior lamella from the tarsus up to the lash roots after a horizontal skin incision at the lid crease. Mattress sutures inserted at the lid margin and through the tarsus, which when pulled and tightly tied reposition the anterior lamella everts the trichiatic lashes	Infection
Anterior Lamellar Repositioning with lid margin splinting [25,97]	Moderate entropion trichiasis	Same as Anterior Lamellar Repositioning, but with a grey line incision at a depth of 2mm	Postoperative lid oedema and/or ecchymosis Lid margin thickening
Anterior Lamella recession with blepharoplasty and supratarsal fixation [142]	Moderate cicatricial entropion without lagophthalmos	Anterior lamella separated from the tarsus (5mm) through a lid margin split at the grey line, recessing and fixing the anterior lamella 3-4mm from the lid margin (with sutures), removing excess anterior lamella, followed by fixing the anterior lamella to the supratarsal area with absorbable sutures to prevent downward migration of the anterior lamella	Eyelid margin thickening
Tarsal Grooving			
Tarsal Wedge Resection [144,145]	Entropion trichiasis with thickened tarsus	Two anterior lamellar incisions are made to remove excessive skin fold, exposing the tarsus and making two angled incisions on the tarsus and then excising tarsal wedge. Insert mattress sutures, when tightened to force the groove to close and evert the eyelid margin	Lid closure defect Overcorrection
Tarsal wedge resection with, anterior lamellar repositioning and lid splinting [26]	Entropion trichiasis with thickened tarsus	A combination of tarsal grooving, anterior lamellar repositioning and lid splinting	Overcorrection
Cuenod Nataf/Anterior tarsotomy [148,149]	All type trichiasis	A modification of the tarsal grooving procedure without tarsal wedge resection, which includes a combination of anterior tarsatomy with a grey line incision	
Tarsal wedge resection with division of orbital septum [146]	Severe entropion trichiasis	Anterior lamellar incision at 3mm distance from the lid margin, dissection of the tarsus from the anterior lamella, and wedge excision of the tarsus, followed by separation of the orbital septum through a horizontal incision and suturing the edge of the orbital septum with the aponeurosis of the levator muscle	Overcorrection, Under correction

Category & Type of Surgical Procedures	Indication	Principle	Common Complications
Anterior lamellar marginal Z-plasty with transverse tarsotomy [147]	Any trichiasis	Three anterior lamellar incisions are made on the anterior lamella. The first at the grey line and separating the two lamellae up to 4-5mm depth; and the second at 4 – 5mm distance above the lid margin through the anterior lamella. This leaves a rectangular anterior lamellar flap. The third incision passes diagonally from the medial edge to the lateral edge creating two triangular anterior lamellar sections that should be transposed using suture. A wedge of tarsus is removed after making transverse tarsotomy at 3mm distance from the lid margin	Postoperative edema Infection Lid margin thickening
Tarsal Excision			
Tarsectomy [127,150]	Severely affected tarso conjunctiva with retraction	Excision of the tarsal plate	Floppy eyelid with lagophthalmos and keratitis Entropion

1.13. Outcome of Trachomatous Trichiasis Surgery

There have been many efforts in the past decades to identify the most reliable and effective surgical procedure for trachomatous trichiasis. Unfortunately, there has not been a perfect surgical procedure. The outcome of trachomatous trichiasis surgery is still one of the major concerns of trachoma control programmes worldwide. Surgical outcomes can be discussed under the following categories: surgical complications, postoperative clinical outcomes and patient reported outcomes.

1.13.1. Surgical Complications

Surgical complications discussed below are those that occur during the surgery or within a few days in relation to the surgery or the surgeon technique. These include excessive bleeding, correction defect, infection, and eyelid closure defect. Others such as division of the eyelid margin, eyelid necrosis, irritation, heaviness of the eyelid margin and loss of cilia were also reported as short-term postoperative complications.[94,125,134]

1.13.1.1. Excessive Bleeding

Bleeding was infrequently reported as complication in trichiasis surgical procedures. This may be because it is fairly uncommon and would be controlled easily. However, surgical procedures that undermine the vascular bed of the eyelid, which is located beneath the orbicularis muscle, are likely to have more bleeding than those confined to the posterior lamella. One clinical trial reported wound bleeding during the two weeks follow-up in 2/124 (1.6%) trial participants, which were operated by the BLTR procedure, while none were reported among those operated by the PLTR.[152] Another clinical trial reported, “excess intraoperative bleeding” on 4 (0.24%) of the eyes randomised to the “standard BLTR” procedure.[94] A retrospective cases review reported bleeding in 4% of the cases with grey line split procedure.[140] A couple of clinical trials, which operated on trichiasis cases using the posterior lamellar tarsal rotation surgery reported a 0.5% postoperative bleeding and a 1.4% “significant” intraoperative bleeding rate.[33,40] Postoperative bleeding was also reported in 2/101 (2%) trial participant undergone tarsal advance and rotation surgery for major trichiasis.[98]

1.13.1.2. Correction Defect

Correction defect such as immediate postoperative overcorrection and under correction probably determine the long-term outcome of surgical procedures. Among the various surgical procedures tried in the past some are particularly related with higher risk of over correction while others relate to under correction.

Overcorrection can be defined as undesired visibility of part of the tarsal conjunctiva (Figure 1.18a). This mainly occur under two conditions: either from high incision distance from the lid margin or excessive tension of mattress sutures. It is generally recommended to aim for slight overcorrection during the time of trichiasis surgery.[108]

Overcorrection rate of between 2% and 3.5% have been reported from BLTR procedure.[128,152,153] A clinical trial comparing the relative effectiveness of different surgical procedures reported more overcorrection in the BLTR surgery than the tarsal advance procedure (2% vs 0%).[128] However, overcorrection could also be produced from tarsal advance procedure due to the advancement of the tarsus up to 4mm anteriorly, although this would disappear within few weeks due to epithelisation.[125,126] In the tarsal grooving procedure a 2.9% overcorrection rate has been reported.[146] In PLTR, a clinical trial reported 0.3% (2/650) over correction rate about 10 days after surgery.[33]

Under correction is characterised by invisibility of the part of or the whole lid margin following trichiasis surgery, which may or may not be associated with lashes touching the eyeball (Figure 1.18b). This occurs in relation to lower incision height to the lid margin or low tension of the mattress sutures. Under correction is probably one of the most common trichiasis surgical complications in programmatic situations. However, it is usually under reported in studies, as most just focus in reporting the postoperative trichiasis, which mostly is the result of the under correction itself.

High rates of under correction (5.7%) have been reported in tarsal grooving procedure from two studies at 5.7% and 20%. [132,146] In one of these studies, under correction was also common at 13% in both PLTR and tarsal advance and rotation procedures.[132] A cohort study that used both the BLTR and PLTR procedure reported that under correction was common in the BLTR procedure (data not provided).[117,147] In one of our clinical trials where under correction was defined as “lash touching or nearly touching the globe” was reported in 0.9% (6/650) of minor trichiasis cases operated in PLTR procedure.[33]

Figure 1.18: Correction defect after TT surgery

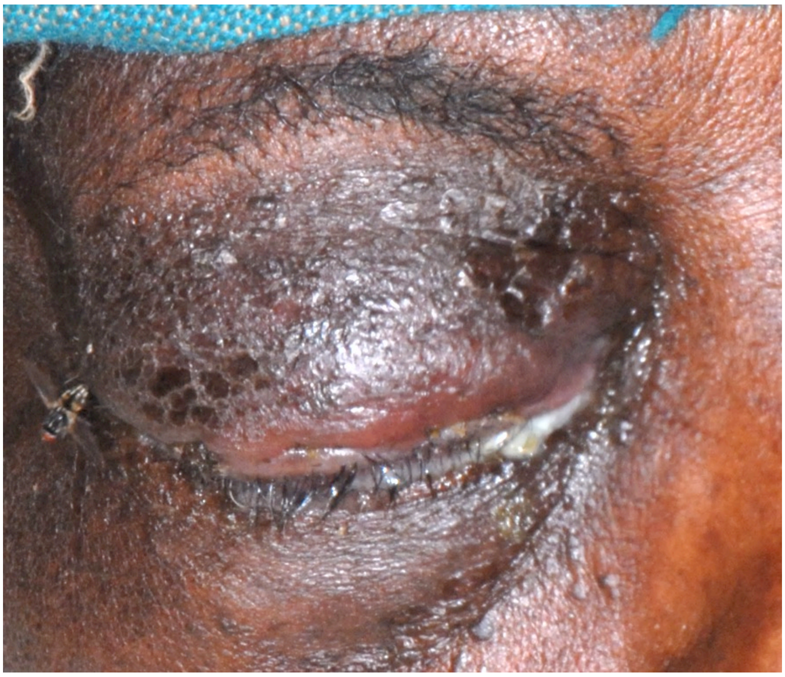
a) Overcorrection

b) Undercorrection

1.13.1.3. Postoperative Infection

Postoperative infection after trichiasis surgery (Figure 1.19) seems to be relatively uncommon. There are probably several reasons for this. Firstly, the use of careful aseptic technique during surgery would contribute to less rate of infection. Secondly, the postoperative antibiotic provided following surgery such as tetracycline eye ointment and azithromycin may help to prevent infection. Thirdly, there may be a degree of underreporting due to poor follow-up. Studies may tend to report those requiring antibiotic treatment and there would be a chance of overlooking those with relatively mild and localised infection. The rate of postoperative infection reported generally is <1% following BLTR and PLTR procedures (range 0.2% - 1.1%).[4,33,40,122,152] An exception is the report from a retrospective case series, in which 1 case out of 23 (3.2%) developed infection following BLTR surgery.[140] In trachoma endemic settings, surgical procedures, which incise the anterior lamella, might have higher risk of infection than those only operate on the tarso-conjunctiva, which would have less exposure to dust and infectious agents. The highest infection rate was 7.4% reported in a recent prospective cohort study following anterior tarsotomy.[147]

Figure 1.19: Postoperative eyelid infection



1.13.1.4. Eyelid Closure Defect

Eyelid closure defect (lagophthalmos) is the inability of the eye to close completely. This condition rarely occurs immediately or within a few weeks after trichiasis surgery. Why and how it happens is less clear, but it is assumed that misplacement of surgical sutures along with unaligned surgical incision may contribute to its development.[154] Eyelid closure defect is usually associated with eyelid contour abnormality, overcorrection, and granuloma.[155]

The frequency of eyelid closure defect following trichiasis surgery ranges between 0.4% and 3.5% (7 years).[4,40,154,156] The exception are the two Oman trials, where 14.3% and 5.1% of major trichiasis cases operated with, tarsal grooving and BLTR surgical procedures respectively developed lid closure defect.[128] In the first trial, lid closure defect was significantly associated with history of previous surgery (47%(32/68), OR 31; 95% CI, 9.0–108). In the second trial, 4%

of eyelids with major trichiasis without eyelid closure defect preoperatively and treated with BLTR surgery, and 1% of the eyelids with minor trichiasis and without eyelid closure defect preoperatively and treated with tarsal advance and rotation surgery developed eyelid closure defect.[98] In most other studies it is unclear if the lid closure defect followed the surgery or existed preoperatively. In one of our trials, 29% of trichiasis cases with major trichiasis had lagophthalmos preoperatively, while only 0.9% were graded to have lagophthalmos 12 month after PLTR surgery.[40] A cross-sectional study conducted in PLTR dominant region of Ethiopia (Amhara) reported a 5.5% postoperative lid closure defect prevalence.[157]

Other than type of surgery and previous history of surgery, surgeon technique is a risk factor for eyelid closure defect.[154] A study reported lid closure rate of 0% to 2% (p=0.003) among surgeons operating in similar set of patients using BLTR surgery. In the same study, although not clear why, evidence of epilation at baseline was associated with lower rate of eyelid closure defect. There was also an insignificant increasing trend of eyelid closure defect with increasing age.[154]

The management of lid closure defect itself is problematic with low success rates, underpinning the importance of avoiding it during surgery. Some of the surgical procedures used to treat lid closure defect in the past have been described in detail in previous sections. In the Reacher et al trial, eyelids with trichiasis and lid closure defect were operated with tarsal advance procedure.[128] This found that among 32 lids operated and followed within 10 months, only 2 (6%) had their lid closure defect treated successfully, while the majority 10 (31%) had failure, and only 9 (28%) had their trichiasis treated. In the second Reacher et al trial, tarsal advance and rotation with incision of the levator (8 eyelids), and tarsal advance with insertion of buccal mucosa graft (11 eyelids) were used to treat lid closure defect.[98] The tarsal advance and rotation with the levator incision resulted no success, while only three (27%) eyelids were successful in the tarsal advance and graft procedure.[98]

1.13.2. Postoperative Clinical Outcomes

In the postoperative clinical outcomes categories are those that occur in relatively longer time after the operation and might not be always the result of the surgery or the surgeon technique. These include granuloma formation, eyelid contour abnormalities, postoperative trichiasis and changes in corneal opacity and visual acuity. These are discussed in detail below.

1.13.2.1. Conjunctival Granuloma

Conjunctival granuloma is a fleshy tissue growth on the tarsal conjunctiva or lid margin that occurs within few weeks of trichiasis surgery (Figure 1.20). Its size varies ranging between 2mm to 15mm. Clinically it can be defined as "a polypoid, friable, purple-red, smooth-surfaced mass".[158] The histopathologic appearance shows lobulated haemangioma with large blood vessels surrounded by capillaries and scattered inflammatory cells.[158] Conjunctival granuloma is suggested to be the result of vigorous healing response of the body to a tissue defect from surgery or trauma. Other than trichiasis surgery, conjunctival granuloma are reported to occur following chalazion surgery, other ocular or adnexal surgery such as strabismus surgery, excision of pterygium or pinguecula, plastic surgery of the eyelid, and scleral buckling, or even following trauma.[158] Granuloma might occur in relation to isolating irritant tissue after the surgery or trauma, or foreign body such as suture fragments.[40,94,155,158]

Following trichiasis surgery 2.9%–22% rate of conjunctival granuloma formation have been reported from various studies.[33,40,94,132,138,154,159,160] Most of the reports were from secondary analysis of clinical trials. It is likely that granulomas might be underreported particularly in studies that did not have frequent early follow-up (within three month) of participants. Granulomas usually occur during the first few weeks following surgery and may be left unnoticed as they may resolve quickly or could be managed at home or by other health professionals before the next follow-up.

The risk factors for conjunctival granuloma formation include type of surgery, type of suture material used, surgeon technique, and patient factors such as demographic and clinical characteristics.

The various types of surgical procedures probably might have different rate of conjunctival granuloma formation. This might be attributed to the way the incisions are made and the amount of tissue defect. Following lid margin splinting procedure with application of scleral graft, 10.3% of the eyes developed granuloma within 2 weeks.[138] A study comparing the relative effectiveness of three trichiasis surgical procedure reported a higher rate of granuloma formation in the tarsal advance and rotation procedure (17%), compared to both terminal tarsal rotation (PLTR), and tarsal grooving procedures that had a 10% granuloma rate.[132] In the PLTR surgical procedure, two of our clinical trials reported, 2.9% and 6.9% granuloma prevalence in patients with minor and major trichiasis respectively.[33,40] One cohort study reported granuloma as the most common complication in PLTR surgery (data not provided).[117]

In contrast, higher rate of granulomas following BLTR surgical procedures have been reported, range between 10% and 22%.[94,159] A clinical trial comparing the relative effectiveness of PLTR and BLTR surgical procedures found that granuloma along with lid notching was more common in the BLTR group than the PLTR (P=0.002, percentages not given).[152] A clinical trial identified that the use of TT clamp to fix the eyelid in BLTR surgery significantly reduces the rate of granuloma formation compared to using the standard haemostats (16.8% vs 22.4%; OR, 0.67; 95% CI, 0.46 – 0.97).[94] The higher rate of granuloma formation in BLTR surgical procedure, particularly when using the clamp was suggested to be from the multiple cuts during the anterior and posterior lamellar incisions performed from two sides of the eyelid.[94]

A trial showed that, among suture materials silk created significantly more conjunctival granuloma than the absorbable polyglactin-910 (8.7% vs 5.7%, p=0.045).[40] In that trial retained silk sutures were found in 2.6% of the eyelid that might initiate inflammatory response and contribute to the higher granuloma rate in the silk group (Figure 1.20c).[40] Another report suggested that a gap between the incised edge of the posterior lamella from inadequate suturing in the PLTR procedure may lead to granuloma formation.[121]

Variation in the rate of conjunctival granuloma formation among surgeons used both the PLTR and BLTR surgeries have been reported, with some surgeons having 2-fold higher rate of granuloma formation than the others.[154,160] This suggests that subtle differences between surgeons in the way the incisions are made and the sutures are placed would probably contribute to the development of granuloma.

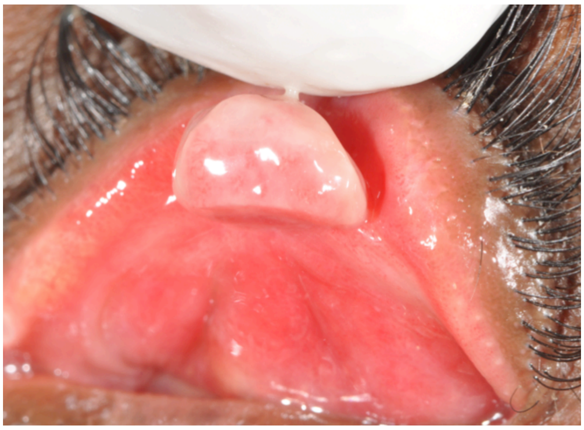
Among the patient reported factors, granuloma was significantly associated with papillary inflammation and successful epilation at baseline.[154,160] In another clinical trial reported higher rate of granuloma in younger (16% in under 30 years) and male (16% vs 8%) participants.[154] In correlation with the above study, an earlier review of 98 granuloma cases following different ophthalmic surgical procedures reported an average age of 34 years.[158]

Conjunctival granuloma often is painless, but easily bleeds or gets ulcerated, which can be very distressing to the patients. Granuloma can be large enough to obscure vision and create a disfiguring look that would have negative psychological impact on the patients and may deter other patients from accepting surgery. Granulomas can be treated easily with a simple shave using a blade after a drop of local anesthesia.

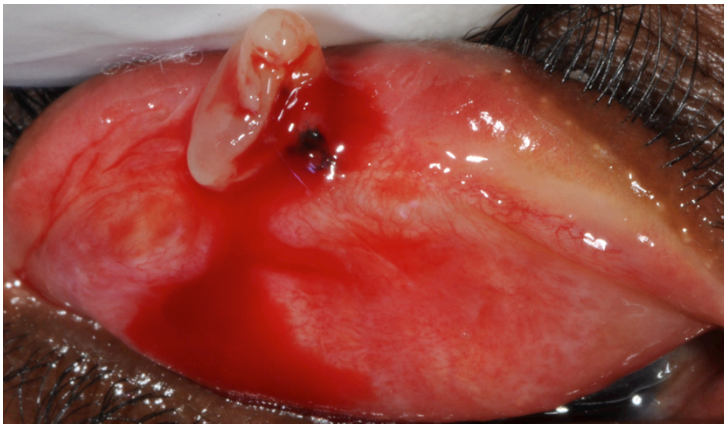
Figure 1.20: Granuloma following trichiasis surgery

a) Granuloma appearance

b) Granuloma on an everted eyelid



c) Suture material induced granuloma



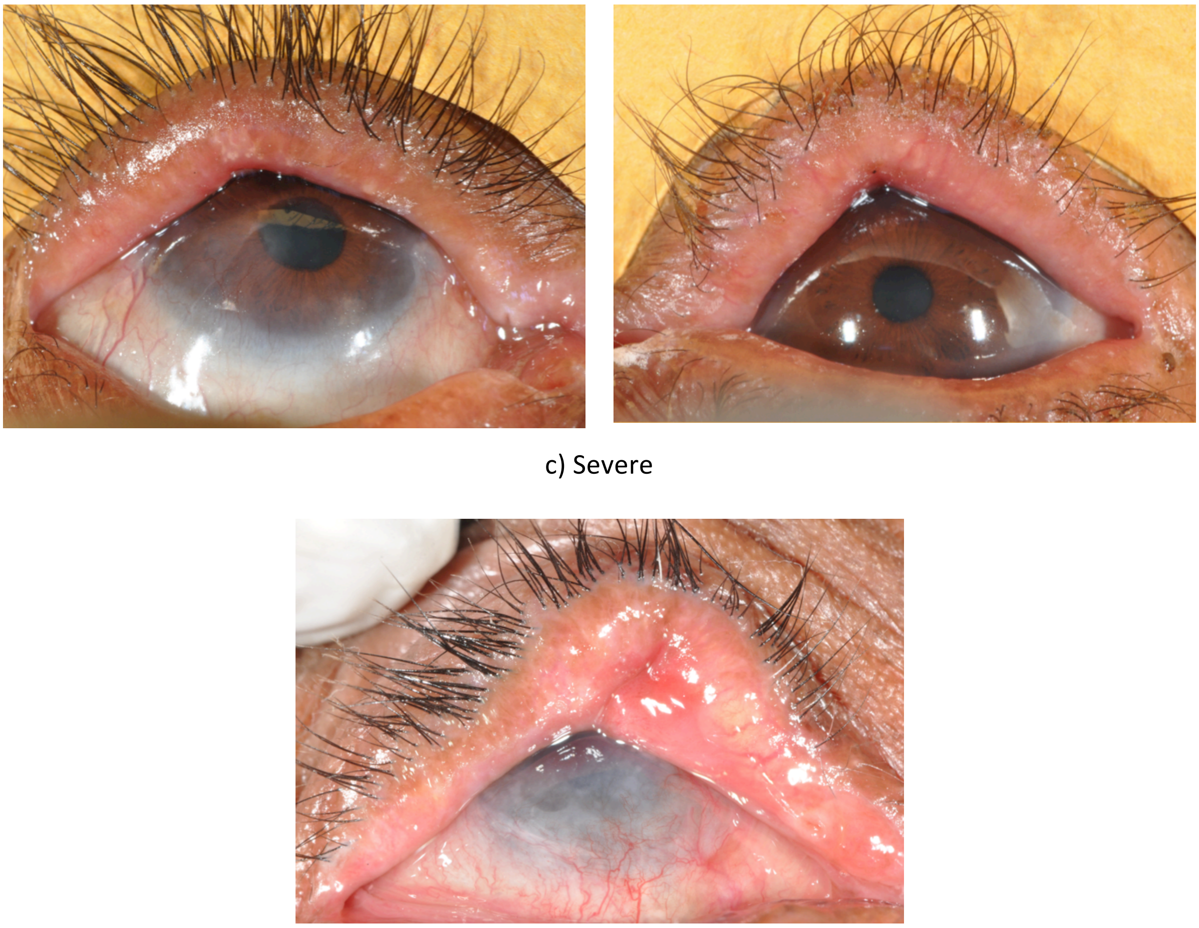
1.13.2.2. Eyelid Contour Abnormality/Notching

Eyelid contour abnormality (ECA) also known as notching can be defined as a vertical or horizontal deviation from the normal contour following trichiasis surgery (Figure 1.21). It can be minor and focal or major deviation involving larger area of the eyelid with risk of eyelid closure defect. Gower et al have classified ECA as mild (vertical deviation of <1mm and affecting <1/3rd of the lid margin), Figure 1.21a; moderate (vertical deviation of 1mm – 2mm or horizontal deviation involving 1/3rd – 2/3rd of the lid margin), (Figure 1.21b); and severe (vertical deviation of >2mm or horizontal deviation involving >2/3rd of the lid margin), (Figure 1.21c).[155]

Figure 1.21: ECA classifications

a) Mild b) Moderate

c) Severe



1.13.2.2.1. Risk factors to ECA

Surgical procedure

The only trial with a head to head comparison of the PLTR and BLTR procedures reported that eyelid notching was more common in the BLTR than the PLTR surgery.[152] However, different non-randomised studies report a range for ECA in the PLTR surgery of 5%–30%, which is higher than the range for BLTR surgery (1.2%–20%).[33,40,94,122,132,154,159] The differences in rates of ECA across these studies could be attributed to the use of different grading systems. The highest rate in the PLTR surgery was reported by Dhaliwal et al, which also showed that the other two compared surgical procedures: tarsal advance and rotation, and tarsal grooving had 20% and 33% ECA respectively.[132] In this study, an additional 10%, 3.3% and 3.3% of eyelids developed an "irregular contour" following PLTR, tarsal advance and rotation, and tarsal grooving procedures, respectively.

In our recent studies we found that PLTR surgery causes eyelid notching in 13% (154/1187) of the major trichiasis cases, and 4.7% (29/617) of the minor trichiasis cases.[33,40] In another study from Tanzania, 6.3% (9/144 eyes) of eyes operated in PLTR surgery had mild to moderate notching which was assumed to be related with "ischemic necrosis of the marginal strip of tarsus".[122] In BLTR surgery, the highest rate of ECA was reported from the PRET trial, which showed that the TT clamp group (16.3%) had relatively lower rate of ECA than the standard instrumentation group (23.7%) by two years.[94] The lowest ECA rate in BLTR (1.2%) was reported from a six weeks follow-up.[154]

Surgeon technique

Significant inter-surgeon variability in the rate of notching (p=0.002) has been reported among five surgeons operating in PLTR procedure.[160] There is evidence that misplacement and imbalance in the tightness of the mattress sutures may lead to the development of ECA.[161]

Baseline disease severity

More severe pre-operative TT is associated with more ECA. Cases with 9 or more trichiasis lashes at baseline had 4 times higher risk of developing ECA than those with less than five lashes.[154] A univariable analysis in another study showed that notching might be associated with baseline papillary inflammation.[160] People above the age of 40 are believed to have 2 times higher risk of developing ECA than their counterparts.[160]

History of previous eyelid surgery

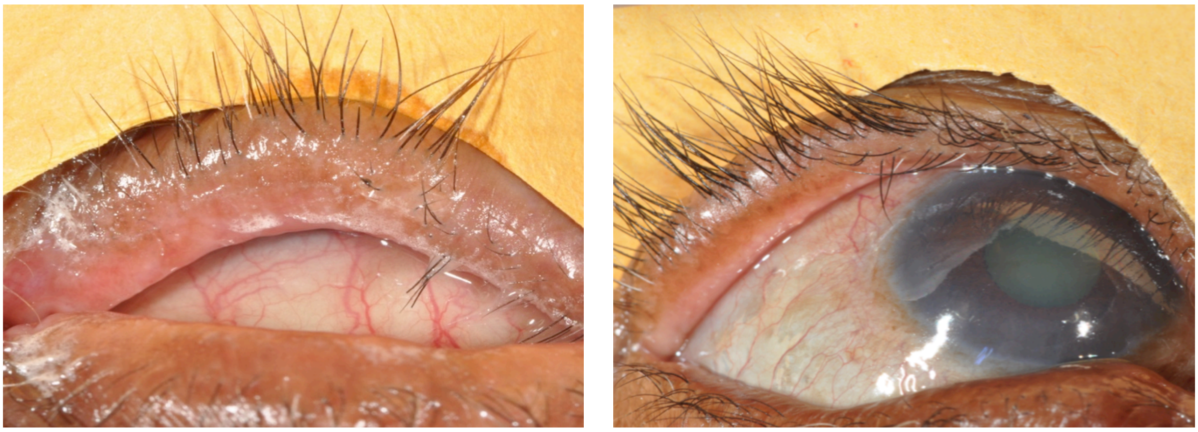
In a recent scientific meeting it is identified that repeat surgeries to treat postoperative TT are associated with increased risk of ECA.[28]

1.13.2.3. Postoperative Trichiasis

Postoperative trichiasis also usually called recurrence (Figure 1.22) is common and a significant problem in preventing blindness from trachoma. It is the most important and frequently used measure of surgical outcome. A recent report in a WHO meeting, indicated that its burden has increased significantly with increasing surgical outputs in the past decade, contributing 10%-75% of the trichiasis cases reported from surveys.[28] Trichiasis returns during the months and years following the surgery. Studies on the outcome of different trichiasis surgical procedures have found trichiasis recurrence rates between 10% at 3 months and 60% at 3 years after surgery, with an average of around 20% at 1 year.[4,5,7,33,40,92-94,98,128,148,154,160,162-164]

There is a consistent pattern to postoperative trichiasis: an initially high rate during the first six months, followed by a slower rate after six months. In a study we conducted in Ethiopia, the incident recurrence rate was 3.5% per month during the first six months, dropping to 0.8% per month after six months (RR 0.24, p=0.0001).[40]

Figure 1.22: Postoperative TT



1.13.2.3.1. Risk factors for postoperative trichiasis

Postoperative trichiasis can be classified as early or late, based on the time of onset. Early postoperative trichiasis occurs within the first six months following surgery, while late postoperative trichiasis occurs after six months following surgery. A number of factors may contribute to the development of early and late postoperative trichiasis. Early postoperative trichiasis might be the result of operation type, surgeon's ability, preoperative disease severity, and patient's wound healing response. Late postoperative trichiasis is probably related to primary disease progression such as progressive conjunctival scarring and inflammation, possibly driven by infection. It is important to understand the reasons for surgical failure and to develop practical treatment strategies to reduce the long-term risk of blindness. Some of these factors are discussed below.

Risk factors for early postoperative trichiasis

Operation type

Operation type is a major determinant of outcome and subtle variations in procedure performance probably affect results.[98,128,165] To date only five randomised trials have compared the relative effectiveness of some of the different surgical procedures suggested for use in the management of trachomatous trichiasis, (Table 1.5A). The first attempt was done by Reacher et al in two clinical trial in Oman some 25 years ago.[98,112,128]

In the first trial, 165 Major TT cases were randomly allocated to receive surgical management in either the BLTR (41), tarsal advance and rotation (21), eversion splinting (24), tarsal advance (41) and tarsal grooving (35).[128] After 5–11 months following enrolment, it found that the BLTR had a higher success rate than eversion splinting (71% vs 29%, p<0.01), tarsal advance (71% vs 27%, p<0.001) and tarsal grooving (71% vs 11%, p<0.001) with "success" being defined as "no eye lash - eye ball contact in the primary position of gaze and complete eye lid closure". The success rate for the tarsal advance and rotation was 46%, which was 25% less than the BLTR. However, this difference was not statistically significant (P>0.05) probably attributable to the lower number of cases enrolled into the tarsal advance and rotation procedures.

In the second trial, 172 minor trichiasis cases were randomised to receive BLTR (52), electrolysis (57) or crayoablation (57), and another 199 cases with major TT to either BLTR (98) or tarsal advance and rotation (101).[98] The BLTR was the successful procedure for both minor and major trichiasis at 80% and 77% respectively compared to electrolysis (29%) and cryoablation (18%) for minor trichiasis; and tarsal advance and rotation (41%) for major trichiasis. These two randomised trials led to the WHO to recommend BLTR for the surgical management of trachomatous trichiasis in endemic settings. However, it is important to note that the widely used PLTR was not one of the operation types included in these earlier trials.

The third trial was conducted by Adamu et al in Ethiopia, the only clinical trial that compared the relative effectiveness of the BLTR and the PLTR surgical procedures.[152] In this trial, 256 eyelids (minor and major TT) were randomised to receive surgical management either using the BLTR (124) or the PLTR (132) surgical procedure. Three months after surgery about 93% (237) of these were re-examined. Among these, 10% in the BLTR and 12% in the PLTR had recurrent trichiasis, the two surgical procedures showing comparable result (p=0.71).

The fourth trial was conducted by Dhaliwal et al in India to compare the efficacy of three surgical procedures for the management of trachomatous entropion. In this trial, 90 cases with moderate or severe trachomatous entropion were randomised (30 cases each) to terminal tarsal rotation/PLTR, tarsal advance and rotation, anterior lamellar repositioning with lid margin split and tarsal wedge resection. The cases were followed for about 6-months. This trial reported two surgical failures (defined as "persistence of entropion or trichiasis within 15 days after surgery") in the tarsal advance and rotation; and one case of recurrence of entropion (defined as "return of symptoms and recurrence of entropion or trichiasis after the 15th postoperative day") in the anterior lamellar repositioning followed by lid split and tarsal wedge resection. The tarsal rotation (PLTR) surgery was reported to be the simplest taking significantly less time than the other two (p<0.0001). All the three procedures provided comparable rate of cosmetic appearance (p=0.1), anatomical correction (p=0.35) and complications (p=0.43). In this trial, the patients enrolled did not have to have trichiasis, and the samples size is too small and the follow-up too short to reach conclusions.

The fifth trial was a non-inferiority trial conducted by Rajak et al in Ethiopia to evaluate the role of epilation in the management of minor trichiasis compared to PLTR surgery. In this trial 1300 minor TT cases were randomised to receive either epilation, with epilation training and two pairs of epilation forceps (650) or surgical management using the PLTR (650). These were evaluated every six-month for 2 years. The primary outcome measure in this trial was “failure” defined as presence of five or more lashes touching the globe or a history of TT surgery at any time during the two years period. The results showed that 13.2% “failed” by two years in the epilation arm, while only 2.2% in the surgery arm. However, the overall recurrence in the surgery arm by two years, defined as one or more lashes touching the eye or repeat surgery, was 17.5%.

The first four clinical trials share the following drawbacks. Firstly, ophthalmologists conducted the surgeries in all of these trials. It is possible that these alternative techniques, which give comparable results when used by very experienced surgeons, may give quite different results in the “real world” situation, when performed by less experienced personnel. Secondly, the surgeries were conducted in hospitals compared to remote low-level health facilities in trachoma endemic settings. Thirdly, the third trial had a relatively short follow-up period to assess the relative performance of the two surgical procedures compared, as differences might take longer to become apparent.[4,92,98,159,164] In addition, the third trial is probably underpowered to detect a difference between these two commonly practiced surgical procedures, which might have relatively lower failure rates compared to other surgical procedures. This basically leaves the important question of which of these two most commonly used surgical procedures (BLTR or the PLTR) is more effective unanswered. Unlike the above four studies the fifth was conducted in programmatic settings with ICEWs doing the surgeries. However, this study does not compare surgical procedures and is only conducted in minor TT cases.

The only other non-randomised cohort study that reported the success rate of the BLTR (“Anterior Tarsotomy” or Ballen/modified Wies technique) and PLTR (“Posterior Tarsotomy”) surgical procedures was conducted in Saudi Arabia.[117] In this study, 1200 consecutive patients with trachomatous cicatricial entropion of different severity underwent surgery using different surgical procedures in four years between 1984 and 1988. Among these, 380 cases with mild to moderate cicatricial entropion, and 500 cases with moderate to severe cicatricial entropion underwent surgery using the BLTR and PLTR procedures respectively. After 2 years (average) follow-up, 27.7% of the BLTR cases "required additional surgery or were lost to follow-up" ("72.3% successfully treated"); while 18% of the cases operated using the PLTR required second surgery, giving a 82% "success" rate. This increased to 92.8% after repeat PLTR surgeries for those who failed after the initial PLTR surgery. In addition, eyelid retraction in BLTR, and localised conjunctival pyogenic granuloma in the PLTR were the two most common complications. Furthermore, under-correction and eyelid crease deformities were common in the BLTR surgery. The results from this cohort study generally suggested that the PLTR probably provides superior results than the BLTR both for the correction of any severity of trachomatous cicatricial entropion, and failed cases after initial surgery. However, again this study was not a head to head comparison of the BLTR and PLTR procedures in a controlled trial, therefore it is unable to provide adequate evidence to inform programmes.[117]

Several other prospective cohort and retrospective cases series have been conducted on surgical outcomes. Most of these are performed to evaluate the outcome of a single surgical procedure, while some compare outcomes of few surgical procedures from a cohort of cases (Table 1.5B). Other randomised clinical trials were also performed to evaluate the effect of additional interventions such as antibiotics following one type of surgical procedure. All of these studies are summarised in (Table 1.6). In summary The reports from these studies showed that postoperative trichiasis ranges from 11% at about 6 months to 61.8% in three years in BLTR;[93,94,159,163,166-168] and from 17% at 9 months to 65% in 7 years in PLTR surgery.[4,29,33,40,92,122,156,164,169,170]

One earlier prospective cohort study conducted on 141 cases undergoing PLTR surgery with a follow-up period ranging between 1 week and 18 months reported a 2.8% (4/141) recurrence rate of trichiasis without the presence of entrioion.[118] In BLTR, the lowest reported recurrence rates were from the STAR trial in Ethiopia (+/- oral azithromycin), ranging between 5.8% and 10.3% at one-year.[5] Our recent RCTs in Ethiopia used PLTR, with an overall recurrence rate of 18.4% at one-year.[33,40] Importantly, surgeons performing surgery in these three RCTs were selected and standardised by the same Ethiopian ophthalmologist. In Cuenod Nataf procedure a recurrence rate of about 9% at one year and 16% at two years were reported.[148,149] Studies conducted on the outcome of other surgical procedures (other than BLTR and PLTR) are summarized in Table 1.7.

Table 1.5: Randomised trials and non-randomised studies comparing trichiasis surgical procedures

Author, Year, Country ***A. Randomised Trials Comparing Surgical Procedures***	Disease severity and Randomisation & Sample size	Outcome measure, Operated by	Response rate, Follow-up period	Recurrence rate	Factors associated with recurrence	Other outcomes
Reacher et al, 1990, Oman [128]	Major TT (1) BLTR, 41 eyelids (2) Tarsal advance and rotation, 24 eyelids (3) Eversion splinting, 24 eyelids (4) Tarsal advance, 41 eyelids (5) Tarsal grooving, 35 eyelids	*Treatment success:* No lash contact in primary position and complete lid closure Ophthalmologist?	153/165 (93%) 5 – 10 months	Treatment Success: (1) 29/41 (71%) (2) 11/24 (46%) (3) 7/24 (29%) (4) 11/41 (27%) (5) 4/35 (11%) *Postoperative TT Rate (1+ lashes)* (1) 11/39 (28%) (2) 11/22 (50%) (3) 15/21 (71%) (4) 27/38 (71%) (5) 22/33 (67%)	History of previous surgery	Defective lid closure after BLTR (5.1%) and tarsal grooving (14.3%)
Reacher et al, 1992, Oman [98]	Minor TT (1) Electrolysis, 57 eyelids (2) Cryoablation, 57 eyelids (3) BLTR, 52 eyelids Major TT (4) BLTR, 98 eyelids (5) Tarsal advance and rotation, 101 eyelids Defective lid closure (6) Tarsal advance and rotation with incision of the levator, 8 eyelids (7) Tarsal advance and graft, 11 eyelids	*Successful surgery:* No lash contact in primary position, no epilation or surgery, complete lid closure, no overcorrection, cosmetically acceptable by the patient and the examiner, no phthisis Ophthalmologist?	94%, At least once in 1.2-25 months period	*Success rate* Minor TT (1) 29.0% (2) 18.0% (3) 80.0% Major TT (4) 77% (5) 41% Defective lid closure (6) 0% (7) 27% *Postoperative TT Rate (1+ lashes)* Minor TT (1) 30/57 (52.6%) (2) 41/57 (71.9%) (3) 6/52 (11.5%) Major TT	*Risk factor for surgical failure* Minor TT History of epilation Major TT Entropion	Defective lid closure (3) 2/52 (3.8%) (5) 1/110 (1.0%) (6) 3/8 (37.5%) (7) 4/11 (36.4% Cosmetic failure (1) 1/57 (1.8%) (2) 1/57 (1.8%) (3) 1/52 (1.9%) (4) 2.0% (2/52) (5) 5/101 (5.0%) Overcorrection (4) 2/98 (2.0%) Phthisis (2) 2/57 (3.5%) Suture granuloma All BLTR surgeries: 19/152

				Defective lid closure (6) 6/8 (75.0)% (7) 8/11 (72/7%)		(5) 2/101 (2.0%)
Author, Year, Country	**Disease severity and Randomisation & Sample size**	**Outcome measure, Operated by**	**Response rate, Follow-up period**	**Recurrence rate**	**Factors associated with recurrence**	**Other outcomes**
Adamu et al, 2002, Ethiopia [152]	All TT severity, BLTR, 124 eyelids PLTR, 132 eyelids	Postoperative TT (1+lashes), Ophthalmologists	All: 92%, 3 months BLTR: 115/124 (92.7%) PLTR: 122/132 (92.4)	BLTR: 10.4% PLTR: 12.3%	Not reported	BLTR procedure Postoperative bleeding, 2/124 (1.6%) Postoperative infection, 1/124 (0.81%) Overcorrection, 4/115 (3.5%) "Lid notching and granuloma" more significant in BLTR than PLTR (p=0.002)
Dhaliwal et al, 2004 India [132]	Moderate and severe trachomatous entropion (1) PLTR (terminal tarsal rotation/PLTR), 30 eyelids (2) Tarsal advance and rotation, 30 eyelids (3) Anterior lamellar repositioning with lid margin split and wedge resection of the tarsus, 30 eyelids	Entropion correction Ophthalmologist	100%, 6 months	(1) 0/30 (0%) (2) 2/30 (6.7%) (3) 1/30 (3.3%)	Not reported	Notching (1) 9/30 (30%) (2) 6/30 (20%) (3) 10/30 (33%) Under correction (1) 4/30 (135) (2) 4/30 (13%) (3) 6/30 (20%) Granuloma (1) 3/30 (10%) (2) 5/30 (18%) (3) 3/30 (10%) Tenting (2) 5/30 (18%) (3) 3/30 (10%) Localised madrosis (3) 3/30 (10%)

Author, Year, Country	Disease severity and Randomisation & Sample size	Outcome measure, Operated by	Response rate, Follow-up period	Recurrence rate	Factors associated with recurrence	Other outcomes
Rajak et al, 2011, Ethiopia [33]	Minor trichiasis: Surgery, 650 patients Epilation, 650 patients	Postoperative TT (1+lashes), IECWs	94%, 2 years	Surgery: 114 (17.5%) Epilation: 298 (45.8%)	Not reported	Surgery arm; Granuloma 2.9% Notching 4.7%
II. Non randomised trials comparing surgical procedures						
Kemp et al, 1986, UK [25]	Retrospective review of 183 eyelids treated based on entropion severity (regardless of cause) - 40% TT cases (1) Minimal entropion (94 eyelids): anterior lamellar repositioning (2) Moderate entropion (49 eyelids): anterior lamellar repositioning +lid split + tarsal wedge resection (for thickened tarsus) + Dissection of the levator aponuerosis and Muller's muscle (for lid retraction) (3) Severe entropion (40 eyelids): Tarsal Advance and rotation + Posterior lamellar lengthening with graft (if insufficient advancement of the posterior lamella)	Recurrence (return) of entropion Oculoplastic surgeon	Retrospective study, minimum 10 months, average 3 years	Trichiasis recurrence (1) 20/94 (21.3%) (2) 8/49 (16.3%) (3) 8/40 (20.0%) Entropion recurrence (1) 30/94 (31.9%) (2) 13/49 (26.5%) (3) 10/40 (25.0%)	Not reported	Not reported

Author, Year, Country	Disease severity and Randomisation & Sample size	Outcome measure, Operated by	Response rate, Follow-up period	Recurrence rate	Factors associated with recurrence	Other outcomes
Babalola, 1988, Nigeria [140]	Retrospective case review of 54 eyelids, with unknown severity BLTR, 31 eyes Grey line split with scleral graft, 23 eyes	Outcome measure not clear Ophthalmologist?	Retrospective study	7/31 (22.6%) 6/23 (26.1%)	Not reported	BLTR Granuloma: 3/31 (9.7%) Infection: 1/31 (3.2%) Grey line split Graft rejection: 7/23 (30.4%) Bleeding: 1/23 (4.3£ Infection: 1/23 (4.3%)
Nasr et al, 1989, Saudi Arabia[117]	Retrospective case review of 960 patients treated based on entropion severity (1) Mild to moderate entropion with conjunctival scarring only (380 patients): BLTR (anterior tarsotomy) (2) Moderate to severe entropion (500 patients): PLTR, + auricular or scleral graft for cases with thin or absent tarsus from previous surgery. (3) Severe entropion with keratinised lid margin (80 patients): Anterior lamellar recession with mucous membrane graft	Recurrence (return) of entropion Ophthalmologist	Retrospective study	Entropion correction 105/380 (27.6%) 90/500 (18.0%), 54/500 (10.8%) required repeat surgery About 50% required further interventions	Not reported	Not reported
Negrel et al, 2000, Morocco [153]	Retrospective review of random sample of patients (740 lids) with all severity Operated using BLTR (91%) and PLTR (9%)	Postoperative TT (1+lashes), Ophthalmologists, general doctors and nurses	Retrospective study	Overall recurrence rate of 15.8% (117/740)	>40 years of age Province of operation Operated by Ophthalmologist or general practitioner	Overcorrection: 17/40 (2.3%) Ptosis: 3/740 (0.4%) Tegumental necrosis with corneal exposure: 1/740 (0.14%) Cutaneous necrosis without corneal exposure: 27/40 (3.6%)

Author, Year, Country	Disease severity and Randomisation & Sample size	Outcome measure, Operated by	Response rate, Follow-up period	Recurrence rate	Factors associated with recurrence	Other outcomes
Khandekar, et al 2001, Oman [93]	Non – concurrent prospective cohort in major TT cases (603) (1) BLTR: 292 patients (2) Electro-epilation: 311 patients	Postoperative TT (1+lashes), Ophthalmologist	81%, average 3.1 years ranging between 1.5 – 5.4 years)	(1) 61.8% (2) 50.6%	*Electro epilation:* Female sex Older age *BLTR* Origin from "high risk region" Infective conjunctivitis Time from surgery	Not reported
Barr et al, 2014, Australia [171]	Retrospective consecutive cases series of 85 eyes with TT severity (1) BLTR: 67 eyes (2) Anterior lamellar repositioning: 18	Postoperative TT (1+lashes), Ophthalmologist	Retrospective Mean follow-up time: (1) 4.5 years (2) 1.8 years	Analysis done just on one calendar year showed (1) 4/6 (66.7%) (2) 1/10 (10%)	Not reported	Not reported

Inter-surgeon variation

Surgical skill is a major determinant of trichiasis surgical outcomes (Figure 1.23). Surgical skill in turn is determined by the aptitude of the surgeon and initial and subsequent on the job trainings. However, despite rigorous trainings and even under tightly standardised clinical trial settings, when surgeons are adhering to the procedures, there are some variations in outcome, suggesting that there are subtle differences between individual surgeons in how they are performing the operations. Different reports indicate that successes of TT surgery vary widely between surgeons, ranging between 0 to 80%.[4,40,94,128,149,159,160,162,172] In one of our studies conducted in Amhara region using the PLTR, the rate of successful TT surgery for an IECW, measured in terms of absence of postoperative TT, was as low as 41% at two years.[40]

Outcome variation may occur regardless of the type or qualification of surgeons. The only randomised trial comparing the outcome of TT surgeries performed by two ophthalmologists and two IECWs (Integrated Eye Care Workers) has found that one of the IECWs had a far lower rate of recurrence at three month compared to the other (6.5% v 13.8%) and both of the ophthalmologists (10.9% and 14.4%) operated in the trial. Similarly, there was a 3.5% variation in recurrence between the two ophthalmologists.[159]

A couple of reports showed that the technique of surgical incision by a surgeon may lead to a marked difference in surgical outcomes.[154,168] Shorter incision length (<22mm) is found to be strongly associated with higher rate of postoperative trichiasis six weeks after BLTR surgery (OR, 3.6; 95% CI, 1.3–9.2).[154] Another study reported that surgeries performed by right handed surgeons using BLTR on the left eyelid are more likely to recur than surgeries performed on the right eyelid (32% vs 25%; p=0.05).[168] The explanation provided for this difference is making an incision on the right eyelid by right handed surgeon is more difficult than making on the left, which might have led to “unintentional modification” on how the surgical incision is performed on the right eyelid, which in turn might have then led to lower recurrence rate on the right eye.[168] However, this observation has not been reported in other studies.

Figure 1.23: Inter-surgeon skill variability determines surgical outcome

Surgical materials

Different surgical instrumentations and suture materials may influence surgical outcomes. The PRET trial compared the use of two surgical instrumentations in BLTR surgery on 3345 eyes: fixing the eyelid using standard haemostats versus TT clamp.[94] This found that a trend towards increased rate of postoperative trichiasis in the TT clamp group compared to the standard haemostat group (43.2% vs 36.6%). However, this trend was reported to be statistically insignificant and in fact there was no significant difference in rate of unfavourable outcome (includes postoperative trichiasis, granuloma and ECA) between the two groups (61% vs 63%).[94]

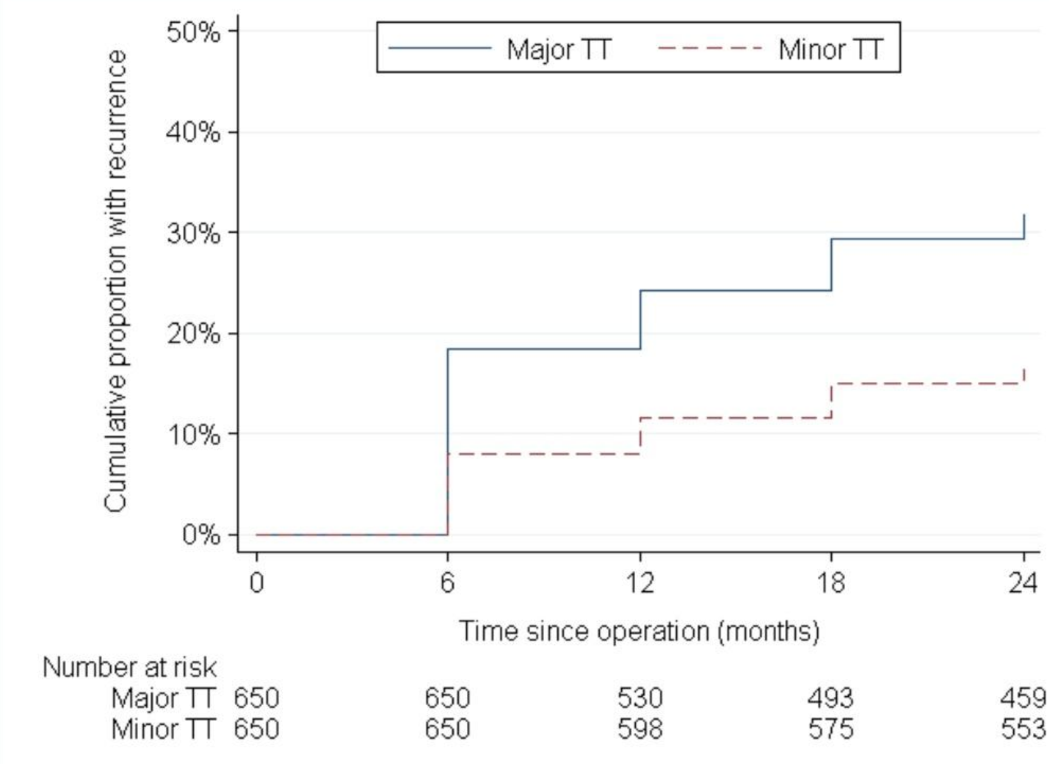
A prospective, non-randomised study conducted on risk factors associated with early surgical failure (within 8 weeks) in BLTR surgery on 638 eyelids in Egypt found that the use of silk suture as opposed to vicryl was associated with surgical failure, defined as one or more lashes touching the eye (RR, 54.82; 95% CI, 7.72 - 389.4).[163] Subsequently we conducted a large randomised controlled trial comparing these two suture materials. We recruited 1300 Major TT cases in Ethiopia, to test the hypothesis that using vicryl has a lower TT recurrence rate one year after surgery than silk sutures. This found no significant difference in the rate of recurrence between the suture materials (vicryl, 18.2%; silk 19.7%).[40]

Preoperative disease severity

Preoperative severe disease characteristics such as major trichiasis and severe degree of entropion have been consistently associated with postoperative trichiasis following both PLTR and BLTR surgeries.[4,40,137,159,160,164,166,167] In one of the randomised trials and its subsequent long term report, cases with 10 or more lashes had about two times higher rate of postoperative TT than those with less number of lashes, both at one year and 4 years after PLTR surgery.[4,164] Two years after PLTR surgery, the rate of postoperative trichiasis in major TT cases was 32.6% compared to 16.9% in minor TT cases (Figure 1.24).[160] Other trials found that major trichiasis cases have higher rate of postoperative TT than cases with minor TT following BLTR surgery.[166,167] Another study after eversion splinting procedure has found cases with trichiasis involving the whole lid margin and with scarred eyelid had more failure rate than those with milder trichiasis (100% vs 95% success rate) at one month.[137]

Figure 1.24: Recurrent TT by pre-operative disease severity

The cumulative proportion of 1300 eyes with recurrent TT stratified by the pre-operative disease severity (Major or Minor TT). Recurrent TT was defined as one or more lashes touching the eye.[33,40]



Studies also reported association between baseline severe entropion and postoperative trichiasis.[5,40,159] In a couple of clinical trials in Ethiopia, increasing risk of postoperative trichiasis from BLTR was associated with increasing severity of preoperative entropion.[5,159] Another study again from Ethiopia but using the PLTR surgical procedure reported association between severe entropion at baseline and postoperative trichiasis both at one (OR, 1.80; 95% CI, 1.36–

2.38; p<0.0001) and two (OR, 1.59; 95% CI, 1.22–2.09; p=0.0008) years after surgery.[40] Baseline severe conjunctival scarring has been associated with higher risk of postoperative trichiasis following Cuenod Nataf surgery (RR, 7.86; 95% CI, 2.87–21.5; p= <0.001).[148,149]

Demographic characteristics

Demographic characteristics such as age and gender are found to be associated with postoperative trichiasis in BLTR and PLTR surgeries.[5,92,154,164] Some studies reported higher rate of postoperative trichiasis in male study participants.[5,164] This is not clear why given that trichiasis is more common in women than males. In contrast, one prospective cohort study of cases treated with BLTR and electro-epilation found that, female cases had significantly higher rate of recurrence than males.[93] Similarly, another study following Cuenod Nataf surgery reported higher rate of recurrence in females than males at 2 years (17% vs 12%).[149]

Older age has been consistently associated with increased rate of postoperative trichiasis in both BLTR and PLTR surgeries.[5,40,92,154,160] In Cuenod Nataf surgery older age has been associated with a two times higher risk of postoperative trichiasis.[148,149] Old age may result in poor wound healing process forcing the eyelid to fall in back to its entropic position.[154,160] In addition, it is likely that trichiasis gets more severe with age due to progression of tarsal conjunctival scarring.

Previous surgery

Repeat surgery is less likely to be successful than primary surgery. In the Reacher et al trial major trichiasis cases with a history of eyelid surgery had a higher rate of failure (postoperative trichiasis and lid closure defect) than first surgery cases: 42% vs 28% after BLTR; 63% vs 53% after tarsal advance and rotation; 82% vs 70% after tarsal advance; and all three surgeries using tarsal grooving in patients with previous history of surgery have failed. Following Cuenod Nataf surgery, patients with a history of previous surgery had twice the risk of developing postoperative trichiasis than those having primary surgery (15% vs 7%).[148,149] In a recent WHO meeting, 42% recurrence and 45% ECA six month after repeat BLTR surgery has been reported from unpublished data.[28] This might be associated with severely scared and deformed tarsus from the preceding surgeries, which all together make tarsal rotation or eyelid eversion difficult. In addition, as discussed above, there is strong evidence that surgical failure and postoperative trichiasis are associated with preoperative disease severity and progressive conjunctival inflammation and scarring, which are likely to persist even after the repeat surgery. For this reason clinical trials tend to exclude patients with a history of previous trichiasis surgery. Consequently, little is known about the success rate of both BLTR and PLTR surgeries performed on lids with history of previous trichiasis surgery.

Wound healing

In conjunctival surgery (such as trabeculectomy for glaucoma) poor outcomes develop because of excessive inflammation and fibrosis during initial wound healing.[173] There are four overlapping phases: Haemostasis, Inflammation, Proliferation, and Remodelling. An imbalance can lead to scarring, primarily mediated by fibroblasts and Matrix Metalloproteinase (MMP) activity.[173] Similar wound healing processes probably occur following trichiasis surgery and may account for a significant component of recurrence within the first few months following surgery.[174] However, there is no adequate data to assert this assumption and studies conducted during early weeks following surgery through intensive follow-up and conjunctiva sampling are still needed to understand the relevance of primary wound healing processes in shaping trichiasis surgical outcomes.

Risk factors for late postoperative trichiasis

Infection

Recurrent infection with *Chlamydia trachomatis* may contribute to progressive conjunctival scarring and recurrent trichiasis following surgery. However, evidence for this is very limited.[4,92,162,166] It was suggested that enhanced antibiotic control of infection at the time of and following surgery might improve the outcome. Three different randomised trials were conducted to assess the effect of Azithromycin following surgery.[4,5,167] The first study was conducted in The Gambia (a country with low levels of endemic trachoma) on 451 people, of which 216 were randomised to Azithromycin group and the rest to the control group following PLTR surgery.[4] This study found that oral azithromycin at time of surgery followed by a repeat at 6 months did not reduce the recurrence rate.

However, in a second study conducted in in Ethiopia, a country with high levels of Chlamydial infection, Azithromycin appeared to reduce the risk of recurrence of trichiasis after BLTR surgery at one year (p=0.047).[5] This trial randomised 1452 trichiasis cases to receive either Azithromycin (968) or tetracycline eye ointment (484). However, a long-term follow-up of the same study participants after three years did not produce lower recurrence rate in the Azithromycin group compared to the tetracycline group (10% vs 13%; RR, 0.78; 95% CI, 0.56 – 1.08).[172]

A third trial was conducted in Nepal, again a country with low levels of endemic trachoma, on 109 patients randomised to Azithromycin (53) or placebo (56).[167] This found that the rate of postoperative trichiasis at 12 month was lower in the azithromycin group among cases with major TT at baseline (21.1% vs 61.5%; p=0.03); but there was a trend towards an increased rate of postoperative TT among patients with minor TT (36.4% vs 10.0%; p=0.075).[167]

A strong association has been found between trichiasis and conjunctival bacterial infection (other than *Chlamydia trachomatis*) before and after surgery.[4,32,92,175] Wide ranges of pathogenic organisms have been isolated from the conjunctiva of trichiasis patients, the commonest being *Streptococcus pneumonia* (upto 26%).[4] The isolation rate increases with increasing severity of trichiasis (number of lashes touching the globe). A year after surgery for trichiasis the bacterial isolation rate was found to be half, suggesting that reducing the burden of trichiasis reduces risk of bacterial infection.[4]

Inflammation and scarring

Severe conjunctival inflammation before and after surgery has been associated with postoperative trichiasis.[4,40,92,162,164,166] Persistent severe conjunctival inflammation in children with trachoma is associated with the subsequent development of the scarring complication of trachoma in later life (conjunctival scarring, trichiasis and corneal opacification).[176] Clinically apparent conjunctival inflammation is frequently found in people with trichiasis.[4,32,34,40,92,162] It is not known what drives this persistent inflammation in individuals with scarring and trichiasis. It is rarely associated with *C. trachomatis* infection, however, other non-chlamydial bacterial pathogens can frequently be cultured from the conjunctiva of individuals with scarring trachoma and trichiasis. It is likely that chronic conjunctival inflammation probably produces progressive scarring of the eyelids leading to trichiasis and corneal opacification both before and after surgery.[40]

Children with active trachoma are consistently found to have increased expression of pro-inflammatory cytokines and chemokines such as Interleukin-1β, IL17A and Tumour Necrosis Factor-α.[75,82,83,177] These probably activate matrix metalloproteinases (MMP), which are enzymes that degrade the extracellular matrix, promote inflammatory cell infiltration and facilitate tissue remodelling and scar formation. In adults with conjunctival scarring there is increased expression (in the conjunctiva) of several MMPs (MMP7, MMP9, MMP12), as well as increased pro-inflammatory factors.[6]

A recent study form a cohort of Ethiopian and Tanzanian cases with trachomatous scarring found a strong association between progressive scarring and increased inflammatory episodes without the presence of C. trachomatis.[19] Chronic conjunctival inflammation was also associated with expression of proinflamatory factors.[19] Two studies examining conjunctival gene expression after trichiasis surgery has been published recently. One of these measured expression of several pro-inflammatory cytokines, MMPs and TIMPs (Tissue inhibitor of Matrix Metalloproteinases) one year after surgery and found evidence of altered tissue remodelling factors in recurrent TT (reduced MMP1/TIMP1), which could favour scarring.[174] The other found that recurrent trichiasis was consistently associated with increased *S100A7* expression, a major pro-inflammatory factor.[178]

Table 1.6: Studies conducted on postoperative TT and other surgical outcomes after BLTR and PLTR surgeries

A. Studies conducted using the BLTR						
Author, Year, Country	**Study design, sample size**	**Type of procedure, operated by**	**Response rate, follow-up period**	**Recurrence rate**	**Factors associated with recurrence**	**Other complications**
Cruz et al, 2015, Saudi Arabia [116]	Prospective cohort, 60 eyelid, 40 patients	BLTR, with lid crease incision and dissection and internal sutures	100%, mean 3 month, range 1 – 12 month	1.7% (only one eyelid)	Not reported	Not reported
Gower et al, 2013, Tanzania[94]	RCT, 1917 patients, 3343 eyes	BLTR, Surgical Technician,	98%, 2 years	TT clamp, 43.2% Standard BLTR 36,6%	Not reported	Granuloma 16.8%, 22.4% ECA 16.3%, 23.7%
Woreta et al, 2012, Ethiopia[172]	RCT, 1452 participants	BLTR, IECWs	>90%, 3 years	Azithromycin, 10% Tetracycline, 13%	Entropion severity Older age Male sex Surgeon	Not reported
Gower et al, 2011, Ethiopia[154]	RCT, 2615 eyelids	BLTR, IECWs	99.5%, 6 weeks	2.3%	Baseline TT severity Shorter incision length (<22mm)	Eyelid closure defect 1.3% ECA 1.2% Granuloma 10.5%
West et al 2006, Ethiopia[31]	RCT, 1452 patients	BLTR, IECWS	96% 12 m	7.4%	Sex, male Severe preoperative entropion No preoperative azithromycin	Not reported
Khandekar et al, 2006, Oman[179]	Historic cohort, 91 patients		69%, 17 years 72 eyes of 63 patients were followed	47.2%	Minor trichiasis	Not reported

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other complications
El Tourkhy et al, 2006, Egypt[163]	Prospective observational, 638 eyelids	BLTR, Ophthalmologists	94% 8 -10 weeks	16.4%	Pre-operative corneal opacity Pre-operative corneal staining Silk sutures Four or more sutures	Not reported
Zhang et al, 2006, Nepal[167]	RCT, 109 patients	BLTR, Ophthalmologist	85% 3 m	5.6%	No post-operative azithromycin treatment Severity of pre-op trichiasis	Not reported
Merbs et al, 2005, Tanzania[168]	Observational cohort, 630 eyes of 384 patients	BLTR, Ophthalmologists	100%, At least 18m	28%	Left eyes	Not reported
West et al, 2005, Tanzania[162]	Observational cohort, 394 patients	BLTR, not stated	100%, At least 18m	28%	Trachomatous inflammation >1 child in household infected with *Chlamydia* District Older age	Not Reported
Alemayehu et al, 2004, Ethiopia[159]	RCT, 1750 lids of 982 patients	BLTR, IECWs and Ophthalmologists	77%, 6 m	14.3%	Trichiasis severity at baseline	Granuloma 14% Lid margin irregularity 6.2%
Zhang et al, 2004, Nepal[166]	RCT, 78 patients with 79 eyelids	BLTR, not stated	Not stated, 6 and 12 m	11.1% at 6/12 25% at 12/12	Chlamydial infection Preoperative trichiasis severity	Not presented

B. Studies conducted using the PLTR

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Rajak et al, 2013, Ethiopia[160]	Prospective cohort study, 1300 patients	PLTR, IECWS	98% of the participants at least once in the following time points; 6m, 12m, 18m and 24m,	6m, 14.3% 12m, 4.9% 18m, 4.5% 24m, 2.2% Overall 2 years, 24.7%	Major TT at baseline Surgeon Lash type (entropic) Older age	Bleeding 1.3% Granuloma 5.7% Notching 13% Residual suture fragment 1.8% Over correction 0.5%
Pearson et al, 2013, Ethiopia[157]	Cross-sectional study, sampled 461 patients	Not indicated but PLTR is used in the study area	363 participated among sampled (84.2%)	9.4%	None were significant	Notching: 16.8% Eyelid closure defect: 5.5% Granuloma: 0.6%
Rajak et al, 2011, Ethiopia[40]	RCT, 1300 patients	PLTR, IECWs	>93%, 1 year	Absorbable suture 18.2% Silk suture 19.7%		Granuloma 8.7%, 5,7% Notching 11.9%, 14.0% Residual suture fragment, 2.6%, 2.0%
Rajak et al, 2010, Gambia[164]	Prospective cohort study, 356 patients	PLTR, Ophthalmic Nurse	94%, 4 years	41%	More than 10 lashes at baseline Baseline conjunctival inflammation	Not reported
Burton et al, 2005, Gambia[92]	Prospective cohort, 162 patients	PLTR, Ophthalmic Nurse	87% 36-48 months	41.6% (24.3% major TT)	Conjunctival inflammation Bacterial infection Older age	Not reported

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Burton et al, 2005, Gambia[4]	RCT, 451 patients	PLTR, Ophthalmic Nurse	94% 12 months	41.3%	Pre-operative TT severity Severe conjunctival inflammation Bacterial infection at 12 months Surgeon	Not reported
Bowman et al, 2002, Gambia[34]	Prospective cohort study, 54 eyes	PLTR, Ophthalmic Nurse	Not clearly stated 12 months	28%	Not reported	Granuloma 15% Lid notching 6% Ptosis 3%
Bowman et al, 2000, Gambia[180]	Retrospective cross-sectional, 65 patients, 115 operated lids	PLTR, Medical Staff and Senior Ophthalmic Assistant	100, median 7 years	55%	Not reported	Not reported
Yeung et al, 1997, Hongkong[169]	Report from 24 eyelids of 19 patients	Posterior tarsal fracture with grey line split, Ophthalmologists?	100%, 2 to 12 months	35%	Not reported	Lid closure defect in 1 participant
Bog et al, 1993, Tanzania[122]	Prospective observational cohort 156 eyes of 94 patients	PLTR, Ophthalmic Nurse	91%, 9-36 months, mean 25.5 months	17.4% (13.9% minor, 3.5% major)	Not reported	1 wound infection Notching 6.3%
Torgersruud, 1950, Ethiopia[118]	Retrospective cohort of 141 eyelids	PLTR	Retrospective, 1 week to 18 months	2.8%	Not reported	Not reported
Halasa et al, 1974, USA[124]	Retrospective cases review of 300 eyes of 154 patients	Ophthalmologists?	6 months to 9 years	3.3% (required operation)	Not reported	Not reported

Table 1.7: Studies conducted on outcomes of surgical procedures other than BLTR and PLTR

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Tarsal Advance						
Welsh, 1969, South Africa[125]	Case series of 177 cases with "advanced trachoma "	Tarsal advance Oculoplastic surgeon	100%, 1 year	0%	Not reported	Loss of cilia Minimal haemorrhage
Tarsal Advance and Rotation						
Seiff et al, 1999, USA[131]	Retrospective cohort In 22 eyelids (7 trachomatous)	Tarsal advance and rotation	Retrospective, average 12.9 months, range 1–48 months	13.6 (3/22)	Not reported	Tarsal buckling in 1 patient (4.5%)
Yagci et al, 2012, Turkey[181]	Prospective cohort of 27 eyelids	Tarsal margin rotation with extended posterior lamellae advancement Ophthalmologist?	100%, average 40 months, range 18–72	0% recurrence	Not reported	Pyogenic granuloma, 11%
Eversion Splinting						
Thommy, 1981, Nigeria[138]	Prospective cohort, 155 eyes of 136 patients	Eversion Splinting: Grey line split, with polyethylene tube as splinter, application of scleral graft Ophthalmologist?	100%, 15 months observation period	7.7%	Not reported	Granuloma 10.3% Partial sloughing of scleral strip 2.6%
Thommy, 1980, Nigeria[139]	Prospective cohort. 341 eyes of 200 patients	Eversion Splinting: Grey line split, with polyethylene tube as splinter, application of eyelid skin graft, Ophthalmologist?	89.7%, Up to 2 years (average 1 and half year)	6.6%, 93.8% "Well maintained"	Not reported	Not reported
Win, 1976, Burma[137]	Retrospective study, 1861 lids	Eversion Splinting: Grey line split, with gauze roll as splinter, Ophthalmologist?	28% 12 months	2%	Severity of pre-operative trichiasis	Not reported

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Tarsal Grooving/Cuenod Nataf						
Ali et al, 2015, Pakistan[147]	Prospective study, 54eyelids of 44 patients with major cicatricial entropion trichiasis	Anterior Lamellar Marginal Z-plasty with transverse tarsotomy Ophthalmologist	100%, 6 month	11%	Not reported	Postoperative edema in all lids Infection: 7.4% Lid margin thickening: 25.9%
Khandekar et al, 2009, Vietnam[149]	Prospective cohort, 648 lids of 472 patients	Modified Cuenod Nataf (without tarsal wedge resection) Ophthalmologist	98%, one year and 2 year	8.9% at one year 15.9% at two years	**At one year** Severe trachomatous scarring at baseline History of eyelid surgery Adjusting sutures **At two years** Operating surgeon Baseline severe trichiasis History of eyelid surgery Adjusting sutures	Not reported
Thanh et al, 2004, Vietnam[148]	Prospective cohort, 636 lids of 472 patients	Modified Cuenod Nataf (without tarsal wedge resection) Ophthalmologist	98% 12 months	10.8%	History of previous surgery Conjunctival scarring Older age Reduced vision	Not reported

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Prachakvej et al, 1978, Thailand[146]	Prospective cohort, 35 yes of 24 patients	Tarsal grooving with division and suturing of the orbital septum with levator aponuerosis	100%, immediate postop	None reported But “90% satisfactory result”	Not reported	Under correction 5.7% Over correction 2.9%
Cockburn, 1943, Libya[144]	Case series of 60 cases with major trichiasis and fibrosed eyelid	Tarsal wedge resection	100%, not clear	0% recurrence (100% success)	Not reported	Not reported
Anterior Lamellar Repositioning						
Aghai et al, 2016, Iran[142]	Prospective interventional cases series of 52 eyelids of 32 patients	Anterior Lamella recession with blepharoplasty and supratarsal fixation	100%, >12 month with mean follow-up of 21 months	25%	Not reported	Eyelid thickening in all cases during the first few weeks
Ahmed et al, 2015, Egypt[97]	Prospective non-comparative study, patients suffering from TT or entropion with short and thin tarsus, 752 eyes of 445 patients	Anterior lamellar repositioning done through lid margin splitting and separation of the two lamellae Ophthalmologist	100% in all follow-ups 3 weeks 3 moth 6 month	3 weeks: 69.1% 3 month: 44% (after treating those with recurrence at 3 weeks with electrolysis) 6 month: 33.9% (after treating those with recurrence at 3 weeks and 3 months with electrolysis)		Postoperative lid edema and/or ecchymosis in all patients Lid margin thickening in all patients Abnormal appearance of the lid: 2.7%

Author, Year, Country	Study design, sample size	Type of procedure, operated by	Response rate, follow-up period	Recurrence rate	Factors associated with recurrence	Other Outcomes
Posterior Lamellar Lengthening						
Hosni, 1974, Egypt[134]	Prospective cohort, 708 eyes of 426 patients	Posterior lamellar lengthening after buccal mucosa graft insertion Ophthalmologist	100%, follow-up period (10 day?) not clear	10% (partial correction 4%; and total failure 6%)	Not reported	Irritation and heaviness of the eyelid margin, 3%
Tarsectomy						
Jones et al, 1976, Iran[127]	Prospective cohort, 36 eyes	Tarsectomy for patients with severe entropion	83.3%, 12 month	15.2%	Not reported	High lid arch (notching), 18.2%

1.13.2.4. Corneal Opacity Change

Corneal opacity changes are reported rarely as trichiasis surgical outcomes. This is probably due to the assumption that established corneal opacity or scar following long term rubbing by trichiasis lashes is less likely to change following trichiasis surgery.[4] Data from clinical trials show that corneal opacity one year after trichiasis surgery improves in 12%–24% and deteriorates in about 10% – 16% of the cases.[4,33,40]

A couple of clinical trials in Ethiopia reported that about 12% – 24% of the trichiasis cases had at least one grade improvement of corneal opacity one year after PLTR surgery. However, similarly, about 10% of the cases also had at least one grade corneal opacity deterioration one year after trichiasis surgery.[33,40] Another trial in the Gambia found that corneal opacity improved in 13% of the eyes but progressed in 16%, which was associated with presence of five or more recurrent trichiasis.[4] However, cases without recurrence have been reported to have corneal opacity progression, suggesting that other factors may contribute to this. In trachoma endemic settings, corneal opacity can be caused by other causes such as cornel infections and trauma both before and after trichiasis surgery. In TT cases, presence of corneal opacity was associated with bacterial infection ($p=0.001$) and severe conjunctival inflammation ($p=0.002$) other than severe trichiasis ($p<0.001$).[4]

1.13.2.5. Visual Acuity Change

It is encouraging that some studies reported improvement in visual acuity after trichiasis surgery, despite the generally held view that trachomatous trichiasis causes irreversible sight loss. The first trial to report visual acuity improvement after trichiasis surgery was the Reacher et al trial. This reported that after adjusting for baseline visual acuity and age, eyes with major TT had half a line of improvement of visual acuity on a Snellen chart ($p<0.001$) one year after TT surgery.[98] Another trial reported borderline improvement in vision after surgery by both BLTR and PLTR procedures ($p=0.052$).[152] In 2005, Burton et al, reported that visual acuity improved in about 58% of the eyes in 12 months from surgery, with 0.14logMar improvement ($p<0.0001$).[4] However, this trial also reported deterioration of vision in 28% of the eyes. In two trials, visual acuity improvement (≥0.1logMar) was also seen in 30% and 23% of cases with major and minor trichiasis respectively one year after trichiasis surgery, while it deteriorated in about a quarter of cases.[33,40] In another prospective cohort study, eyes that had TT surgery improved by 0.13logMar on average after six months, compared to eyes that did not have surgery which only had 0.08 logMar change (OR, 1.65; 95% CI, 1.04–2.70).

Improvement in vision after trichiasis surgery might be attributable to several reasons. Firstly, the surgery would remove the trichiatic lashes and discharge from the visual axis.[4,33,98,182] Secondly, the removal of the constantly rubbing lashes would contribute to corneal epithelium restoration, less corneal edema, photophobia and epiphora.[7] Corneal opacities can sometimes fade with time.

On the other hand the reasons for visual acuity deterioration might be associated with other ocular changes and development of conditions such as cataract. Cataract is the first blinding condition in most trachoma endemic settings. The age group most affected by TT are those above 50 years, which are also more commonly affected by age related cataract. It is possible that cases might develop or progress to advanced stage of cataract within one-year period after TT surgery.

1.13.3. Patient Reported Outcomes

Patient reported outcomes probably determine the community's view of TT surgery delivery and acceptance of it. The patient reported outcomes mostly focus around improvement on vision, pain, photophobia and daily living. Studies have generally reported high rates of satisfaction from patients after surgery. In a trial from The Gambia, 77% of trial participants reported subjective improvement of vision and another 94% reported that they are more comfortable in the operated eye one year after PLTR surgery.[4] In a trial from Ethiopia, 78% of patients in the surgery arm group (78%) reported vision improvement at 12-month follow-up. In another study about 99% of study participants reported that the pain and photophobia they had was no longer bothering them six-months after BLTR surgery.[182]

The only clinical trial that compared patient satisfaction with the cosmetic outcome of three surgical procedures found no significant difference between the surgical procedures compared: PLTR 28(93%), tarsal advance and rotation 27(90%), and tarsal grooving 27(90%). This study also reported that more than 93% of the trial participants gained symptomatic relief seven days after their surgeries.[132] None of these studies measured quality of life of trichiasis patient before or after surgery, except three other studies: two cohort studies and one qualitative study.[41,183,184] These are discussed later in the quality of life section (section 1.17).

1.14. Managing TT Surgical Services

Currently there is an unprecedented effort to scale-up global trichiasis surgical productivity and improve outcomes. However, programmes face many challenges in delivering a high volume and high quality trichiasis surgical service. The number of surgeries performed worldwide is less than anticipated to clear the huge trichiasis backlog. TT surgery services quality is increasingly becoming a significant concern for program managers, the patients and the community at large. Poor quality surgeries may have profound multiple impacts on surgical programmes and communities. These may range from psychosocial impacts, deterring patients' from accepting trichiasis surgery; to having direct financial implications to the programme as managing these require huge resources and specialized surgical skills, which in most trachoma endemic countries are scantly available. It is therefore important not only to focus on the number of trichiasis surgeries performed but also on the quality of the surgery, through high quality and standardized training of surgeons and on-going technical supportive supervision (Figure 1.25).

There are several important elements to delivering an efficient high quality TT surgical service: choosing the most effective surgical procedure, choosing the right people to perform the surgery and training them well, choosing the appropriate service delivery model, providing on-going supportive supervision and well organised management, and monitoring of outcomes.

1.14.1. Which Surgical Procedure?

During the past few decades, various surgical procedures have been used in the management of trachomatous trichiasis. Not all these procedures are easy to perform and do not always provide a reasonable success rate. The choice of surgical procedure is influenced by the severity of trichiasis and the skill of the surgeon. It has been suggested that no single surgical procedure is suited to manage all cases of trichiasis and different surgical procedures should be used depending on the disease severity.[25,105] Whilst this is probably a reasonable suggestion, it is not particularly practical in typical trachoma endemic settings. Practicing different sets of surgical procedures on wide variety of entropion trichiasis severity would require high level training and skill which are not usually available.

Following the two Reacher trials and its relative simplicity to the other surgical procedures, the WHO recommended the BLTR surgical procedure for the management of all types of entropic trichiasis in endemic settings.[112] However, at the same time the PLTR surgical procedure was already extensively used in many trachoma endemic countries. Retraining of PLTR surgeons in the BLTR procedures would be resource intensive for low-income countries. This led the WHO to recommend new programmes should use the BLTR, however, existing programmes should use the already established surgical procedures "unless the incidences of surgical failure, complications or recurrence of TT are high".[90] Subsequently the PLTR procedure has become acceptable alternative to the BLTR surgical procedures and then included in later editions of the WHO trichiasis surgery training manual.[108,143]

Data from various studies suggested that these two tarsal rotation procedures are probably the most effective options for various degrees of TT severity and they are probably simpler than the other types of operation. However, there was insufficient data on their relative effectiveness. Programmes chose to use either procedures usually based on personal preferences of those who started the programme. However, the huge trichiasis backlog and the current need to scale-up surgical programmes necessitates identifying the safest, simplest and most effective surgical procedure for the management of TT. Therefore there was a need to rigorously examine which of the two operations performs better under operational conditions. This has been a research priority question for several years.

1.14.2. Who Should Do The Surgery?

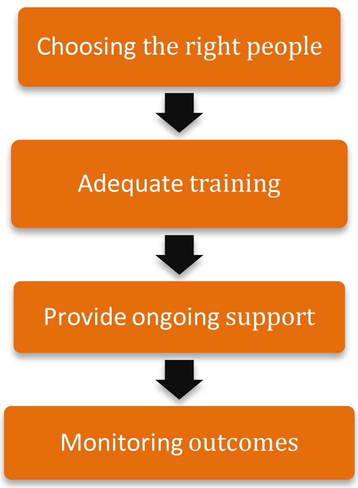
The TT backlog in endemic countries requires prompt action. This requires training a large number of personnel in a short period of time on the most simple, safe and effective surgical procedure. In most trachoma endemic countries, there are not enough ophthalmologists to treat people with TT. Therefore in many programmes there has been a task shift, with trichiasis surgery being performed by mid-level health workers. These are sometimes referred to as Integrated Eye Care Workers (IECWs), who have received focused training on trichiasis surgery.

Results from a clinical trial and subsequent programmatic experience suggest that IECWs can perform TT surgery to a similar standard to ophthalmologists.[159] For instance, in Amhara Region, an area with the highest trichiasis backlog worldwide, hundreds of IECWs have been trained and deployed during the last 10 years.[185] However, this has many challenges including identifying appropriate trainees, providing high quality surgical training, locating and equipping them in relatively remote rural areas and providing sustained supportive supervision.[185]

1.14.2.1. Selecting TT Surgeons

Candidates for TT surgery training need to be selected carefully. It is not uncommon to see IECWs selected for training by rotation rather than their aptitude and interest. Programmes should ensure that individuals selected for IECWs training should have both the aptitude for surgery and the interest to serve in relatively remote rural health facilities.[185,186] They should be selected based on previous experience with eye examinations, experience in giving injections, knowledge of sterile surgical techniques, demonstrated manual dexterity, and good eyesight.[108] In a recent WHO scientific meeting it was indicted that IECWs selection for training should also be supported with a mannequin-based screening test.[28]

Figure 1.25: Managing surgical quality



1.14.2.2. Surgical Training

Training of IECWs should strictly follow the recent WHO Trichiasis Surgery for Trachoma Manual.[108] The training usually takes about 4 weeks, divided into theoretical training, supervised hospital based and practical field training (Figure 1.26). IECWs need to be rigorously assessed based on the specified criteria for certification. Experienced and specifically standardised ophthalmologist for trichiasis surgery training should lead and conduct the training. Where training is cascaded through others, there needs to be rigorous standardization to ensure the surgery is taught correctly. The WHO recommends using a mannequin-based training programme known as **HEAD START** (**H**uman **E**yelid **A**nalogue **D**evice for **S**urgical **T**raining **A**nd Skills **R**einforcement in **T**rachoma) for training of IECWs.[28] This would provide trainees with the opportunity to learn and practice all the major steps of the trichiasis surgical procedure prior to operating on real patients.

Figure 1.26: Surgical trainings should largely be practical

1.14.2.3. Surgeon Retention

Attrition is one of the major challenges of sustaining trichiasis surgical services. In some programmes it has been difficult to maintain services because individuals who have been trained in TT surgery may be moved or promoted, and are therefore no longer available to provide a service. In Amhara Region Trachoma Control Programme, one of the largest and most productive trachoma control programmes worldwide, among the IECWS trained between 2001 and 2008, 59% were no longer in a position to perform TT surgery.[185] Among the attrition surgeons, 55% were promoted to a more senior position out of the TT surgical service within their health offices, and another 30% were receiving long-term training, while the other 15% were working within the private or NGO sector.[185] Worryingly, during the time of leaving the surgical post, nearly half of the IEWs were not replaced by another IECW in their health facility.[185] Programmes should think carefully on how to retain their trichiasis surgeons at least for few years based on their local context. For example, to address the above situation, the Amhara Region, Ethiopia programme makes an agreement with the trainee to work in the programme for at least 1 year following training, or pay 15,000 ETB as compensation if relocation is requested. Programmes should create a favourable and encouraging employment environment and devise a method of continuously supporting and motivating IECWs after they have been deployed.[185]

1.14.3. Service Delivery Approach

Different service delivery models can be adapted based on local needs and availability of resources. The most common once are the static or health facility based, the outreach or campaign, and mobile team approaches. The static approach is probably more sustainable and less resource intensive with the advantage of being integrated with other health care activities. This is useful in areas where there is a relatively low burden of TT. The outreach approach on the other hand tends to be more productive than the static service. In the Gambia, a village-based surgery significantly increased surgical uptake compared to the health facility based surgery (66% v 44%, OR 2.46, 95% CI 1.29 to 4.68).[180] Amongst the TT surgeries performed in one year in Amhara Region, Ethiopia, about 86% were performed in outreach services compared to only 14% being performed in static services.[185] The average productivity of surgeons in outreach programme was 64 surgeries/year/surgeon, while it was 10 surgeries/year/surgeon in static programme.[185] The overall productivity rate for a surgeon working in such high backlog area using either of these two approaches was only 41 cases per year, which was comparable with a report from Tanzania of 22 cases per year.[185,187]

In many trachoma endemic countries, there are insufficient trichiasis surgeons to clear the current trichiasis backlog through the traditional static and outreach models. Individuals trained in trichiasis surgery usually have many other responsibilities. In high burden areas, more productive approaches that deliver high quality and high volume surgery are needed. One approach is deploying a dedicated mobile team of trichiasis surgeons, which travel to districts of high trichiasis burden. With good coordination and communication with communities in need, a single team can do hundreds of surgeries within a few weeks. In addition, with such an approach the quality of surgery is likely to be higher due to the high volume and the increased opportunities for supportive supervision.

Despite a village based surgical service, trichiasis patients tend to decline surgery mainly for three reasons: concern about surgical outcomes, misinformation on the time required before engaging to usual daily activity after surgery and fear of surgical pain.[188] There is an assumption among TT cases that exposure to sunlight or fire smoke will lead to recurrence or bad outcome. Therefore it is important to devise an approach, which can address the concerns of trichiasis patients and their relatives through discussion and counselling. One such approach would be training and deploying community based trichiasis screeners and counsellors, who can identify cases, address their concerns with discussion and bring them to the mobile surgical team.[188] In addition, gaining political support at all administrative levels is mandatory for success of surgical programmes.[188]

1.14.4. Supportive Supervision

Continued supportive supervision is crucial both for improving output and outcome of trichiasis surgery. However, unfortunately surgical programmes often tend to overlook its importance. Lack of supportive supervision has been cited among the major reasons for poor surgical productivity.[185,187] Among "supervisors" interviewed in a study in Amhara, about half never met with their surgeons to discuss trichiasis surgery.[185] On the other hand, even if conducted, the quality of supportive supervision may be an issue in most trachoma control programmes.

Supportive supervision is a process of guiding, helping, training and encouraging staff to improve their performance so that they can provide high-quality health services. Instead of fault finding, it encourages two-way communication between the supervisor and the supervisee so that they can together identify malpractices, and prevent them from happening again and uses the visit as an opportunity for building knowledge and skill and thereby enhance productivity and promote quality service.

Supervisors themselves require a standardized training on supportive supervision processes and skills.[186] Supervisors need to have all the necessary clinical knowledge and have been successfully performing quality trichiasis surgery themselves, so that are capable of transferring skills and providing hands-on, on the job training in all aspects of TT surgery to ensure high-quality sustainable surgical service. In addition, the supervisors should have the necessary programme management skills, therefore would be competent in providing comprehensive support to the IECWs and other members of the surgical team on building and leading effective surgical team, organising TT surgery campaigns, and managing logistics and supplies. It is usually advised to conduct supportive supervision in a team. This allows supervisors to complement each other on the different aspects of supportive supervision skills.[186]

1.14.5. Managing Supplies

Inadequate surgical consumables mean no surgery. One of our studies found a significant association between performing more surgery and reported good availability of surgical consumables.[185] Surgical kit availability means that the IECWs have the necessary surgical material with them at the health facility at all times so that they can provide surgical service anytime patients present. Buying surgical consumables and materials is not sufficient to effectively run a surgical programme. However, it requires regular logistical planning, supply chain management and material audit at all levels.[185] The necessary consumables and equipment required for trichiasis surgery are listed in the WHO Trichiasis Surgery for Trachoma Manual.[108]

1.15. Trachoma and Poverty

Poverty is not the direct cause of trachoma as not all poor people acquire trachoma. However, poverty and trachoma are highly correlated. Trachoma overwhelmingly affects poor and marginalised communities, predominantly in Africa and Asia. Poor communities often have limited access to clean water and sanitation, and crowded living conditions. These factors have been repeatedly associated with trachoma, probably because they promote the spread of *C. trachomatis* infection.

Blindness or visual impairment from trachoma is likely to lead to loss of income at the individual level, which may contribute to family or individual financial poverty. The burden of disability caused by trachoma was estimated at 1.3 million DALYs, with economic losses of 5-8 billion USD/year.[2,189] However, the effect of trachoma on income may begin prior to the visual impairment. The pain and photophobia from trichiasis alone are disabling, and may exacerbate the pre-existing financial strain/poverty. Previously healthy productive adults can be rendered dependent on others and unable to work or fully care for themselves due to the trichiasis, compounding poverty. The economic loss from trichiasis alone due to lost productivity was estimated to be about three billion USD per year.[2,189]

1.15.1. Poverty: Definitions and Classifications

Poverty has been historically linked to lack of income.[190] However, income is just one of the several features of poverty. Poverty, is a multidimensional condition mainly characterised by deprivation ranging from lack of resources to inability to operate and participate in society. The World Bank defines poverty as “a pronounced deprivation in wellbeing”.[191] There are two forms of poverty: Absolute poverty and relative poverty.

The 1995 United Nations summit defines absolute poverty as ''a condition characterised by severe deprivation of basic human needs, including food, safe drinking water, sanitation, health, shelter, education and information".[192] Absolute poverty, which also known as extreme poverty is measured based on a fixed scale – the poverty line. Below this line exists the absolute poverty. This scale is usually expressed in terms of the minimum subsistence available for an individual to fulfil basic minimal needs. The assumption behind absolute poverty measurement is that people require the same amount of resources to survive. Absolute poverty measure is the same across all countries and cultures and does not fluctuate through time.[193] It focuses on an individual's ability for consumption independent of changes in income distribution. In 2015, the World Bank defined absolute poverty as "living on less than $1.90 Purchasing Power Parity (PPP) per day".[194]

The advantage of the absolute poverty measure is that it provides same standards for everyone and allows comparison across all societies and time points.[191,193] This is particularly helpful to compare effect of policies and progress being made. However, this could also be its major drawback as the amount of resource required for survival may not be the same in all communities and time points. For instance, people living in regions with different weather patterns might require different resources for survival. This drawback of the absolute poverty measure can be overcome by using a relative measure.[193]

Relative poverty is lack of resources in comparison to other members of the society.[191,193] People fall into a relative poverty category if they are deprived of resources and opportunities that are normally available to other members of their society. Unlike absolute poverty, relative poverty is directly related to the individual's social and economic status in a given community and measures inequality. Hence, it refers to socioeconomic status (SES), another broad term that has been interchangeably used as a poverty measure. SES refers to the social and economic position of an individual or a household in a given community. This status or position can be given by measures of level of education, income and type of occupation.[195]

1.15.2. Measuring Poverty or SES in Low Income Settings

In low and middle income countries (LMICs) resources are often shared within household. Therefore, the economic impact of a condition or intervention affects not only the individual but also the whole family. Subsequently, wealth or poverty in LMICs should be measured at household level.[196,197] Household economic welfare can be measured objectively based on income, consumption expenditure and ownership of assets and housing characteristics.

Among the more subjective tools used to assess household economic welfare are self and peer rated wealth assessments.[196] Poverty also can be measured in a multidimensional domain scale or single non-monetary domains such as household educational and literacy level, occupational status, and in nutritional measures.[196,197] These measures are discussed below.

1.15.2.1. *Income*

Income is probably the first tool used to measure poverty. Income is usually calculated in terms of earnings in a given time. Measuring income is relatively simple, requiring small amount of data that can be collected with in short period of time. It is considered useful method in high-income settings. However, measuring income in low resource settings is problematic.[191,196,197]

Firstly, people in low-income settings do not know or tend to forget their actual earnings. Either they may have multiple sources of earnings or may only earn very little in form of money, as they tend to get food from own production or through self-employment. Secondly, even if they actually know their income, people tend to not disclose their full income figure particularly those that are considered from illegitimate sources. Thirdly, income tends to be affected by seasonal or even monthly variations. Therefore measurement at one point in time may not always provide a full and accurate picture of socioeconomic status. Fourthly, income measurement is often dependent on the earnings of the household head and do not always capture the contribution of other members of the household. For instance, remittance by a family member residing in another place might be overlooked.[191,196,197]

1.15.2.2. *Consumption Expenditure*

Alternatively, how the income, food and other goods from any sources such as home production or gifts have been actually used can be measured through consumption analysis.[196] Consumption measures the ability of a household to meet its needs and access services.[197] Data on payments made to services and all lists of items consumed by every member of the household, including frequencies and quantities, during a given time (usually per month) is collected. Then the value of these is summed for the household using a price index and then divided by the number of the household members. This provides per capita household consumption expenditure, which can be used to measure absolute poverty.[196] Consumption measure does not include expenses towards capital expenditures such as buying a house; and transfer expenditures such as payments made for taxes or interests.[198]

Consumption expenditure has the following advantage over income. It is more stable than income as families are less likely to change their consumption expenditure to a short term fluctuation of income or home production.[196,197] It is believed that people adjust and regulate their expenditures based on their permanent income rather to their current income.[197,199]

On the other hand this method has its own limitations. First of all, poverty measurement based on consumption would require collecting data on nearly hundred items.[200] This is not only cumbersome to collect and analyse but also is resource intensive. This makes it less appealing for use in epidemiological studies and trials.[196] Second, it is highly likely to be affected by recall bias. People tend to forget what they have consumed in the last few days.[191,196,197] The choice of recall period probably is important to minimize bias. However, this is also problematic as some expenditures are daily while others such as rent or school fees could be paid over a period of time. The interviewee might be unaware of some consumption by other member of the household. In addition, some people may not want to disclose what they have consumed leading to under measurement. Third, the items consumed from home production and those that are soled in the market might have differing qualities.[197]

1.15.2.3. Asset Based Measures

Asset based measures have been largely used in demographic and health surveys.[201-204] In this method data on ownership of various durable assets housing characteristics and access to basic services by a household are collected. The durable assets include radio, bicycle, TV, refrigerator etc. Housing characteristics include, the materials that the house is built with such as the wall, roof and floor materials. Data on access to electric city, water and sanitation facilities are also collected.[202,203,205,206]

In asset based measures it is important to use locally relevant proxies of assets.[203] For instance in most low income settings, ownership of electrical appliances such as TV and refrigerator or other assets such as ownership of car or bicycle might not be relevant as only few or none of the households in such settings would own these. Instead, locally relevant measure of wealth such as ownership of animals, land and durable plants should be included to measure inequality in such settings (Figure 1.27). Locally relevant items can be derived though community discussions.[203]

The asset index has the following strengths. Firstly, it is relatively simple to collect making it feasible for use in various epidemiological and clinical studies.[196] Secondly, evidence suggests that asset based measurement of wealth or poverty measures the long-term financial status of a household, and is less vulnerable to short-term fluctuations than income and consumption expenditure.[202,205,206] This advantage makes it more suitable over the other methods for use in low-income settings.[207] Thirdly, it is a useful if one attempts to measure relative poverty. However, this also could be a limitation as it precludes regional or international comparability.[208]

Among other limitations, quality of assets owned is an issue in asset based socio-economic status classification. Some households might have higher quality or brand of assets compared to others which own similar assets, which cannot be captured with asset index analysis.[203] However, this is probably less of an issue in a rural homogenous community. As explained above, asset variables need to be locally relevant. Otherwise, using the standard asset variables used in surveys for both urban and rural locations would provide a falsely high socioeconomic classification for the urban households, as these are more likely to own a TV or refrigerator and have access to services such as electricity and water than their rural counterparts. In addition to using context and locally relevant asset variables, it is recommended to make separate analysis for urban and rural locations, to overcome such misclassifications.[197,203] Asset analysis is not sensitive to short term changes as it measures long-term accumulation of wealth and not considered a useful measure to assess the impact of an intervention in a relatively short time frame.[196] Analysis and interpretation of asset data is often complex.[197,202,203]

Figure 1.27: Poverty/ wealth measures in low-income settings

a) Housing characteristics b) Durable household assets c) Agricultural assets

1.15.2.3.1. Analysing Asset Data

Once the data is collected an asset index is constructed by assigning weight to each asset.[197] This can be done in a number of ways. One is to sum the number of assets that each household owns. However, this method allocates equal weight for the different types of assets. Another method is using the value of the item to give weight to it. Alternatively, relatively high weight can be given to those that are owned by a smaller proportion of the population under study. The other and most popular option is using principal component analysis (PCA) to construct asset based poverty or wealth index.[202,203,205]

PCA is a multivariate statistical technique mainly used for data reduction and describes a series of uncorrelated linear combinations of the asset variables that contain most of the variance.[202,203,205] The output of PCA provides a table of principal components with factor scores for "n" number of variables (eg. PC1, PC2..., PC28 for 28 asset variables). All components of the PCA contain the same information as the original variables.[205] However this information is partitioned across the different principal components, where the components and their scores are orthogonal (uncorrelated) to each other and the initial components contain more information than the later.[202] Accordingly, the first principal component has the greatest information while the last component has the list uncorrelated additional information. The factor score of the first principal component is considered an appropriate measure of wealth and socio-economic status providing the maximum discrimination (variance) between households. It is particularly considered to be a measure of the household's long-term wealth.[202,203,205]

The following steps are usually employed in constructing a socio-economic index using principal component analysis. First categorical variables should be coded into dummy variables. Then a descriptive analysis of all asset indicators should be conducted to identify variables that should be included and excluded in the PCA.[202,203,205] PCA is effective in capturing inequality when the distribution of variables is not uniform across the households. Indicators that are unevenly distributed across households or those with higher standard deviation carry the highest weights in PCA. Variables either owned by few households or owned by almost all the households will have the list variability or standard deviation (close to zero), which would be given low weight, thereby would have less value in differentiating socioeconomic status or inequality.[202,205] Accordingly, indictors that are owned by only a few or almost all the households can be excluded from the PCA.[203] Second, the distribution of the asset factor scores of the first PCA should be plotted to determine whether truncation and clumping are issues in the data and to ensure whether the data is adequate enough to proxy inequality among that specific study group.[202,203] Truncation occurs when there are higher number of variables with low distribution which would therefore carry low weight in the PCA and won't have much use in differentiating inequality between households or different socioeconomic stratums.[202,203] To avoid truncation, assets that are owned by few households should be excluded from PCA. However, this might again lead to clumping. Clumping is clustering of households in small numbers and occurs when insufficient numbers of asset indicators are used.[202,203] These two conditions may limit the study from producing useful information from the asset index. Therefore, one should consider balancing between the type and number of variables used. The third step is, classifying the households into the desired groups based on their socio-economic scores, usually in quintiles.[202,203,205]

1.15.2.4. Participatory Measures / Peer Rated Wealth

Participatory measures are wealth or poverty rankings of a household by their own community.[197] These methods are used when other survey methods explained above are not useful or inefficient in capturing the socio economic positions of households in a community. The participatory wealth ranking methods also are used to complement other poverty measures. Different approaches can be used to measure socioeconomic status using participatory measures. The common method involves dividing members of the community in smaller groups, define wealth and poverty with in each group and then ask each group to rank households in their community from the poorest to the wealthiest until an agreement is reached in ranking the households.[197,209] Another approach would be asking randomly selected "peers" of a particular household to rate the wealth of the household on a given scale.

These approaches help to capture community perspective and allow incorporating local values. They are also relatively easy to conduct compared to other poverty measures such as consumption measures. However, such community participatory wealth ranking methods can only be done in a relatively small community. They are not suitable to be used in divided and heterogeneous communities.[197] Participatory wealth rankings can also be influenced by easily visible assets. There are also concerns that comparison of such methods within and across different approaches are difficult and may yield weak agreements.[197,210] The participatory wealth ranking methods are not applicable to assess the impact of an intervention.[196]

1.15.2.5. Self-Rated Wealth

Self-rated wealth is a subjective measure of socioeconomic status by the study participants themselves.[200,211,212] In these methods, participants are asked to rate the wealth of their households on a given scale in relation to other households in their community. One of such approaches is the Economic Ladder Question (ELQ), in which participants are asked to rate the socioeconomic status of their households in a pictorial ladder with the bottom representing the poorest and the top the wealthiest.[200,213] Another approach is giving participants a list of reordered wealth rankings to choose from.[197,212]

Its limitation arises from its subjectivity and often it is not clear how well the participants are ranking their households. There might be a tendency among participants to rate themselves as "middle class" in an attempt to avoid calling themselves poor or wealthy.

1.15.2.6. Multidimensional Poverty Index (MPI)

The multidimensional poverty index measures acute poverty at the individual level.[214,215] The concept behind the multidimensional poverty index is that, poverty has multiple features that should be measured with several indicators that capture its complexity.[214] The one-dimension measures such as income fail to constitute the multiple factors that contribute to poverty. For instance income could be higher in some communities, but other issues such as child mortality might be greater than anticipated. Overall, income indicates who is income poor while MPI indicates who is multidimensionally poor. Compared to income, MPI provides data that would significantly help in shaping policy.[214]

MPI measures poverty in three dimensions: Health, Education and Living Standard; using ten indicators.[215] The health indicators are, nutrition and child mortality; education indicators are years of schooling and school attendance; while the living standard indicators include availability of cooking fuel, improved sanitation, safe drinking water, electricity, flooring and assets. In MPI, a person who is deprived in three of the 10 indicators is considered poor. The MPI do not only tell who is poor (incidence of poverty), but also how poor they are (intensity of poverty) giving opportunity in identifying the poorest of the poor.[215] In addition MPI allows comparison across communities and countries.[214,215] The MPI, however, is not useful if one attempts to measure household level poverty.

Using the MPI instead of the monetary based absolute poverty measure ($1.90 a day) increases the burden of poor people worldwide.[216] For instance, based on the MPI measure, 544 million people are poor in Africa, while this number is reduced to 388 million when the $1.90 absolute poverty line is used.[216] This disparity between the two numbers is huge in East Africa, with 70% and 33% are MPI poor and $1.90 a day poor, respectively. Worldwide, 1.6 billion people are multidimensionally poor. Over half of African population is in multidimensional poverty. Among these the majority are found in East and West African countries, with the MPI poorest region being East Africa. The highest pocket of poverty is found in the Sahel belt that includes Ethiopia. In 2011, based on the MPI, 87% of Ethiopians are poor compared to only 34% using the below $1.90/day absolute poverty measurement scale.[216]

1.15.2.7. Nutritional Measures

Nutritional poverty can be measured in the following ways. Food security measures the uncertainty on the availability of nutritionally adequate foods in community. Calories consumed can be also measured using a consumption diary, and then people can be categorised based on the amount of calories taken from different items. Anthropometric measures are also used to measure malnutrition in children. Accordingly children can be categorised as “stunted” or “wasted” based on their age and height.[196]

1.15.2.8. Other Non-monetary Measures

The non-monetary domains such as literacy, education status, and occupation and school participation can also be used to measure household poverty status. The advantage of these methods is they are relatively simple to collect. However, they tend to provide only crude estimates of poverty status and are less sensitive to interventions.[196]

Literacy and level of education achieved can be used as proxy for socioeconomic status.[196] These can be measured at the individual level or the household head. Among the limitation of using education as a measurement for poverty is, it is often affected by social values given to education, which can be affected by place, culture and time.[197] Some low-income setting communities might give lower value to education than others. Some might tend to send only male children to school. In some rural settings, such as Ethiopia, it is not uncommon to see “rich” but illiterate families with not a single year of formal education.

Type and level of occupation can also be used as proxy for socio-economic status. However, in low-income settings most people are self-employed and employment is often seasonal making its use and comparability complex. In addition, there might be differences in categorisation of occupations into socioeconomic stratums among communities, indicating that this is context specific. For instance, "farming" can be considered a lower level of employment in some settings, while others might categorise it to higher status.[197]

1.15.3. Which Poverty Measures are Used and Why

Among the above measures, three relative poverty measures were used for the project of this thesis. The asset based poverty, peer-rated wealth and self-rated wealth measures. The choice of these measures among the others was based on both applicability and feasibility.

The asset based poverty measure was particularly chosen for its key feature of measuring long-term poverty of a household. Trachomatous trichiasis is the long-term squeal of trachoma that starts from child hood and probably is associated with long-term household socio-economic status. Therefore, measuring the association between trachoma and poverty requires such tool that can reflect the long-term living standards of the individual and his/her families. As discussed above, both income and consumption expenditure measure current socio-economic status and are particularly affected by seasonality and recall bias respectively. While it has this advantage, asset based measurement also provides comparable socioeconomic classification of households with consumption expenditure measures.[205] The MPI measures acute individual level poverty, while the other non-monetary and nutritional measures capture a single dimension of poverty. In addition, in terms of feasibility, the asset data is simple to collect and can be easily nested within a clinical trial comparing the relative effectiveness of two commonly used surgical procedures in the management of TT.

The self-rated wealth and peer-rated wealth measures were mainly chosen for triangulation of the asset-based analysis. The socio-economic perception of oneself probably would influence his/her behaviours and interaction with the environment. There is evidence that self-rated wealth socio-economic classifications are comparable to other objective methods such as consumption expenditures and income in low-income countries.[211,212,217,218]

1.15.4. Studies Conducted on Trachoma and Poverty

Although trachoma has been long considered a disease of poverty, it is surprising that not many studies have been conducted to quantitatively elicit this association. The only study that assessed poverty status among trachoma cases (active and TT) was conducted by Jansen et al.[219] This collected household asset data as a measure of living standard in Tanzania and Vietnam among trachoma cases. The results showed that trachoma was prevalent among the poor in Tanzania. However, this association was not seen in Vietnam. In contrast, trachoma was more prevalent among the better off than the poorest households. This probably is due to the implementation of successful trachoma control programme in the poorest communities in Vietnam, which was not the case in the Tanzanian districts. In addition, there is sampling variation between the two countries as in Vietnam the study sample used was from districts selected three years ago for a disease prevalence study, during which there might be an attrition of the study sample population, particular the poor for work to non-study districts.[219]

Other risk factor studies showed that trachoma is more prevalent in communities with signs of lower socioeconomic standards such as illiteracy, poor hygienic practices, child hood mortality, poor housing condition, living in a crowded households and social inequalities.[220-231] For instance a case-control study among women in Tanzania, found that women with trichiasis cases were twice as likely to be uneducated than their non-trichiatic counterparts.[221] In addition, female trichiasis cases were more likely to be found in houses with poor living standards, to have multiple child deaths, and tend to never have been married. A cases control study in Ethiopia showed that TT cases are more likely to be illiterate and had poor hygiene practices.[222]

Active trachoma in Nepal was associated with lower socioeconomic status, crowding and less access to water.[220] A community based cross-sectional study conducted in Amhara Region, Ethiopia showed that children with active trachoma were 3 times and 5 times more likely to be from low-income and illiterate families, respectively.[228] Another similar study conducted in the same region showed that, children with active trachoma were 2.4 times more likely to be from low-income households. This study also asked household heads to rate their household socioeconomic status, and household heads with active trachoma cases were 4 times more likely to rate their household "poor" than the non-active trachoma children households.[212] Again, in Amhara Region, severe active trachoma in children was associated with living in a household with thatch roof (OR, 1.3; 95% CI, 1.0—1.5 and no electricity (OR, 2.4; 95% CI, 1.3—

4.3).[229] Children with active trachoma had poor face hygiene, illiterate mother, and poor access to water and latrine facilities.[232]

1.15.5. Economic Overview of Ethiopia

Ethiopia's economy is dominated by agriculture, accounting for 83.4% of the labour force, 43.2% of the Gross Domestic Product (GDP) and 80% of exports.[55]

In 2007, the working age group dependency ratio was estimated at 93 dependants per 100 persons.[55] Literacy level was low at 36% in people above the age of 15 years. Females had a lower literacy rate than males (51% vs. 63%, respectively).[204] In 2014 education Gross Attendance Ratio (GAR) for primary school, the percentage of the primary school students among the official primary school age population (7 – 14 years), was 86.8%.[204] In 2011, only 23% and 34% of the population had access to electricity and piped water respectively.[233]

Ethiopia is considered one of the poorest economies worldwide. However, it has made positive progress in recent years with an average of 11% in annual growth rate during the last 10 years.[234] In 2000, 55% of the population lived in extreme poverty. However in 2011, based on the <$1.90 per day international poverty line, this figure was down to 33%.[234] Based on the national poverty line of 3781 Birr per adult per year in 2011 prices, 29.6% of the population lived below this poverty line.[233] In 2015, the annual per capita earning in Ethiopia was $590.[234] Life expectancy in Ethiopia increased from 52 years in 2000 to 63 years in 2011.[233]

Data was collected using the asset based wealth index in 2014 in a mini demographic survey. This found that, about 46% of the rural population is in the poorest and poor quintiles; while in contrast about 94% of the urban population was in the rich and richest quintile.[204] This difference is however probably due to the fact that asset based wealth indicators used in surveys are biased towards the urban populations due to their dependence in measuring ownership of household assets that are less likely to be available in rural setups (such as TV, refrigerator, bicycle, car etc). Among the 9 regional states of the country Afar, Somali and Gambela regions had 79.4%, 73.4%, and 67.2% of their population respectively at the poorest and poor quintiles.[204]

1.16. Activity Participation in Low Income Settings

In most trachoma endemic settings, employment opportunities are often limited and household income is mainly generated from engagement in non-paid household, outdoor and agricultural activities. These are carried out by all family members regardless of age and gender. For instance women, who are 3 times more affected by TT than men, usually participate in both household and agricultural activities, including caring for family members, cooking, farming and processing agricultural products.[51] In Sub-Saharan Africa, agriculture accounts for nearly 60% of employment of women.[235] Participation in non-paid or non-monetized household and outdoor activities is estimated to make a $16 trillion "invisible" monetary contribution to global economic output and between 20% and 60% of national GDP in some regions.[235,236] Therefore in low-income settings, the impact of a condition or intervention on productive activity engagement affects not just the individual but potentially the whole family.

1.16.1. The Impact of TT and TT Surgery on Activity Participation

There is some evidence suggesting that trichiasis can interfere with physical functioning.[184,237,238] However, there is no adequate data on the extent to which TT impacts daily household and outdoor productive activities, and leisure or social activities. TT may limit participation in productive and leisure activities. However, measuring engagement or participation in an activity would not give the full picture of its impact on productivity. TT may also limit performance in execution of tasks even if the person is engaged in an activity. For instance, a woman from a low resource setting might still be engaged in a productive activity with lots of difficulty due to visual impairment or lots of pain or both from the trichiasis as she may not have choice; but probably may have very low productivity due to the disabling effect of the trichiasis. In addition, TT cases might seek assistance to finish or execute an activity, which again cannot be measured by looking at engagement in an activity alone. However, no studies are available that have made an in-depth exploration of the impact of TT on the above three parameters: participation in productive and leisure activities, difficulty in executing productive and leisure activities, and assistance received in executing activities.

Trachomatous trichiasis is treated with corrective eyelid surgery to stop the abrasive damage to the cornea with the aim of reducing the risk of sight loss.[90] However, the surgery also may improve overall wellbeing and thereby the individual's capacity to engage in household and agricultural activities by effectively treating the pain and discomfort from the trichiasis. A longitudinal study in Ethiopia assessed the six-month effect of trichiasis surgery on physical functioning using a locally appropriate questionnaire. This study found that trichiasis surgery increased the proportion of trichiasis patients performing physical activities without difficulty.[184] Other than this, there are no longitudinal studies' measuring the long-term effect TT surgery has on engagement and ability in execution of a range of activities.

1.16.2. Measuring Activity Participation

The 'stylised activity list' developed for the World Bank's Living Standards Measurement Survey (LSMS) allows one to assess participation in various productive and leisure activities before and after trichiasis surgery.[239] This tool has been recently used to measure the impact of cataract on activity participation and the change that cataract surgery brought on activity participation of operated cases in three low and middle-income countries.[240,241] The same tool has been adapted in this project to measure the impact of TT and its corrective surgical management on the participation and performance of cases on productive and leisure activities.

1.17. Impact of Trachomatous Trichiasis on Quality of Life

Trichiasis results in significant morbidity and can have a profound effect on many aspects of the individual's life. Trichiasis alone, without visual impairment, could affect quality of life and significantly limit functioning from the marked pain that it causes.[41] However, we know relatively little about the impact that TT has on the lives of people or the effect that the surgical treatment has on quality of life and functioning.

Quality of Life (QoL) is a broad concept referring to the general well-being of the individual. The WHO defines it as an "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".[242] Clinical outcomes do not provide the full picture of the impact of a condition on the life of the individuals and their families. In eye care the most common measure of the impact of a disease or an intervention is visual acuity. However, for patients the most important thing is usually not whether their vision is 6/18 or 6/6 following a certain intervention, but rather, the impact it has on their overall functioning in life.[196] Measuring quality of life is becoming an important aspect of health and health intervention measurements.

1.17.1. Measuring Quality of Life

QoL can be measured quantitatively and qualitatively. Quantitative tools used to measure quality of life can be classified into: tools measuring the broader concept, which can evaluate the overall experience of life; and health related quality of life (HRQoL) tools. The broad QoL tools measure the multidimensional nature of quality of life such as physical, psychological, social, environmental, financial and educational functioning of the individual and consider health as just one domain contributing to a person's quality of life. An example of such tools is the personal wellbeing index (PWI) that measures standard of living, achievements in life, personal relationships, personal health, personal safety, community connectedness, security and spirituality.[196,243] This thesis does not intend to measure this and is specifically focuses on measuring HRQoL in TT patients.

1.17.1.1. Health Related Quality of Life Tools

In assessing QoL there is always a debate about whether to use the standard QoL tools or develop more locally relevant tools. The locally developed tools, compared to the standard broad QoL tools, are more likely to be culturally acceptable and capture locally relevant issues. However, on the other hand developing new tools by itself is a complex process and is one big project requiring lots of time. In addition, results from locally developed tools would lack comparability across different populations, which is one of the strengths of the standard internationally tested QoL tools.

The HRQoL tools could be further divided into: tools measuring disease specific quality of life and generic HRQoL. It is often recommended in research to use both the disease specific and generic HRQoL tools as they provide complementary information. In this project we used both tools to assess QoL of TT patients and the impact that trichiasis surgery has on vision and health related quality of life.

1.17.1.1.1. Disease Specific Quality Of Life Tools

The disease specific quality of life tools range from those measuring the functional ability of patients such as restriction in daily activity in relation to a specific disease to the impact of a condition to a broader area of health such as psychological and social aspects. The advantages of such tools are focusing on relevant factors and explore patient experience of a specific disease condition or intervention, reducing burden of interview and data collection. They are particularly responsive to change following an intervention. Among such tools are the vision related quality of life (VRQoL) tools.

Few tools have been developed to measure VRQoL of patients. The tools that have been tried previously in different sets of patients and potentially could have been used in this project are summarised in Table 1.8. Most of the tools focus on assessing vision related physical functioning and do not adequately capture the psychological domain of quality of life except the WHO/PBD-VF20 tool. In addition, this is the only tool that evaluates how ocular pain and discomfort impacts QoL, making it a preferable tool for assessing QoL in TT patients. This tool has been evaluated and showed good psychometric properties in studies conducted on cataract cases with visual impairment in Kenya, Bangladesh and the Philippines.[244-246] However, it has never been applied to measure VRQoL in trichiasis patients.

WHO Vision Related QoL Tool

The World Health Organisation/Prevention of Blindness and Deafness–20 item Visual Function (WHO/PBD-VF20) questionnaire is a comprehensive VRQoL tool designed to explore the overall eyesight, ocular pain and discomfort, general functioning and psychosocial factors related to vision.[247] This tool contains 20 questions sub-divided into three subscales: visual symptom, general functioning and psychosocial. Each question has a 5-point response option: 1 indicates the highest and 5 the lowest score. The first two questions measure the eyesight and amount of pain or discomfort the person is experiencing. The psychosocial questions assess the frequency of experiencing a specific vision-related problem, while the remaining items measure the difficulty associated with overall performance.

Table 1.8: Summary of VRQoL used before

	Authors and Tools			
	WHO/PBL VF 20 ***Vision related quality of life tool*** [247]	***Fletcher et al '97;*** ***Measurement of vision function in cataract patients*** [248]	***Van Dijk et al '99*** ***Visual function assessment in low-income countries*** [249]	***Frick et al '01*** ***Physical functioning assessment in trichiasis patients*** [237]
Scale	5 scale: Non, mild, moderate, severe, extreme/can't do	4 scale: very good, good, fair, poor	4 scale: no problem, little problem, a lot of problem, can't do	
QoL Domain				
General Vision	Rate eye sight using both eyes	-	-	-
Ocular Pain/Discomfort	Has pain/discomfort	-	-	-
Vision Difficulty				
Distance vision difficulty	Going down steps or stairs Noticing obstacles Going to activities outside the house Recognising people from a distance of 20 meters Seeing irregularities in the path when walking	Problem recognising people across the street	Recognising potholes, stones or branches while walking Problem in recognising faces (distance not clear)	Recognising faces (distance not clear)
Near vision difficulty	Searching for something Recognising face at near distance Seeing level of container when pouring Seeing close object, coins/notes etc. Doing activities that require close-up vision eg. Sewing	Recognising the face of a person standing near Recognising very small or minute objects on the hands Locating something when its is surrounded by a lot others	Difficulty reading Difficulty in differentiating notes Difficulty in recognising food on a plate Sorting stone from rice or beans Sewing or making baskets or mats	-
Glare	Difficulty because of glare from bright light	Recognising a person when in bright light Seeing with bright lights shining on the eyes	-	-
Light/dark/sensory adaption	Seeing when coming inside after being in bright sunlight	Adjusting to darkness after being in bright light Adjusting to bright light after being in dark place	-	-

QoL Domain	Authors and Tools			
	WHO/PBL VF 20 ***Vision related quality of life tool*** [247]	***Fletcher et al '97;*** ***Measurement of vision function in cataract patients*** [248]	***Van Dijk et al '99*** ***Visual function assessment in low-income countries*** [249]	***Frick et al '01*** ***Physical functioning assessment in trichiasis patients*** [237]
Colour vision difficulty	Seeing differences in colours	Recognising colours	-	-
Depth of perception	-	When reaching to an object (to take a glass), how much problem in finding it because it is further away or closer than you thought	-	-
Night vision difficulty	-		Walking around in night	-
Peripheral vision difficulty	-	Noticing objects off to the side		-
Physical Functioning Limitation	Carry out usual work	The extent eyesight limits on daily activities	Difficulty cooking, chopping vegetables, or pouring water Difficulty tending garden Difficulty repairing own house	Walking outside the village Going to the market Helping with the farm Weeding Housework Gathering food for charcoal Gathering fire wood Cooking Caring for children
Social Functioning Limitation	Hesitant to participate in social functions	-	Participating in social activities such as wedding and funerals	Attending parties
Psychological/Mental Wellbeing	Ashamed or embarrassed Worry that you may lose your remaining eye sight How often felt that burden to others	-	-	-
Activities of Daily Living	-	-	Difficulty using the latrine without assistance	Bathing, dressing, eating, transfer
Comment	Relatively comprehensive addressing visual functioning in all domains and is the only tool that included pain and discomfort. More appropriate to assess QoL in TT patients.	It focuses on vision difficulty and overlooks important domains such as the social and psychological domains. It does not capture pain and discomfort as originally prepared to measure QoL in cataract patients.	It focuses on distance and near vision functions and overlooks the psychological domain. It does not capture the effect of pain and discomfort.	Limited to physical functioning and activity of daily living as originally developed to assess how disabling or limiting TT is.

1.17.1.1.2. Generic Health Related Quality of Life Tools

Generic HRQoL tools are capable of assessing a range of health concepts and can be used irrespective of specific disease or condition.[196] Among the advantages of these tools is, they are comprehensive and cover multiple domains of health from the individual's perceptions of his/her own health to social and environmental functioning. However, they are probably relatively less responsive to changes following intervention. There are multiple tools that measure generic HRQoL such as the Short Form-36 (SF-36), the EuroQoL EQ-5D, Sickness Impact Profile (SIP), and the WHOQoL tools. Among the WHOQoL tools we used the WHOQoL-BREF.

The WHOQOL-BREF Tool

The WHOQOL-BREF, the shortened version of the WHOQOL-100 tool, is a cross cultural tool and has been widely used in different socio-economic settings and has good applicability in low and middle-income countries (LMIC) as it was developed from concept across 20 countries in Africa, Asia and Latin America, which is why it is selected for use in this project among other HRQoL tools.[196,250,251] It contains 26 questions, which assess QoL across four domains: physical health, psychological, social relationships and environment in the past four weeks.[242,252,253] The first two questions assess general QoL and health. The physical health domain assesses activities of daily living, pain and discomfort, dependency in medical care, mobility, energy and fatigue, sleep and rest, and work capacity. The psychological domain incorporates body image and appearance, feelings, self-esteem, beliefs and cognitive states. The social relationships domain includes sexual relationship, social support and personal relationships. The environment domain is constructed from items on financial resources, freedom and security, home and physical environment, access to health and social care, information, transport and participation in leisure activities. Each item is scored on a 5-point scale. The Amharic version used in this project was provided by the WHO and has been previously validated and used in Ethiopia.[254-256]

1.17.2. Studies on QoL of TT Patients

1.17.2.1. Studies on Impact of TT on VRQoL

Only very limited studies have been conducted to assess VRQoL of TT patients. Few studies have measured functional ability of TT patients.[237,238] These studies however, did not use standard tools and were focused on exploring the effect of trichiasis on physical functioning only. The psychological and social impacts of trichiasis and its related visual impairment have often been overlooked.

The first attempt was by Frick et al, which assessed the association between TT and functional status in cases without visual impairment.[237] This study adapted a tool used to assess visual function and quality of life in Cataract patients in India and additional items were generated from interviews with key informants.[248] The items included were on social activity such as visiting neighbours and attending parties; physical functioning such as walking outside the village, going to the market, recognizing faces, helping with the farm, weeding, housework, gathering wood for charcoal, gathering firewood, cooking, and caring for children; and activities of daily living such as bathing, dressing, feeding, and transfer. Study participants were asked to rate the degree of difficulty they had in performing each activity from a 4-point scale ranging from no difficulty to not be able to do activity. This study found that, women with trichiasis but without visual impairment had a comparable degree of disability to those with visual impairment; and the combined effect of trachomatous trichiasis and visual impairment leads to greater functional limitations.[237]

Another study from Tanzania, which used the same study population and physical functioning tools as used by Frick et al to collect data on cataract and trachomatous trichiasis cases. This found that trachomatous trichiasis caused a similar level of vision related physical disability with cataract (11% vs 17%).[238]

1.17.2.2. Studies on Impact of TT Surgery on VRQoL

Again, no adequate studies have been conducted to assess the impact of TT surgery on VRQoL. One study has been conducted by Wolle et al in Ethiopia to measure the impact of corrective eyelid surgery on physical functioning of 411 TT patients.[184] The physical functioning questions were derived from the above Frick et al questionnaire with "Ethiopian specific factors" such as making enjera (bread) and grinding coffee added to it. The TT cases using a 5 to 7 point scale, ranging from no difficulty to unable to do the activity, rated the questions before and 6 months after corrective eyelid surgery. This study found that the percentage of TT cases "reporting no difficulty in physical functioning increased by 32.6%" six-months after TT surgery. In addition, this showed that visual improvement was an important determining factor for improvement in physical functioning after TT surgery. Severe entropion at baseline predicted improvement in physical functioning suggesting that TT cases with severe diseases benefit a lot from TT surgery.[184]

1.17.2.3. *Studies on HRQoL of TT Patients*

The data on the impact of trichiasis and trichiasis surgery on HRQoL of patients is also limited. One hospital based prospective interventional study conducted in India has compared the quality of life of 60 trichiasis and entropion cases with 60 age, sex and socio-economic status matched patients without trichiasis using the WHOQOL-BREF tool.[183] The study showed that trichiasis patients have poorer quality of life than the non-trichiatic patients in the physical and psychological domain regardless of the presence of visual impairment prior to intervention (epilation for minor trichiasis and surgery for entropion and major trichiasis). Two to four weeks after the intervention, quality of life scores improved in the physical, psychological and environmental domain regardless of visual improvement.[183]

However, this Indian study had a number of limitations. Firstly, about two third of the "trichiasis cases" had no trichiasis (only entropion), which precludes drawing conclusions about the change in the QoL of TT patients. Secondly, 19 cases with minor trichiasis received epilation management, which might give different level of QoL improvement compared to cases that had corrective eyelid surgery. Thirdly, there was less than one month of follow-up in this Indian study during which the surgical wound healing process might influence QoL results. Fourthly, the study used hospital control many of whom had other potentially impairing conditions which might influence their QoL scores.

A relatively inclusive qualitative study in Niger by Palmer et al explored the impact of trichiasis on QoL in women.[41] The study participants were women with trichiasis, had trichiasis, and received surgical management for trichiasis. This found that trichiasis affected overall wellbeing of these individuals ranging from health to social status and religious participation, which in turn led to loss of security. On the other hand trichiasis surgery improved QoL regardless of the presence of postoperative TT. [41]

Table 1.9: Studies measuring quality of life of TT patients

Author, Year, Country	Study Design, aim	QoL Tools Used, domains	Study participants	Results
Frick et al, 2001, Tanzania [237]	Cross sectional study, measures limitation of physical functioning in trichiasis patients with and without visual impairment	Locally relevant physical functioning tools exploring degree of difficulty in performing activities in 4-point scale. See Table 1.8	People above the age of 40 from 6 randomly selected villages 1) No trichiasis and no visual acuity loss (n=2025), 2) No trichiasis and visual acuity loss (n=792), 3) Trichiasis and no visual acuity loss (n=88), 4) Trichiasis and visual acuity loss (n=112).	a) Trichiasis without visual impairment limited physical functioning of women with a level similar with visual impairment. b) Trichiasis with visual impairment lead to greater degree of limitation in physical functioning in women
Lia et al, 2004, Tanzania [238]	Cross sectional study, assess the impact on vision related physical difficulties with daily activities caused by trichiasis, cataract, and both trichiasis and cataract	Same as the tool used by Frick et al	2743 people above the age of 40 from 6 randomly selected villages	1) Prevalence: a) TT, 5.5% b) Cataract, 11.9% c) TT and Cataract, 1.5% 2) Vision related physical difficulty scores a) Participants with neither trichiasis nor cataract, 0 b) With TT, 0.38 c) With Cataract, 0.50 d) TT and Cataract, 0.70 3) Association of vision related physical disability with a) TT: OR, 5.07; 95% CI 1.15–22.34 b) Cataract: OR, 7.55; 95% CI, 1.87–30.47 c) TT and Cataract: OR 17.40; 95% CI, 1.95–155.40
Dhaliwal , 2004, India [183]	Prospective interventional case control study, determine HRQoL of cases with trichiasis and entropion before and 15 to 30 days after intervention (surgery/epilation for minor TT cases)	WHOQOL – BREFF; Physical, Psychological, Social and Environment domains	1) 60 cases with trichiasis and entropion, among which half have visual impairment 2) 60 hospital based controls without trichiasis or entropion, among which half have visual impairment	1) HRQoL of trichiasis and entropion cases was poorer than that of controls in the physical, psychological and environment domain. 2) HRQoL scores of cases improved after intervention in all domains except the social domain regardless of visual improvement
Wolle et al, 2011, Ethiopia [184]	Prospective interventional cohort, evaluate physical functioning in TT cases before and six-months after surgery.	Same as the tool used by Frick et al, with Ethiopia specific factors added	411 trichiasis cases above the age of >18 years had baseline and follow-up data six month after TT surgery	1) The percent of participants reporting no difficulty in physical functioning increased by 32.6% 2) Physical functioning improvement associated with vision improvement and severe entropion at baseline
Palmer et al, 2014, Niger [41]	Qualitative study, understand effect of TT on QoL of women	Qualitative method on defining QoL, exploring effect of TT on physical functioning, loss of security, stigmatisation and family burden; and the impact of TT surgery on QoL using in-depth interviews	23 women: 10 who have TT, and 13 who have had surgery for TT	1) QoL defined as: "health, security, family, social status and religious participation. 2) "Trichiasis caused severe pain and loos of health, leading to loss of security", which affected "social, economic and religious activities and caused burden on their families" 3) Surgery improved QoL regardless of postoperative TT

2. Research Project Overview

2.1. Study Setting

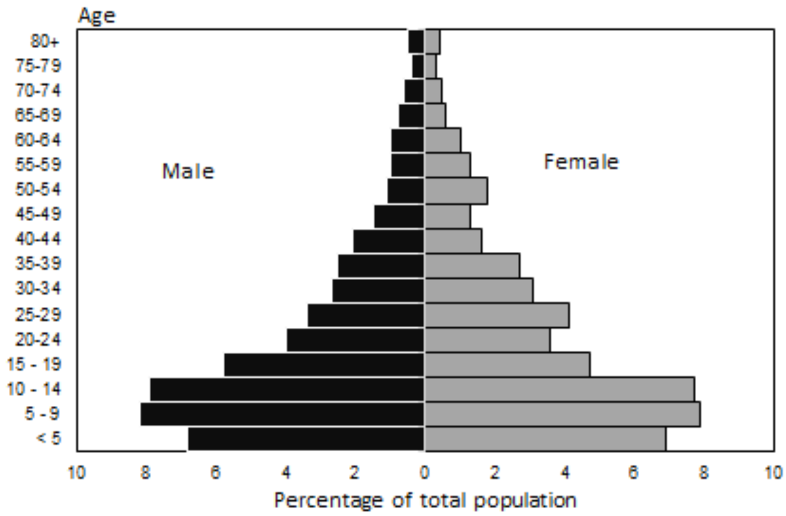
This project was conducted in Amhara Region of Ethiopia. As discussed in earlier section Ethiopia has one of the highest burden of trachomatous trichiasis worldwide and among its region Amhara is the most affected.

Figure 2.1: Map of Ethiopia showing Amhara Region

2.1.1. Ethiopia: country profile

Ethiopia has a total area of 1.1 million km^2 with diversified geography ranging between peaks of 4550m above sea level to depressions of 110m below sea level (Figure 2.1).[55] It is the second most populous country in Africa with a projected 99 million population in 2016, of which 84% is rural.[257] Ethiopia's population is predominantly young with under 15 years, 15–65 years and above 65 years of ages constituting 44%, 52% and 4% of the population respectively, Figure 2.2. Male:Female ratio is balanced (with 101 males per 100 females) and reproductive age (15–49 years) women constitute 24% of the population.[204] Average household size is about 5 persons. The Ethiopian population is estimated to be growing at a rate of 2.6% annually.[55]

Figure 2.2: Population pyramid of Ethiopia, 2014 [204]



Ethiopia has nine regional states and two city administration councils. These are subdivided into 84 zones, which are in turn subdivided into 826 administrative Woredas (districts). These Woredas are subdivided into more than 17,000 kebeles (villages), which are the smallest administrative units in the country.[55]

Ethiopia has three-tier health care delivery system.[55] The first level is a district level health system. This is comprised of a primary hospital covering between 60,000 and 100,000 people, under which health centres, each serving between 15,000 and 25,000 population are contained. Each health centre in turn is comprised of about 5 Health Posts in average, each serving 3000 – 5000 village population. The second level is a referral hospital serving 1–1.5 million people. The third level is a Specialised Hospital covering 3.5–5 million population. There are about 1.9 hospital beds per 10,000 people, that is by far the lowest globally. In Sub-Saharan Africa the average is 9 beds to 10,000 people.[55]

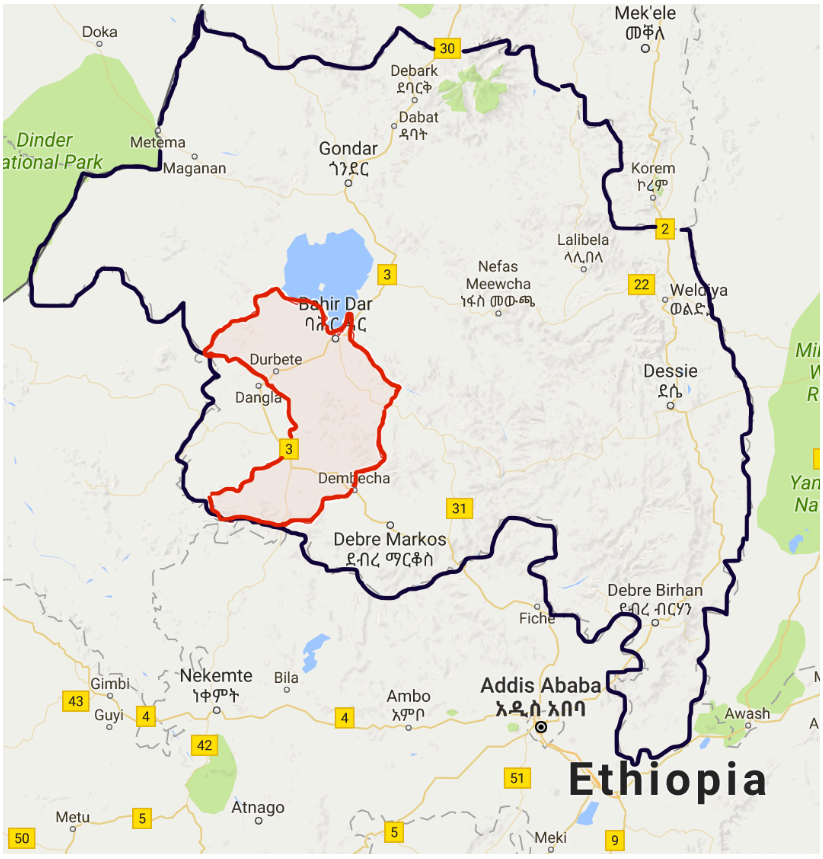
Ethiopia's population has one of the highest morbidity and mortality rates.[55] In 2010 under five-mortality rate was reported to be 100/1000. More than 90% of childhood deaths are from common and largely preventable communicable diseases.[55] More than 1.2 million people are blind in Ethiopia. About 87% are due to avoidable causes: Cataract (50%), Trachoma (12%) and Refractive Errors (8%).[258]

2.1.1.1. Amhara Region

Amhara Region is one of the 9 regional states of Ethiopia. It is located in the Northwest part of Ethiopia. Amhara Region has a total area of 170,000 square kilometres (Figure 2.3). According to the Ethiopian Central Statistic Agency projection, the region's population in 2016 is about

20.14 million.[257] About 88% of the population is rural, most of which are subsistence farmers. The capital city of Amhara region is Bahirdar, where our research project coordination office is based.

Figure 2.3: Map of Amhara Region with West Gojam Zone within the red boundary



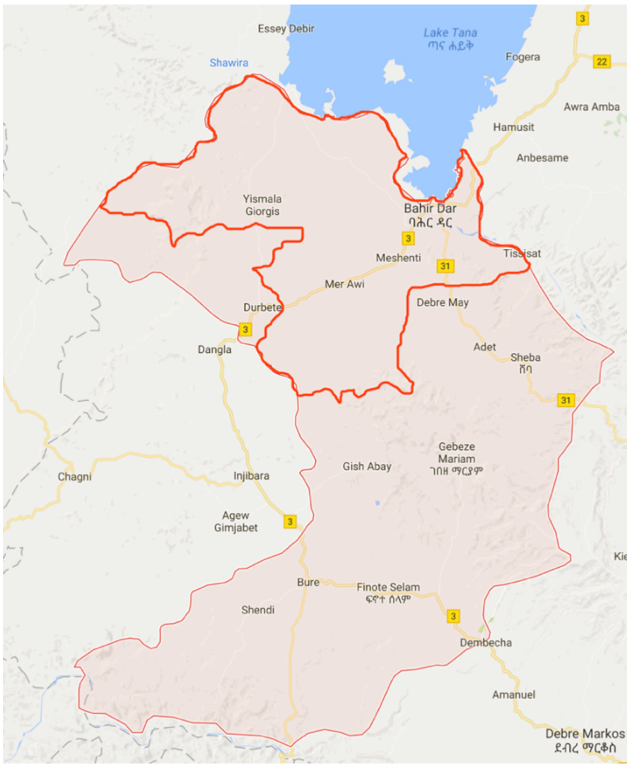
Amhara Region is one of frequently drought affected regions of the country; with about 35% of its districts chronically affected with drought. Average household size is 4.3 (persons).[204] The region has one of the lowest literacy rates with about 54% of females and 47% of males having no formal education.[204] Based on the 2014 asset based poverty index analysis, 24% and 25% of the regions population were in the poorest and poor quintiles; while 26%, 17% and 8% were in the middle, rich and richest quintiles respectively.[204]

Amhara Region has 17 hospitals, 654 health centres, 3046 health posts, 332 primary eye care units and 7 secondary eye care units. In addition, it has 7 private hospitals and more than 1020 different private health institutions. Despite these health facilities, the heath care utilisation culture of the community is disappointing. It is not uncommon, to see people passing away without visiting a health facility. In fact a survey conducted on health care utilisation in the region reported that among people who were reported dead, and sick during the survey, more than 40% and 61% respectively did not visit health facility.[259]

2.1.1.1.1. West Gojam Zone

Amhara region is further divided into 11 zones, and 167 woredas. The woredas are further divided into 3,435 kebeles. West Gojam zone is one of the 11 zones; our project field activities are based here. It covers 13,311 square kilometres. It has a population of 2.4 million, of which about 90% is rural.[257] West Gojam is further divided into 14 woredas. The fieldwork of this study was conducted in three districts of West Gojam Zone: Mecha, North Achefer and Bahirdar Zuria Woredas, between February 2014 and April 2015 (Figure 2.4).

Figure 2.4: Study participants' recruitment area in West Gojam Zone



2.1.2. Research Partnership

This project is executed through a collaborative research partnership between the Amhara Regional Health Bureau (ARHB), The Carter Center trachoma control programme and the International Centre for Eye Health (ICEH) at the London School of Hygiene & Tropical Medicine (LSHTM). These three organisations have worked together on trichiasis surgery research since 2007, and have a strong track record. Trichiasis surgeons operating in this trial have been seconded from the ARHB and all project field activities have been conducted under a close collaboration with the district health office departments under the ARHB. TCC is a not-for-profit, non-governmental organisation working on an extensive trachoma control programme in the region for 15 years. All administrative support including financial management and staff appointments for this project have been delivered by TCC. The study coordination office has been located in Bahirdar, within the TCC Amhara Region Bureau, with a large, experienced field research team.

2.2. Research Questions

1) **Which of the two commonly used surgical procedures (BLTR or PLTR) provides the best results in the management of trachomatous trichiasis under programmatic conditions?**

   Rationale: The two commonest trichiasis surgical procedures (BLTR and PLTR) have not been compared in an adequately sized randomised trial with sufficient follow-up time. The important question of which of these two commonly used alternatives gives the best results under programmatic conditions remains unanswered. Therefore, there was a need to rigorously examine with an appropriate sample size and an adequate follow-up period in a programmatic setting, which of the two operations (BLTR or PLTR) performs better. This question was identified as a research priority several years ago by the WHO/GET2020 meeting.[260] If one of these procedures does indeed turn out to have better results, this would have major implications for how the surgery is performed and results will be fed directly to guide policy.

   Primary Outcome: Rate of postoperative TT by 12 month

   Secondary Outcomes: Rate of intra and postoperative complications, patient reported outcomes

2) **What factors predict TT surgical outcomes one year after BLTR and PLTR surgeries?**

   Rationale: There is currently a major global effort to scale up surgical services to clear the current trichiasis backlog by 2020. However, unfavorable outcomes following TT surgery are undermining these efforts. Reports indicate that the burden of unfavorable outcomes such as postoperative TT, eyelid contour abnormality and granuloma may have increased significantly with increasing surgical outputs.[28] These have negative social and psychological impact, and are deterring patients' from accepting trichiasis surgery. On the other hand, the management of unfavorable surgical outcomes is often challenging, underpinning the need to maximize the success on the initial operation to prevent unfavorable outcomes, which in turn require in-depth study of predictors of unfavorable outcomes. The trial above would provide a unique opportunity to investigate factors that are associated with unfavorable outcomes in both of the commonly used BLTR and PLTR surgeries.

Outcome measures: Preoperative, intra operative and postoperative factors predicting postoperative TT, eyelid contour abnormality and granuloma separately for PLTR and BLTR surgeries.

3) What is the relationship between trachomatous trichiasis and poverty?

Rationale: Trachoma has been long considered a disease of the poor. However, very surprisingly there is very little quantitative data that investigates this association. Many epidemiological studies link trachoma with factors normally associated with poverty. However, not all poor people get TT and it is possible that the people vulnerable to developing this blinding complication of trachoma are the poorest members of the poorest communities. Conversely, the disability caused by TT could lead to reduced productivity, unemployment and loss of income, putting additional financial pressure on an already strained household. These issues have not been adequately investigated before.

Outcome measures: classification of TT cases households using a poverty index of asset based, peer-rated and self-rated measurements, relative to non-trichiatic neighbours.

4) What is the impact of trachomatous trichiasis on quality of life?

Rationale: There is clear evidence that visual impairment generally reduces QoL.[244-246] However, relatively little is known about the impact that trachomatous trichiasis has on the overall wellbeing of affected people with and without the presence of visual impairment. The marked pain and the photophobia from TT alone may greatly hamper the vision and health related QoL of affected individuals. However this has not been studied adequately. Few previous studies mainly assessed the impact of TT on physical functioning; and the psychological and social effects of TT have usually been overlooked.

Outcome measures: Vision and health related quality of life score of TT patients, relative to their non-trichiatic neighbours.

5) **What is the impact of trachomatous trichiasis surgery on quality of life?**

Rationale: TT surgery is mainly conducted to reduce the risk of sight loss. However, the benefits of surgery may go beyond preventing vision loss and in fact may help to restore the physical, social, psychological, environmental and economic wellbeing of individuals through improving vision and reducing pain and discomfort. However, detailed empirical data on the impact of surgery on QoL is lacking.

Outcome measures: Change in QoL score of TT patients one year after TT surgery, relative to their non-trichiatic neighbours.

6) **What is the impact of trachomatous trichiasis surgery on activities of daily living?**

Rationale: In trachoma endemic settings, employment opportunities are often limited and household income is mainly generated through engagement of family members in agricultural activities. TT may limit engagement with productive activities and ability to execute activity without difficulty and assistance that would together result in loss of household income. TT surgery may improve the individual's capacity to engage in household and agricultural activities by effectively treating the pain and discomfort from the trichiasis. However, there are no data demonstrating that this assumption is true.

Outcome measures: Change in proportion of TT cases engaging in productive and leisure activities, performing productive and leisure activities without difficulty and assistance, relative to their non-trichiatic neighbours.

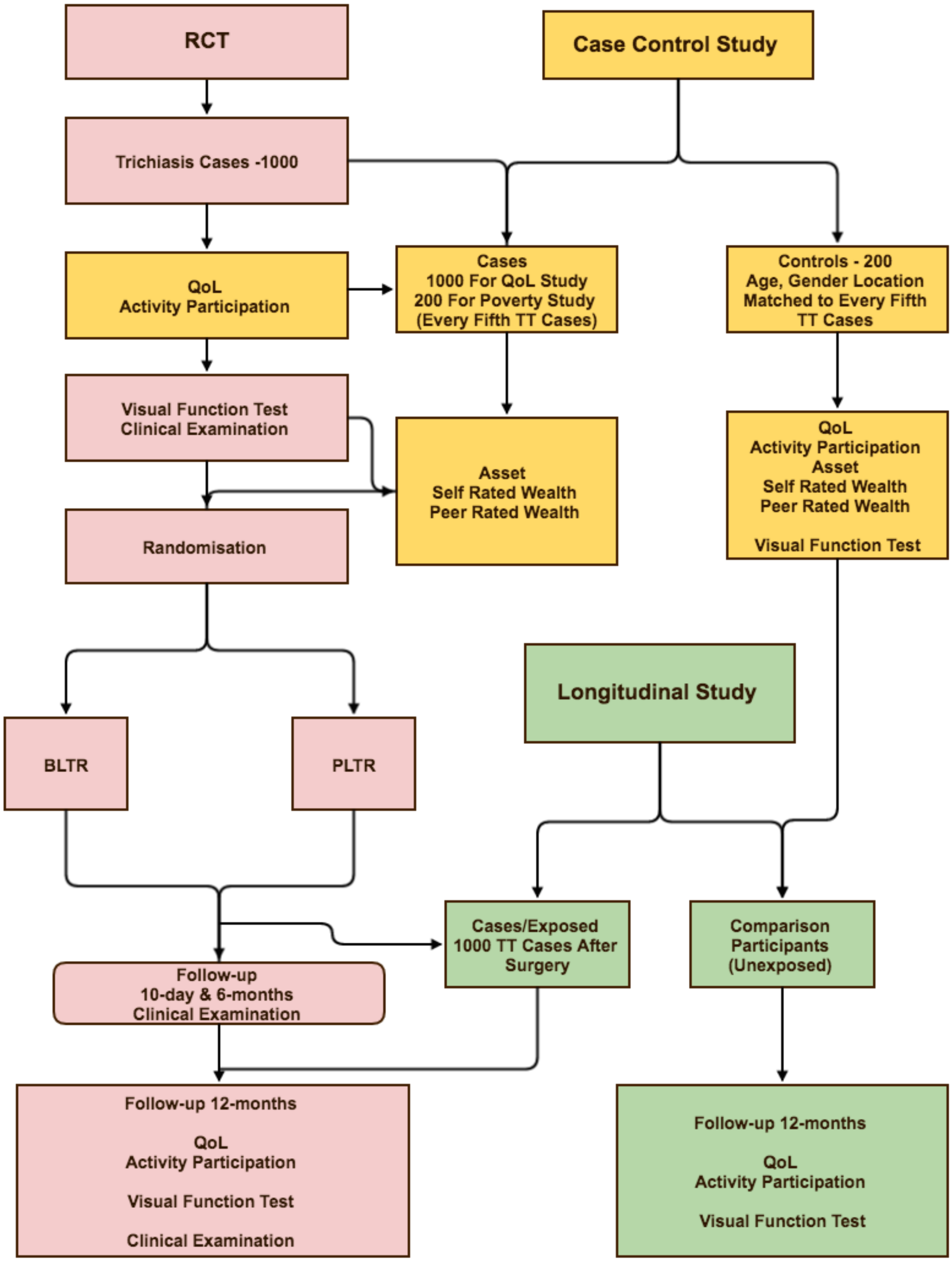
2.2. Study Project Structure

This project was structured as three integrated studies (Figure 2.5). The first is a randomised clinical trial comparing the relative effectiveness of the two surgical procedures. In this trial, research questions 1 and 2 would be addressed.

The second is a cases-control study nested within the clinical trial. In this, the trial participants are used as "cases"; and "controls" are selected from the same villages as the cases with matching criteria. In this study design, research questions 3 and 4 would be answered.

The third is a longitudinal study, which explores the change in QoL and activity participation of cases one year after surgery and compares the results with the change in the "comparison participants" recruited as controls at baseline. In this study design, research questions 5 and 6 would be answered. The summaries of methods for each of these studies design are presented below.

Figure 2.5: Research programme structure



3. Study Methodology

3.1. Randomised Controlled Trial of BLTR vs PLTR Surgeries

A prospective double-masked, randomised clinical trial (RCT) was conducted to investigate which of the two commonly used alternative surgical procedures for the treatment of trachomatous trichiasis provides the better result in terms of reduced recurrence. Individuals with un-operated TT were randomised to one of the following two intervention arms: 1) Bilamellar tarsal rotation surgery (BLTR), performed under local anaesthesia; 2) Posterior lamellar tarsal rotation surgery (PLTR), performed under local anaesthesia.

3.1.1. Sample Size

The sample size was calculated based on the following assumption. From the STAR trial, the one-year TT recurrence rate using the BLTR was about 10% (tetracycline group).[5] In our recent trials in Ethiopia involving patients with a similar severity of disease to the STAR trial, we found PLTR had a one-year recurrence rate of 18%.[40] We estimate we will need a sample of 836 to detect a reduction in TT recurrence from 18% to 10%, with 90% power and 95% confidence. Therefore, we recruited 1000 (500 in each arm), to allow for about 15% loss to follow-up.

3.1.2. Preparatory Activities

3.1.2.1. Inter-observer Agreement for Clinical Examination

The field grader at baseline and 12-month follow-up (EH, observer B) and the reference grader (MJB, Observer A) independently graded 135 eyelids in December 2013 using the detailed and modified trachoma grading system used in this thesis (Figure 3.1). The inter-observer correspondence for the main outcome measures is shown in Table 3.1. Similarly, independent examinations of 209 eyelids were performed by observer B (EH), and the six-month follow-up assessor (SA, observer C) in July 2014. The inter-observer agreement for the main outcome measures is described in Table 3.2. Weighted kappa-score analysis was employed for ordinal variables.

Table 3.1: Inter-observer score (Observer A vs B, agreement highlighted in yellow)

Outcome Measures	Observer A	Observer B grades									Kappa score
Primary outcome		0	1							Total	
	0	26	1							27	0.91
	1	3	105							108	
	Total	29	106							135	
		0	1	2	3					Total	0.89
Conjunctival scar grade	0	1	0	0	0					1	
	1	0	3	2	0					5	
	2	0	0	80	3					83	
	3	0	0	5	21					26	
	Total	1	3	87	24					115 å	
		0	1	2	3					Total	0.85
Trichiasis grade	0	17	1	0	0					18	
	1	8	7	0	3					18	
	2	0	1	4	1					6	
	3	1	0	2	90					93	
	Total	26	9	6	94					135	
		0	1-2	3-5	6-9	10-14	15-20	21-30	31+	Total	0.83
Lash count	0	34	1	1	0	0	0	0	0	49	
	1-2	1	35	7	0	0	0	0	0	33	
	3-5	0	8	19	6	0	0	0	0	28	
	6-9	0	0	2	9	4	0	0	0	1	
	10-14	0	0	0	0	5	1	0	0	20	
	15-20	0	0	0	0	0	1	0	0	2	
	21-30	0	0	0	0	0	0	0	0	0	
	31+	0	0	0	0	0	0	0	1	2	
	Total	35	44	29	15	9	2	0	1	135	
Evidence of epilation		0	1							Total	
	0	58	15							73	0.67
	1	7	24							61	
	Total	65	69							134	
		0	1	2	3					Total	0.61
Size of epilation	0	58	14	2	0					74	
	1	7	31	9	0					47	
	2	0	4	5	0					9	
	3	0	0	3	2					5	
	Total	65	49	19	2					135	
Entropion grade		0	1	2	3	4				Total	0.52
	0	26	16	3	0	0				45	
	1	8	26	6	0	0				40	
	2	2	13	26	2	0				43	
	3	0	1	1	1	0				3	
	4	0	0	3	0	1				4	
	Total	36	56	39	3	1				135	

		0	1	2	3	4	5	6	Total	0.75
Corneal scar grade	0 (C0)	27	19	3	0	0	0	0	49	
	1 (C1)	2	24	5	0	2	0	0	33	
	2 (C2a)	2	1	23	1	1	0	0	28	
	3 (C2b)	0	0	0	1	0	0	0	1	
	4 (C2c)	0	0	2	2	15	1	0	20	
	5 (C2d)	0	0	0	0	1	1	0	2	
	6 (C3	0	0	0	0	0	0	2	2	
	Total	31	44	33	4	19	2	2	135	

å 20 cases with TT surgery excluded

Table 3.2: Inter-observer score (Observer B vs C, agreement highlighted in yellow)

Outcome Measures	Observer B	Observer C grades									Kappa score
Primary outcome (PTT)		0	1							Total	
	0	168	2							170	0.95
	1	1	38							39	
	Total	*169*	*40*							*209*	
ECA		0	1	2	3					Total	0.86
	0	148	7	0	0					155	
	1	5	37	1	0					43	
	2	0	1	10	0					11	
	3	0	0	0	0					0	
	Total	*153*	*45*	*11*	*0*					*209*	
Granuloma		0	1							Total	
	0	205	0							205	0.96
	1	0	4							4	
	Total	*205*	*40*							*209*	
Trichiasis grade		0	1	2	3					Total	0.93
	0	160	1	1	0					162	
	1	1	12	0	1					14	
	2	0	0	3	0					3	
	3	2	0	0	28					30	
	Total	*163*	*13*	*4*	*29*					*209*	
Lash count		0	1-2	3-5	6-9	10-14	15-20	21-30	31+	Total	0.84
	0	174	3	0	0	0	0	0	0	177	
	1-2	5	15	0	0	0	0	0	0	20	
	3-5	0	3	6	0	0	0	0	0	9	
	6-9	0	0	0	1	1	0	0	0	2	
	10-14	0	0	0	1	0	0	0	0	1	
	15-20	0	0	0	0	0	0	0	0	0	
	21-30	0	0	0	0	0	0	0	0	0	
	31+	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	
	Total	*179*	*21*	*6*	*2*	*1*	*0*	*0*	*0*	*209*	
Evidence of epilation		0	1							Total	
	0	195	2							197	0.92
	1	0	12							12	
	Total	*195*	*14*							*209*	

Outcome Measures	Observer B	Observer C grades									Kappa score
		0	1	2	3					Total	0.88
Size of epilation	0	195	2	0	0					197	
	1	0	5	1	0					6	
	2	0	1	2	1					4	
	3	0	0	0	2					2	
	Total	*195*	*8*	*3*	*3*					*209*	
Entropion grade		0	1	2	3	4				Total	0.76
	0	141	6	3	0	0				150	
	1	10	10	5	0	0				25	
	2	1	4	24	2	0				31	
	3	0	0	1	2	0				3	
	4	0	0	0	0	0				0	
	Total	*152*	*20*	*33*	*4*	*0*				*209*	
		0	1	2	3	4	5	6	7	Total	0.81
Corneal scar grade	0 (C0)	68	4	0	0	1	0	0	0	73	
	1 (C1)	15	26	2	1	3	0	0	0	47	
	2 (C2a)	2	8	25	3	3	0	0	0	41	
	3 (C2b)	0	0	0	3	0	0	0	0	3	
	4 (C2c)	1	0	3	1	25	2	0	0	32	
	5 (C2d)	0	0	0	1	0	9	0	0	10	
	6 (C3	0	0	0	0	0	0	2	0	2	
	7 (C4)	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*1*	
	Total	*86*	*38*	*30*	*9*	*32*	*11*	*2*	*1*	*209*	
Conjunctival scar grade, after surgery		1	2	3	4	5				Total	0.56
	1	0	0	0	0	0				0	
	2	0	1	4	0	0				5	
	3	0	0	47	18	1				66	
	4	0	0	14	63	3				80	
	5	0	0	0	4	6				10	
	Total	*0*	*1*	*65*	*85*	*10*				*161*[å]	
Level of correction (Central)*		0	1	2	3	4				Total	0.92
	0	46	0	1	0	0				47	
	1	0	2	1	1	0				4	
	2	2	0	142	3	0				147	
	3	0	0	2	8	0				10	
	4	0	0	0	0	1				1	
	Total	*48*	*2*	*146*	*12*	*1*				*209*	

*å 45 cases without TT surgery excluded. *Level of correction grading; 0 = no surgery; 1=overcorrection, 2=adequate correction, 3=partial under-correction, 4=under-correction.*

Figure 3.1 Inter-observer examination

3.1.2.2. *Team Training and Piloting*

Two field coordinators, ten field data collectors, a data entry clerk and two driver logisticians were appointed. These were provided practical training on the data collection tools, standard operating procedures and good clinical practices for five days. The vision related QoL and activity participation questionnaires were translated and back translated into Amharic (local language). For the health related QoL data collection, the WHO approved Amharic version WHOQoL-BREF was used. The fieldwork process and all data collections tools have been pilot tested in trichiasis surgical outreach. The interview including the QoL and activity participation data collection took between 40 and 60 minutes per participant to complete. Modifications were made to some of the questionnaires according to local understanding and contexts.

3.1.3. Trachomatous Trichiasis Cases

3.1.3.1. *Case Definition*

Trachomatous Trichiasis cases in this study were defined as: individuals with one or more eyelashes touching the eyeball or with evidence of epilation in either or both of the eyes, and tarsal conjunctival scarring.

3.1.3.2. *Inclusion Criteria*

1. Trachomatous Trichiasis with tarsal conjunctival scarring
2. Adults (≥18 years)
3. Agree to be randomly allocated to one of the two alternative operative procedures
4. Agree to re-examination at six and twelve months after surgery

3.1.3.3. *Exclusion Criteria*

1. Age less than 18 years
2. Previous eyelid surgery

3. Medically unfit, BP systolic >170, diastolic >110.
4. Pregnant
5. Patients with trichiasis from other eyelid pathologies, such as:
    - Blepharitis
    - Steven Johnson syndrome
    - Burn
    - Trauma
    - Eyelid muscle sub-laxity due to aging
    - Herpes zoster
    - Ocular cicatricial pemphigoid

3.1.4. Recruitment

Recruitment of trichiasis cases was done through community-based identification and by organising community-based surgical outreach campaigns (this is the current established practice in this part of Ethiopia) between February and May 2014. A mobile eye care team systematically visited communities in the districts, as per the programmes standard practice. People with trichiasis were identified mainly through door-to-door screening of older members of the community (≥15 years of age) for trichiasis through trained community based screeners and counsellors (Eye Ambassadors), Figure 3.2. Other methods such as community mobilization in markets and churches were also used. The recruitment was achieved within 4 months period.

Figure 3.2: Eye Ambassadors training

a) Theoretical training b) Practical training

3.1.5. Triaging Procedure

The following triaging procedure was used during the surgical outreach campaigns:

a. All people presenting at the recruitment location were examined using magnifying loupes and a torch for trichiasis (Figure 3.3). To check for exclusion criteria they were asked their ages and history of previous surgery. If they are a woman of childbearing age, they were also asked whether they might be pregnant.

b. ***Patients TT and no exclusion criteria:*** were invited to enrol in the trial. The study information sheet was read to them in Amharic. If they are willing they were then taken through the informed consent process.

c. ***Patients with TT and an exclusion criterion:*** were excluded from enrolment into the study, but were offered appropriate standard treatment (Epilation or Surgery).

d. ***Patients with non-trachomatous eye disease:*** were excluded from enrolment into the trial, and:

    i. Those with trachomatous eye disease but without trichiasis were offered standard treatment

    ii. Non-emergency conditions: manageable conditions at field setup were provided treatment. Otherwise a clear instruction to attend the nearest eye unit with a referral letter was provided.

    iii. Emergency conditions: were referred immediately to the nearest eye health facility or hospital

e. Trichiasis patients refusing surgery:

These were counselled to undergo surgery. If they still refused, they were offered epilation forceps with clear instruction on how to do the epilation.

Figure 3.3: Trial participants triaging

a) Examination for TT

b) Handing trial card for eligible cases

3.1.6. Baseline Assessment

Visual acuity and contrast sensitivity were measured. A single observer examined the participants' eyes with magnifying loupes and a torch for signs of trachoma using the detailed WHO grading system, with additional assessment of entropion and trichiasis severity (See Appendix III, section 9 for data record form), (Figure 3.4).[37] Digital photographs were taken of eyelid and cornea for independent grading. A photograph of their faces was also taken to help confirm identity at follow-up. Once the examination is completed the patient was guided to a separate area where the surgical procedure was being randomly allocated.

Figure 3.4: Examination and photography

a) Ocular examination

d) Clinical photography

3.1.7. Surgical Intervention

3.1.7.1. Surgeon Training and Standardisation

The Amhara Region trachoma control programme, which is supported by The Carter Center has trained more than 1000 trichiasis surgeons on the PLTR surgical procedure in the last 10 years. Among these surgeons, eight certified and highly productive trichiasis surgeons from West Gojam Zone and 1 ophthalmic nurse from Bahirdar Hospital were selected, trained and certified in the WHO recommended BLTR trichiasis surgical procedure by an experienced Ethiopian ophthalmologist. These were then sent back to their health facilities and practiced BLTR surgical procedure for about six months. Then they were called back for second assessment, standardisation and recertification by two assessors on both PLTR and BLTR surgical procedures. Six surgeons (5 TT surgeons and one ophthalmic nurse) who were regularly performing all component steps of both operations correctly, using the WHO certification procedures were chosen to operate in the trial, (Figure 3.5).

Figure 3.5: Surgeon training and standardisation

a) Practical training

b) Standardization using WHO checklist

3.1.7.2. *Randomisation, Allocation Concealment and Masking*

The randomised allocation was concealed in opaque, sequentially numbered envelopes. The sequences were prepared by a statistician independent of every other aspect of the trial, who securely hold the master list of the allocated treatment. To ensure reasonable balance in the allocation of treatments in different locations, the sequences were blocked into groups. The size of the blocks was random, were determined by the independent statistician and not divulged to the study team.

Directly after baseline clinical examination, patients were randomised into either of the treatment arms: BLTR Surgery or PLTR Surgery to the next available surgeon. Among the 6 surgeons, 2 or 3 operated at the same time on any given recruitment day. As surgical recurrence rates can vary between surgeons, each surgeon had their own randomisation sequence. The randomisation administrator along with this next available surgeon opened the next randomisation envelop to learn which operation to use on this patient. In bilateral cases, both eyes received the same operation. The outcome observers were masked to the intervention arm until the end of the trial.

3.1.7.3. Surgical Management

Based on the randomisation the surgical procedures used were the BLTR and PLTR. The procedure for these strictly followed the procedure described in the WHO trichiasis surgery manual. These two procedures are described in earlier section (section 1.12.3.1).

All the surgeries were performed free of charge in district and cluster health centres and health posts. All procedures followed strict aseptic technique. The patient needed to lie flat while the surgery is done. For both surgical procedures the eyelid and the surrounding area were cleaned, before the face is covered with a sterile towel with appropriate opening to access the eyelid. Then the conjunctiva is anaesthetised with a drop of topical anaesthetic (tetracaine). The conjunctival sac was cleaned using a drop of topical povidone iodine 5% ophthalmic solution. Then local anaesthetic (lidocaine 2% with adrenaline [1:100,000]) was injected into the skin of the eyelid to prevent pain during the surgery. After both surgeries, tetracycline eye ointment was applied on the sutured lid prior to patching it for about 12 hours.

All patients were provided with 1% tetracycline eye ointment with instructions of how to apply it twice a day for two weeks. The trichiasis surgeons and the surgical assistants demonstrated to all patients and/or their relatives the amount of the tetracycline ointment to be applied and the part of the eyelid it shall be applied.

3.1.8. Intraoperative Assessment

During the operations, three well-trained and standardised nurses measured and document the incision length, incision distance from the lid margin, suture position and tension, duration of surgery and complications (Figure 3.6a). The operated lid was examined for degree of correction, eyelid contour abnormality and lid closure immediately after the completion of the surgery (Figure 3.6b). Then two photographs of the operated eyelid were taken in up gaze and primary position (straight) at the end of the operation for independent grading. Just before the patients exited the operation room, they were asked to rate the pain they experienced during the surgery. Please see Appendix III, section 10 for the intraoperative observations data record form.

Figure 3.6: Intra and postoperative measurements and observations

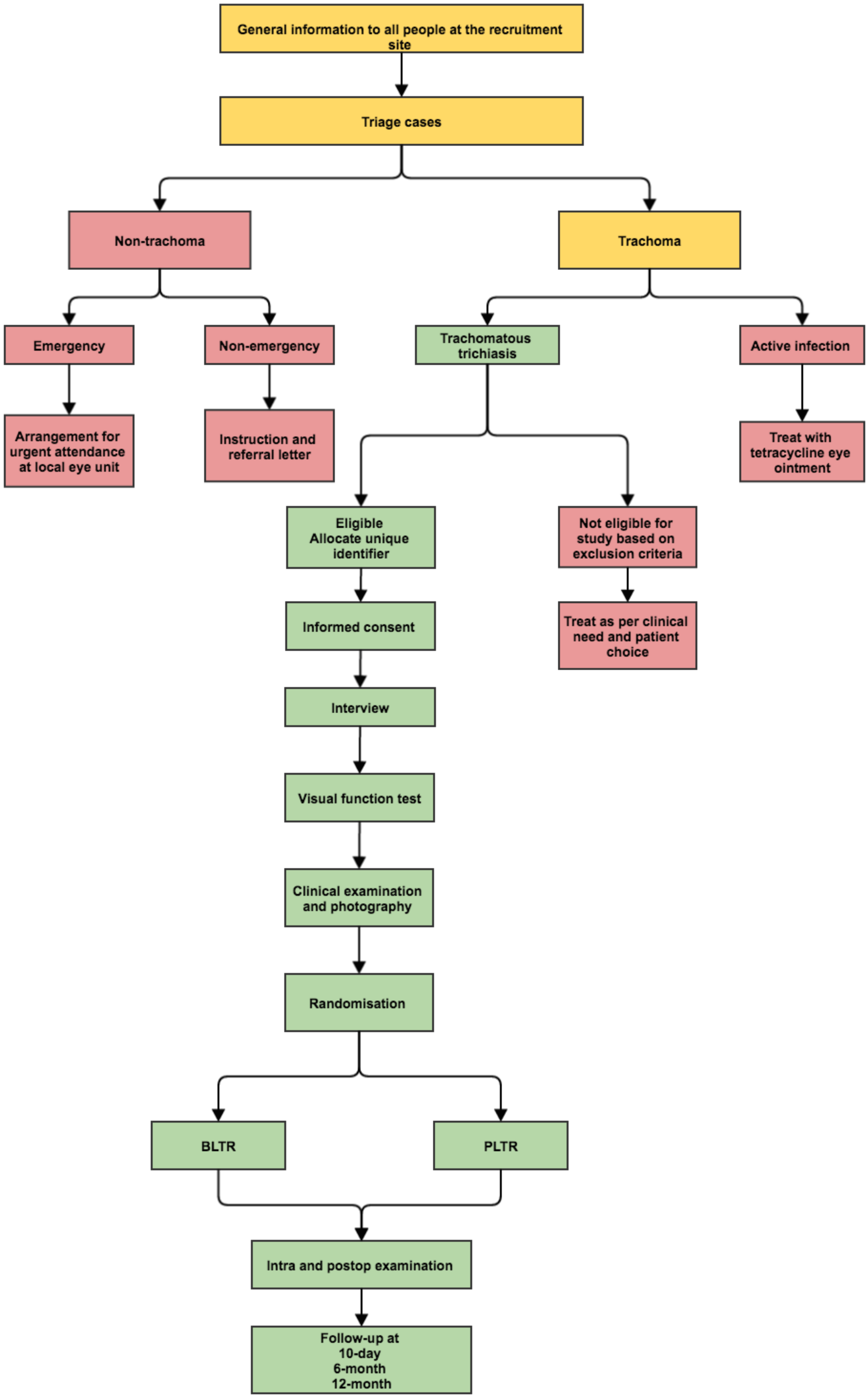
a) Intra operative measurement

b) Intra operative observations

3.1.9. Follow-up Assessment

Trial participants were re-assessed at three time points at 7-10 days, 6-months and 12-months from the point of enrolment. All participants were given appointment cards for their next follow-up and were reminded a week prior to the follow-up date. The "village development army" and the 1 to 5 village organization system, and the Eye Ambassadors were used to locate the subject's home and aid the follow-up process. Participants who did not present for their follow-up visit were traced (Figure 3.8). Reasons for the loss to follow-up were identified. If sick or moved within accessible areas, a follow-up assessment was arranged in their houses or villages. These helped to achieve high follow-up rates.

Figure 3.7: Participant enrolment procedure for the RCT



At the 7-10 day follow-up operated eyelids were examined for postoperative trichiasis level of correction and sign of infection and other postoperative complications and outcomes; and were asked based on a predesigned questionnaire by a trained Health Officer. Patients were asked to rate the pain they experienced between the surgery and the suture removal date. Then the sutures were removed.

Figure 3.8: Study participants tracking

At the 6 and 12 moth follow-ups, visual acuity and contrast sensitivity were measured and the operated eyes were examined mainly for postoperative TT, level of correction, eyelid contour abnormality, granuloma, corneal opacity, and conjunctival scarring and inflammation. They were also asked about their satisfaction with the outcome of the surgery they had for treating the trichiasis and the cosmetic appearance of the eyelid. Photographs of the operated eyelid were taken after covering the incision area of the upper eyelid with specifically designed occluder (Figure 3.9) for independent photographic grading, to validate the field grading.

Figure 3.9: Photograph of upper eyelid taken with occluder to cover incision area

During the follow-ups, the faces of the participants were compared with the full-face photograph taken at baseline to confirm participant identity. All participants with postoperative trichiasis at follow-ups were offered surgical treatment or epilation. Participants with other ocular conditions were advised and referred to the nearest eye health facility.

3.2. Cases Control Studies

Case control studies were nested with in the Randomised Controlled Trial 1) To quantitatively measure the association between trachomatous trichiasis and relative household poverty and; 2) To evaluate the impact of trachomatous trichiasis on quality of life.

3.2.1. Trachomatous Trichiasis and Relative Household Poverty

3.2.1.1. Participants

Cases: for this study were every fifth consecutive TT cases enrolled into the above clinical trial, which gives a sample of 200 cases.

Controls: were individuals without clinical evidence or a history of trichiasis (including surgery and epilation), and who came from households without a family member with trichiasis or a history of trichiasis. One control was individually matched to each trichiasis case by location, sex and age (+/- two years).

3.2.1.2. Controls Recruitment

The research team visited the sub-village (30–50 households) of the trichiasis case requiring a matched control. A list of all potentially eligible people living in the sub-village was compiled with the help of the sub-village administrator. One person was randomly selected from this list using a lottery method, given details of the study and invited to participate if eligible. If a selected individual refused or was ineligible, another was randomly selected from the list. When eligible controls were not identified within the sub-village of the case, recruitment was done in the nearest neighboring sub-village, using the same procedures.

3.2.1.3. Data Collection

Household poverty was measured using a) asset based poverty index, b) peer-rated wealth and c) self-rated wealth in the households of both cases and controls (Appendix III, section 12, 6 and 11 respectively). For the asset based poverty analysis data was mostly collected by observation and through interview with the household head (if other than study participant), Figure 3.10. To measure peer rated wealth, three member of village administration living in the same village ("Got") with the cases and the controls were randomly selected and asked to rate the socio-economic status of the household under study on a five point scale. Then the responses were later averaged to produce a score of the household's socioeconomic status in relative to the other households in the village. Similarly, for the self-rated wealth, study participants were asked to rate the socioeconomic or wealth status of their household in relative to other household in their villages.

In addition, to evaluate how much TT impends engagement in productive and leisure activities, data was collected on activity participation using a modified 'stylised activity list' developed for the World Bank's Living Standards Measurement Survey (LSMS), Appendix III, section 4).[239] Participants were asked whether they had been involved in each of a list of common daily activities during the last week. If they were involved in an activity, they were asked to rate how much difficulty they had in doing that particular activity; and whether or not they have received assistance during the previous week while doing the activity.

Figure 3.10: Collecting asset data

3.2.2. Impact of Trachomatous Trichiasis on Quality of Life

Controls are the same with the poverty study above, except that the cases for this QoL study are all 1000 trichiasis cases enrolled into the clinical trial comparing the two surgical procedures.

Data on VRQoL and HRQoL was collected using the WHO/PBD VFQ(20) and WHOQOL-BREF respectively, from both cases and controls (Figure 3.11). These tools are discussed in section 1.17.1 of this thesis in detail.

Figure 3.11: Collecting quality of life data

3.3. Longitudinal Studies

The longitudinal studies were again parts of the clinical trial and the nested cases control study with in the trial. "Cases/exposed" in these were the 1000 trichiasis cases enrolled into the trial and "comparison participants/unexposed" were the 200 controls recruited into the case control studies. The studies were conducted to measure 1) The impact of TT surgery QoL and; 2) The impact of TT surgery on daily living.

For the former, data on VRQoL and HRQoL were collected 12-months after enrolment from cases (after trichiasis surgery) and comparison participants using the same tools used at the baseline. The difference in QoL change between baseline and 12-months follow-up within cases and comparison participants; and the difference of the baseline – follow-up QoL score differences between cases and comparison participants were compared. In addition, factors predicting QoL change among trichiasis cases were looked at.

For the later, data on activity participation, difficulty and assistance were collected in both cases and comparison participants 12-months after enrolment (after trichiasis surgery for cases), Figure 3.12. The change in proportion of cases engaging in productive and leisure activities, executing productive and leisure activities without difficulty and assistance were analysed and compared with the changes in the comparison participants, which did not receive any intervention.

Figure 3.12: Collecting data on activity participation

3.4. General Methods Summary

3.4.1. Ethics Approval

The London School of Hygiene & Tropical Medicine's Ethics Committee and Emory University IRB representing The Carter Center have approved this study project. Then this was reviewed and approved again in Ethiopia by the National Health Research Ethics Review Committee (NRERC) of the Ethiopian Ministry of Science and Technology. The Food Medicine And Healthcare Administration And Control Authority of Ethiopia (FMHACA) has provided a regulatory approval for the clinical trial. The Amhara Regional Health Bureau Review Board provided full support for the conduct of the study project in the region.

3.4.2. Informed Consent

Participants were informed about the nature of the study and asked if they would be willing to participate. Cases were asked if they would be willing to be randomised to alternative surgical procedures and be followed for a year. The information document was read to them in Amharic, Figure 3.13. They have been clearly told that close-up photographs of the eyelids and cornea as well as the face will be taken.

Information on asset data was collected after an informed consent was given by the household head in addition to the informed consent by the study participant. The informed consent process was conducted by experienced and well-trained field workers; which were supported by an Ophthalmic Officer trained in eyelid surgery and the details of the study, and therefore competent to provide answers to questions.

Figure 3.13: Informed consent with independent witness

3.4.3. Data Management

Data were archived in the locked, dedicated study office, which is located within the secure compound of the Carter Center programme office in Bahirdar. Paper data were filed based on registration number and were only accessed by the trial coordinators. The data were double entered in to Microsoft Access and stored in a password protected computer isolated from the internet in this secured office. All data record forms were scanned and stored in PDFs. Both text and picture data were backed-up in five password protected external hard drives regularly. Participants' identification data was only used for the registration and follow-up process. Analysis was done using an annonymised dataset. Picture data were only collected and stored in electronic copy in a password protected computer.

3.4.4. Study Monitoring

An independent Data and Safety Monitoring Board (DSMB) was appointed by the trial steering committee. These were 5 people, all independent of the running of the trial with relevant clinical and epidemiological experience. The DSMB monitored recruitment and implementation of procedures as per standard protocols. The DSMB met three times during the recruitment and follow up periods to assess the safety of the trial procedures. The DSMB visited the study sites once during recruitment.

4. Posterior Lamellar Versus Bilamellar Tarsal Rotation Surgery for Trachomatous Trichiasis in Ethiopia: A Randomised Controlled Trial

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RESEARCH PAPER COVER SHEET FOR RESEARCH PAPERS ALREADY PUBLISHED

Section A - Student details

Student	Esmael Habtamu Ali
Principal Supervisor	Prof Matthew Burton
Thesis Title	Trachomatous Trichiasis: Surgical Management and Impact

Section B - Published Paper Details

Where was the work published?	Lancet Global Health
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If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	Work part of the PhD registration
Have you retained the copyright for the work?	Yes. Please see first page of the published paper where the following is indicated: *"Copyright © Habtamu et al. Open Access article distributed under the terms of CC BY"*
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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper	With senior colleagues I designed the study and prepared the protocol / SOP, led the research project and collected data, analysed data and wrote the first draft of the paper with edits from my supervisor and co-authors.

Student Signature: Esmael Habtamu Ali Date: 15th December 2016

Supervisor Signature: Prof. Matthew Burton
Date: 1st December 2016

Posterior lamellar versus bilamellar tarsal rotation surgery for trachomatous trichiasis in Ethiopia: a randomised controlled trial

Esmael Habtamu, Tariku Wondie, Sintayehu Aweke, Zerihun Tadesse, Mulat Zerihun, Zebideru Zewudie, Amir Bedri Kello, Chrissy H Roberts, Paul M Emerson, Robin L Bailey, David C W Mabey, Saul N Rajak, Kelly Callahan, Helen A Weiss, Matthew J Burton

Summary

Background Eyelid surgery is done to correct trachomatous trichiasis to prevent blindness. However, recurrent trichiasis is frequent. Two procedures are recommended by WHO and are in routine practice: bilamellar tarsal rotation (BLTR) and posterior lamellar tarsal rotation (PLTR). This study was done to identify which procedure gives the better results.

Methods A randomised, controlled, single masked clinical trial was done in Ethiopia. Participants had upper lid trachomatous trichiasis with one or more eyelashes touching the eye or evidence of epilation, in association with tarsal conjunctival scarring. Exclusion criteria were age less than 18 years, recurrent trichiasis after previous surgery, hypertension, and pregnancy. Participants were randomly assigned (1:1) to either BLTR or PLTR surgery, stratified by surgeon. The sequences were computer-generated by an independent statistician. Surgery was done in a community setting following WHO guidelines. Participants were examined at 6 months and 12 months by assessors masked to allocation. The primary outcome was the cumulative proportion of individuals who developed recurrent trichiasis by 12 months. Primary analyses were by modified intention to treat. The intervention effect was estimated by logistic regression, controlled for surgeon as a fixed effect in the model. The trial is registered with the Pan African Clinical Trials Registry (number PACTR201401000743135).

Findings 1000 participants with trichiasis were recruited, randomly assigned, and treated (501 in the BLTR group and 499 in the PLTR group) between Feb 13, 2014, and May 31, 2014. Eight participants were not seen at either 6 month or 12 month follow-up visits and were excluded from the analysis: three from the PLTR group and five from the BLTR group. The follow-up rate at 12 months was 98%. Cumulative recurrent trichiasis by 12 months was more frequent in the BLTR group than in the PLTR group (110/496 [22%] *vs* 63/496 [13%]; adjusted odds ratio [OR] 1·96 [95% CI 1·40–2·75]; p=0·0001), with a risk difference of 9·50% (95% CI 4·79–14·16).

Interpretation PLTR surgery was superior to BLTR surgery for management of trachomatous trichiasis, and could be the preferred procedure for the programmatic management of trachomatous trichiasis.

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Introduction

Trachoma, a neglected tropical disease caused by *Chlamydia trachomatis*, is the leading infectious cause of blindness.[1] Recurrent infection drives progressive conjunctival scarring, which turns the lid and eyelashes in towards the eye (trichiasis) resulting in pain and eventually blinding corneal opacification. About 1·2 million people are irreversibly blind from this disease and about 7·2 million have trichiasis.[1,2] WHO recommends the SAFE strategy for trachoma control: Surgery for trichiasis, Antibiotics, Facial cleanliness, and Environmental improvement.[3] Trichiasis surgery reduces the risk of sight loss by correcting the in-turned eyelid, thus stopping the corneal damage. Surgery involves an incision through the scarred upper eyelid, parallel to the lid margin, outward rotation, and suturing in the corrected position.[4] Due to the limited number of ophthalmologists in most trachoma-endemic countries, surgery is usually done by non-physicians with limited training, equipment, and time.[3] Given these constraints, the technique needs to be simple, safe, and quick to do, whereas at the same time giving consistently good results.

Unfortunately, trichiasis frequently recurs after surgery. This outcome represents a substantial limitation in preventing sight loss from trachoma. Studies have reported trichiasis recurrence rates between 10% at 3 months and up to 60% at 3 years, with an average of around 20% at 1 year.[5–14] Several factors contribute to recurrent trichiasis, including preoperative disease severity, surgeon skill, and surgical procedure.[15] Among these, operation type is a major determinant of outcome and subtle variations in procedure performance probably affect results.[10,11,16] Many different surgical procedures have been used to correct trichiasis, with some evidence that

Research in context

Evidence before this study

Members of our study group recently published a systematic review of the management of trachomatous trichiasis (Burton and colleagues, 2015). When preparing this systematic review, we searched CENTRAL, Ovid MEDLINE, Embase, ISRCTN registry, ClinicalTrials.gov, and WHO ICTRP. We searched until May 7, 2015, using the search terms "trachoma" and "trichiasis". See the review's appendix for full search methods for each database. We identified one previous randomised trial (Adamu and Alemayehu, 2002), which compared variants of the BLTR and PLTR procedure done by ophthalmologists in a teaching hospital environment in Ethiopia; 153 patients were randomly assigned and followed for 3 months. No evidence of a difference in outcome was found. However, this earlier study was constrained by a small sample size and short duration. The surgery was performed in a teaching hospital setting by ophthalmologists, in contrast to the health centre provision by non-physicians typical of trachoma control programmes, limiting the conclusions that can been drawn.

Added value of this study

Our trial was designed to compare the two most common operations used to treat trachomatous trichiasis to determine which gives the best results in terms of disease recurrence and complications in a programmatic setting. The results show that the PLTR was superior to BLTR because it had a substantially lower trichiasis recurrence rate by 1 year and fewer intraoperative and immediate postoperative complications.

Implications of all the available evidence

This study provides evidence of superiority of PLTR, suggesting that it could be the best procedure for the programmatic management of trachomatous trichiasis. We suggest that new surgical trainees in both established and new programmes be trained in the PLTR procedure. Another trial examining the outcomes of PLTR surgery done by surgeons previously trained in BLTR surgery should be considered.

bilamellar tarsal rotation (BLTR) is better than others to which it has been formally compared.[10,11,15,17] However, it is important to determine which is the best of these options.

About 20 years ago several procedures were compared with the BLTR operation in randomised controlled trials.[10,11] The findings from these trials showed that the BLTR procedure had the lowest trichiasis recurrence rate of the procedures compared (about 20% at 1 year), leading WHO to recommend it as the preferred operation.[3] However, the most commonly used alternative procedure, the posterior lamellar tarsal rotation (PLTR) or Trabut operation, was not included in these earlier trials. One earlier randomised trial from Ethiopia compared variants of the BLTR and PLTR, and found no difference. However, that trial was relatively small, with only 3 months' follow-up and was done by ophthalmologists in a teaching hospital, precluding conclusions for control programmes that do the vast majority of trichiasis surgery.[13]

There is an unprecedented effort to scale up global trichiasis surgery output and improve outcomes, to clear the huge trichiasis backlog. This effort requires training many trichiasis surgeons on the easiest, safest, and most successful operation with the least recurrence and complications. There is an urgent need to examine rigorously which of these two most frequently performed operations has the best outcomes in a programmatic setting, with an adequate sample size and follow-up period. This question was identified as a research priority several years ago by the WHO Alliance for the Global Elimination of Trachoma by 2020 (GET2020).[18] The aim of our trial was to determine whether BLTR or PLTR surgery gives superior results under programmatic conditions.

Methods

Study design and participants

This was a single-masked, individual-randomised, controlled trial done in Ethiopia. Adults with trachomatous trichiasis were randomly allocated to either BLTR or PLTR surgery, stratified by surgeon, and followed up for 1 year. The study was approved by the Ethiopian National Health Research Ethics Review Committee, the London School of Hygiene & Tropical Medicine Ethics Committee, Emory University Institutional Review Board, and the Ethiopia Food, Medicine and Healthcare Administration and Controls Authority. The trial was done in compliance with the Declaration of Helsinki and International Conference on Harmonisation–Good Clinical Practice. An independent data and safety monitoring committee oversaw the trial.

Participants had upper lid trachomatous trichiasis with one or more eyelashes touching the eye or evidence of epilation, in association with tarsal conjunctival scarring. We excluded people with trichiasis due to other causes, recurrent trichiasis after previous surgery, hypertension, pregnancy, and those under 18 years. Patients were recruited mainly through community-based screening in three districts of West Gojam Zone, Amhara Region, Ethiopia. Recruitment and surgery were performed in community level health centres. Written informed consent in Amharic was obtained before enrolment from participants. If a participant was unable to read and write, the information sheet and consent form were read to them and their consent recorded by thumbprint.

Randomisation and masking

Participants were randomly assigned (1:1) to either PLTR or BLTR surgery for each surgeon, with random block sizes of 4 or 6. Randomisation was stratified by surgeon because of potential intersurgeon variability. The sequences were computer-generated by an independent statistician. Separate allocation sequences for each surgeon were concealed in sequentially numbered, sealed, opaque envelopes. A person independent of all other aspects of the trial prepared these envelopes.

On most recruitment days, two surgeons operated simultaneously. Following baseline examination, participants were allocated to the next available surgeon. A fieldworker was responsible for implementing the intervention assignment in a dedicated area. The fieldworker and surgeon jointly confirmed the allocation and recorded this in the surgical logbook. The different surgical equipment sets for the two procedures were kept separately. The randomisation fieldworker and surgeon jointly collected the appropriate surgical set for the allocated procedure. Surgeons and patients were aware of the allocation. The two examiners (EH, SA) who were responsible for clinical observations at baseline, 6 months, and 12 months were masked to the allocation. They were not involved in the allocation process, surgery, postoperative care, or the 10 day follow-up. The intraoperative and 10 day observations were made by separate fieldworkers who could not be masked to the allocation.

Procedures

At the preoperative assessment before randomisation, demographic characteristics were recorded. Presenting logMAR (logarithm of the minimum angle of resolution) visual acuity at 2 m was measured using PeekAcuity software on a smartphone in a dark room.[19] For visual acuities of counting fingers or less, logMAR values were attributed as follows: counting fingers, 2·0; hand movements, 2·5; perception of light, 3·0; and no perception of light, 3·5.[8] We assessed contrast sensitivity with a prototype smartphone-based test that presents calibrated grey scale spots against a white background, which are identified by touch.

Eyes were examined by a single examiner (EH) using 2·5× binocular loupes and torch, and graded using the Detailed WHO FPC Grading System.[20] Lashes touching the eye were counted and subdivided by the part of the eye contacted: cornea, lateral, or medial conjunctiva. Trichiasis subtypes were recorded: metaplastic, misdirected, and entropic.[21] Clinical evidence of epilation was identified by broken or newly growing lashes, or areas of absent lashes. Upper lid entropion was graded by assessing the degree of eyelid margin inward rotation.[21] Corneal scarring was graded using a previously described detailed system.[20] Three standardised high-resolution digital photographs of trichiasis, cornea, and tarsal conjunctiva were taken, using a Nikon D90 digital SLR camera with 105 mm macro lens and R1C1 flash units.[22]

Before recruitment, nine experienced trichiasis nurse-surgeons, already trained, certified, and regularly performing PLTR surgery were trained in BLTR surgery. We followed the procedures described in the WHO Trichiasis Surgery for Trachoma manual.[4] After training, surgeons were carefully observed throughout five operations and certified as correctly doing the procedure following the standardisation checklist.[4] Surgeons then returned to their usual workplace, and regularly performed BLTR for 6 months. They then returned for repeat standardisation, assessment, and certification on both PLTR and BLTR procedures by two assessors. Before

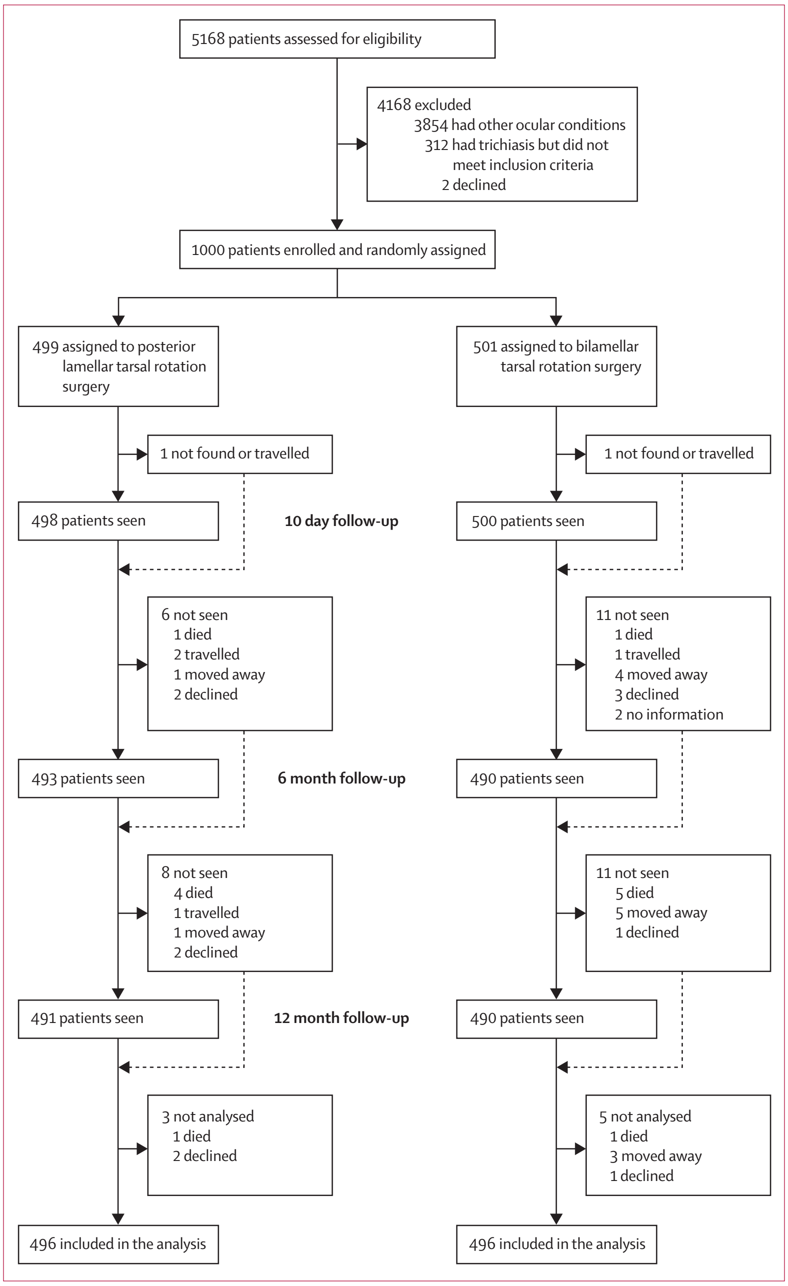

Figure: Trial profile

	Baseline		12 months	
	PLTR group (n=499)	BLTR group (n=501)	PLTR group (n=491)	BLTR group (n=490)
Sex (female)	388 (78%)	377 (75%)	..	..
Age, years (mean, SD)	47·2 (15·0)	47·5 (14·9)	..	..
Illiterate	441 (88%)	445 (89%)	..	..
Best corrected logMAR visual acuity in study eye				
−0·1 to 0·3	141 (28%)	137 (27%)	175 (36%)	169 (34%)
0·3 to 0·7	190 (38%)	209 (42%)	186 (38%)	212 (43%)
0·7 to 1·1	107 (21%)	103 (21%)	90 (18%)	78 (16%)
1·1 to 2·0	18 (4%)	18 (4%)	10 (2%)	10 (2%)
CF/HM/PL	37 (7%)	27 (5%)	25 (5%)	15 (3%)
NPL	6 (1%)	7 (1%)	4 (1%)	5 (1%)
Not possible to measure	..	..	1 (<1%)	1 (<1%)
Entropion grade				
0	11 (2%)	7 (1%)	467 (95%)	446 (91%)
1	93 (19%)	85 (17%)	17 (3%)	39 (8%)
2	315 (63%)	334 (67%)	6 (1%)	5 (1%)
3	71 (14%)	66 (13%)	1 (<1%)	0
4	9 (2%)	9 (2%)	0	0
Trichiasis (number of lashes)				
No trichiasis	..	..	445 (91%)	405 (83%)
None (epilating)	38 (8%)	44 (9%)	7 (1%)	13 (3%)
1–5	316 (63%)	312 (62%)	37 (8%)	66 (13%)
6–9	87 (17%)	87 (17%)	1 (<1%)	5 (1%)
10–19	41 (8%)	46 (9%)	1 (<1%)	1 (<1%)
20+	17 (3%)	12 (2%)	0	0
Mean (SD)*	5·6 (6·6)	5·4 (5·7)	2·7 (2·7)	2·6 (2·5)

(Table 1 continues on next page)

commencing the trial, each surgeon had done about 100 BLTR procedures (median 117, range 94–137). The best six surgeons did the surgery in this trial: they were all certified as consistently performing all component steps of both operations correctly, using the WHO certification procedures.

The procedures are described in detail in the WHO manual.[4] Briefly, in the PLTR the eyelid is everted, an incision is made through the tarsal conjunctiva and tarsal plate (posterior lamella), parallel to and 3 mm above the lid margin. The posterior lamella is separated from the anterior lamella (orbicularis muscle and skin). Three sutures are placed to externally rotate and fix the eyelid. In the BLTR the eyelid is fixed with a clamp (Waddell type), of an appropriate size.[23] A full-thickness incision is made through the anterior and posterior lamellae, parallel to and 3 mm above the lid margin. Three sutures are placed to externally rotate and fix the eyelid. Surgery was done under subcutaneous local anaesthesia (2–3 mL of lidocaine 2%, with adrenaline). In both surgical procedures, 4/0 silk sutures with 3/8th circle, 19 mm cutting needles were used. Surgery duration was measured and complications documented. Post-operatively, operated eyes were padded for 1 day and tetracycline eye ointment 1% was self-administered twice daily for 2 weeks. Participants were not given perioperative oral azithromycin because it is not the operational practice to use it in this region.

Participants were examined at 10 days, 6 months, and 12 months after operation. At 10 days, data were collected on patient-reported outcomes (improvement in preoperative symptoms, postoperative pain, and functioning). Participants were examined for recurrence, degree of lid eversion, infection, granulomata, and eyelid contour abnormality (ECA) before suture removal.

At 6 months and 12 months participants were re-examined following the same procedures as for baseline (SA at 6 months and EH at 12 months). The examiners were standardised and had very strong agreement for the primary outcome in grading validation studies (κ=0·95). Based on severity, trichiasis cases were categorised into minor trichiasis with less than six lashes or evidence of epilation in less than one third of the lid margin, and major trichiasis with six or more lashes or evidence of epilation in one third or more of the lid margin. The degree of entropion correction was graded as follows: (grade 1) extra eversion: main lashes point superiorly, whole lid margin visible, and tarsal plate surface visible; (grade 2) lid margin eversion: lashes point superiorly, whole lid margin visible, and tarsal surface not visible; (grade 3) partial lid margin entropion: some parts of the lashes might point anteriorly and some part of the lid margin not visible; (grade 4) total lid margin entropion: lashes might point inferiorly or towards the globe and lid margin is not visible. We considered grade 1 over-correction, grade 2 normal correction, and grades 3 and 4 under-correction. Granulomata were defined as fleshy tissue growth of at least 2 mm on the tarsal conjunctiva or at the edge of the eyelid.[12] Grading of ECAs was based on the PRET trial method: mild, vertical deviation from the natural contour less than 1 mm in height and affecting more than one third of horizontal eyelid length; moderate, vertical deviation from the natural contour 1–2 mm in height or affecting one third to two thirds of horizontal eyelid length; severe, vertical deviation from the natural contour more than 2 mm in height or a defect more than two thirds the horizontal eyelid length.[24] These were regrouped as: clinically non-significant ECA, which included mild ECA; and clinically significant ECA, which included moderate-to-severe ECA. The clinically significant ECAs also included other ECAs such as divot, which is a scarred depression or tissue loss including lashes at the eyelid margin. Visual acuity and contrast sensitivity were measured at 12 months. Data on patient-reported outcomes were collected at 12 months. Individuals with recurrent trichiasis during follow-up were offered repeat surgery. Participants with other ophthalmic pathology (eg, cataract) were referred.

High-resolution digital photographs of upper eyelid, cornea, and tarsal conjunctiva were taken at 6 months and 12 months.[22] To address potential concerns of bias which might arise from identifying procedure type from surgical scars, the upper eyelid photograph was taken after covering the incision area with a shaped occluder to prevent any unmasking of the independent photograph grader (an ophthalmologist with 15 years' experience of examining for trachomatous trichiasis). Images were viewed on a 15 inch high-resolution "retina" screen (Apple). Trachomatous trichiasis was considered to be present if there was one or more lashes touching the eye, identified by the lashes deviating over the globe and appearing to touch the eye.

Outcomes

The primary outcome was the cumulative proportion of individuals who developed recurrent trichiasis by 12 months. Recurrent trichiasis was defined as one or more lashes touching the eye or clinical evidence of epilation, or a history of repeat trichiasis surgery by 12 months. A-priori defined secondary outcome measures were: recurrent trichiasis at 6 months and 12 months; trichiasis recurrence difference by surgeon; trichiasis recurrence difference by baseline disease severity; number, type, and location of recurrent lashes at 12 months; corneal opacity, vision, and contrast sensitivity changes at 12 months; intraoperative, immediate, and late postoperative surgical complications (bleeding, infection, and granulomas); ECA at 12 months; and patient-reported outcomes.

Statistical analysis

In the STAR trial, the 1 year trichiasis recurrence rate using BLTR surgery was about 10% (tetracycline group).[5] In our recent trials in Ethiopia involving patients with a similar severity of disease to the STAR trial, we found PLTR surgery had a 1 year recurrence rate of 18%.[8] A sample of 836 participants was estimated to have 90% power and 95% confidence to detect a similar difference in recurrent trichiasis (18% *vs* 10%). Therefore, we aimed to recruit 1000 cases (500 in each group), to allow for about 15% loss to follow-up.

Data were double-entered into Access 13 (Microsoft) and transferred to Stata 11 (StataCorp) for analysis. For participants who had bilateral surgery, we randomly designated one eye to be the study eye for the analysis. A modified intention-to-treat analysis was done, with primary outcome data analysed on all participants seen at either the 6 month or 12 month follow-up or both. Those not seen at either of these follow-up visits were excluded from the analysis.

The primary outcome and binary secondary outcomes were compared between the two surgical groups with logistic regression analyses to estimate the odds ratio (OR) and 95% CI. All comparisons between the two surgical procedures were controlled for surgeon as a fixed effect in the model to account for the stratified randomisation. The risk difference in the primary outcome (recurrent trichiasis by 12 months) between BLTR and PLTR procedures was estimated. The possibility of effect modification between group and a-priori defined factors such as surgeon, preoperative trichiasis severity, papillary inflammation, age, and sex was investigated by including interaction terms in the model and using a likelihood ratio test to assess statistical significance of the interaction term. Ordered categorical secondary outcomes (changes in visual acuity and corneal opacity, bleeding, and patient-reported outcomes) were compared between the two surgical interventions using ordinal logistic regression. Categorical secondary outcomes (type and location of recurrent lashes, ECAs, and entropion correction) were analysed using multinomial logistic regression to estimate relative risk ratio (RRR) and 95% CI. Negative binomial regression

	Baseline		12 months	
	PLTR group (n=499)	BLTR group (n=501)	PLTR group (n=491)	BLTR group (n=490)
(Continued from previous page)				
Lash location				
None (epilating)	38 (8%)	45 (9%)	7 (15%)	13 (15%)
Corneal with or without peripheral	450 (90%)	451 (90%)	30 (65%)	59 (69%)
Peripheral only	11 (2%)	5 (1%)	9 (20%)	13 (15%)
Corneal opacity				
None (CC0)	121 (24%)	132 (26%)	155 (32%)	159 (32·5)
Peripheral (CC1)	204 (41%)	201 (40%)	140 (29%)	157 (32·0)
Off centre faint (CC2a)	94 (19%)	94 (19%)	98 (20%)	85 (17%)
Off centre dense (CC2b)	19 (4%)	11 (2%)	7 (1%)	4 (1%)
Central faint (CC2c)	48 (10%)	50 (10%)	77 (16%)	76 (16%)
Central dense (CC2d)	7 (1%)	7 (1%)	10 (2%)	5 (1%)
Total central dense (CC3)	4 (1%)	6 (1%)	2 (<1%)	4 (1%)
Phthisis (CC4)	2 (<1%)	0	2 (<1%)	0
Tarsal conjunctiva inflammation				
None (P0)	6 (1%)	9 (2%)	9 (2%)	12 (2%)
Mild (P1)	117 (23%)	131 (26%)	104 (21%)	98 (20%)
Moderate (P2)	306 (61%)	297 (59%)	332 (68%)	321 (66%)
Severe (P3)	70 (14%)	64 (13%)	46 (9%)	59 (12%)
Tarsal conjunctival scarring				
None (C0)	0	0	..	..
Mild (C1)	51 (10%)	56 (11%)	..	..
Moderate (C2)	373 (75%)	367 (73%)	..	..
Severe (C3)	75 (15%)	78 (16%)	..	..
Recurrent trichiasis by surgeon†				
1	..	..	8/89 (9%)	27/91 (30%)
2	..	..	14/95 (15%)	17/93 (18%)
3	..	..	12/84 (14%)	17/85 (20%)
4	..	..	10/92 (11%)	17/91 (19%)
5	..	..	6/47 (13%)	12/47 (26%)
6	..	..	13/89 (15%)	20/89 (22%)

Data are n (%) unless otherwise stated. BLTR=bilamellar tarsal rotation. PLTR=posterior lamellar tarsal rotation. CF=counting fingers. HM=hand movement. PL=perception of light. NPL=no perception of light. *Excluding those with no lashes touching the eyeball. †Data are n/N (%).

Table 1: **Baseline and 12 month characteristics of participants**

	PLTR group	BLTR group	OR or RRR (95% CI)	p value
Cumulative recurrence by baseline trichiasis severity*				
Minor trachomatous trichiasis	26/266 (10%)	36/257 (14%)	1·47 (0·85–2·53)	0·16
Major trachomatous trichiasis	37/230 (16%)	74/239 (31%)	2·29 (1·46–3·59)	0·0003
Cumulative recurrence by baseline entropion severity*				
None or mild	11/102 (11%)	28/90 (31%)	3·98 (1·80–8·80)	0·0007
Moderate	37/314 (12%)	59/331 (18%)	1·59 (1·02–2·49)	0·04
Severe	15/80 (19%)	23/75 (31%)	2·04 (0·95–4·37)	0·07
Number of recurrent lashes (mean, SD)†	2·67 (2·72)	2·65 (2·45)	0·97‡ (0·71–1·32)	0·84
Types of recurrent lashes§				
Entropic	4/46 (9%)	10/85 (12%)	1·79¶ (0·48–6·69)	0·38
Metaplastic (base outcome)	32/46 (70%)	55/85 (65%)	1	..
Misdirected	3/46 (6%)	7/85 (8%)	1·37¶ (0·32–5·99)	0·67
Epilating	7/46 (15%)	13/85 (15%)	1·26¶ (0·43–3·69)	0·68
Location of recurrent lashes§				
Corneal or corneal and peripheral (base outcome)	30/46 (65%)	59/85 (69%)	1	..
Peripheral	9/46 (20%)	13/85 (15%)	0·82¶ (0·30–2·22)	0·69
Epilating	7/46 (15%)	13/85 (15%)	1·08¶ (0·37–3·12)	0·89
Visual acuity change‖				
Worse	123/490 (25%)	111/489 (23%)	0·97 (0·77–1·23)	0·81
Same	172/490 (35%)	198/489 (41%)		
Better	195/490 (40%)	180/489 (37%)		
Contrast sensitivity‖				
Worse	114/490 (23%)	100/489 (20%)	1·05 (0·83–1·32)	0·71
Same	149/490 (30%)	165/489 (34%)		
Better	227/490 (46%)	224/489 (46%)		
Corneal opacity change‖				
More opacity	84/491 (17%)	68/490 (14%)	1·19 (0·92–1·55)	0·19
No change	329/491 (67%)	338/490 (69%)		
Less opacity	78/491 (16%)	84/490 (17%)		
Entropion grade change‖				
<2 grade change or no change	119/491 (24%)	113/490 (23%)	1·07 (0·79–1·44)	0·67
≥2 grade change	372/491 (76%)	377/490 (77%)		

Data are n/N (%), unless otherwise stated. BLTR=bilamellar tarsal rotation. PLTR=posterior lamellar tarsal rotation. OR=odds ratio. RRR=relative risk ratio. *Analysis done using logistic regression adjusted for surgeon to see the effect of the two surgical procedures on cumulative recurrence (by 12 months) across baseline trichiasis and entropion severity level. †Analysis done using negative binomial regression. ‡Incidence rate ratio. §Multinomial logistic regression. ¶Relative risk ratio. ‖Ordinal logistic regression.

Table 2: **Secondary clinical outcomes and changes in clinical phenotype at 12 months**

was used to analyse the difference in the number of recurrent lashes touching the eye between the two intervention groups. The signed-rank test was used to analyse visual acuity and contrast sensitivity changes between baseline and the 12 month follow-up. The risk of trichiasis recurrence difference by surgeon between the two surgical interventions was analysed using logistic regression adjusted for baseline disease severity such as entropion and trichiasis. To investigate the possibility of a learning curve effect during recruitment, the trichiasis recurrence rates for the first 50% of cases to be recruited versus the second 50% of cases recruited for each surgeon were compared using logistic regression adjusted for baseline disease severity such as entropion and trichiasis. The trial is registered at the Pan African Clinical Trials Registry (PACTR201401000743135).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Feb 13, 2014, and May 31, 2014, 5168 people were examined for eligibility, of whom 1314 (25%) had trachomatous trichiasis (figure). The remaining 3854 had other ocular conditions. Of the 1314 trichiasis cases, 312 did not meet inclusion criteria, largely because they had previously received surgery for trichiasis. Of the 1002 eligible participants, two (<1%) declined surgery. Thus, 1000 trichiasis cases consented, were enrolled, and randomly assigned (501 in the BLTR group and 499 in the PLTR group).

Participants were reassessed at 10 days (range 7–14) for suture removal, 6 months, and 12 months after enrolment. Almost all (98%) participants were examined at each follow-up. At 10 days, two people had travelled to another region, and had sutures removed in their new locality. Eight (1%) participants were not seen at either 6 month or 12 month follow-up visits and were therefore excluded from the analysis: three from the PLTR group and five from the BLTR group. Hence, primary outcome data were available and analysed for 992 (99%): 496 in each group.

Baseline demographic and clinical characteristics were balanced between the trial groups (table 1). The majority of the participants were female (77%) and their mean age was 47·3 years. The two groups were comparable for visual acuity and prevalence of corneal opacity, conjunctival inflammation, scarring, entropion, and trichiasis. There was evidence of epilation in 588 (59%) participants: 281 (56%) in the PLTR group and 307 (61%) in the BLTR group; among these 82 (8%) in both groups had successfully epilated, with no lashes touching. Major trichiasis was present in 145 (29%) of the PLTR group and 144 (29%) of the BLTR group. About 90% of the participants in both groups had corneal lashes (table 1). PLTR surgery took slightly less time than BLTR surgery (15 min 33 s *vs* 16 min 39 s; p<0·0001).

By 12 months, the primary outcome, cumulative recurrent trichiasis, had developed in 173 (17%) of 992 study eyes. Cumulative recurrence was significantly more frequent in the BLTR group (110/496 [22%]) than in the PLTR group (63/496 [13%]); after adjusting for surgeon, the OR was 1·96 (95% CI 1·40–2·75; p=0·0001). The risk difference for recurrent trichiasis between BLTR

	PLTR group	BLTR group	OR or RRR (95% CI)	p value
Intraoperative or postoperative bleeding*				
Mild	490/499 (98%)	477/501 (95%)	2·76 (1·27–6·00)	0·01
Moderate	8/499 (2%)	18/501 (4%)		
Excessive	1/499 (<1%)	6/501 (1%)		
Sign of infection at 7–14 days†‡	9/498 (2%)	37/500 (7%)	4·44 (2·11–9·33)	0·0001
Granuloma by 12 months†	26/496 (5%)	11/496 (2%)	0·41 (0·20–0·83)	0·01
Lagophthalmos (present)	3/491 (1%)	7/490 (1%)		
Eyelid contour abnormality at 12 months§				
None (base outcome)	371/491 (76%)	404/490 (82%)	1	··
Clinically non-significant (mild)	89/491 (18%)	49/490 (10%)	0·50¶ (0·34–0·73)	0·000
Clinically significant (moderate-to- severe)	31/491 (6%)	37/490 (8%)	1·10¶ (0·66–1·81)	0·72
Central correction at 12 months§				
Corrected (base outcome)	468/491 (95%)	454/490 (93%)	1	··
Over-corrected	12/491 (2%)	6/490 (1%)	0·52¶ (0·19–1·39)	0·19
Under-corrected	11/491 (2%)	30/490 (6%)	2·81¶ (1·39–5·68)	0·004
Medial correction at 12 months§				
Corrected (base outcome)	469/491 (96%)	450/490 (92%)	1	··
Over-corrected	0	0		··
Under-corrected	22/491 (4%)	40/490 (8%)	1·90¶ (1·11–3·26)	0·02
Lateral correction at 12 months§				
Corrected (base outcome)	486/491 (99%)	469/490 (96%)	1	··
Over-corrected	1/491 (<1%)	0	··	··
Under-corrected	4/491 (1%)	21/490 (4%)	5·44¶ (1·85–16·00)	0·002

Data are n/N (%), unless stated otherwise. BLTR=bilamellar tarsal rotation. PLTR=posterior lamellar tarsal rotation. OR=odds ratio. RRR=relative risk ratio. *Ordinal logistic regression. †Logistic regression. ‡Erythematous swelling and discharge. §Multinomial logistic regression. ¶Relative risk ratio.

Table 3: **Complications and eyelid contour abnormalities**

and PLTR procedures was 9·50% (95% CI 4·79–14·16). There was no evidence of effect modification between group and a-priori defined other factors on the primary outcome, including surgeon.

The primary outcome analysis using the photograph grading results was similar to the field grading. By 12 months, cumulative recurrent trichiasis was recorded for 250 (25%) of 992 study eyes. Recurrence was significantly more frequent in the BLTR group than in the PLTR group (32% *vs* 19%; OR 1·97 [95% CI 1·47–2·65]; p<0·0001). The risk difference for recurrent trichiasis between BLTR and PLTR procedures was 12·5% (95% CI 7·2–17·8).

At 10 days, recurrent trichiasis was present in three study eyes, one in the PLTR group and two in the BLTR group. At 6 months, recurrent trichiasis was present in 114 (12%) of 983 study eyes, and was significantly more frequent in the BLTR group than the PLTR group (71 [14%] *vs* 43 [9%]; OR 1·77 [95% CI 1·19–2·65]; p=0·0001). At 12 months, recurrent trichiasis was present in 131 (13%) of 981 study eyes and again remained significantly more frequent in the BLTR group than the PLTR group (85 [17%] *vs* 46 [9%]; OR 2·04 [95% CI 1·39–2·99]; p=0·0003).

There was no evidence of a difference in the risk of trichiasis recurrence between surgeons by 12 months for either PLTR (p=0·80) or BLTR (p=0·44), or for a learning curve during the course of the trial for either procedure. For PLTR, recurrence risks during the first and second half of recruitment were 32 (13%) of 248 and 31 (12%) of 248, respectively (p=0·68). For BLTR, recurrence risks during the first and second half of recruitment were 55 (22%) of 247 and 55 (22%) of 249, respectively (p=0·93).

The number, type, and location of recurrent lashes were comparable between the two groups (tables 1 and 2). BLTR surgery had more frequent recurrence than PLTR surgery for major trichiasis cases and across all baseline entropion grades. There was no evidence of a difference in visual acuity, contrast sensitivity, corneal opacity, and entropion changes at 12 months between the two groups (table 2). However, compared with the baseline, at 12 months there was a statistically significant overall improvement in visual acuity (baseline median logMAR, 0·6 [IQR 0·3–0·8] *vs* 12 month median logMAR, 0·5 [0·2–0·7]; signed-rank test, p<0·0001) and contrast sensitivity (baseline median contrast sensitivity, 3% [2–5] *vs* 12 month contrast sensitivity, 2% [1–3]; signed-rank test, p<0·0001) in the entire combined study sample.

After adjusting for surgeon, there was evidence of a difference in odds of intraoperative, immediate, or late postoperative complications between the two surgical interventions (table 3). There was more intraoperative and immediate postoperative bleeding in the BLTR surgery group than the PLTR surgery group (OR 2·76

	PLTR group	BLTR group	OR* (95% CI)	p value
Pain during surgery				
None	441/499 (88%)	441/501 (88%)	1·04 (0·71–1·53)	0·84
Mild	40/499 (8%)	39/501 (8%)		
Moderate	7/499 (1%)	11/501 (2%)		
Severe	11/499 (2%)	10/501 (2%)		
Pain between surgery and suture removal				
None	347/498 (70%)	309/500 (62%)	1·46 (1·12–1·89)	0·004
Mild	94/498 (19%)	107/500 (21%)		
Moderate	38/498 (8%)	56/500 (11%)		
Severe	19/498 (4%)	28/500 (6%)		
Satisfaction with the effect of surgery on the trichiasis at 12 months				
Satisfied	463/491 (94%)	452/490 (92%)	1·39 (0·84–2·31)	0·20
Neither satisfied nor dissatisfied	13/491 (3%)	16/490 (3%)		
Dissatisfied	15/491 (3%)	22/490 (4%)		
Satisfaction with the cosmetic appearance at 12 months				
Satisfied	465/491 (95%)	461/490 (94%)	1·14 (0·66–1·97)	0·64
Neither satisfied nor dissatisfied	10/491 (2%)	7/490 (1%)		
Dissatisfied	16/491 (3%)	22/490 (4%)		

Data are n/N (%), unless stated otherwise. BLTR=bilamellar tarsal rotation. PLTR=posterior lamellar tarsal rotation. OR=odds ratio. *Ordinal logistic regression.

Table 4: **Patient-reported outcomes**

[95% CI 1·27–6·00]; p=0·01), and also more postoperative infection in the BLTR surgery group than the PLTR surgery group (OR 4·44 [95% CI 2·11–9·33]; p=0·0001; table 3). Granulomata were less frequent in the BLTR group compared with the PLTR group (OR 0·41 [95% CI 0·20–0·83]; p=0·01; table 3).

The frequency of clinically non-significant (mild) ECA at 12 months was lower in the BLTR surgery group than the PLTR surgery group (RRR 0·50 [95% CI 0·34–0·73]; p<0·0001; table 3). However, there was no evidence of a difference in the frequency of clinically significant (moderate-to-severe) ECA between the two groups (RRR 1·10 [95% CI 0·66–1·81]; p=0·72; table 3). A similar pattern in ECA was found by independent photograph grading. Clinically mild ECA at 12 months was less frequent in the BLTR group (27/484 [5%]) than in the PLTR group (58/489 [12%]; RRR 0·43 [95% CI 0·27–0·70]; p=0·001). However, again we found no evidence of a difference in moderate-to-severe ECA between the two groups (BLTR, 4% *vs* PLTR, 5%; RRR 0·76 [95% CI 0·41–1·44]; p=0·40). There was evidence of more under-correction at 12 months with BLTR surgery than PLTR surgery (table 3).

There was no evidence of a difference between groups in the patient-reported pain experienced during surgery (p=0·84; table 4). However, participants in the BLTR group reported more pain and discomfort during the days between surgery and suture removal than the PLTR group (OR 1·46 [95% CI 1·12–1·89]; p=0·004; table 4). There was no evidence of a difference in patient satisfaction between the two groups for treatment of trichiasis (p=0·20) or the cosmetic appearance of the operated eyelid (p=0·64; table 4).

Discussion

Around 7 million people have trachomatous trichiasis and require high-quality surgical intervention.[2] A major global effort exists to scale up surgical programmes. However, high postoperative trichiasis recurrence rates are undermining trachoma control.[25] Identifying the surgical intervention with the lowest recurrence rate has been a research priority for many years.[18] In this trial, we compared the relative effectiveness of the two most commonly used operations and found that PLTR surgery has a significantly lower trichiasis recurrence rate at 12 months than BLTR surgery, particularly for more severe cases.

Considerable care was taken to ensure that the surgeons did both procedures using the WHO-described method with equal precision.[4] We trained surgeons who had been previously taught PLTR to do the BLTR procedure. This approach was chosen, rather than training novice surgeons simultaneously in both procedures, to reduce the learning curve to achieve proficiency in the new procedure.[26] During training and standardisation, before the commencement of the trial, each surgeon did about 100 BLTR operations and was confirmed by two assessors to be performing the procedure per protocol, using the WHO Certification process.[4]

There is clear evidence that during the trial the surgeons continued to do both operations consistently well and that the recorded difference in the primary outcome was not attributable to having learnt the BLTR procedure more recently. First, there were only three recurrent cases by 10 days, indicating that primary surgical failure was rare. If the recorded differences in recurrence were due to poor surgical technique, we would anticipate this to be more apparent by 10 days. This finding suggests that the subsequent difference in the primary outcome is attributable to fundamental differences in the surgical method that achieves a more stable and long-lasting correction in the case of PLTR surgery. Second, trichiasis recurrence rates between the first and second half of recruitment were very similar. If surgeons were still on a BLTR learning curve, a lower recurrence rate in the second half of recruitment would have been anticipated. Third, there was no significant difference in recurrence for either surgical procedure between surgeons. Finally, the recurrence rates for both procedures were generally similar to or lower than those reported in other trials, with the exception of the STAR trial which reported a lower BLTR recurrence rate.[5–14]

The only other trial to compare BLTR and PLTR procedures was done in Ethiopia.[13] This trial reported comparable outcomes for the two procedures: BLTR, 10·4%, and PLTR, 12·3%, recurrence at 3 months. However, this earlier study had a number of constraints. First, it was under-powered to detect a difference (153 patients, 256 eyes operated). Second, it was done at a tertiary teaching hospital by ophthalmologists. By contrast, most programmatic trichiasis surgery is done by non-physicians with limited training in remote, low-level, health facilities. Alternative techniques might give different results in more programmatic settings. Third, the 3 month follow-up period was too short to assess the relative performance because differences might take longer to become apparent.[6,7,11,27,28]

The PLTR surgical procedure did better than BLTR for several secondary outcomes. A higher rate of postoperative infection occurred following BLTR, probably because of the skin incision. All infections were treated successfully with oral antibiotics. The skin and orbicularis incision probably also explains the greater intraoperative and postoperative bleeding and postoperative pain that occurred with the BLTR procedure because these structures have an extensive vascular and sensory supply. These are important considerations for improving surgical uptake, which might be reduced by patient reports of pain and bleeding. Participants reported very high levels of satisfaction with the cosmetic outcome and effect of surgery in alleviating the trichiasis in both groups at 12 months. There was no difference by group. However, some caution needs to be taken in drawing firm conclusions from such data; the questions were asked by members of the study team, and there could be some reticence in expressing dissatisfaction in this context. Of note, the Kenyan National Trachoma Control Programme recently switched from the BLTR to PLTR surgery because of reports of widespread patient dissatisfaction with the appearance of the full-thickness incision in BLTR surgery. Under-correction was more frequent with BLTR surgery at 12 months, suggesting it is less effective at correcting underlying entropion.

We found that BLTR had a lower rate of mild ECAs. We consider this degree of ECA to be clinically and cosmetically non-significant because the vertical deviation from the lid contour is less than 1 mm. It is possible that this difference reflects consistently greater degrees of evertion with PLTR. There was no difference in moderate-to-severe ECA by group. Conjunctival granulomata developed more frequently after PLTR surgery.[8] Granulomata are probably a vigorous healing response that occurs in a tissue defect.[12] The additional rotation effected by the PLTR might create a larger posterior lamella defect and thereby a higher likelihood of granuloma formation. However, they are usually a minor complication that either self-resolve or need only a simple shave under topical anaesthesia. In the earlier comparison of BLTR and PLTR in Ethiopia, both eyelid notching and granulomata were significantly more common in the BLTR group than in the PLTR group (p=0·002).[13]

We think that it is biologically plausible that the PLTR achieves a more effective and stable correction of the entropion and trichiasis due to a key difference in technique from the BLTR. In the PLTR procedure, the lower edge of the dissected upper portion of the tarsal plate is drawn down and tucked into the dissected space between the anterior lamella and the lower portion of the tarsal plate behind.[4] Once healed, this provides a wedge of tissue that continues to rotate the distal end of the eyelid outwards, and stabilise the correction.

This study has several strengths. It had a large sample size and very high follow-up rates. Demographic and clinical characteristics were balanced between groups. The surgeons were rigorously trained and standardised to ensure the procedures were done correctly.

A potential design limitation in a trial of these two procedures is the risk of unmasking at the time of follow-up observations because some BLTR cases might very occasionally have a faint skin scar. The baseline, 6 month, and 12 month observers were masked to the randomisation. However, to independently assess the primary outcome for observer bias, photographs in which the upper lid skin was covered by a mask were graded. We found that the analysis of primary outcome using field and photograph grading were comparable, showing no systematic bias in the field grading. The observations of some of the secondary outcomes made during the operative procedure and at 10 days were impossible to mask. The use of surgeons who had previously been trained in PLTR and then provided with a second round of training in BLTR could be viewed as a potential limitation. However, we think that there was ample pre-trial training, practice, and assessment to bring the surgeons to a proficient standard, and that there is clear evidence that during the trial high standards were maintained, as discussed above. In this trial we used silk sutures, which were removed at 10 days. Although absorbable sutures such as polyglactan-910 (vicryl) offer the operational advantage of not needing to be removed, we have previously found in a randomised trial that silk and absorbable sutures have comparable outcomes, and therefore it is unlikely that the outcome of this present study would be modified by their use.[8]

Overall, the PLTR procedure was superior to the BLTR in terms of lower trichiasis recurrence and fewer intraoperative and immediate postoperative complications. All other factors being equal, PLTR could be the preferred procedure for the programmatic management of trachomatous trichiasis. We suggest new surgical trainees in both established and new programmes should be trained in the PLTR procedure. Additionally, consideration could be given to further research to investigate whether individuals previously trained to do BLTR surgery need to be re-trained in PLTR surgery.

Contributors

EH and MJB did the literature search. EH, ABK, PME, RLB, DCWM, SNR, KC, HAW, and MJB were responsible for the study conception and design. EH, TW, SA, ZT, MZ, ZZ, ABK, and MJB collected the data. EH, HAW, and MJB did the statistical analysis. EH, HAW, and MJB were responsible for the interpretation of the data. EH and MJB drafted the manuscript. All authors critically revised the manuscript for important intellectual content. RLB, DCWM, and MJB obtained the funding. TW, SA, ZT, MZ, ZZ, ABK, CHR, PME, and KC provided administrative, technical, or material support. MJB was the study supervisor.

Declaration of interests

We declare no competing interests.

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5. Predictors of Trachomatous Trichiasis Surgery Outcome

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Student Signature: Esmael Habtamu Ali Date: 15th December 2016

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Predictors of Trachomatous Trichiasis Surgery Outcome

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Abstract

Purpose: Unfavorable outcomes following Trachomatous Trichiasis (TT) surgery are undermining the global trachoma elimination effort. This analysis was done to identify predictors of postoperative TT (PTT), Eyelid Contour Abnormalities (ECA) and conjunctival granuloma in the two most common TT surgery procedures; Posterior Lamellar Tarsal Rotation (PLTR) and Bilamellar Tarsal Rotation (BLTR).

Design: Longitudinal data analysis from a randomised, controlled, single masked clinical trial.

Participants: One thousand TT cases with lashes touching the eye or evidence of epilation, in association with tarsal conjunctival scarring.

Methods: Cases were randomly allocated and received either BLTR (501) or PLTR (499) surgery. Disease severity at baseline; and surgical incisions, sutures and corrections were graded during and immediately after surgery. Participants were examined at 6 and 12-months by assessors masked to allocation.

Main outcome measures: PTT, ECA and conjunctival granuloma.

Results: Data were available for 992 (99.2%) trial participants (496 in each arm). There was strong evidence that performing more peripheral dissection with scissors in PLTR (OR=0.70; 95% CI=0.54–0.91; p=0.0078) and BLTR (OR=0.83; 95% CI=0.72–0.96; p=0.0095) independently protected PTT. Old age, baseline major trichiasis and mixed location lashes; and immediate postoperative central under-correction independently predicted PTT in both surgical procedures. Peripheral lashes in PLTR (OR=5.91; 95% CI=1.48–23.5; p=0.012) and external central incision height ≥4mm in BLTR (OR=2.89; 95% CI=1.55–5.41; p=0.0009) were independently associated with PTT. Suture interval asymmetry of >2mm (OR=3.18; 95% CI=1.31–7.70; p=0.010) in PLTR; and baseline conjunctival scarring in BLTR (OR=1.72; 95% CI=1.06–2.81; p=0.030) were independently associated with ECA. Old age was independently associated with ECA in both PLTR (<0.0001) and BLTR (p=0.031). There was substantial inter-surgeon variability in ECA rates for both PLTR (Range, 19.0%–36.2%) and BLTR (Range, 6.1%–28.7%) procedures. In PLTR surgery, irregular posterior lamellar incision at the centre of the eyelid (OR=6.72; 95% CI=1.55–29.04; p=0.011) and ECA (OR=3.08; 95% CI=1.37–6.94; p=0.0066) resulted in conjunctival granuloma formation.

Conclusions: Poor TT surgical outcomes were associated with inadequate peripheral dissection, irregular incision, asymmetric suture position and tension, and inadequate correction; in addition to preoperative disease severity, lash location and age. Addressing these will improve TT surgical outcomes.

Introduction

Visual impairment from trachoma, results from the in-turning of eyelashes that scar the cornea (trachomatous trichiasis (TT)). It remains the leading infectious cause of blindness worldwide.[1,2] TT is a consequence of progressive conjunctival scarring caused by recurrent infection with *Chlamydia trachomatis.* It causes painful corneal abrasion, introduces infection and alters the ocular surface, eventually leading to irreversible blindness from corneal opacification (CO). Approximately 3.2 million people have un-treated TT, and 2.4 million people are visually impaired from trachoma worldwide of whom an estimated 1.2 million are irreversibly blind.[3,4]

The World Health Organisation (WHO) recommends corrective eyelid surgery to reduce the risk of visual impairment from TT.[5] The surgery involves an incision through the eyelid parallel to and a few millimetres above the lid margin. The terminal portion of the lid is externally rotated and sutured in the corrected position.[6] In trachoma endemic countries surgery is usually performed by non-physician health workers.[6] There is currently a major global effort to scale up surgical services to clear the current trichiasis backlog by 2020, with more than 200,000 surgeries being performed annually.[7]

However, unfavorable outcomes following TT surgery are undermining these efforts.[8] Reported rates of postoperative TT (PTT) vary considerably, however, 20% recurrence at one year is typical.[9-15] Moreover, a report from the Global Trachoma Mapping Project suggests the number of cases with unfavorable outcomes, including PTT, have increased significantly with increasing surgical output.[8] Other adverse outcomes, such as eyelid contour abnormalities (ECA) and granuloma following surgery, which occurs in 5%–30% of cases, may have negative social and psychological impact and deter other patients from accepting trichiasis surgery.[16 10,13 17-19]

Several clinical trials have reported unfavourable outcomes to be associated with surgical quality, type of surgical procedure and preoperative disease severity.[10-14] PTT rates between surgeons have been reported to range from 0% to 80%.[10,12-14,20] We have previously reported the outcome of a randomised controlled trial (RCT) comparing the Bilamellar Tarsal Rotation (BLTR) and the Posterior Lamellar Tarsal Rotation (PLTR) operations.[11] The PLTR had a substantially lower rate of postoperative trichiasis and was more effective in severe TT cases than BLTR; although, BLTR surgery had lower rate of granuloma formation.

Management of unfavorable surgical outcomes is often challenging.[8] Firstly, it requires additional programmatic resources and specialized surgical skills.[8] Secondly, the management of postoperative trichiasis is more challenging and probably has less good outcomes than a primary procedure.[8]

Therefore, every effort must be made to avoid unfavorable outcomes at the primary operation. The pre, intra and postoperative factors that lead to unfavorable outcomes after TT surgery need to be studied and understood. Here, we investigate factors that are associated with unfavorable outcomes (PTT, ECA and Granuloma) following BLTR and PLTR surgery, and identify potential approaches to minimize them.

Methods

Ethics statement

This study was approved by the Ethiopian National Health Research Ethics Review Committee, London School of Hygiene & Tropical Medicine Ethics Committee, and Emory University Institutional Review Board. Written informed consent in Amharic was obtained prior to enrolment from participants. If a participant was unable to read and write the information sheet and consent form were read to them and their consent recorded by thumbprint. An independent Data and Safety Monitoring Committee oversaw the trial. The trial was conducted in compliance with the Declaration of Helsinki and International Conference on Harmonisation–Good Clinical Practice. The trial is registered with the Pan African Clinical Trials Registry (PACTR), http://www.pactr.org; PACTR201401000743135.

Study design and participants

This was a single-masked, individual-randomised, controlled trial conducted in Ethiopia. The trial methodology has been previously reported in detail.[11] Briefly, we recruited 1000 TT cases with one or more lashes touching the eye or evidence of epilation, in association with tarsal conjunctival scarring. People with trichiasis due to other causes, recurrent trichiasis after previous surgery, uncontrolled hypertension, pregnancy and under 18 years were excluded. Recruitment was done through community-based screening in three districts of West Gojam Zone, Amhara Region, Ethiopia between February and May 2014. We trained and standardised six trichiasis surgeons in both the PLTR and BLTR surgery. We used the WHO TT surgery training and certification manual.[6] Participants were randomised to either PLTR or BLTR (using the Waddell clamp) surgery, in a 1:1 allocation ratio for each surgeon. In both surgical procedures 4/0 silk sutures with 3/8th circle, 19 mm cutting needles were used.

Clinical assessments

At baseline, eyes were examined and graded using the Detailed WHO FPC Grading System.[21] Lashes touching the eye were counted and sub-divided by the part of the eye contacted/location: cornea, lateral, or medial. Trichiasis sub-types were recorded as metaplastic, misdirected, or entropic.[22] Three trained nurses made intra and immediate postoperative observations. The incision length was measured using a silk suture thread, which was measured against a ruler. The incision height was measured between the incision and the eyelid margin with a sterile ruler. In PLTR surgery we measured the posterior lamellar incision, while in BLTR the measurement was done for the skin incision. The incision was examined to determine regularity and whether it ran parallel to the lid margin. The scissor cuts made to complete the incision medially and laterally were counted. Data on the number, symmetry and tension of the sutures were collected. Suture tension was considered "regular" if there is equal tension or firmness across all the sutures; and "irregular" if at least one of the sutures was either insufficiently tight or excessively tight compared to the others. The spacing between sutures was considered "symmetrical" if the difference in space between the central and medial sutures, and the central and lateral sutures was ≤2mm; and "asymmetrical" if this difference was >2mm. The degree of entropion correction was graded using a previously described system.[11] Two (primary gaze and up gaze) high-resolution digital photographs of the operated eye were taken before placing the dressing.

Participants were re-examined at 10-days, 6-months and 12-months post-operatively. At 10-days, PTT, degree of lid eversion, infection and granulomata were documented before suture removal. At 6 and 12-months participants were re-examined following the same procedures as for baseline. Eyelid contour abnormalities (ECA) were graded according to the PRET trial method.[23] Mild ECA were considered to be "clinically insignificant"; and moderate and severe ECA were grouped together as "clinically significant". The surgical incision scar height, the distance between the incision scar line in the tarsal conjunctiva and the eyelid margin, was measured in millimetres using a ruler for the medial, central and lateral part of the eyelid. Presenting distance vision was measured at baseline and 12-months using "PeekAcuity" software on a Smartphone in a dark room.[24] Three standardised high-resolution digital photographs of trichiasis, cornea and tarsal conjunctiva were taken, using a Nikon D90 digital SLR camera with 105mm macro lens and R1C1 flash units at baseline, 6 and 12 month follw-ups.[25]

Statistical analysis

The sample size was determined based on the assumptions described in the primary paper of this trial.[11] Data were double-entered into Access (Microsoft) and transferred to Stata 11 (StataCorp) for analysis. For participants who had bilateral surgery, we randomly designated one eye to be the 'study eye' for the analysis. The three main unfavourable TT surgical outcome measures used here are PTT, ECA and granuloma. PTT was defined as one or more lashes touching the eye or clinical evidence of epilation, or a history of repeat trichiasis surgery by 12-months. ECA was considered for any type and severity of ECA. A Granuloma was defined as a fleshy tissue growth of at least 2mm on the tarsal conjunctiva or at the edge of the eyelid. The analysis of ECA was based on the participants seen at 12-months, while the analysis of PTT and granuloma included all participants seen at least once during the 6 and 12-months follow-ups.

Based on severity, TT cases were categorised into Minor Trichiasis with <6 lashes or evidence of epilation in <1/3rd of the lid margin, and Major Trichiasis with ≥6 lashes or evidence of epilation in ≥1/3rd of the lid margin. To analyse the association between trichiasis severity and corneal opacity the detailed corneal opacity grading was converted into the WHO grading system. Mixed postoperative lash location by 12-months were defined as lashes touching more than one location at either the 6-month follow-up or the 12-month follow-up or during both follow-ups. The same definition was used for mixed postoperative lash types by 12-months.

Univariable and multivariable association of factors with major trichiasis at baseline, PTT by 12-months, ECA at 12 month and granuloma by 12-months, all binary outcomes, were analysed using logistic regression to estimate the odds ratio (OR) and 95% confidence interval (CI) for both surgical procedures separately. Likelihood ratio test was used to decide on the variables that should be included in the final multivariable logistic regression model. P-value for trend was calculated for ordered categorical exposure variables such as papillary grade, tarsal conjunctival scar, corneal opacity, visual acuity, and age. Categorical secondary outcomes (such as level of correction, and ECA severity) were analysed using multinomial logistic regression to estimate relative risk ratio (RRR) and 95% CI. Correlation between postoperative trichiasis lashes location and type with preoperative trichiasis lashes and locations were analysed using Fisher's exact test due to small observations. Correlation between surgical incision height and incision scar height were analysed using paired t-test.

Results

Participant Flow

The participant flow for this trial has previously been described in detail.[11] In summary, 98% of the participants were examined at all three follow-up time points. At 12-months 491 (98.4%) and 490 (97.8%) from the PLTR and BLTR arm were re-assessed, respectively. PTT data was available for 992 (99.2%) participants, 496 in each arm, who were reassessed on at least one occasion during the 12-month period.

Demographic and Baseline Clinical Characteristics

Baseline demographic and clinical characteristics were analysed for the 992 trial participants who were seen at one or more follow-up. The majority of the participants were female (758, 76.4%), and the mean age was 47.0 (SD, 14.7) years. Baseline clinical characteristics were balanced between the two surgical procedures, Table 1. Major trichiasis was present in 46.4% (230/496) and 48.2% (239/496) of the PLTR and BLTR cases, respectively. Most cases had moderate or severe entropion: PLTR (394/496, 79.4%), BLTR (406/496, 81.8%). Most individuals in both PLTR (381/496, 76.8%) and BLTR (374/496, 75.4%) groups had lashes in contact with the cornea. Metaplastic lashes were common: PLTR: 223/496 (45.0%;) BLTR: 205/496 (41.3%), Table 1.

Factors associated with preoperative TT severity in all cases are presented in Table 2. In a multivariable analysis, major TT was significantly associated with females, increasing corneal opacity, older age, increasing conjunctival scarring and increasing conjunctival inflammation, Table 2.

Postoperative Trachomatous Trichiasis

By 12-months, postoperative trichiasis was present in 173/992 (17.4%) cases: PLTR 63/496 (12.7%), BLTR 110/496 (22.2%), Table 1. Most of the cases of postoperative TT by 12-months were minor trichiasis (PLTR: 56/63, 80.9%; BLTR: 97/110, 88.2%). Metaplastic lashes were the most common type of PTT lashes after both procedures: PLTR (37/63, 58.3%) and BLTR (66/110, 60.0%). The most common location of PTT in both PLTR (32/63, 50.8%) and BLTR (55/110, 50.0%) surgery was corneal, Table 1.

PLTR surgery

Univariable and multivariable analysis of factors associated with postoperative TT by 12-months following PLTR surgery are presented in Table 3. In a multivariable analysis, there was strong evidence that performing more medial and lateral dissections using scissors to increase the length of surgical incision had a protective effect against PTT (OR, 0.70; 95% CI, 0.54–0.91; p=0.0078). ECA at 12-months was associated with a lower rate of PTT (5.0% vs 15.4%; OR, 0.24; 95% CI, 0.09–0.60; p=0.0023). On the other hand, there was evidence that PTT was independently associated with: older age (p-value for trend = 0.048), baseline major trichiasis (16.1% vs 9.8%; OR, 1.97; 95% CI, 1.09–3.56; p=0.025), peripheral lashes (36.4% vs 10.0%; OR, 5.91; 95% CI; 1.48–23.5; p=0.012), and mixed location lashes (22.8% vs 10.0%; OR 2.24; 95% CI, 1.09–4.59; p=0.028) as compared to corneal lashes; and immediate postoperative central under-correction compared to adequate correction (36.4% vs 12.5%; OR, 4.97; 95% CI, 1.15–21.5; p=0.032). Cases with irregular suture tension had a two times higher rate of PTT compared to those with regular suture tension (26.7% vs 12.3%). However, this was not statistically significant (p=0.11). There was no evidence of association between PTT and surgeon, Table 3. Increased severity of baseline conjunctival scarring was significantly associated with major PTT by 12-months (Mild, 0/4 [0.0%]; Moderate, 4/51 [7.8%); Severe, 3/8 [37.5%]; OR, 7.40; 95% CI, 1.34–40.8; p-value for trend=0.022).

Incision height: There was no evidence of a significant association between surgical incision height of ≥4mm from the lid margin and PTT, although it tended to give a slightly lower rate of PTT compared to <4 mm incision height (9% vs 13%), Table 3. Incision height of <4mm was not associated with under correction. However, a surgical incision height of ≥4mm was associated with immediate postoperative overcorrection at the corresponding site than a surgical incision height of <4mm in PLTR surgery: central (27.3% [15/55] vs 10.1% [45/444]; RRR, 3.32; 95% CI, 1.70–6.50; p=0.0004) and lateral (15.6% [7/45] vs 5.3% [24/454]; RRR, 3.10; 95% CI, 1.25–7.67; p=0.014). We analysed the correlation between incision height and incision scar. The postoperative internal incision scar height measured at 12-months was significantly higher than the intraoperative internal incision height of PLTR surgery: (i) central mean, 5.0mm vs 3.1mm; difference, 1.9mm; 95% CI, 1.83–1.99; p<0.0001; (ii) medial mean, 4.3mm vs 3.1mm; difference: 1.2mm; 95% CI, 1.17–1.33; p<0.0001; (iii) lateral mean, 4.3mm vs 3.0mm; difference, 1.3mm; 95% CI, 1.22–1.40; p<0.0001.

BLTR surgery

Univariable and multivariable analysis of factors associated with PTT by 12-months in BLTR surgery are presented in Table 4. In a multivariable analysis, there was strong evidence that performing more medial and lateral dissections using scissors to increase the length of surgical incision had a protective effect on PTT (OR, 0.83; 95% CI, 0.72–0.96; p=0.009). Older age (P-value for trend = 0.076), baseline major trichiasis (31.0% vs 14.0%; OR, 1.88; 95% CI, 1.12–3.15; p=0.017), mixed location lashes compared to corneal only lashes (46.7% vs 16.8%; OR, 4.44; 95% CI, 2.38–8.28; p<0.0001) and immediate postoperative central under-correction compared to adequate correction (60.0% vs 22.6%; OR, 5.04; 95% CI, 1.23–20.6; p=0.024) were independently associated with PTT, Table 4. Age ≥60 years (OR, 2.05; 95% CI, 1.29–3.25; p=0.0024) and major TT at baseline (OR, 2.77; 95% CI, 1.76–4.34; p<0.0001) were independently associated with major PTT by 12-months following BLTR surgery.

Incision height: In a univariable analysis, lids with external surgical incision height of ≥4mm from the lid margin were more likely to have PTT compared to those with <4mm external incision height (central 37.6% vs 19.0%; medial, 33.3% vs 19.5%; lateral, 32.1 vs 19.4%). However, in a multivariable model, this association was only significant for the central external incision height (OR, 2.89; 95% CI, 1.55–5.41; p=0.0009), Table 4. Incision height was not associated with under or overcorrection in BLTR (data not shown). On the other hand, in a univariable analysis, internal conjunctival incision scar height of ≥4mm measured at 12-months was associated with less PTT at 12-months than <4mm internal incision scar height (central 20.7% vs 42.9%; medial, 19.1% vs 35.5%; lateral, 20.0% vs 27.9%). But again, in multivariable analysis, this association was only significant for the medial internal incision scar height (OR, 0.39; 95% CI, 0.21–0.72; p=0.0027). The intraoperative external skin incision height in BLTR was higher than the internal conjunctival incision scar height measured at 12-months: (i) central mean, 5.4mm vs 3.1mm; difference, 2.3mm; 95% CI, 1.16–2.36; p<0.0001; (ii) medial mean, 4.7mm vs 3.1mm; difference: 1.6mm; 95% CI, 1.45–1.66; p<0.0001; (iii) lateral: mean, 4.5mm vs 3.2mm; difference, 1.3mm; 95% CI, 1.22–1.42; p<0.0001.

Postoperative Lash Location

We analysed whether post-operative trichiasis tended to reoccur in the same sector of the eyelid as it was found pre-operatively. Participants with baseline medial only, lateral only and mixed lashes had significantly higher rate of postoperative lashes in the same area only, compared to those with no baseline lashes in these areas of the eyelid in PLTR: i) medial (66.7% [2/3] vs 2.3% [11/493]; Fisher's exact test p=0.002); ii) lateral (25.0% [2/8] vs 0.61% [3/488]; Fisher's exact test p=0.002) and iii) mixed location lashes (4.6% [3/66] vs 0.93% [4/430]; Fisher's exact test p=0.05); and in BLTR, mixed location lashes (17.3% [13/75] vs 2.1% [9/421]; Fisher's exact test p<0.001). Figure 1 illustrates this association. However, such correlation was not seen between preoperative and postoperative corneal only lashes for both PLTR (6.8% [26/381] vs 6.1% [7/115]; Fisher's exact test p=1.0) and BLTR (11.0% [41/374] vs 13.1% [16/122]; Fisher's exact test p=0.52) procedures.

There was strong evidence that PTT location by 12-months significantly correlates to areas of immediate postoperative under-correction, Figure 1. Participants with immediate postoperative central under-correction had a significantly higher rate of central PTT by 12-months than those with immediate post-operative adequate central correction in both PLTR (36.6% [4/11] vs 7.5% [32/425]; OR, 7.01; 95% CI, 1.95–25.2; p=0.0029) and BLTR (60.0% [6/10] vs 15.3% [65/424]; OR, 8.28; 95% CI, 2.27–30.2; p=0.0013) surgeries. The medial and lateral analyses were not possible due to insufficient events.

Eyelid Contour Abnormalities

Eyelid contour abnormalities were present in 206/981 (21.0%) participants at 12-months: PLTR 120/491 (24.4%), BLTR 86/490 (17.6%), Table 1. Univariable and multivariable analysis of factors associated with ECA in PLTR and BLTR surgery are presented in Table 5. Inter-surgeon variability is an important factor for ECA in both PLTR (range, 19.0%–36.2%) and BLTR (range, 6.1% – 28.7%) procedures, Table 5. In both procedure old age predicted ECA. Between sutures distance asymmetry of >2mm (Figure 2) in PLTR (52.2% vs 23.1%; OR, 3.18; 95% CI, 1.31–7.70; p=0.0028); and baseline conjunctival scarring in BLTR (p-value for trend=0.030) were independently associated with ECA. The use of 4 mattress sutures in BLTR surgery halved the rate of ECA compared to 3 mattress sutures (9.5% vs 19.1%; p=0.03). However, this was not significant in a multivariable analysis, Table 5. In separate multivariable analysis on the predictors of clinically significant ECA in PLTR surgery, cases with ≥ 60 years age, (12.1% [14/116] vs 4.5% [17/375]; RRR, 3.91; 95% CI, 1.79–8.56; p=0.0006) and operated by surgeon 5 (17.0% vs <8%; RRR, 3.23; 95% CI, 1.01–10.4; p=0.049) had higher risk of developing clinically significant ECA than their counterparts.

Conjunctival Granuloma

Conjunctival granuloma were documented in 37/992 (3.7%) participants during the 12 month period: PLTR 26/496 (5.2%), and BLTR 11/496 (2.2%), Table 1. The development of a granuloma following PLTR surgery was independently associated with (i) a posterior lamellar incisions that was irregular or not parallel to the lid margin in the central 1/3rd of the eyelid (OR, 6.72; 95% CI, 1.55–29.04; p=0.011) and (ii) ECA (OR, 3.08; 95% CI, 1.37–6.94; p=0.0066), Table 6. There was a non-significant trend for cases with suture tension irregularity having a higher rate (three-fold) of granuloma, compared to those with regular suture tension in both PLTR (5.0% vs 13.3%) and BLTR (2.1% vs 6.7%) procedures. Preoperative disease severity, age, and surgeon were not associated with granuloma in both surgeries. There were no significant associations with granuloma following BLTR, Table 6.

Figure 1: Immediate post-operative undercorrection. The pictures on the left are the immediate postoperative pictures of patient with central under-correction. The pictures on the right are the 12-month follow-up pictures of the same eye showing postoperative TT at the same area.

Figure 2: Suture distance asymmetry resulting in ECA. The pictures on the left are the immediate postoperative pictures showing asymmetry between suture intervals. The pictures on the right are the 12-month follow-up pictures of the same eye with ECA.

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Table 1: Clinical and demographic characteristics of cases seen at baseline and at 12-months

Characteristic	Baseline				By 12 Months			
	PLTR		BLTR		PLTR		BLTR	
	n/496	(%)	n/496	(%)	n/496	(%)	n/496	(%)
Sex, Female	385	(77.6%)	373	(75.2%)	-	-	-	-
Age in years, Mean (SD)	47.0	(15.0)	47.5	(14.9)	-	-	-	-
Entropion grade*								
None/mild (grade 0 & 1)	102	(20.6%)	90	(18.1%)	484	(98·6%)	485	(99.0%)
Moderate (grade 2)	314	(63.3%)	331	(66.7%)	6	(1.2)	5	(1.0%)
Severe (grade 3 and 4)	80	(16.1%)	75	(15.1%)	1	(0.2)	0	(0.0%)
Trichiasis severity								
No trichiasis	-	-	-	-	433	(87.3)	386	(77.8%)
Minor trichiasis	266	(53.6%)	257	(51.8%)	56	(11.3)	97	(19.6%)
Major trichiasis	230	(46.4%)	239	(48.2%)	7	(1.41)	13	(2.6%)
Lash location								
No trichiasis	-	-	-	-	433	(87.3%)	386	(77.8%)
Epilating	38	(7.7%)	42	(8.5%)	7	(1.4%)	21	(4.2%)
Corneal only	381	(76.8%)	374	(75.4%)	32	(6.5%)	55	(11.1%)
Medial only	3	(0.6%)	0	(0.0%)	12	(2.4%)	7	(1.4%)
Later only	8	(1.6%)	5	(1.0%)	5	(1.0%)	5	(1.0%)
Corneal + Peripheral	66	(13.3%)	75	(15.1%)	7	(1.4%)	22	(4.4%)
Lash Type								
No trichiasis	-	-	-	-	433	(87.3%)	386	(77.8%)
Epilating	38	(7.7%)	42	(8.5%)	7	(1.4%)	21	(4.2%)
Entropic only	126	(25.4%)	117	(23.4%)	5	(1.0%)	8	(1.6%)
Metplastic only	223	(45.0%)	205	(41.3%)	37	(7.5%)	66	(13.3%)
Misdirected only	9	(1.8%)	13	(2.6%)	2	(0.4%)	4	(0.8%)
Mixed	100	(20.2%)	119	(23.4%)	12	(2.4%)	11	(2.2%)
Eyelid Contour Abnormality*								
None	-	-	-	-	371	(75.6%)	404	(82.4%)
Clinically insignificant	-	-	-	-	89	(18.1%)	49	(10.0%)
Clinically significant	-	-	-	-	31	(6.3%)	37	(7.6%)
Granuloma	-	-	-	-	26	(5.2%)	11	(2.2%)

*Data analysed from 12-months examination (PLTR, N = 491; BLTR, N = 490)

Table 2: Univariable and multivariable analysis of baseline factors associated with preoperative TT

Variable	Minor TT		Major TT		Univariable Analysis			Multivariable analysis		
	n/525	*(%)*	*n/475*	*(%)*	*OR*	*(95% CI)*	*P-value*	*OR*	*95% CI*	*P-value*
Preoperative Major TT										
Sex, Female	372	(70.9%)	393	(82.7%)	1.97	(1.45 – 2.67)	<0.0001	2.29	(1.64 – 3.21)	<0.0001
Age, mean (SD)	46.1	(14.6%)	48.7	(15.2%)	1.01	(1.01 – 1.03)	0.0049	1.02	(1.01 – 1.03)	0.016
Lash location										
Corneal only	428	(81.5%)	331	(69.7%)	0.52	(0.39 – 0.70)	<0.0001	0.65	(0.41 – 1.05)	0.080
Peripheral only	10	(1.9%)	6	(1.3%)	0.66	(0.24 – 1.83)	0.42	-	-	-
Mixed	46	(8.8%)	97	(20.4%)	2.67	(1.83 – 3.89)	<0.0001	-	-	-
Lash type										
Entropic	146	(27.8%)	97	(20.4%)	0.67	(0.50 – 0.89)	0.0067	0.70	(0.49 – 1.01)	0.057
Metaplastic	229	(43.6%)	201	(42.3%)	0.95	(0.74 – 1.22)	0.68	-	-	-
Misdirected	21	(4.0%)	2	(0.4%)	0.10	(0.02 – 0.43)	0.0021	0.22	(0.05 – 0.99)	0.048
Mixed	88	(16.7%)	134	(28.2%)	1.95	(1.44 – 2.64)	<0.0001	1.45	(1.01 – 2.06)	0.045
Lower lid TT	36	(6.9%)	54	(11.4%)	1.74	(1.12 – 2.71)	0.014	1.52	(0.94 – 2.44)	0.087
Papillary grade										
None	10	(1.9%)	5	(1.1%)	1.84	(1.50 – 2.25)	<0.0001	1.54	(1.23 – 1.94)	0.0002†
Mild	167	(31.8%)	81	(17.1%)						
Moderate	298	(56.8%)	305	(64.2%)						
Severe	50	(9.5%)	84	(17.7%)						
Tarsal conjunctiva scar										
Mild	76	(14.5%)	31	(6.5%)	2.23	(1.72 – 2.91)	<0.0001	2.08	(1.54 – 2.82)	<0.0001†
Moderate	398	(75.8%)	342	(72.0%)						
Severe	51	(9.7%)	102	(21.5%)						
Corneal scar										
CCO	171	(32.6%)	82	(17.3%)	1.61	(1.37 – 1.89)	<0.0001	1.30	(1.09 – 1.56)	0.0041†
CC1	205	(39.1%)	200	(42.1%)						
CC2	143	(27.2%)	173	(36.4%)						
CC3	6	(1.1%)	20	(4.2%)						
Best corrected logMAR visual acuity										
-1.0 – 0.29	169	(32.2%)	109	(22.9%)	1.19	(1.07 – 1.33)	0.0017	-	-	-
0.3 – 0.69	207	(39.4%)	192	(40.4%)						
0.7 – 1.0	94	(17.9%)	116	(24.4%)						
1.1 – 1.9	22	(4.2%)	14	(2.9%)						
2.0 – 3.0/CF, HM, LP	29	(5.5%)	35	(7.4%)						
3.5/NLP	4	(0.8%)	9	(1.9%)						

Note: Analysis made using logistic regression. † P- value for trend

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Table 3: Univariable and multivariable association of factors with postoperative trichiasis by one year after PLTR surgery

Demographic and Clinical Factors	Postoperative TT N=496		Univariable Analysis			Multivariable Analysis		
	n/N	*(%)*	*OR*	*(95% CI)*	*p-value*	*OR*	*(95% CI)*	*p-value*
Gender								
Male	17/111	(15.3%)	0.75	(0.41 – 1.32)	0.35	-	-	-
Female	46/385	(12.0%)						
Age								
18 – 29	3/59	(5.1%)	1.18	(0.98 – 1.41)	0.077†	1.23	(1.00 – 1.50)	0.047†
30 – 39	8/85	(9.4%)						
40 - 49	18/123	(14.6%)						
50 - 59	17/108	(15.7%)						
60 - 69	10/74	(13.5%)						
70+	7/47	(14.9%)						
Trichiasis severity								
Minor	26/266	(9.8%)	1.77	(1.04 – 3.03)	0.037	1.97	(1.09 – 3.56)	0.025
Major	37/230	(16.1%)						
Baseline entropion								
E0	1/11	(9.1%)	1.40	(0.96 – 2.06)	0.080†	-	-	-
E1	10/91	(11.0%)						
E2	37/314	(11.8%)						
E3	12/71	(16.9%)						
E4	3/9	(33.3%)						
Lash types at baseline								
Epilating	6/38	(15.8%)	1.36	(0.52 – 3.56)	0.54	-	-	-
Entropic	14/126	(11.1%)	0.91	(0.46 – 1.80)	0.78	-	-	-
Metaplastic	27/223	(12.1%)	1	-	-	-	-	-
Misdirected	0/9	(0.0%)	-	-	-	-	-	-
Mixed lashes (binary)	16/100	(16.0%)	1.38	(0.71 – 2.70)	0.34	-	-	-
Lash Location								
Epilating	6/38	(15.8%)	1.69	(0.66 – 4.31)	0.27	1.72	(0.64 – 4.62)	0.29
Corneal	38/381	(10.0%)	1	-	-	1	-	-
Peripheral	4/11	(36.4%)	5.16	(1.44 – 18.4)	0.012	5.91	(1.48 – 23.5)	0.012
Corneal + Peripheral	15/66	(22.7%)	2.65	(1.36 – 5.17)	0.0041	2.24	(1.09 – 4.59)	0.028
Conjunctival scarring, baseline								
1	4/49	(8.2%)	1.05	(0.62 – 1.79)	0.85†	-	-	-
2	51/372	(13.7%)						
3	8/75	(10.7)						
Eye								
Right	31/250	(12.4%)	1.06	(0.62 – 1.79)	0.84	-	-	-
Left	32/246	(13.0%)						
Surgeon *(Relative to surgeon 4)*								
1	8/89	(9.0%)	0.81	(0.30 – 2.16)	0.67	0.57	(0.20 – 1.63)	0.29
2	14/95	(14.7%)	1.42	(0.60 – 3.37)	0.43	1.40	(0.56 – 3.50)	0.48
3	12/84	(14.3%)	1.37	(0.56 – 3.35)	0.49	0.74	(0.27 – 2.04)	0.56
4	10/92	(10.9%)	1	-	-	-	-	-
5	6/47	(12.8%)	1.20	(0.41 – 3.53)	0.74	1.62	(0.47 – 5.55)	0.45
6	13/89	(14.6%)	1.40	(0.58 – 3.39)	0.45	0.73	(0.27 – 1.97)	0.54
Number of medial and lateral dissections, median (range)								
No recurrence	1	(0 – 26)	0.78	(0.63 – 0.96)	0.018	0.70	(0.54 – 0.91)	0.0078
Recurrence	0	(0 – 5)						
Immediate postop central correction								
Corrected	53/425	(12.5%)	1	-	-	1	-	-
Over corrected	6/60	(10.0%)	0.78	(0.32 – 1.90)	0.58	0.73	(0.28 – 1.90)	0.52
Under corrected	4/11	(36.4%)	4.01	(1.14 – 14.2)	0.03	4.97	(1.15 – 21.5)	0.032
Number of mattress sutures¥								
3 sutures	52/401	(13.0%)	0.92	(0.46 – 1.85)	0.82	-	-	-
4 sutures	11/91	(12.1%)						
Suture tension across sutures								
Regular	59/481	(12.3%)	2.60	(0.80 – 8.43)	0.11	-	-	-
Irregular	4/15	(26.7%)						

Demographic and Clinical Factors	Postoperative TT N=496		Univariable Analysis			Multivariable Analysis		
	n/N	***(%)***	***OR***	***(95% CI)***	***p-value***	***OR***	***(95% CI)***	***p-value***
Surgical incision height in mm*								
Central								
<4mm	58/442	(13.1%)	0.66	(0.26 – 1.77)	0.42	-	-	-
≥4mm	5/54	(9.3%)						
Medial								
<4mm	58/438	(13.2%)	0.62	(0.24 – 1.61)	0.32	-	-	-
≥4mm	5/58	(8.6%)						
Lateral								
<4mm	59/452	(13.0%)	0.67	(0.23 – 1.93)	0.45	-	-	-
≥4mm	4/44	(9.1%)						
Surgical scar height in mm								
Central								
<4mm	5/27	(18.5%)	0.63	(0.23 – 1.72)	0.37	-	-	-
≥4mm	58/464	(12.5%)						
Medial								
<4mm	16/95	(16.8%)	0.66	(0.36 – 1.23)	0.19	-	-	-
≥4mm	47/396	(11.9%)						
Lateral								
<4mm	15/106	(14.1%)	0.86	(0.46 – 1.61)	0.65	-	-	-
≥4mm	48/385	(12.5%)						
Eyelid contour abnormality (ECA)								
No	57/371	(15.4%)	0.29	(0.12 – 0.69)	0.0052	0.24	(0.09 – 0.60)	0.0023
Yes	6/120	(5.0%)						

Note: Analysis made using logistic regression. Dashed lines indicated that variables are excluded from the final model after likelihood ratio test.

† P-value for trend; indicating that the odds of developing postoperative TT increases with increasing age.

¥ n=492, 4 cases with 5 mattress sutures excluded from analysis

**Surgical incision height in PLTR surgery is measured from the cut edge of the posterior lamella to the lid margin.*

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Table 4: Univariable and multivariable association of factors with postoperative trichiasis by one year after BLTR surgery

Demographic and Clinical Factors	Postoperative TT N=496		Univariable Analysis			Multivariable Analysis		
	n/N	*(%)*	*OR*	*95% CI*	*p-value*	*OR*	*95% CI*	*p-value*
Gender								
Male	23/123	(18.7%)	1.32	(0.79 – 2.21)	0.28	-	-	-
Female	87/373	(23.3%)						
Age, median (IQR)								
18 – 29	10/48	(20.8%)	1.26	(1.09 – 1.46)	0.0005[†]	1.26	(1.06 – 1.49)	0.0076[†]
30 – 39	16/106	(15.1%)						
40 - 49	17/107	(15.9%)						
50 - 59	25/103	(24.3%)						
60 - 69	24/82	(29.3%)						
70+	18/50	(36.0%)						
Trichiasis severity								
Minor	36/257	(14.0%)	2.75	(1.76 – 4.30)	<0.0001	1.88	(1.12 – 3.15)	0.018
Major	74/239	(31.0%)						
Baseline entropion, increasing severity								
E0	2/7	(28.6%)	1.05	(0.76 – 1.45)	0.76[†]	-	-	-
E1	26/83	(31.3%)						
E2	59/331	(17.8%)						
E3	17/66	(25.8%)						
E4	6/9	(66.7%)						
Lash types at baseline,								
Epilating	10/42	(23.8%)	1.25	(0.57 – 2.75)	0.58	-	-	-
Entropic	23/117	(19.7%)	0.98	(0.55 – 1.73)	0.94	-	-	-
Metaplastic	41/205	(20.0%)	1	-	-			
Misdirected	0/13	(0.0%)	-	-	-	-	-	-
Mixed lashes (binary)	36/119	(30.2%)	1.73	(1.03 – 2.92)	0.038	-	-	-
Lash Location								
Epilating	10/42	(23.8%)	1.54	(0.72 – 3.30)	0.26	1.44	(0.61 – 3.39)	0.41
Corneal	63/374	(16.8%)	1	-	-	1	-	-
Peripheral	2/5	(40.0%)	3.29	(0.54 – 20.1)	0.20	3.77	(0.57 – 25.1)	0.17
Corneal + Peripheral	35/75	(46.7%)	4.32	(2.55 – 7.33)	<0.0001	4.44	(2.38 – 8.28)	<0.0001
Conjunctival scarring, baseline								
1	8/54	(14.8%)	1.65	(1.09 – 2.52)	0.0191[†]	1.59	(0.94 – 2.68)	0.08[†]
2	78/366	(21.3%)						
3	24/76	(31.6%)						
Eye								
Right	55/237	(23.2%)	0.89	(0.58 – 1.36)	0.60	-	-	-
Left	55/259	(21.2%)						
Surgeon *(Relative to surgeon 4)*								
1	27/91	(29.7%)	1.84	(0.92 – 3.67)	0.086	1.31	(0.59 – 2.89)	0.51
2	17/93	(18.3%)	0.97	(0.46 – 2.05)	0.94	0.73	(0.31 – 1.73)	0.48
3	17/85	(20.0%)	1.09	(0.51 – 2.30)	0.82	0.57	(0.23 – 1.45)	0.24
4	17/91	(18.7%)	1	-	-	-	-	-
5	12/47	(25.5%)	1.49	(0.64 – 3.46)	0.35	1.86	(0.69 – 5.03)	0.22
6	20/89	(22.5%)	1.26	(0.61 – 2.61)	0.53	1.08	(0.46 – 2.52)	0.86
Number of medial and lateral dissections, median (range)†								
No recurrence	2	(0 – 17)	0.91	(0.82 – 1.01)	0.063	0.83	(0.72 – 0.96)	0.0095
Recurrence	1	(0 – 11)						
Immediate postop central correction								
Corrected	96/424	(22.6%)	1	-	-	1	-	-
Over corrected	8/62	(12.9%)	0.51	(0.23 – 1.10)	0.086	0.43	(0.18 – 1.03)	0.059
Under corrected	6/10	(60.0%)	5.12	(1.42 – 18.5)	0.013	5.04	(1.23 – 20.6)	0.024
Number of mattress sutures[¥]								
3 sutures	89/394	(22.6%)	0.80	(0.46 – 1.41)	0.44	-	-	-
4 sutures	18/95	(18.9%)						
Suture tension across sutures								
Regular	105/481	(21.8%)	1.79	(0.60 – 5.35)	0.30	-	-	-
Irregular	5/15	(33.3%)						

Demographic and Clinical Factors	Postoperative TT N=496		Univariable Analysis			Multivariable Analysis		
External surgical incision height in mm*								
Central								
<4mm	78/411	(19.0%)	2.58	(1.56 – 4.26)	0.0002	2.89	(1.55 – 5.41)	0.0009
≥4mm	32/85	(37.6%)						
Medial								
<4mm	78/400	(19.5%)	2.06	(1.26 – 3.37)	0.0038	-	-	-
≥4mm	32/96	(33.3%)						
Lateral								
<4mm	75/387	(19.4%)	1.97	(1.22 – 3.16)	0.0052	-	-	-
≥4mm	35/109	(32.1%)						
Surgical scar height in mm								
Central								
<4mm	9/21	(42.9%)	0.35	(0.14 – 0.85)	0.021	-	-	-
≥4mm	97/468	(20.7%)						
Medial								
<4mm	27/76	(35.5%)	0.43	(0.25 – 0.73)	0.0018	0.39	(0.21 – 0.72)	0.0027
≥4mm	79/413	(19.1%)						
Lateral								
<4mm	29/104	(27.9%)	0.64	(0.39 – 1.06)	0.085	-	-	-
≥4mm	77/385	(20.0%)						
Eyelid contour abnormality (ECA)								
No	92/404	(22.8%)	0.72	0.39 – 1.31	0.28	-	-	-
Yes	15/86	(17.4%)						

Note: Analysis made using logistic regression. Dashed lines indicated that variables are excluded from the final model after likelihood ratio test.

† P-value for trend; indicating that the odds of developing postoperative TT increases with increasing age.

¥ n=489, 7 cases with 5 mattress sutures excluded from analysis

** Surgical incision height in BLTR surgery was measured externally on the skin*

Table 5: Univariable and multivariable association of factors with Eyelid Contour Abnormality (ECA) at one year, by type of surgery

Demographic and Clinical Factors	PLTR (N=491)								BLTR (N=490)							
	ECA		Univariable			Multivariable			ECA		Univariable			Multivariable		
	n/N	*(%)*	*OR*	*95% CI*	*p-value*	*OR*	*95% CI*	*P-value*	*n/N*	*(%)*	*OR*	*95% CI*	*p-value*	*OR*	*95% CI*	*p-value*
Gender																
Male	26/110	(23.6%)	1.06	(0.64 – 1.74)	0.82	-	-	-	21/121	(17.4%)	1.02	(0.59 – 1.75)	0.95	-	-	-
Female	94/381	(24.7%)							65/369	(17.6%)						
Age, continuous																
18 – 29	8/59	(13.6%)	1.39	(1.20 – 1.62)	<0.0001†	1.39	(1.20 – 1.62)	<0.0001†	5/48	(10.4%)	1.14	(0.98 – 1.34)	0.092†	1.20	(1.02 – 1.42)	0.031†
30 – 39	11/85	(12.9%)							17/106	(16.0%)						
40 - 49	27/123	(21.9%)							18/106	(17.0%)						
50 - 59	32/108	(29.6%)							20/101	(19.8%)						
60 - 69	25/73	(34.2%)							14/81	(17.3%)						
70+	17/43	(39.5%)							12/48	(25.0%)						
Trichiasis severity																
Minor	61/264	(23.1%)	1.17	(0.77 – 1.76)	0.46	-	-	-	43/256	(16.8%)	1.11	(0.70 – 1.78)	0.65	-	-	-
Major	59/227	(26.0%)							43/234	(18.4%)						
Conjunctival scarring, baseline																
1	13/47	(27.7%)	0.74	(0.48 – 1.13)	0.16†	-	-	-	5/52	(9.6%)	1.52	(0.96 – 2.42)	0.077†	1.72	(1.06 – 2.81)	0.029†
2	94/370	(25.4%)							65/366	(17.7%)						
3	13/74	(17.6%)							16/72	(22.2%)						
Surgeon *(Relative to surgeon 3)*																
1	21/86	(24.4%)	1.37	(0.66 – 2.86)	0.40	1.13	(0.53 – 2.44)	0.74	10/91	(11.0%)	1.90	(0.62 – 5.81)	0.26	1.87	(0.60 – 5.81)	0.28
2	27/95	(28.4%)	1.69	(0.83 – 3.41)	0.14	1.60	(0.78 – 3.28)	0.20	25/92	(27.2%)	5.75	(2.08 – 15.9)	0.0007	5.84	(2.07 – 16.4)	0.0008
3	16/84	(19.0%)	-	-	-	-	-	-	5/82	(6.1%)	1	-	-	-	-	-
4	19/90	(21.1%)	1.14	(0.54 – 2.39)	0.73	0.99	(0.46 – 2.14)	0.98	11/91	(12.1%)	2.12	(0.70 – 6.38)	0.18	2.13	(0.70 – 6.52)	0.18
5	17/47	(36.2%)	2.41	(1.08 – 5.40)	0.033	2.39	(1.04 – 5.49)	0.040	10/47	(21.3%)	4.16	(1.33 – 13.05)	0.014	4.40	(1.37 – 14.2)	0.013
6	20/89	(22.5%)	1.23	(0.59 – 2.58)	0.58	1.15	(0.54 – 2.44)	0.72	25/87	(28.7%)	6.21	(2.25 – 17.2)	0.0004	5.81	(2.07 – 16.3)	0.0009
Number of mattress sutures																
3 sutures	103/396	(26.0%)	0.65	(0.37 – 1.16)	0.15	-	-	-	74/388	(19.1%)	0.44	(0.21 – 0.92)	0.030	-	-	-
4 sutures	17/91	(18.7%)							9/95	(9.5%)						

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Demographic and Clinical Factors	PLTR (N=491)								BLTR (N=490)							
	ECA		Univariable			Multivariable			ECA		Univariable			Multivariable		
	n/N	*(%)*	*OR*	*95% CI*	*p-value*	*OR*	*95% CI*	*P-value*	*n/N*	*(%)*	*OR*	*95% CI*	*p-value*	*OR*	*95% CI*	*p-value*
Sutures distance																
Symmetric	108/468	(23.1%)	3.64	(1.56 – 8.47)	0.0028	3.18	(1.31 – 7.70)	0.010	77/457	(16.8%)	1.85	(0.83 – 4.14)	0.13	-	-	-
Asymmetric*	12/23	(52.2%)							9/33	(27.3%)						
Suture tension across sutures																
Regular	116/476	(24.4%)	1.13	(0.35 - 3.61)	0.84	-	-	-	82/475	(17.3%)	1.74	(0.54 – 5.61)	0.35	-	-	-
Irregular	4/15	(26.7%)							4/15	(26.7%)						
Immediate postop central correction																
Corrected	104/421	(24.7%)	1	-	-				67/419	(16.0%)	1	-	-	1	-	-
Over corrected	16/59	(27.1%)	1.13	(0.61 – 2.10)	0.69	-	-	-	17/61	(27.9%)	2.03	(1.09 – 3.76)	0.025	2.45	(0.95 – 6.30)	0.063
Under corrected	0/11	(0.0%)	-	-	-				2/10	(20.0%)	1.31	(0.27 – 6.32)	0.73	2.03	(0.59 – 6.96)	0.26
Surgical incision height in mm																
Central																
<4mm	109/438	(24.9%)	0.79	(0.39 – 1.59)	0.51	-	-	-	74/407	(18.2%)	0.76	(0.39 – 1.47)	0.42	-	-	-
≥4mm	11/53	(20.7%)							12/83	(14.5%)						
Medial																
<4mm	109/434	(25.1%)	0.71	(0.36 – 1.42)	0.338	-	-	-	72/396	(18.2%)	0.79	(0.42 – 1.47)	0.45	-	-	-
≥4mm	11/57	(19.3%)							14/94	(14.9%)						
Lateral																
<4mm	110/448	(24.5%)	0.93	(0.44 – 1.95)	0.85	-	-	-	74/384	(19.3%)	0.53	(0.28 – 1.03)	0.060	-	-	-
≥4mm	10/43	(23.3v)							12/106	(11.3%)						
Surgical scar height in mm																
Central																
<4mm	3/27	(11.1%)	2.70	(0.79 – 0.91)	0.11	-	-	-	9/21	(42.9%)	0.26	(0.11 – 0.64)	0.0035	0.31	(0.12 – 0.82)	0.018
≥4mm	117/464	(25.2%)							77/468	(16.4%)						
Medial																
<4mm	19/95	(20.0%)	1.37	(0.79 – 2.38)	0.26	-	-	-	21/76	(27.6%)	0.49	(0.28 – 0.86)	0.014	-	-	-
≥4mm	101/396	(25.5%)							65/413	(15.7%)						
Lateral																
<4mm	25/106	(23.6%)	1.06	(0.64 – 1.76)	0.82	-	-	-	22/104	(21.1%)	0.74	(0.43 – 1.28)	0.28	-	-	-
≥4mm	95/385	(24.7%)							64/385	(16.6%)						

Note: Analysis made using logistic regression. Dashed lines indicated that variables are excluded from the final model after likelihood ratio test

** Spaced between >2 mm symmetry difference between each other*

ECA = Eyelid Contour Abnormality

† P-value for trend; testing if there is linear association between ECA and the variable of interest.

Table 6: Univariable and multivariable association of factors with Conjunctival Granuloma in one year, by type of surgery

Demographic and Clinical Factors	PLTR (N=496)								BLTR (N=496)				
	Granuloma		Univariable			Multivariable			Granuloma		Univariable		
	n/N	(%)	OR	95% CI	p-value	OR	95% CI	P-value	n/N	(%)	OR	95% CI	p-value
Gender													
Male	7/111	(6.3%)	0.77	(0.32 – 1.88)	0.57	-	-	-	4/123	(3.2%)	0.57	(0.16 – 1.98)	0.37
Female	19/385	(4.9%)							7/373	(1.9%)			
Age, continuous													
18 – 29	4/59	(6.8%)	1.00	(0.76 – 1.30)	0.98†	-	-	-	0/48	(0.0%)	1.20	(0.79 – 1.79)	0.39†
30 – 39	5/85	(5.9%)							1/106	(0.9%)			
40 - 49	5/123	(4.1%)							3/107	(2.8%)			
50 - 59	3/108	(2.8%)							4/103	(3.9%)			
60 - 69	7/74	(9.5%)							3/82	(3.7%)			
70+	2/47	(4.3%)							0/50	(0.0%)			
Trichiasis severity													
Minor	15/266	(5.6%)	0.84	(0.38 – 1.87)	0.67	-	-	-	6/257	(2.3%)	0.89	(0.27 – 2.97)	0.85
Major	11/230	(4.8%)							5/239	(2.1v)			
Surgeon *(Relative to surgeon 3)*													
1	5/89	(5.6%)	1.82	(0.42 – 7.87)	0.42	-	-	-	2/91	(2.2%)	1.90	(0.62 – 5.81)	0.26
2	3/95	(3.2%)	1	-	-	-	-	-	1/93	(1.1%)	1	-	-
3	9/84	(10.7%)	3.68	(0.96 – 14.1)	0.42	-	-	-	3/85	(3.5%)	3.37	(0.34 – 33.0)	0.30
4	3/92	(3.3%)	1.03	(0.20 – 5.26)	0.97	-	-	-	2/91	(2.2%)	2.07	(0.18 – 23.2)	0.56
5	2/47	(4.3%)	1.36	(0.22 – 8.45)	0.74	-	-	-	1/47	(2.1%)	2.00	(0.12 – 32.7)	0.63
6	4/89	(4.5%)	1.44	(0.31 – 6.34)	0.64	-	-	-	2/89	(2.2%)	2.11	(0.19 – 23.7)	054
Central incision in relation to lid margin													
Regular/parallel	23/486	(4.7%)	8.6	(2.1 – 35.5)	0.0029	6.72	(1.55 – 29.0)	0.011	1/13	(7.7%)	-	-	-
Irregular/unparalleled or slanted	3/10	(30.0%)							25/483	(5.2%)			
Surgical incision height in mm													
Central													
<4mm	21/442	(4.7%)	2.05	(0.74 – 5.67)	0.17	-	-	-	8/411	(1.9%)	1.84	(0.48 – 7.1)	0.37
≥4mm	5/54	(9.3%)							3/85	(3.5%)			
Sutures distance													
Symmetric	23/472	(4.9%)	2.79	(0.77 – 10.0)	0.12	-	-	-	10/463	(2.2%)	1.42	(0.18 – 11.4)	0.74
Asymmetric *	3/24	(12.5%)							1/33	(3.1%)			
Suture tension across sutures													
Regular	24/481	(5.0%)	2.93	(0.62 – 13.7)	0.17	-	-	-	10/481	(2.1%)	3.36	(0.40 – 28.1)	0.26
Irregular	2/15	(13.3%)							1/15	(6.7%)			
ECA													
No	13/371	(3.5%)	3.35	(1.51 – 7.43)	0.0030	3.08	(1.37 – 6.94)	0.0066	8/404	(2.0%)	1.79	(.46 – 6.89)	0.40
Yes	13/120	(10.8%)							3/86	(3.5%)			

*Note: Analysis made using logistic regression. Dashed lines indicated that variables are excluded from the final model after likelihood ratio test. * Spaced between >2 mm symmetry difference between each other.* † P-value *for trend; testing if there is linear association between conjunctival granuloma and the variable of interest.*

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Discussion

Poor outcomes from TT surgery affect both the individual and the TT programme as a whole. A good understanding of the factors that increase the likelihood of an adverse outcome is crucial for surgeons, surgical trainers and programme planners. In this study we explored factors associated with postoperative trichiasis, ECA and granuloma formation following PLTR and BLTR surgeries. The results showed a range of intra and immediate postoperative factors are probably vital in shaping trichiasis surgery outcomes.

Postoperative TT

Peripheral dissections

Perhaps one of the most useful findings of this study was that performing more medial and lateral dissection using scissors to increase the length of surgical incision markedly reduced the rate of postoperative TT for both PLTR and BLTR. A longer incision allows the distal fragment to rotate adequately and once secured with sutures, it pulls back less to the original entropic position. Additionally, the longer incision probably allows the most medial and lateral extents of the lid to rotate more freely, thereby successfully correcting the peripheral trichiasis. Failing to extending the ends of the incision further to the peripheries of the lid margin is a common error in PLTR surgery that later leads to peripheral recurrence.[26]

Baseline lash location was an important determinant of postoperative TT for both surgeries. Peripheral TT lashes and mixed location lashes were substantially more likely to recur than corneal only lashes in PLTR surgery; while mixed location lashes were more likely to recur than corneal only lashes in BLTR surgery. This may be attributable to an insufficiently long surgical incision, failing to correct the extremes of the eyelid. An earlier study has reported comparable results, where eyelids with shorter incisions had a four-fold higher rate of recurrent TT than those with longer incision length.[27] Training should focus on how to make proper peripheral dissections using scissors to achieve adequate rotation.

Incision height

There was a trend towards lower recurrence rate in cases with ≥4mm incision height from the lid margin in PLTR surgery. Higher incision height creates a larger distal segment that rotates more freely, pulling the lashes further away from the globe. In contrast, BLTR surgery cases with central incision height of ≥4mm had nearly two times more postoperative TT than those with <4 mm incision height. This difference might be attributed to the following. Firstly, it is possible that in BLTR, despite a higher incision height, the distal fragment does not rotate as well as the PLTR. In a prospective cohort study, among 380 patients with mild to moderate trachomatous cicatricial entropion operated using BLTR with an incision made at >3mm distance from the lid margin (on the eyelid crease), 275 (72.3%) had adequate results after two years.[28] In comparison, in the same study, among 500 patients with moderate to severe cicatricial entropion and operated using PLTR with an incision made at about 2mm from the grey line, 410 (82%) had adequate results after about 2 years.[28] These results suggest that compared to the PLTR, the BLTR still might have a lower success rate even with a slightly higher incision height. This might be related to the fact that there is no dissection between the two lamellae in BLTR. Without this dissection, there may still be too much tension holding the large distal segment or pulling it back to the entropic position. Secondly, in our study the incision height in the BLTR is measured from the skin immediately after the incision. However, this distance may not be accurate due to the distension of the skin by the local anaesthetic. The incision in the posterior lamella is likely to be stable, and may not necessarily correspond to the skin incision measurement. Thirdly, higher incisions result in more than the intended over correction. Therefore the surgeons would apply low tension eversion sutures as per the WHO training manual, which later, despite the high incision, might result in under correction and then PTT.[6]

A report from the PRET trial on the effect of surgical scar height on trichiasis surgical outcomes showed that eyelids with central incision scar height of <4.5mm had more recurrence one year after BLTR surgery than those with higher incision heights.[29] This is consistent with our findings of a trend to lower postoperative trichiasis rates in cases with ≥4mm internal incision scar height in both PLTR and BLTR surgeries. However, we also found that internal incision scar height is not correlated with intraoperative incision heights in both PLTR and BLTR. The scar height is significantly higher than the intraoperative incision height with a mean difference ranging between 1.2mm and 2.3mm across the eyelid. This suggests that other factors such as progressive scarring might have a role in determining the position of the surgical scar in 12-months. Overall, these results indicate that the current WHO recommended surgical incision height of about 3mm should be maintained for both PLTR and BLTR surgeries. The height of the incision to be made should be marked prior to the infiltration of the anaesthesia.

Suture tension

Irregular suture tension at the end of surgery was associated with more PTT in both PLTR and BLTR surgeries, although this was not statistically significant. Suture tension is an essential part of trichiasis surgery as the outward rotation of the entropic eyelid is dependent on how tight the sutures are tied. Irregularity in the suture tension would lead to under correction around the loosely tied eversion sutures. Eyelid position reverts quickly after the surgery, particularly as the swelling settles down and the sutures can appear looser few days after the surgery, failing to hold the distal portion of the eyelid to the intended corrected position. There are no reports on the effect of suture tension on surgical outcomes. The WHO trichiasis surgery training manual recommends that all sutures should be "tightened firmly enough to produce a slight overcorrection". Correct placement and adequate tightening of eversion sutures should be mastered during trainings before the trainees operate on patients.

Patient related factors

In addition to preoperative lash location discussed above, preoperative major trichiasis and older age were independent predictors of PTT for both surgical procedures in this and other clinical trials.[10,12,14,17,27,29-31] These were also predictors for major PTT in BLTR (but not in PLTR) surgery in this study. Operating on severe trichiasis cases is often difficult due to severe tarsal conjunctival scarring and associated lid shortening.[27,30] Our study showed that, major trichiasis was associated with more severe conjunctival scarring at baseline than minor TT. Severe conjunctival scarring and old age may affect wound healing, resulting in the eyelid reverting to its entropic position.[27,30] Preoperative major trichiasis and older patients should ideally be treated by the most experienced surgeon available to minimize failure.

Eyelid Contour Abnormality

Suture spacing asymmetry of >2mm increased the rate of ECA by more than two fold in PLTR surgery. Unequal suture positioning probably creates unbalanced forces that distort the lid margin.[30] TT surgical training programmes must emphasise the importance of meticulous surgical technique and accurate suture placement. Smooth insertion and then suturing of the cut end of the large fragment tarsus into the pocket created through dissection between the two lamellae at the distal fragment in alignment with where it has been dissected should be emphasized in initial and subsequent trainings of PLTR surgery. The use of four mattress sutures was associated with reduced ECA, probably because there is less opportunity for uneven suture placement. ECA rates for both PLTR and BLTR varied by surgeons. In our study, two surgeons had consistently higher rates of ECA for both procedures. This indicates that despite rigorous training and extensive experience subtle differences in how the incisions are made and the sutures are positioned may result in ECA. In addition, the primary objective of TT surgery is to treat the TT. Therefore, trainings and standardizations often focus more on how to achieve effective outward rotation and avoid surgical failure and recurrence than on how to prevent ECA.

Higher incision scar at the center of the eyelid was associated with a lower ECA rate in BLTR surgery. We would expect the opposite. However, this fits with the above finding that despite a higher incision the distal fragment in BLTR surgery may not be rotated adequately, resulting in higher rates of failure and less over-rotation or notching. A similar result has been reported from another study, where the proportion of cases with ECA was lower in those with scar height of ≥4.5mm.[29] ECA were more frequent in older people following PLTR and BLTR surgery in this study, possibly because older individuals already have more distorted eyelids from the more advanced tarsal scarring or because the older eyelid is more pliable and therefore more susceptible to irregular suture tensions and forces. Similar results have been reported in earlier studies that used BLTR.[27,30]

Conjunctival Granuloma

Conjunctival granuloma is more common in the PLTR surgical procedure. This is consistent with findings in other studies.[19,28,30] There was evidence that an irregular/slanted posterior lamellar incision in the central third of the eyelid increased the rate of granuloma formation by more than six-fold in PLTR surgery. This finding is consistent with the mechanism of granuloma formation we had previously hypothesised in relation to tissue defects following PLTR surgery.[11] An irregular posterior lamellar incision may leave a larger defect in the tarsal conjunctiva; while a smooth posterior lamellar incision would achieve a quick wound healing process. It has been reported that a gap between the incised edge of the posterior lamella from inadequate suturing in PLTR surgery may lead to granuloma formation.[26] We found irregular suture tension tends to result in higher rates of granuloma formation in both PLTR and BLTR surgeries. Other studies have reported retained suture fragments as a potential causes for granuloma formation; and it is possible that this in conjunction with the open conjunctival defect increases the likelihood of granuloma formation in PLTR.[27] Granuloma was much less likely after BLTR, presumably because the operation, which used the Waddell clamp, does not leave a significant conjunctival defect.[13]

Strengths and Limitations

This study has a very high follow-up rate of a large cohort of patients, providing good power to examine the determinants of the outcomes of both PLTR and BLTR surgery. Three well trained nurses made intra and immediate postoperative observations. The surgical incision in the BLTR surgery was measured externally on the skin, which could be a more variable measure than the incision and scar height on the posterior lamella. The potential design limitations of such a surgical trial, such as risk of unmasking during the operation, and in the follow-ups due to surgical scars have been discussed previously in detail.[11] However, independent photograph grading analysis showed there was no evidence of systematic bias in the field grading.[11] Moreover, procedure unmasking is less likely to be an issue in this particular analysis as determinants of surgical outcome were analysed within each surgical procedure. It is possible that other unstudied factors in this trial such as genetic predisposition, imbalance in the initial wound healing process and progression of conjunctival inflammation and scarring could influence TT surgical outcomes.

Conclusions

Overall, specific surgical factors such as inadequate peripheral dissection, irregular incision, asymmetric suture position and tension, and inadequate correction along with preoperative TT severity and location; and old age determine outcomes following TT surgery. These are relatively straightforward to address during surgical training and surgical practice and should be incorporated into TT surgery programmes with further studies to assess their impact in the field. Surgical training should provide practical training on how to identify surgery related predictors of unfavourable outcome and manage these immediately during or after the completion of the surgery. Trainings should be supported by HEAD START (mannequin-based training programme) and the use of trichiasis surgery training DVD.[8,32] Surgical outcomes monitoring should be strengthened. A system for frequent and regular supportive supervision and active follow-up of patients should be implemented. Surgeons with consistently undesirable surgical outcomes should be identified and causes of poor surgical outcomes should be explored. Further research is needed on how to improve surgical outcomes, on the effect of immediate postoperative correction of an unfavorable outcome, and on how to manage postoperative TT and clinically significant ECA.

Contributors

EH and MJB did the literature search. EH, SNR, KC, HAW, and MJB were responsible for the study conception and design. EH, TW, SA, ZT, MZ, BG, GSW, and HD collected the data. EH, HAW, and MJB did the statistical analysis. EH, SNR, HAW, and MJB were responsible for the interpretation of the data. EH drafted the manuscript. All authors critically revised the manuscript for important intellectual content. MJB obtained the funding. TW, SA, ZT, MZ, BG, GSW, HD, and KC provided administrative, technical, or material support. MJB was the study supervisor.

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6. Trachoma and Relative Poverty: A Case Control Study

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RESEARCH PAPER COVER SHEET FOR RESEARCH PAPERS ALREADY PUBLISHED

Section A - Student details

Student	Esmael Habtamu Ali
Principal Supervisor	Prof Matthew Burton
Thesis Title	Trachomatous Trichiasis: Surgical Management and Impact

Section B - Published Paper Details

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Have you retained the copyright for the work?	Yes. Please see first page of the published paper where the following is indicated: *"Copyright: © 2015 Habtamu et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited."*
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Section D - Multi-authored Work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper	With senior colleagues I designed the study and prepared the protocol / SOP, led the research project and collected data, analysed data and wrote the first draft of the paper with edits from my supervisor and co-authors.

Student Signature: Esmael Habtamu Ali Date: 15th December 2016

Supervisor Signature: Prof. Matthew Burton
Date: 1st December 2016

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RESEARCH ARTICLE

Trachoma and Relative Poverty: A Case-Control Study

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Abstract

Background

Trachoma is widely considered a disease of poverty. Although there are many epidemiological studies linking trachoma to factors normally associated with poverty, formal quantitative data linking trachoma to household economic poverty within endemic communities is very limited.

Methodology/Principal Findings

Two hundred people with trachomatous trichiasis were recruited through community-based screening in Amhara Region, Ethiopia. These were individually matched by age and gender to 200 controls without trichiasis, selected randomly from the same sub-village as the case. Household economic poverty was measured through (a) A broad set of asset-based wealth indicators and relative household economic poverty determined by principal component analysis (PCA, (b) Self-rated wealth, and (c) Peer-rated wealth. Activity participation data were collected using a modified 'Stylised Activity List' developed for the World Bank's Living Standards Measurement Survey. Trichiasis cases were more likely to belong to poorer households by all measures: asset-based analysis (OR = 2.79; 95%CI: 2.06–3.78; p<0.0001), self-rated wealth (OR, 4.41, 95%CI, 2.75–7.07; p<0.0001) and peer-rated wealth (OR, 8.22, 95% CI, 4.59–14.72; p<0.0001). Cases had less access to latrines (57% v 76.5%, p = <0.0001) and higher person-to-room density (4.0 v 3.31; P = 0.0204) than the controls. Compared to controls, cases were significantly less likely to participate in economically productive activities regardless of visual impairment and other health problems, more likely to report difficulty in performing activities and more likely to receive assistance in performing productive activities.

all the data and had final responsibility for the decision to submit for publication.

Competing Interests: The authors have declared that no competing interests exist.

Conclusions/Significance

This study demonstrated a strong association between trachomatous trichiasis and relative poverty, suggesting a bidirectional causative relationship possibly may exist between poverty and trachoma. Implementation of the full SAFE strategy in the context of general improvements might lead to a virtuous cycle of improving health and wealth. Trachoma is a good proxy of inequality within communities and it could be used to target and evaluate interventions for health and poverty alleviation.

Author Summary

Trachoma has long been considered a disease of poverty. However, there is surprisingly little direct data that formally quantifies the relationship between trachoma and economic poverty, and none that specifically focuses on trichiasis. We compared 200 people with trachomatous trichiasis (TT) to 200 people (controls) without the condition, who were matched on age and sex, living in the same community, in Amhara Region, Ethiopia. We measured household relative poverty using three measures: household assets, self-rated wealth and peer-rated wealth. We also measured activity participation. We found TT case households were poorer by all relative economic measures. We found cases less likely to participate in economically productive activities regardless of visual impairment and other health problems, more likely to report difficulty and need assistance performing activities. The results suggest that the causative relationship between poverty and trachoma could possibly be bidirectional: poor households are more affected by trachoma and trichiasis reduces productivity even prior to development of visual impairment, which may exacerbate poverty. Implementation of the SAFE strategy in the context of general socioeconomic improvements might lead to a virtuous cycle of improving health and wealth. Trachoma could be used as proxy of inequality and to target and evaluate interventions for health and poverty alleviation.

Introduction

Trachoma is leading infectious cause of blindness worldwide [1]. Trachomatous trichiasis (TT) is the late stage consequence of repeated conjunctival *Chlamydia trachomatis* infection in which eyelashes turn towards the eye, causing pain and eventually irreversible blinding corneal opacification (CO). About 229 million people live in trachoma endemic areas, and approximately 7.3 million have untreated TT [2,3]. More than 2.4 million people are visually impaired from trachoma worldwide, among which between 439,000 and 1.2 million are estimated to be irreversibly blind [2,4]. The WHO recommends the SAFE Strategy for trachoma control [5]. This involves **S**urgery for trichiasis, **A**ntibiotics for infection, **F**acial cleanliness and **E**nvironmental improvements to suppress chlamydial infection and transmission.

Trachoma has long been considered a disease of poverty [6]. It is believed that the decline in trachoma observed in Europe, North America and elsewhere over the last century, in the absence of specific control measures, was largely attributable to general improvements in socio-economic status [7,8]. Trachoma remains prevalent in developing and marginalised communities, particularly in Africa, where crowded living conditions are common and access to clean water, sanitation and health care are often limited [6,8,9]. However, not all people living in such settings acquire active or scarring trachoma. It is possible that, within apparently homogeneous communities, the individuals who are most vulnerable to developing the blinding complications of trachoma are the poorest members of the poorest communities, although this has not been adequately investigated [10]. Moreover, the disability that TT causes may lead to reduced productivity, unemployment and loss of income, putting additional financial pressure on an already strained household [11–13]. The effect of trachoma on income may begin prior to the visual impairment, with the pain and the photophobia from trichiasis limiting function [13,14]. Of note, blindness has generally been associated with lower socio-economic status [15–17].

In low and middle income countries (LMICs) resources are often shared within households. Therefore, relative wealth or poverty in LMICs needs to be measured at household level, as the economic impact of a medical condition or intervention potentially affects the whole family [18]. In low-income settings estimating income can be difficult, as many people are self-employed and incomes are subject to significant short-term fluctuations [18,19]. In addition, people may earn from sources that they do not wish to disclose. Consumption expenditure data are considered more reliable than income data [16,19]. However, this method is subject to recall bias and requires detailed questionnaires, which are time consuming and costly to administer [19]. An alternative approach is to use a range of asset and housing characteristics as proxy indicators for household wealth and socio-economic status [19,20]. A key advantage of this approach is that it measures the long-term financial status of a household, and is less vulnerable to short-term fluctuations than income and consumption expenditure [19,20]. On the other hand, asset score only measure relative poverty, which may preclude regional or international comparability.

There is surprisingly little direct data that formally quantifies the relationship between trachoma and economic poverty, and none that specifically focuses on the scarring sequelae. The aim of this study was to investigate in detail the relationship between poverty and trachomatous trichiasis through an asset-based analysis, self-rated and peer-rated wealth measures, and participation in productive activities.

Methods

Ethics Statement

This study was reviewed and approved by the Food, Medicine and Healthcare Administration and Control Authority of Ethiopia, the National Health Research Ethics Review Committee of the Ethiopian Ministry of Science and Technology, Amhara Regional Health Bureau Research Ethics Review Board Committee, the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee, and Emory University Institutional Review Board. Written informed consent in Amharic was obtained prior to enrolment from participants. If the participant was unable to read and write, the information sheet and consent form were read to them and their consent recorded by thumbprint.

Study Design and Participants

This case-control study was nested within a clinical trial of two alternative surgical treatments for trichiasis. From the 1000 trichiasis cases recruited into the trial, every fifth consecutive case was also enrolled into this economic poverty study and matched to a non-trichiasis control. This approach was chosen for logistical and methodological reasons, in order to identify and collect data from controls within the shortest possible time period following case recruitment. Cases were defined as individuals with one or more eyelashes touching the eyeball or with evidence of epilation in either or both eyes in association with tarsal conjunctival scarring. People with trichiasis of other causes, recurrent trichiasis and those under 18 years were excluded. Trichiasis cases were identified mainly through community-based screening. Trichiasis screeners and counsellors (Eye Ambassadors) visited every household in their target village, identified and referred trichiasis cases to health facilities where surgical services were provided. Some individuals self-presented or were referred by local health workers. Recruitment was mainly from three districts of West Gojam Zone, Amhara Region, Ethiopia between February and May 2014. This area has one of the highest burdens of trachoma worldwide [21].

Controls were individuals without clinical evidence or a history of trichiasis (including surgery and epilation), and who came from households without a family member with trichiasis or a history of trichiasis, as we wanted to measure household level relative poverty, which requires comparison of trichiasis case households with households without trichiasis cases. One control was individually matched to each trichiasis case by location, sex and age (+/- two years). The research team visited the sub-village (30–50 households) of the trichiasis case requiring a matched control. A list of all potentially eligible people living in the sub-village of was compiled with the help of the sub-village administrator. One person was randomly selected from this list using a lottery method, given details of the study and invited to participate if eligible. If a selected individual refused or was ineligible, another was randomly selected from the list. When eligible controls were not identified within the sub-village of the case, recruitment was done in the nearest neighbouring sub-village, using the same procedures.

Data Collection

Data on detailed demographic characteristics were collected. Household economic poverty was measured through (a) Asset based wealth indicators, (b) Self-rated wealth, and (c) Peer-rated wealth. Activity participation data was collected using a modified 'Stylised Activity List' developed for the World Bank's Living Standards Measurement Survey [22]. Visual acuity of both cases and controls were measured and cases underwent detailed trachoma examination.

Asset-based wealth inequality indicators. Data on 60 asset variables were collected. This included (i) housing characteristics and utilities, (ii) ownership of durable assets, and (iii) ownership of agricultural assets. Most data were collected through direct observation. Data on access to water was not collected as it is mainly supplied by government and non-governmental organisations, therefore would not directly reflect the household's wealth but rather general infrastructure development in the area. Households were asked about their financial savings and whether they had loans from the government at the time of data collection.

Self and peer-rated wealth indexes. The participants were asked the question: "*How well-off do you think your household is in relation to the other households in the village*?" They were then asked to choose one of the following options: (1) very poor, (2) poor, (3) average, (4) wealthy or (5) very wealthy. Three members of the village administration team (peers of both the cases and the controls) were then randomly selected and independently asked the question: *"How well-off do you think [Name of household head] household is in relation to the other households in the village*?*"* for both the case and the control households. They were asked to choose one of the five levels.

Activity participation data. The 'Stylised Activity List' tool contains a list of common activities in different subgroups: household activities, paid work, work for own use, leisure activities and personal activities.[22,23] Participants were asked if they had participated in any of the activities in the subgroups in the last week. If they had undertaken a specific activity in the last week, they were asked the question *"How much difficulty did you have in doing [Activity] in the last week*?*"* and asked to choose one of the following options: (0) extreme/not able to do, (1) a lot of difficulty, (2) some difficulty, (3) little difficulty, (4) no difficulty; and another question whether they have done the activity (1) fully assisted, (2) with some assistance, (3) with no assistance.

Visual acuity and clinical examination. Presenting LogMAR (Logarithm of the Minimum Angle of Resolution) visual acuity at two metres was measured using "PeekAcuity" software on a smartphone in a dark room [24]. The ophthalmic examination was conducted in a dark room using a 2.5x binocular magnifying loupe and a bright torch. Clinical signs were graded using the Detailed WHO Follicles Papillae Cicatricae (FPC) Grading System [25].

Sample Size

To detect a difference in asset-based principal component analysis (PCA) similar to that found in the Cataract Impact Study (mean and standard deviation of asset based PCA score in cataract cases and their controls 0.6 and 2.0; and 0.3 and 2.6, respectively) with an alpha of 0.05 and 95% power, at least 346 (173 in each group) participants were required [16]. We recruited 200 trichiasis cases and 200 age, sex and location matched non-trichiasis controls.

Analysis

Data were double-entered into Access (Microsoft) and transferred to Stata 11 (StataCorp) for analysis. Conditional logistic regression was used to compare basic characteristics of matched cases and controls.

Asset index analysis. Descriptive and summary statistics of all asset indicators were calculated. A PCA was used to analyse the asset-based wealth or inequality indicator data in order to classify households into different socio-economic levels [19,20,26–28]. Variables owned by less than 5% or more than 95% of the participants' households were excluded from the PCA as they would have the least weight and less value in differentiating socio-economic status or inequality. The PCA was conducted separately to generate a factor score for each of the three subset asset indices: (1) housing and utilities, (2) durable assets and (3) agricultural assets, and for all asset variables combined [19,20,27]. The control households were grouped into quintiles based on the overall asset index socio-economic score (SES). Then the case households were classified based on the "cut points" of the controls' socio-economic quintiles. We performed matched univariable and multivariable conditional logistic regression analyses to investigate the relationship between asset-based household economic poverty and case-control status. A stratified analysis was performed to test whether the observed association persisted in different groups. Logistic regression adjusted for clustering using robust standard errors was used for stratified analyses of all economic poverty measures by age, sex, marital status and vision, and variables of insufficient frequencies (such as government loan) for matched analysis. Likelihood ratio tests were used to obtain p-values in categorical exposure variables. To test for robustness of the asset index a Spearman rank correlation coefficient was employed to examine whether the three sub-set asset indices produce similar classifications of SES to the overall asset index. To adjust for multiple comparisons, we used the Benjamini and Hochberg method, assuming a false discovery rate (FDR) of 5% [29].

Self and peer-rated wealth indexes. The wealth scores provided by the three peers were averaged. The association between self and peer-rating of household socio-economic status and case-control status was examined using conditional logistic regression. The self-rated and peer-rated wealth scores were converted into a score out of one hundred, using the formula: ([individual score–lowest possible score]/[Highest possible score—lowest possible score])x100. Lower scores indicate a worse score (0 the lowest possible score) and higher scores indicates better score (100 the highest score) [30]. The mean scores were compared between cases and controls using the Wilcoxon rank-sum test. The correlations of the self-rated wealth, the peer-rated wealth and the asset index based socio-economic classifications of households were compared using Spearman rank correlation coefficient.

Activity and participation data. Activities undertaken (paid employment and commission work) and not undertaken (talking with friends) by <1% participants were excluded from the analysis. Activities were regrouped into productive household activities, outdoor activities, paid work, agricultural activities and leisure activities. The association between participation in an activity and case-control status were analysed using conditional logistic regression adjusting for self-reported health problems occurring in the last month. Logistic regression adjusted for clustering (using robust standard errors), age, sex and self-reported health problems was used to analyse the difference in activity participation between cases and controls stratified by vision, and to analyse the association between case-control status and difficulty in doing an activity and receiving assistance.

Clinical data. Presenting visual acuity in the better eye was used in analysis. For visual acuities of counting fingers or less, LogMAR values were attributed as follows: counting fingers, 2.0; hand movements, 2.5; perception of light, 3.0; and no perception of light, 3.5 [31]. The LogMAR visual acuity scores were categorised using the WHO classification: normal vision, ≥6/18; moderate visual impairment, <6/18 to ≥6/60; severe visual impairment, <6/60 to ≥3/60; and blind, <3/60. Corneal opacity grading and trichiasis grading in the more affected eye was undertaken to test their association with household economic poverty among trichiasis cases. Based on their severity, trichiasis cases were categorised into Minor Trichiasis cases with <6 lashes or evidence of epilation in <1/3rd of the lash margin; and Major Trichiasis cases with ≥6 lashes or evidence of epilation in ≥1/3rd of the lash margin.

Results

Demographic and Clinical Characteristics of Participants

Cases and controls were well matched in terms of location, gender and age and had similar levels of literacy, household size and household occupation (Table 1). Compared to the controls, the trichiasis cases were less likely to be married, more likely to be either unemployed or work as daily labourers, less likely to have a family member with formal education and more likely to have experienced a health problem during the last month. As expected, cases were more likely to be visually impaired than the controls (37.0% v 3.0%, respectively; OR = 69.0; 95%CI 9.58–496.82; p<0.0001)

Distribution of Assets

The asset variables used in the PCA are described in Table 2 and their summary statistics are shown in S1 Table. The PCA was based on a combination of 28 asset values. The other 32 measured assets were excluded as they were present in less than 5% or more than 95% of the participants' households. Households were generally poor. About 67% had a latrine, among which 65% were of the "non-improved" pit latrine type without a concrete slab. About half (54%) had their cattle dwelling within the main house. Ownership of durable assets such as mobile phones and radio was low (<30%). Only 17% of the households had access to electricity. About 12% of the households had taken a government loan. Overall, cases had fewer household and agricultural assets than controls and were more likely to have a government loan (Table 2). There was no difference in the ownership of the house they were living in (92.0% vs 94%, p = 0.22), or access to electricity (18·5% v 16·5%, p = 0·40). Case households had fewer rooms (1.22 vs 1.55, p<0·0001), and had a higher density of persons per room than the controls: 4.0, 95%CI 3.6–4.4 vs 3.3, 95%CI 3.0–3.6 respectively (P = 0.020).

Table 1. Demographic and clinical characteristics of individual participants and their households.

Variables	Cases		Controls		P-value
	n / 200	(%)	n / 200	(%)	
Individual					
Age (years), mean (SD)	46.1	(13.5)	45.9	(13.3)	
Gender, female	167	(83.5)	167	(83.5)	
Illiterate	177	(85.5)	170	(85.0)	0.25
Marital status					
Married	130	(65.0)	162	(81.0)	0.0001‡
Widowed	38	(19.0)	27	(13.5)	
Divorced	27	(13.5)	9	(4.5)	
Single	5	(2.5)	2	(1.0)	
Job					
Farmer	158	(79.0)	168	(84.0)	0.006‡
Employed/self employed	9	(4.5)	17	(8.5)	
Daily labourer	14	(7.0)	4	(2.0)	
No job	19	(9.5)	11	(5.5)	
Visual acuity–better eye					
Normal (≥6/18)	126	(63.0)	194	(97.0)	<0.0001†
Moderate visual impairment (<6/18 to ≥6/60)	65	(32.5)	4	(2.0)	
Severe visual impairment (<6/60 to ≥3/60)	5	(2.5)	1	(0.5)	
Blind (<3/60)	4	(2)	1	(0.5)	
Self reported health problem in the last month					
No	115	(57.5)	172	(86.0)	<0.0001
Yes	85	(42.5)	28	(14.0)	
Household					
Family size, mean (SD)	4.9	(2.4)	5.1	(2.0)	0.17
Highest family education					
No formal education	41	(20.5)	22	(11.0)	0.006†
Primary school	74	(37.0)	74	(37.0)	
Secondary/high school	70	(35.0)	82	(41.0)	
Higher education	15	(7.5)	22	(11.0)	
Highest family job					
Farmer	165	(82.5)	169	(84.5)	0.29‡
Employed/self employed	18	(9.0)	21	(10.5)	
Daily labourer	16	(8.0)	9	(4.5)	
No job	1	(0.5)	1	(0.5)	

Analysis is done by conditional logistic regression.

‡ Combined p-value from likelihood ratio-test.

† P-value for trend.

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Asset Index Factor Scores

The overall asset index accounts for 21% of the total variance (S1 Table). Among the three subset asset indices, the agricultural asset indicators had the highest factor scores and accounted for the highest weights in measuring wealth in this population. In contrast, the housing characteristics and utilities index, except for the number of metal roof sheets, had generally lower factor scores and contributed lower weights in estimating wealth than the other two subset

Table 2. Descriptive and summary statistics for all 28 asset variables that were included in the principal component analysis.

Variables	Cases (200)		Controls (200)		P-values*
	n or mean	(% or S.D.)	n or mean	(% or S.D.)	
Housing characteristics and utilities					
Own current house	184	(92.0%)	188	(94.0%)	0.22
Number of rooms, mean (SD)	1.22	(S.D. 0.61)	1.55	(S.D. 0.08)	<0.0001
Roof made of metal	175	(87.5%)	195	(97.5%)	0.0010
Number of metal roof sheets	41.3	(24.3%)	59.8	(29.3%)	<0.0001
Own other houses	16	(8.0%)	19	(9.5%)	0.58
Latrine availability	114	(57.0%)	153	(76.5%)	<0.0001
Separate kitchen area	56	(28.0%)	96	(48.0%)	<0.0001
Cattle dwelling within main house	117	(58.5%)	99	(49.5%)	0.04
Cattle dwelling outside main house	30	(15.0%)	66	(33.0%)	<0.0001
Access to Electricity	33	(16.5%)	37	(18.5%)	0.40
Ownership of durable household materials					
Phone	38	(19.0%)	59	(29.5%)	0.005
Radio	44	(22.0%)	72	(36.0%)	0.003
Number of household furniture, mean (SD)	0.99	(S.D. 0.73)	1.49	(S.D. 0.97)	<0.0001
Cart	6	(3.0%)	21	(10.5%)	0.002
Agricultural assets (plants, land, animals)					
Mango Trees	10	(5.0%)	21	(10.5%)	0.03
Guava Trees	7	(3.5%)	18	(9.0%)	0.02
Lemon Trees	10	(5.0%)	23	(11.5%)	0.02
Banana trees	12	(6.0%)	24	(12.0%)	0.04
Buckthorn trees	123	(61.5%)	151	(75.5%)	0.0004
Coffee land	10	(5.0%)	27	(13.5%)	0.004
Equaliptous land	79	(39.5%)	135	(67.5%)	<0.0001
Teff land in Hectares, mean (SD)	0.81	(S.D. 0.63)	1.11	(S.D. 0.77)	<0.0001
All lands in Hectares, mean (SD)	0.88	(S.D. 0.66)	1.19	(S.D. 0.80)	<0.0001
Animal Ownership					
Cattle, mean (SD)	2.76	(S.D. 3.06)	4.46	(S.D. 3.25)	<0.0001
Sheep/Goat, mean (SD)	1.24	(S.D. 2.23)	2.11	(S.D. 2.71)	<0.0002
Horse/mule/donkey, mean (SD)	0.35	(S.D. 0.73)	0.74	(S.D. 0.82	<0.0001
Chicken, mean (SD)	2.32	(S.D. 4.02)	3.46	(S.D. 4.43)	0.0065
Government loan	49	(24.5%)	1	(0.5%)	<0.0001‡

* All p-values were derived from conditional logistic regression, with the exception of those for government loan‡, which used logistic regression models adjusted for clustering using robust standard errors method. Using the Benjamini and Hochberg method, only tests with a p-value below 0·0387 have a False Discovery Rate of <5%.

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indices. Among all indices, number of oxen and cows owned (0.324), the number of metal roof sheets (0.320) and amount of land owned in hectares (0.319) had the highest weights in estimating wealth. In contrast, access to electricity (-0.096) having cattle dwelling within the main house (-0.024) and having a government loan (-0.038) had negative weights. Fig 1 illustrates the distribution of the subset and overall asset indices, in order to determine whether clumping or truncation were present in this data. Overall, there was evidence of truncation and clumping when the three subset indices (Fig 1A to 1C) are used separately. However, the distribution of

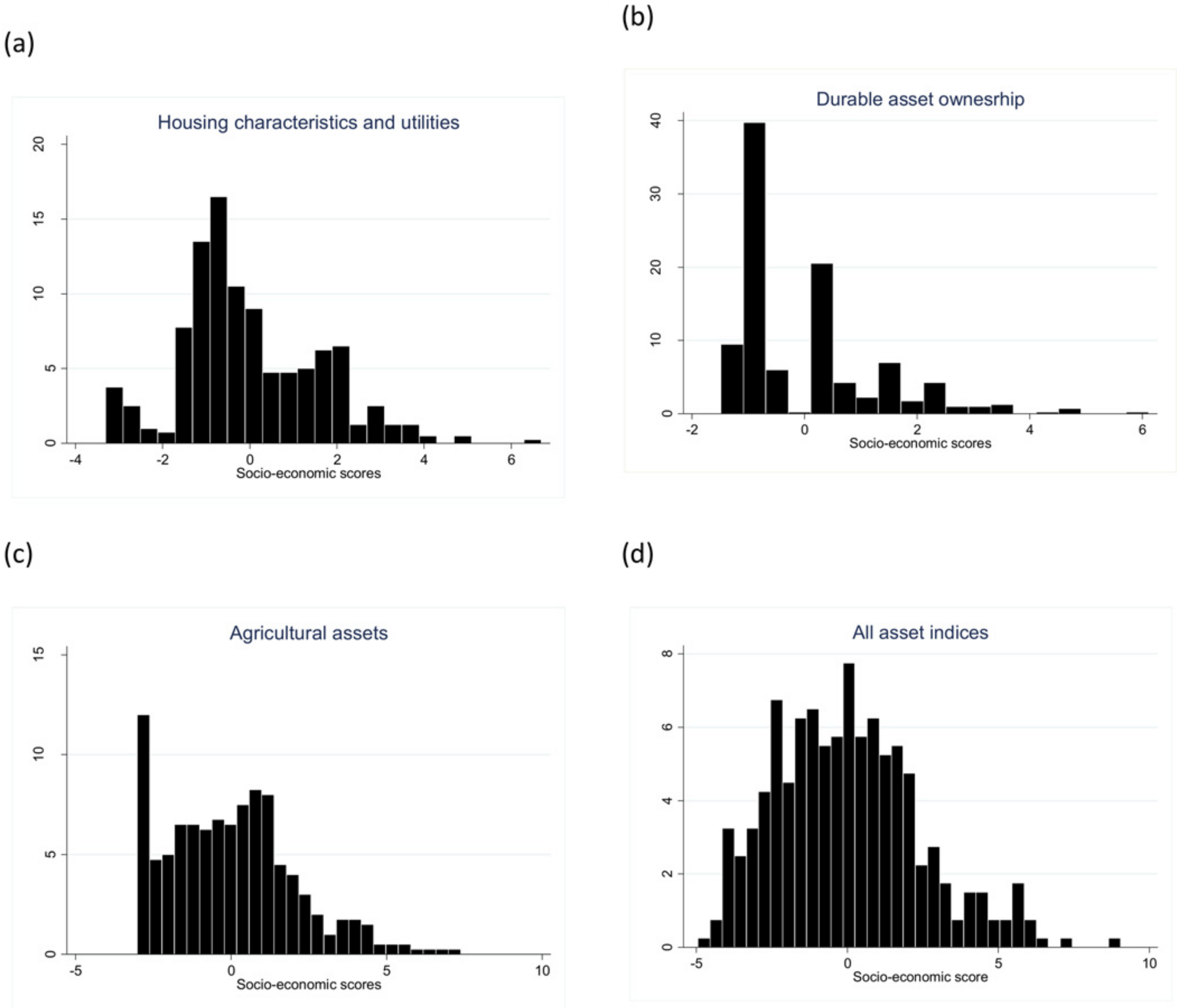

Fig 1. Distribution of socio-economic scores for (a) housing characteristics and utilities, (b) durable assets, (c) agricultural assets and (d) all assets combined.

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the overall combined factor scores was much smoother; and clumping and truncation were not observed (Fig 1D).

Asset Based Household Economic Poverty and Trichiasis

There was a strong association between being a trichiasis case and asset based household economic poverty: OR = 2.79; 95%CI, 2.06–3.78; p<0.0001 (Table 3). This relationship persisted after adjusting for marital status, and highest family education (OR = 2.78; 95%CI, 2.00–3.87; p<0.0001). For stratified analyses we combined "richest" and "rich" with "middle" because of small numbers, to create a "middle & above" category with three levels of socio-economic status measure to facilitate data modelling. Compared to the controls, trichiasis cases were more likely to be from the poorest (OR = 2.65; 95%CI, 2.05–3.42; p<0.0001) households than from

Table 3. Association between household economic poverty and trachomatous trichiasis.

Poverty Index	Cases (200)		Controls (200)		Univariable analysis			Adjusted analysis [a]		
	n	(%)	n	(%)	OR	(95% CI)	P-value	OR	(95% CI)	P-value
Overall asset index[†]										
Richest	9	(4.5)	40	(20.0)	2.79	(2.06–3.78)	<0.0001	2.78	(2.00–3.87)	<0.0001
Rich	20	(10.0)	40	(20.0)						
Middle	17	(8.5)	40	(20.0)						
Poor	51	(25.5)	40	(20.0)						
Poorest	103	(51.5)	40	(20.0)						
Self-rated wealth index[‡]										
Very wealthy	1	(0.5)	1	(0.5)	4.41	(2.75–7.07)	<0.0001	3.99	(2.43–6.54)	<0.0001
Wealthy	4	(2.0)	29	(14.5)						
Average	95	(47.5)	135	(67.5)						
Poor	67	(33.5)	32	(16.0)						
Very poor	33	(16.5)	3	(1.5)						
Peer-rated wealth index[‡]										
Very wealthy	1	(0.5)	5	(2.5)	8.22	(4.59–14.72)	<0.0001	9.10	(4.79–17.270)	<0.0001
Wealthy	8	(4.0)	35	(17.5)						
Average	48	(24.0)	124	(62.0)						
Poor	80	(40.0)	30	(15.0)						
Very poor	63	(31.5)	6	(3.0)						

Socio-economic classification of cases and controls into quintiles based on the first principal component factor scores of the overall asset index and; self and peers ranking of households' wealth. Analysis is done using conditional logistic regression for trend after likelihood ratio-test for non-linearity.

[a] Marital status and highest family education included in the matched analysis model.

[†] The case households were classified based on the "cut points" of the controls' socio economic quintiles.

[‡] Socioeconomic classification households as rated by the study participants and their peers.

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the middle & above households (Table 4). In the stratified analysis, the association between asset based household economic poverty and trichiasis persisted regardless of age, gender, marital status, and in people with normal visual acuity after adjusting for the matching variables and family education (Table 4).

Self and Peer-Rated Wealth Indexes and Trichiasis

On both the self-rated and peer-rated scores, the households of trichiasis cases were rated poorer than controls (Table 3). This association persisted in both self-rated (OR = 3.99; 95%CI, 2.43–6.54; $p<0.0001$) and peer-rated (OR = 9.10; 95%CI, 4.79–17.27; $p<0.0001$) wealth measures after adjusting for marital status and highest family education. Compared to the controls, the trichiasis case households were more likely to be rated as poorest and poor rather than middle or affluent by themselves (OR = 3.74; 95%CI, 2.55–5.49; $p<0.0001$) and their peers (OR = 10.57; 95%CI, 6.42–17.41; $p<0.0001$) compared to the other households in their villages (Table 4). Using the 0 to 100 scale (poorest to richest), the mean self-rated scores for cases and controls were 34.1 v 49.1 ($p<0.0001$) and for peer-rated scores they were 27.5 v 50.3 ($p<0.0001$). The association of lower self-rated and peer-rated wealth with trichiasis persisted regardless of age, gender, marital status, and in people with normal visual acuity after adjusting for the matching variables and family education (Table 4).

Table 4. The relationship between household economic poverty and trachomatous trichiasis using the asset index, self-rated wealth index and peer-rated wealth index, stratified by age, sex, marital status and vision.

Category	Asset Index					Self Rated Wealth Index					Peer Rated Wealth Index				
	Cases	Controls	OR	(95% CI)	P-value	Cases	Controls	OR	(95% CI)	P-value	Cases	Controls	OR	(95% CI)	P-value
All (n = 400)	**200**	**200**				**200**	**200**				**200**	**200**			
Middle & Above	23.0%	60.0%	2.7	(2.05–3.42)	<0.0001	50.0%	82.5%	3.7	(2.55–5.49)	<0.0001	28.5%	82.0%	10.6	(6.4–17.4)	<0.0001
Poor	25.5%	20.0%				33.5%	16.0%				40.0%	15.0%			
Poorest	51.5%	20.0%				16.5%	1.5%				31.5%	3.0%			
Age [a‡]															
Young (n = 200)	**104**	**96**				**104**	**96**				**104**	**96**			
Middle & Above	24.0%	58.3%	2.6	(1.83–3.70)	<0.0001	61.5%	89.6%	3.4	(1.86–6.27)	0.0001	39.4%	87.5%	9.4	(4.63–19.3)	<0.0001
Poor	26.9%	21.9%				25.0%	9.4%				33.7%	11.5%			
Poorest	49.0%	19.8%				13.5%	1.0%				26.9%	1.0%			
Old (n = 200)	**96**	**104**				**96**	**104**				**96**	**104**			
Low	21.5%	61.9%	3.3	(2.17–5.10)	<0.0001	37.5%	76.0%	4.1	(2.46–6.99)	0.0001	16.7%	76.9%	13.6	(6.39–29.0)	<0.0001
Medium	24.0%	18.3%				42.7%	22.1%				46.9%	18.3%			
High	54.2%	20.2%				19.8%	1.9%				36.5%	4.8%			
Sex [b]															
Male (n = 66)	**33**	**33**				**33**	**33**				**33**	**33**			
Middle & Above	36.4%	75.8%	4.4	(2.04–9.49)	0.0002	48.5%	84.9%	5.7	(1.68–19.2)	0.0053	30.3%	93.9%	27.3	(5.13–145)	0.0001
Poor	33.3%	21.2%				51.5%	15.1%				54.5%	6.1%			
Poorest	30.3%	3.0%				0.0%	0.0%				15.2%	0.0%			
Female (n = 334)	**167**	**167**				**167**	**167**				**167**	**167**			
Middle & Above	20.4%	56.9%	2.5	(1.85–3.25)	<0.0001	50.3%	82.0%	3.56	(2.38–5.32)	<0.0001	28.1%	79.6%	9.3	(5.54–15.7)	<0.0001
Poor	33.9%	19.8%				29.9%	16.2%				37.1%	16.8%			
Poorest	55.7%	23.3%				19.8%	1.8%				34.7%	3.6%			
Marital status [c]															
Married (n = 292)	**130**	**162**				**130**	**162**				**130**	**162**			
Middle & Above	33.1%	67.9%	2.9	(2.10–3.96)	<0.0001	64.6%	88.9%	4.5	(2.63–7.55)	<0.0001	40.8%	90.7%	13.1	(6.66–25.8)	<0.0001
Poor	33.8%	20.4%				28.5%	11.1%				44.6%	8.6%			
Poorest	33.1%	11.7%				6.9%	0.0%				14.6%	0.6%			
Unmarried* (n = 108)	**70**	**38**				**70**	**38**				**70**	**38**			
Middle & Above	4.3%	26.3%	3.1	(1.57–6.01)	0.0011	22.9%	55.3%	3.1	(1.65–5.91)	0.0005	5.7%	44.7%	6.27	(2.81–14.0)	<0.0001
Poor	10.0%	18.4%				42.9%	36.8%				31.4%	42.1%			
Poorest	85.7%	55.3%				34.3%	7.9%				62.9%	13.2%			
Visual acuity [a]															
Normal (n = 320)	**126**	**194**				**126**	**194**				**126**	**194**			
Middle & Above	27.0%	61.3%	2.5	(1.91–3.66)	<0.0001	57.1%	84.0%	4.0	(2.49–6.33)	<0.0001	32.5%	83.5%	11.1	(6.00–20.6)	<0.0001
Poor	26.2%	19.6%				30.2%	15.0%				41.3%	13.9%			
Poorest	46.8%	19.1%				12.7%	1.0%				26.2%	2.6%			
VI (n = 80)[†]	**74**	**6**				**74**	**6**				**74**	**6**			
Middle & Above	16.2%	16.7%	5.0	(0.28–89.5)	0.28	37.8%	33.3%	2.6	(0.24–26.9)	0.43	21.6%	33.3%	11.5	(2.43–54.5)	0.0021
Poor	24.3%	33.3%				39.2%	50.0%				37.8%	50.0%			
Poorest	59.5%	50.0%				23.0%	16.7%				40.5%	16.7%			

We merged "richest/very wealthy" and "rich/wealthy" with "middle" because of small numbers at these highest extremes of the distribution, to create a combined "middle & above" category in the three socio-economic status indexes, to facilitate data modelling. Analysis was done using logistic regression for trend, adjusted for clustering using robust standard errors method. Using the Benjamini and Hochberg method, only tests with a p-value below 0.0053 have a False Discovery Rate of <5%.

[a] adjusted for age, sex, marital status and highest family education.

[b] adjusted for age, marital status and highest family education.

[c] adjusted for age, sex and highest family education.

[‡] To classify participants into young and old age groups, the median value of age was used as a cut-off point.

* Unmarried includes: single, divorced and widowed.

[†] VI includes: moderate visual impairment, severe visual impairment and blindness. Cont = Controls; VI = Visual impairment.

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Reliability and Correlation of Economic Poverty Measures

The asset based socio-economic classification of households was found to be robust and produced similar ranking of households when the overall index was compared with the different subset indexes; the Spearman rank correlation coefficient ranged between 0.88 and 0.94. A Spearman rank correlation coefficient between asset index and self-rated wealth index, asset index and peer-rated wealth index, and self and peer-rated wealth indexes were 0.58, 0.70 and 0.63, respectively.

Activity Participation and Trichiasis

Trichiasis cases were significantly less likely to participate in household, outdoor, agricultural and leisure activities, even after controlling for the presence of other health problems during the preceding month, (Table 5). However, the trichiasis cases were slightly more likely to participate in daily labouring and self-employment activities such as selling goods. These associations persisted in multivariable analysis after controlling for self reported health problems during the preceding month, except for leisure activities. In stratified analyses by vision, trichiasis cases with normal vision were significantly less likely to participate in processing of agricultural products and in productive outdoor activities such as fetching wood and travelling compared to controls with normal vision (Table 5).

After adjusting for the matching variables and self reported health problems, trichiasis cases were significantly more likely to report difficulty in performing all productive and leisure activities than the controls: >66% of the cases reported difficulty in all productive activities in contrast to <5% of controls (Table 6). Similarly, trichiasis cases were significantly more likely to report receiving assistance in doing all productive activities compared to controls. In contrast to other activities, higher proportions of trichiasis cases received assistance particularly in agricultural activities such as farming, animal husbandry and processing agricultural products (Table 6).

Factors Associated with Asset Based Household Economic Poverty in Trichiasis Cases

In a univariable analysis (Table 7), being a household head with trichiasis had a strong association with economic poverty (OR = 3.29; 95%CI, 1.89–5.75; p<0.0001) while visual impairment had a borderline association (OR = 1.71; 95%CI, 0.98–2.97; p = 0.058). Not having a marriage partner (OR = 9.41; 95%CI, 4.16–21.31; p<0.0001), no family member with formal education (OR = 4.95; 95%CI, 1.73–14.16; p = 0.0028) and a main family job of daily labouring (OR = 19.64; 95%CI, 2.32–166.49; p = 0.0063) as opposed to farming were independently associated with economic poverty (Table 7). Families in which there were more people of a productive age were less likely to be poor than their counterparts (OR = 0.32; 95%CI, 0.16–0.60; p = 0.0005) (Table 7). In a multivariable analyses, participating in animal husbandry (OR = 0.05; 95%CI, 0.02–0.12; p<0.0001) and agricultural product processing (OR = 0.50; 95% CI, 0.27–0.91; p = 0·024) activities were independently associated with wealthier households while house cleaning (OR = 2.05; 95%CI, 1.03–4.08; p = 0.042) and self employment (OR = 2.77; 95%CI, 1.25–6.18; p = 0.012) activities were associated with poorer households.

Discussion

Poverty is a complex multidimensional issue that encompasses not only deprivation of material possessions but also wider issues such as nutrition, health and education [32,33]. Many different approaches have been taken to measuring "poverty", both in absolute and relative terms

Table 5. Associations between participation in an activity during the last week and case-control status; and stratified analyses by vision.

Activity	Cases		Controls		Adjusted Analysis [c]			Normal Vision (N 320) [d]					Visually Impaired (N 80) [d]				
	n/200	(%)	n/200	(%)	OR	95% CI	P-value	Cases (n = 126)	Control (n = 194)	OR	(95% CI)	P-value	Cases (n = 74)	Control (n = 6)	OR	(95% CI)	P-value
Productive household activities																	
Cooking and cleaning dishes	166	(83.0)	168	(84.0)	0.63	(0.12–3.26)	0.58	84.1%	84.0%	0.94	(0.61–1.46)	0.7930	81.1%	83.3%	0.26	(0.03–2.49)	0.24
House cleaning	156	(78.0)	167	(83.5)	0.20	(0.05–0.77)	0.02	81.7%	83.5%	0.82	(0.53–1.29)	0.3961	71.65	83.3%	0.20	(0.02–2.34)	0.20
Washing clothing	99	(49.5)	129	(64.5)	0.49	(0.29–0.82)	0.006	55.6%	66.5%	0.59	(0.34–1.01)	0.0563	33.2%	0.0%	-	-	-
Looking after family member	129	(64.5)	137	(68.5)	0.99	(0.61–1.60)	0.97	72·2%	69.1%	1.18	(0.69–2.04)	0.5458	51.4%	50.0%	0.33	(0.06–1.79)	0.20
Productive outdoor activities																	
Shopping/ Marketing	125	(62.5)	151	(75.5)	0.53	(0.31–0.90)	0.02	69.0%	76.8%	0.68	(0.38–1.23)	0.20	51.3%	33.3%	0.89	(0.18–4.39)	0.88
Fetching wood	78	(39.0)	153	(76.5)	0.09	(0.04–0.20)	<0.0001	42.1%	77.3%	0.21	(0.13–0.35)	<0.0001	33.9%	50.0%	0.23	(0.04–1.46)	0.12
Fetching water	151	(75.5)	170	(85.0)	0.38	(0.18–0.79)	0.01	79.4%	86.1%	0.55	(0.29–1.04)	0.07	68.9%	50.0%	0.89	(0.20–3.99)	0.88
Travelling	73	(36.5)	116	(58.0)	0.37	(0.23–0.60)	0.0001	34.9%	59.3%	0.36	(0.21–0.61)	0.0002	39.2%	16.7%	2.28	(0.23–22.1)	0.48
Paid work																	
Daily labouring	13	(6.5)	4	(2.0)	6.30	(0.79–50.95)	0.08	7.9%	2.1%	2.48	(0.87–7.11)	0.09	4.0%	0.0%	-	-	-
Self employment [a]	38	(19.0)	25	(12.5)	2.08	(1.01–4.27)	0.05	24.6%	12.9%	2.39	(1.40–4.10)	0.002	9.5%	0.0%	-	-	-
Agricultural activities																	
Farming	93	(46.5)	118	(59.0)	0.55	(0.32–0.94)	0.03	48.4%	59.8%	0.72	(0.46–1.11)	0.14	43.2%	33.3%	1.28	(0.20–8.02)	0.79
Animal raring	130	(65.0)	165	(82.5)	0.23	(0.10–0.52)	0.0003	71.4%	83.5%	0.59	(0.37–0.96)	0.04	54.0%	50.0%	0.53	(0.13–2.21)	0.38
Processing agricultural products	95	(47.5)	160	(80.0)	0.16	(0.08–0.31)	<0.0001	50.8%	81.4%	0.24	(0.14–0.41)	<0.0001	41.9%	33.3%	0.74	(0.11–4.93)	0.75
Leisure activities																	
Social visits	141	(70.5)	149	(74.5)	0.88	(0.53–1.48)	0.64	69.8%	75.8%	0.88	(0.51–1.54)	0.67	71.6%	33.3%	3.46	(0.50–23.9)	0.21
Attending ceremonies	43	(21.5)	59	(29.5)	0.61	(0.33–1.11)	0.11	21.4%	30.4%	0.75	(0.44–1.25)	0.27	21.6%	0.0%	-	-	-
Attending social meetings	16	(8.0)	31	(15.5)	0.46	(0.20–1.04)	0.06	11.1%	16.0%	0.82	(0.44–1.53)	0.53	2.7%	0.0%	-	-	-
Relaxing activities [b]	40	(20.0)	64	(32.0)	0.49	(0.29–0.83)	0.009	23.0%	31.4%	0.69	(0.40–1.20)	0.19	14.9%	50.0%	0.13	(0.02–0.90)	0.039

[a] Selling goods

[b] Listening to radio, Reading, Watching TV.

[c] Conditional logistic regression adjusted for self reported health problem in the last month. Visual impairment included moderate visual impairment, severe visual impairment and blindness. A dashed line indicates that comparison is not possible.

[d] Analysis was done using logistic regression adjusted for clustering using robust standard error methods and adjusted for age and self reported health problem. Odds ratios are relative to the controls. In the stratified analyses by vision, using the Benjamini and Hochberg method, only tests with a p-value below 0.002 have a False Discovery Rate of <5%.

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Table 6. Association between case-control status and having difficulty in doing an activity and receiving assistance to do it among those who have done the activity in the past week.

Activity	Difficulty with activity					Assisted with activity				
	Cases		Controls			Case		Control		
	n/N	(%)	n/N	(%)	P value	n/N	(%)	n/N	(%)	P value
Productive household activities										
Cooking and cleaning dishes	142/166	(85.5)	4/168	(2.4)	<0.0001	25/166	(15.1)	1/168	(0.6)	0.001
House cleaning	130/156	(83.3)	3/167	(1.8)	<0.0001	19/156	(12.2)	1/167	(0.6)	0.004
Washing clothing	66/99	(66.7)	1/129	(0.8)	<0.0001	13/99	(13.1)	0/129	(0.0)	-
Looking after family member	75/129	(58.10	1/137	(0.7)	<0.0001	27/129	(20.9)	1/137	(0.7)	0.0002
Productive outdoor activities										
Shopping /Marketing	96/125	(76.8)	4/151	(2.6)	<0.0001	4/125	(3.2)	1/151	(0.7)	0.38
Fetching wood	64/78	(82.1)	4/153	(2.6)	<0.0001	7/78	(9.0)	2/153	(1.3)	0.005
Fetching water	110/151	(72.8)	5/170	(2.9)	<0.0001	22/151	(14.6)	1/170	(0.6)	0.002
Travelling	62/73	(84.9)	2/116	(1.7)	<0.0001	7/73	(9.6)	1/116	(0.9)	0.05
Paid work										
Daily labouring	10/13	(76.9)	0/4	(0.0)	-	1/13	(7.7)	0/4	(0.0)	-
Self employment	27/38	(71.0)	1/25	(4.0)	0.0001	4/38	(10.5)	0/25	(0.0)	-
Agricultural activities										
Farming	81/93	(87.1)	0/118	(0.0)	-	27/93	(29.0)	2/118	(1.7)	<0.0001
Animal raring	98/130	(75.4)	5/165	(3.0)	<0.0001	63/130	(48.5)	20/165	12.1	<0.0001
Processing agricultural products	80/95	(84.2)	1/160	(0.6)	<0.0001	12/95	(12.6)	0/160	(0.0)	-
Leisure activities										
Family/Social visits	57/141	(40.4)	2/149	(1.3)	<0.0001	2/141	(1.4)	0/149	(0.0)	-
Attending ceremonies	26/43	(60.5)	0/59	(0.0)	-	1/43	(2.3)	0/59	(0.0)	-
Attending social meetings	8/16	(50.0)	0/31	(0.0)	-	1/16	(6.2)	0/31	(0.0)	-
Relaxing activities [a]	12/40	(30.0)	2/64	(3.1)	0.003	0/40	(0.0)	1/64	(1.6)	-
Activities of daily living	79/200	(39.5)	2/200	(1.0)	<0.0001	6/200	(3.0)	0/200	(0.0)	-

The denominators are the number of participants who did the activity in the past week. Analysis was done using logistic regression adjusted for clustering using robust standard errors method and adjusted for the matching variables (age & sex) and self reported health problem. Only P-values are presented as the cell sizes of the majority were too small for calculation of odds ratio. Using the Benjamini and Hochberg method, only tests with a p-value below 0.005 have a False Discovery Rate of <5%. A dashed line indicates that comparison is not possible.

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[34]. In general, these involve a survey methodology to capture estimates of income or consumption and methods that take into account broader issues of health and education such as the Multidimensional Poverty Index [34].

According to the 2011 World Bank estimates, 29.6% (Urban, 25.7%; Rural, 30.4%) of Ethiopians live below the national absolute poverty line (defined as 3781 Birr) and 30.7% live on less than US$1.25 PPP (purchasing power parity) a day [35]. Using asset indicators, the World Bank defines a household as being deprived "when none of these assets are owned by the household: fridge, phone, radio, TV, bicycle, jewelry, or vehicle" [35]. According to these criteria, 53% of rural households in Ethiopia were in deprivation in 2011. However, these are narrowly defined assets and most of these would not be commonly found in a rural Ethiopian community, irrespective to the level of wealth [35].

In this study we compared individuals with trichiasis to matched controls from within the same communities in Amhara Region, Ethiopia using three different measures of relative poverty: Asset Index, Self-Rated Wealth Index and Peer-Rated Wealth Index. These measures

Table 7. Univariable and multivariable ordinal logistic regression for household economic poverty among the 200 trichiasis cases only.

Variable	OR	95% CI	p-value
Univariable analysis			
Trichiasis case is household head	3.29	(1.89–5.75)	<0.0001
Marital status, being single/widowed/divorced	12.14	(5.71–25.82)	<0.0001
Productive age family members ≥3	0.17	(0.09–0.30)	<0.0001
Highest family education, No formal education	8.09	(3.24–20.20)	<0.0001
Highest family job			
Farmer (reference)	1	-	-
Self employed/employed	7.00	(1.97–24.81)	0.003
Daily Labourer	20.11	(2.60–155.50)	0.004
Trichiasis severity (Major TT)	0.93	(0.55–1.57)	0.78
Visual impairment	1.71	(0.98–2.97)	0.06
Multivariable logistic regression			
Marital status, Single/widowed/divorced	9.41	(4.16–21.31)	<0.0001
Productive age family members ≥3	0.32	(0.16–0.60)	0.0005
Highest family education, No formal education	4.95	(1.73–14.16)	0.003
Highest family job			
Farmer (reference)	1	-	-
Self employed/employed	6.63	(1.62–27.11)	0.008
Daily Labourer	19.64	(2.32–166.49)	0.006

Analysed based on the classification of participants and households into quintiles (richest to poorest) using the overall asset index. Ordinal logistic regression was used to identify correlates of asset based socio-economic status (ordered categorical variable) in a univariable and multivariable analysis. Variables that were associated with the outcome on univariable analyses at a level of p<0.05 were included in the multivariable analysis and then those with p<0.2 were retained in the final model after likelihood ratio-test.

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allow us to understand whether people with TT were relatively poorer than their neighbours, even within these very poor communities. We performed a PCA of household assets to stratify the participants into economic groupings. The variance explained by the first principle component was similar to the range reported in other similar studies (between 11% and 27%) [19,20,27,36]. The asset index used in this study is probably a reasonable proxy for consumption expenditure as we collected data on a sufficiently broad set of asset indicators that are capable of capturing living standards and wealth inequalities based on local values [37].

Participant and Household Characteristics

The age distribution, gender profile and literacy status of the trichiasis cases in this study were comparable with those reported in our earlier studies in Ethiopia as well as other studies of trichiasis patients elsewhere in Sub-Saharan Africa [31,38–40]. This suggests that the results are probably generalizable for this region of Ethiopia at least. The households of trichiasis cases were significantly less well off than controls in terms of ownership of almost all asset indicators measured. Consistent with the literature, trichiasis cases had significantly smaller and more crowded households [6,41]. Cases had less latrine access and more kept their cattle within the house, which is consistent with observations that active trachoma is associated with poor sanitation access [41–43]. These differences reflect a gap in the implementation of the "E" component of the SAFE strategy, which needs on-going emphasis in this region.

Trachoma and Poverty

We have found clear evidence from each measure that even within trachoma-endemic communities individuals and households affected by trichiasis are significantly economically poorer than those that are not. Within endemic communities some individuals or families appear to be more severely affected by the disease and develop sight-threatening complications. This raises the important question of whether the association between poverty and trichiasis arises from a general state of impoverishment or whether there are a number of critical factors that primarily drive the relationship that might be amenable to focused intervention. The data we present here suggest that the relationship between poverty and trachoma could possibly be bidirectional.

Poverty may contribute to trachoma. This study provides evidence that even within superficially homogeneous endemic communities relative poverty plays a major part in the vulnerability of families to scarring disease. Firstly, trichiasis cases were more likely than the controls to come from households where the main family job is daily labouring and from families with no or lower formal education. Both of these factors have a major influence on income and health awareness, which in turn increase the vulnerability of the family to trachoma. Consistent with this, studies from Malawi, Tanzania and Ethiopia identified that children from lower socio-economic households had a higher prevalence of active trachoma than their counterparts indicating an association between poverty and active trachoma [10,44,45]. Secondly, previously described risk factor associations for active trachoma such as crowding and poor access to latrine, characterised the households of the trichiasis cases in this study. Such conditions are believed to promote the transmission of *Chlamydia trachomatis* within endemic communities, sustaining higher prevalence levels. Poorer households and communities may be less likely to have either the resources or the awareness to access treatment and sustain a sufficiently hygienic environment to control trachoma [8,17,46,47]. Households with higher income were more likely to have a latrine than their counterparts in a study conducted in the same area [48].

Trachoma may also contribute to poverty. Poor health frequently results in loss of productivity through disability and diversion of resources [11]. Trichiasis and its associated visual impairment probably lead to a loss of income, exacerbating pre-existing poverty in a "vicious cycle" [12,13]. Previously healthy and productive adults can be rendered dependent on others, unable to work or fully care for themselves due to pain, photophobia or visual impairment [13]. We found clear evidence of reduced activity and participation among trichiasis cases. Trichiasis cases were less likely than the controls to participate in productive household activities, outdoor activities (shopping/marketing, fetching wood and water) and agricultural activities (farming, animal husbandry and processing agricultural products). The stratified analysis found trichiasis cases with normal vision are less likely to participate in outdoor and agricultural activities than controls. This is consistent with a study of Tanzanian women with trichiasis without visual impairment, who had a degree of functional limitation which was comparable to those with visual impairment [14]. We found evidence that households with fewer economically productive adults and where the family head had trichiasis tended to be poorer. Conversely, households where trichiasis cases participated in agricultural activities were better off. Even where the trichiasis cases were undertaking specific activities, they reported much more difficulty and greater need for assistance than the controls. Similarly in another study, trichiasis cases reported difficulty in performing day-to-day farming activities [49]. These observations all point towards households with someone with trichiasis being under greater financial strains through reduced income contribution and greater needs and dependence of the person with trichiasis. The burden of disability caused by trachoma has been estimated between 171,000 and 1.3 million DALYs, with economic losses of 5–8 billion

USD/year [4,12,13]. The economic loss from trichiasis alone due to lost productivity was estimated to be 3 billion USD/year [12,13].

Study Strengths

This study comprehensively assesses the relationship between trachoma and economic poverty using four different measures, with a robust process to select suitable community controls. The asset index quantifies the long-term economic welfare of trachoma affected communities, which is important as trachoma and its sequelae are probably related to long-term SES [19,20]. The asset index has the practical advantage that it is much less affected by recall or measurement bias during data collection [19]. Most of the housing characteristics, utilities and durable assets were collected through direct observation minimising miss-measurement. Broad ranges of asset data were collected increasing the power of the study in the following ways. Clumping and truncation, potential problems that can arise with PCA of asset data and compromise its suitability for defining socio-economic strata, did not occur when all asset indices were combined into a single index. This indicates that the data from this study is sufficient to measure economic status and effectively infer inequality between different socio-economic strata and that in this region assessment of economic status by asset measurement requires a wider pool of parameters, particularly including agricultural assets. Encouragingly, the asset based poverty measure was moderately and strongly correlated with the self-rated and peer-rated wealth measures.

Limitations of the Study

Poverty is a complex multidimensional problem with many causes and manifestations. Therefore there are many ways in which poverty can be measured. Here we only examined the economic aspect using relative measures such as low asset ownership. We use the first principal component (PC1) to measure socio-economic status. However, there is no clear description of the number of principal components to use and often the factor scores derived from the other principal components are difficult to interpret [27]. Despite the comparability of the amount of variance explained by PC1 with other studies, there is uncertainty whether the first component alone sufficiently explains all the pertinent variation. Asset scores are usually developed to be locally relevant, to allow ranking of people within the same community with respect to poverty. Unfortunately, socio-economic classifications based on asset ownership quintiles measure relative poverty within a given context and face the limitation of lacking international comparability. Therefore, between region or country comparison of SES should be done with caution [28]. We did not collect consumption or expenditure data, and so were not able to assess absolute poverty levels.

Although a community based screening method was used to identify trichiasis cases, it is possible that some cases might have been missed, which could potentially introduce non-response bias. Similarly, it is possible that some potential controls were not listed by the sub-village administrators. Self and peer-rated wealth are subjective measures, which might have suffered from the tendency to favour ranking households in the middle of the distribution. The activity participation data relied on the participant's recall ability on what s/he had done in the last week. Finally, our results suggest that a bidirectional relationship may possibly exist between trachoma and poverty. However, the authors recognise that inference about causality is speculative as it is not possible to draw firm conclusions from a cross-sectional observational study such as this.

Conclusions

In this study we found a clear association between trichiasis and household economic poverty by all three economic measures. Trichiasis cases were more likely to have economically poor households and less likely to participate in productive activities regardless of visual impairment, more likely to report difficulty in performing productive activities and more likely to need assistance in performing activities than controls. These suggest that the causative relationships between poverty and trachoma may possibly involve bidirectional interaction: poor households are more affected by trachoma and the scarring sequelae of trachoma and trichiasis reduces productivity even prior to the development of visual impairment, which might lead to additional poverty.

These data are anticipated to be useful in advocacy and to support programme leaders and funders to secure resources to promote trachoma prevention linked to socio-economic development in trachoma-endemic communities. Implementation of the full SAFE strategy in the context of general improvements might lead to a virtuous cycle of improving health and wealth. Trachoma is a good proxy of inequality within communities and it could be used to target and evaluate interventions for health and poverty alleviation. Measuring the effect of trichiasis surgery on household economic poverty through longitudinal studies would provide an indication of the relative contribution of trichiasis to poverty, as improved health potentially leads to improved productivity and income.

Supporting Information

S1 Checklist. STROBE Checklist.
(DOCX)

S1 Table. Summary statistics and principal component factor scores for asset variables used in the Principal Component Analysis (PCA).
(PDF)

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Author Contributions

Conceived and designed the experiments: EH PME HK SP HW MJB. Performed the experiments: EH TW SA ZT MZ ZZ MJB. Analyzed the data: EH HAW MJB. Wrote the paper: EH TW SA ZT MZ ZZ KC PME HK RLB DCWM SNR SP HAW MJB.

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S1 Table: Summary statistics and principal component factor scores for asset variables used in the Principal Component Analysis (PCA).

Variables	Summary Statistics		Factor score for PC1				A change from 0 to 1	Means of all indicators asset index by quintile				
	Mean	*SD*	*Housing*	*Durable assets*	*Agricultural assets*	*All*	*Fi/Si*	*Poorest*	*poor*	*Middle*	*Rich*	*Richest*
Housing characteristics and utilities												
Own the house	0·930	0·255	0·006			0·161	0·635	0·804	1·000	1·000	1·000	1·000
Number of rooms	1·383	0·730	0·441			0·154	0·208	1·182	1·286	1·281	1·617	1·980
Roof made of metal	0·925	0·264	0·315			0·143	0·538	0·804	0·978	1·000	1·000	1·000
Number of metal roof sheets	50·58	28·48	0·435			0·320	0·011	27·20	51·99	58·84	64·57	89·47
Cattle dwelling within the main house	0·540	0·499	-0·365			-0·024	-0·050	0·441	0·802	0·789	0·383	0·245
Cattle dwelling separate to the main house	0·240	0·428	0·424			0·242	0·570	0·028	0·110	0·175	0·600	0·735
Has latrine	0·668	0·472	0·178			0·078	0·161	0·503	0·769	0·789	0·700	0·776
Kitchen separate from the main house	0·380	0·486	0·256			0·035	0·072	0·378	0·275	0·368	0·400	0·571
Access to electric	0·175	0·380	0·216			-0·096	-0·261	0·329	0·099	0·053	0·033	0·184
Own other house/s	0·088	0·283	0·245			0·046	0·152	0·056	0·143	0·000	0·100	0·163
Ownership of durable assets												
Phone	0·243	0·429		0·562		0·076	0·175	0·224	0·154	0·175	0·283	0·490
Radio/tape recorder	0·290	0·454		0·509		0·180	0·394	0·133	0·209	0·228	0·500	0·714
Number of furniture	1·243	0·892		0·534		0·141	1·279	1·021	1·176	1·228	1·383	1·857
Cart	0·068	0·251		0·373		0·123	0·498	0·021	0·011	0·035	0·150	0·245
Agricultural assets												
Mango Tree	0·078	0·268			0·192	0·152	0·582	0·007	0·044	0·035	0·117	0·347

Guava Tree	0·063	0·242			0·170	0·138	0·583	0·000	0·033	0·070	0·083	0·265
Lemon Tree	0·083	0·275			0·213	0·170	0·629	0·014	0·011	0·053	0·150	0·367
Banana Tree	0·090	0·287			0·213	0·178	0·620	0·007	0·011	0·105	0·183	0·347
Buckthorn trees	0·685	0·465			0·284	0·173	0·503	0·343	0·758	0·895	0·983	0·939
Coffee land	0·093	0·290			0·143	0·107	0·362	0·028	0·066	0·070	0·167	0·265
Equaliptous tree land	0·535	0·499			0·315	0·247	0·499	0·112	0·626	0·877	0·767	0·918
Teff and other cereals, land in Hectares	0·961	0·713			0·375	0·301	0·426	0·417	0·901	1·237	1·342	1·872
All land in Hectares	1·032	0·751			0·392	0·319	0·429	0·447	0·933	1·292	1·463	2·089
Number of oxen and cows	3·605	3·267			0·369	0·324	0·099	0·930	3·286	4·772	5·267	8·612
Number of horses and mules	0·540	0·797			0·289	0·258	0·327	0·042	0·341	0·895	0·933	1·469
Number of sheep and goats	1·670	2·518			0·274	0·219	0·087	0·427	1·286	1·789	2·833	4·449
Number of chickens	2·889	4·263			0·235	0·190	0·045	0·853	2·582	3·737	4·033	7·000
Household took government loan	0·125	0·331				-0·038	-0·112	0·140	0·231	0·070	0·050	0·041
Overall index	0·000	2·392										
Eigenvalues associated with PC1			2·54	1·88	4·31	5·72						
Share of variance associated with PC1			25%	41%	33%	21%						
Number of variables used			10	4	13	28						
KMO sample adequacy test			0·56	0·65	0·79	0·79						

This table shows the summary statistics of the all asset indicators used in the PCA in the first two columns. In the next 4 columns, the factor score of the first principal component for each three indices and when all indicators are combined as a single indicator is presented. The factor scores are the weight assigned to each asset indicator, normalised by its mean and standard deviation, in the linear combination of the variable that constitutes the first principal component. The 7th column shows the factor score of each indicator divided by its standard deviation. This shows how much owning an asset contributes to the index compared to not owning in dummy variables. A positive value reflects an increase and a negative value a reduction in the asset score. The last five columns show the mean value of the asset ownership across the five socio-economic groupings of case and controls together classified based on the "cut points" of the controls' *first factor score quintiles. In most of the asset indicators with positive and negative factor scores, the mean asset ownership of assets increased and decreased respectively from poor to rich households.*

7. The Impact of Trachomatous Trichiasis on Quality of Life: A Case Control Study

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RESEARCH PAPER COVER SHEET FOR RESEARCH PAPERS ALREADY PUBLISHED

Section A - Student details

Student	Esmael Habtamu Ali
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Have you retained the copyright for the work?	Yes. Please see first page of the published paper where the following is indicated: *"Copyright: © 2015 Habtamu et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited."*
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Section D - Multi-authored Work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper	With senior colleagues I designed the study and prepared the protocol / SOP, led the research project and collected data, analysed data and wrote the first draft of the paper with edits from my supervisor and co-authors.

Student Signature: Esmael Habtamu Ali Date: 15th December 2016

Supervisor Signature: Prof. Matthew Burton
Date: 1st December 2016

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RESEARCH ARTICLE

The Impact of Trachomatous Trichiasis on Quality of Life: A Case Control Study

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Abstract

Background

Trachomatous trichiasis is thought to have a profound effect on quality of life (QoL), however, there is little research in this area. We measured vision and health-related QoL in a case-control study in Amhara Region, Ethiopia.

Methodology/Principal Findings

We recruited 1000 adult trichiasis cases and 200 trichiasis-free controls, matched to every fifth trichiasis case on age (+/- two years), sex and location. Vision-related quality of life (VRQoL) and health-related quality of life (HRQoL) were measured using the WHO/PBD-VF20 and WHOQOL-BREF questionnaires. Comparisons were made using linear regression adjusted for age, sex and socioeconomic status. Trichiasis cases had substantially lower VRQoL than controls on all subscales (overall eyesight, visual symptom, general functioning and psychosocial, p<0.0001), even in the sub-group with normal vision (p<0.0001). Lower VRQoL scores in cases were associated with longer trichiasis duration, central corneal opacity, visual impairment and poor contrast sensitivity. Trichiasis cases had lower HRQoL in all domains (Physical-health, Psychological, Social, Environment, p<0.0001), lower overall QoL (mean, 34.5 v 64.6; p<0.0001) and overall health satisfaction (mean, 38.2 v 71.7; p<0.0001). This association persisted in a sub-group analysis of cases and controls with normal vision. Not having a marriage partner (p<0.0001), visual impairment (p = 0.0068), daily labouring (p<0.0001), presence of other health problems (p = 0.0018) and low self-rated wealth (p<0.0001) were independently associated with lower overall QoL scores in cases. Among cases, trichiasis caused 596 (59%) to feel

all the data and had final responsibility for the decision to submit for publication.

Competing Interests: The authors have declared no competing interests exist.

embarrassed, 913 (91.3%) to worry they may lose their remaining eyesight and 681 (68.1%) to have sleep disturbance.

Conclusions/Significance

Trachomatous trichiasis substantially reduces vision and health related QoL and is disabling, even without visual impairment. Prompt trichiasis intervention is needed both to prevent vision loss and to alleviate physical and psychological suffering, social exclusion and improve overall well-being. Implementation of the full SAFE strategy is needed to prevent the development of trachomatous trichiasis.

Author Summary

There is clear evidence that visual impairment generally reduces quality of life. However, relatively little is known about the impact that trachomatous trichiasis (TT) has on the lives of affected people with and without the presence of visual impairment. We measured the impact of TT on vision and health-related quality of life in 1000 people with TT using standard WHO quantitative tools and compared these with 200 trichiasis-free controls, matched to every fifth trichiasis case on age, sex and location. We found TT cases had lower vision and health related quality of life than controls regardless of visual impairment and other health problems suggesting the burden of TT goes beyond visual loss. The results provide solid data for advocacy and encourage programme leaders and funders to secure resources to promote trichiasis intervention. Trichiasis causes considerable physical and psychosocial trauma including sleep disturbance, low self-esteem and possibly a less stable marriage regardless of visual impairment. These suggest that, timely treatment is needed not only to prevent visual loss but also alleviate physical and psychological suffering and social exclusion of TT patients, thereby improving their physical and psychological health, general functioning and social relations.

Introduction

Trachoma is the leading infectious cause of blindness worldwide [1]. About 229 million people live in trachoma endemic areas [2]. The disease starts in early childhood with repeated episodes of *Chlamydia trachomatis* infection. This triggers conjunctival inflammation of the upper eyelid, which leads to scarring. The scarring causes the eyelid to turn in (entropion) and the eyelashes to scratch the eye, which is known as trachomatous trichiasis (TT). Visual impairment and blindness develop when the cornea is damaged directly or indirectly by the trichiasis and ocular surface dysfunction, leading to corneal opacification (CO). Approximately 7.3 million people have un-treated trichiasis [3]. It is estimated that 2.4 million people are visually impaired from trachoma worldwide, among which between 439,000 and 1.2 million are estimated to be irreversibly blind [2,4].

Clinical examination provides little insight into the impact a condition has on the overall functioning and life of an affected individual and their family. Trichiasis can cause ocular pain and impaired vision but it can also have a profound effect on broader aspects of general health and well-being [5]. However, there is very limited data on the effect of trichiasis and its associated visual impairment on quality of life (QoL). QoL is a broad concept that refers to an "individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [6]. It can be measured quantitatively by a variety of tools including health-related quality of life (HRQoL) tools and tools measuring broader concepts to evaluate the overall experience of life [7]. HRQoL tools can be further divided into those measuring disease-specific quality of life (e.g. vision related QoL) and generic HRQoL [7].

A comprehensive vision related quality of life (VRQoL) measure has been developed by the World Health Organization (WHO): WHO/PBD-VF20 (World Health Organisation/ Prevention of Blindness and Deafness—Visual Functioning 20 item questionnaire) [8]. This tool was designed to explore the eyesight, ocular pain and discomfort, general functioning and psychosocial factors related to vision. WHO/PBD-VF20 has been evaluated and showed good psychometric properties in studies of people with visual impairment from cataract in Kenya, Bangladesh and the Philippines [9–11]. However, it has not been used to measure VRQoL in people living with trichiasis.

Generic HRQoL tools assess a range of health related issues and can be used irrespective of disease entity [7,12]. The WHOQOL-BREF is one such tool, which has been developed and validated across 20 countries in Africa, Asia and Latin America [12–16]. A hospital-based study in India used the WHOQOL-BREF to compare the QoL of 60 "trachomatous entropion" patients with age, sex and socio-economic status matched hospital patients without entropion or trichiasis [5]. However, about two-thirds of the cases had entropion without trichiasis, which precludes drawing conclusions about the QoL of trichiasis patients and the controls were not necessarily representative of the population.

Relatively little is known about the impact that trichiasis has on the lives of affected people. In this case-control study we measured the impact on vision and health-related QoL in Ethiopia, using standard WHO quantitative tools.

Methods

Ethics Statement

This study was reviewed and approved by the Food, Medicine and Healthcare Administration and Control Authority of Ethiopia, the National Health Research Ethics Review Committee of the Ethiopian Ministry of Science and Technology, Amhara Regional Health Bureau Research Ethics Review Board Committee, the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee, and Emory University Institutional Review Board. Written informed consent in Amharic was obtained prior to enrolment from participants. If the participant was unable to read and write, the information sheet and consent form were read to them and their consent recorded by thumbprint.

Study design and Participants

This case-control study was nested within a clinical trial of two alternative surgical treatments for trichiasis. For the trial 1000 trichiasis cases were recruited, and these were also enrolled into this QoL study. Cases were defined as individuals with one or more eyelashes touching the eyeball or with evidence of epilation in either or both eyes in association with tarsal conjunctival scarring. People with trichiasis from other causes, recurrent trichiasis and those <18 years of age were excluded. Trichiasis cases were identified mainly through community-based screening. Trichiasis screeners and counsellors (Eye Ambassadors) visited every household in their target village, identified and referred trichiasis cases to health facilities where surgical services were provided. Some cases self-presented or were referred by local health workers. Recruitment was done mainly from three districts of West Gojam Zone, Amhara Region, Ethiopia between February and May 2014. This area has one of the highest burdens of trachoma worldwide [17].

We recruited 200 matched controls to every fifth consecutive trichiasis case. Controls were individuals without clinical evidence or a history of trichiasis (including epilation), and who came from households without a family member with trichiasis or a history of trichiasis. Controls were individually matched with every fifth trichiasis case by location, sex and age (+/- two years). The research team visited the sub-village (30–50 households) of the trichiasis case that required a matched control. A list of all potentially eligible people living in the sub-village of the case was compiled with the help of the sub-village administrator. One person was randomly selected from this list using a lottery method, given details of the study and invited to participate if eligible. If a selected individual refused or was ineligible, another was randomly selected from the list. When eligible controls were not identified within the sub-village of the index case, recruitment was done in the nearest neighbouring sub-village, using the same procedures.

Quality of life instruments

VRQoL. The WHO/PBD-VF20 was used to assess VRQoL [8]. It contains 20 questions sub-divided into three subscales: visual symptom, general functioning and psychosocial. Each question has a 5-point response option: one indicates the highest and five the lowest score. The first two questions measure the eyesight and amount of pain or discomfort the person is experiencing. The psychosocial questions assess the frequency of experiencing a specific vision-related problem, while the remaining items measure the difficulty associated with overall performance. Two translators translated the tool into Amharic independently. The two translations were compared and differences were discussed and resolved to develop a single, final version.

HRQoL. The WHOQOL-BREF was used to assess HRQoL [13]. It contains 26 questions, which assess QoL across four domains: physical health, psychological, social relationships and environment in the past four weeks [6,12,13]. The first two questions assess general QoL and health. Each item is scored on a 5-point scale. The Amharic version used in this study was provided by the WHO and has been previously validated and used in Ethiopia [18–20].

Data collection

The VRQoL and HRQoL were administered orally by six trained Amharic speaking interviewers, because of the low literacy rate amongst participants. Data from trichiasis cases were collected at health facilities at the time of enrolment into the clinical trial, prior to surgery. Data from the controls were collected at their homes.

Data were also collected on general health problems and self-rated socioeconomic status (SES). For the self-rated socio-economic status, participants were asked to rate the wealth of their households in relation to other households in their village by choosing one of the following options: (1) very poor, (2) poor, (3) average, (4) wealthy or (5) very wealthy. In addition, data were collected on social relations, marriage and sleeping, through semi-structured questions including: "Do you feel ashamed or embarrassed due to the trichiasis?", "Do you worry that you may lose your remaining eyesight due to the trichiasis?", "Do you have a sleeping problem?" and "If yes, do you think your sleeping problem is related with the trichiasis?"

Presenting LogMAR (Logarithm of the Minimum Angle of Resolution) visual acuity at two metres was measured using "PeekAcuity" software on a Smartphone in a dark room [21]. We assessed contrast sensitivity with a prototype smartphone based test that presents the individual with calibrated grey scale spots against a white background, which they have to identify by touching the screen (www.peekvision.org). Unlike visual acuity, which is measured with high contrast, contrast sensitivity perhaps more accurately reflects the person's everyday visual experience in varying conditions. Patients with normal visual acuity may have profound contrast sensitivity impairment. Therefore it is useful to measure contrast sensitivity while investigating VRQoL, as impairment could lead to decreased functioning and quality of life [22]. The ophthalmic examination was conducted using a 2.5x binocular magnifying loupe and a bright torch. Clinical signs were graded using the Detailed WHO FPC Grading System [23].

Sample size

The sample size was calculated with the aim of detecting a three point difference in mean QoL score between trichiasis cases and controls [5]. The sample size of 1000 cases and 200 controls has 90% power to detect even minimal effect of trichiasis on QoL with an effect size of about 0.27 (effect size = QoL score difference (3)/SD (11)) with a Type I error of 5%.

Analysis

Data were double-entered into Access (Microsoft), cleaned in Epidata 3.1 and transferred to Stata 11 (StataCorp) for analysis. Data were analysed as follows:

VRQoL. All items were grouped and scores added into their respective subscales: "General Vision" subscale (1 question); "Visual Symptoms" subscale (3 questions); "General Functioning" subscale (12 questions); and "Psychosocial" subscale (4 questions) [8]. The subscale scores were then converted into a scaled value out of one hundred, using the formula: ([individual score—lowest possible score]/[highest possible score—lowest possible score]) X100. Therefore, the person with the lowest possible VRQoL score would receive a scaled value of "0" and the person with the highest possible VRQoL score receives a scaled value of "100" [11].

HRQoL. Data were analysed following the WHOQOL protocol [6,13]. Three negatively framed items were reversed into a positive frame so higher scores denote higher QoL. To generate domain scores, questions were grouped into their respective domains and their scores totalled. The mean score of all items included in the domain was calculated and then multiplied by four. These scores then transformed to a 0 to 100 scale with the formula specified in the manual to allow comparison between domains made of unequal number of items [6].

Clinical data. The presenting visual acuity in the better eye was used in this analysis. For visual acuities of counting fingers or less, LogMAR values were attributed as follows: counting fingers, 2.0; hand movements, 2.5; perception of light, 3.0; no perception of light, 3.5 [24]. The LogMAR visual acuity scores were then categorised based on the WHO classifications: Normal vision, $\geq$6/18; moderate visual impairment, <6/18–$\geq$6/60; severe visual impairment, <6/60–$\geq$3/60; and blind, <3/60. Contrast sensitivity scores were grouped into quartiles. Corneal opacity and trichiasis grading in the more affected eye was used to test the association of these with QoL in trichiasis cases. Based on their trichiasis severity, cases were categorised into Minor Trichiasis (<6 lashes or evidence of epilation in <1/3rd of the lash margin) and Major Trichiasis ($\geq$6 lashes or evidence of epilation in $\geq$1/3rd of the lash margin). Corneal opacity grading was categorised as either (i) no opacity/peripheral opacity or (ii) opacity involving the visual axis.

Comparison of cases and controls. All comparisons of cases and controls were adjusted for the matching variables: age and sex. The VRQoL analysis was also adjusted for socio-economic status and the HRQoL analysis adjusted for both socio-economic status and presence of health problems during the previous four weeks, as these factors may confound the association between trachomatous trichiasis and QoL. Logistic, linear and ordinal logistic regression methods were used for binary, continuous and ordered categorical outcome variable analysis, respectively. Linear regression models and the t-test were employed to compare significant differences in QoL scores and to generate mean and mean differences between cases and controls in each QoL subscale and domain, respectively.

Factors associated with QoL among cases. Linear regression was used to investigate the relationship between various factors with each VRQoL and HRQoL domain score (continuous variable) in trichiasis cases in a univariable and multivariable analysis. Tests for trend were undertaken in case of ordered categorical independent variables and significance was assessed using p-value for trend. Likelihood ratio-tests were employed to obtain p-values in categorical exposure variables. Variables that were associated with the outcome on univariable analyses at a level of $p<0.05$ were included in the multivariable analysis and then those with $p<0.2$ were retained in the model. To adjust for multiple comparisons, we used the Benjamini and Hochberg method, assuming a false discovery rate (FDR) of 5% [25].

Psychometric property evaluation. Construct validity of the VRQoL data was assessed through known-group difference and convergence validity using a linear regression model. In the HRQoL data discriminant (to distinguish differences between cases and controls) and construct validity were assessed using linear regression and Pearson's correlation respectively. Cronbach's alpha was used to test for internal consistency and reliability of the VRQoL and HRQoL data.

Results

Demographic and clinical characteristics of participants

Cases and controls were adequately matched for age (Table 1) and for geographical distribution across the 20 administrative units where recruitment was conducted. There were proportionately slightly more females among the 200 controls (83%) than the 1000 cases (76%). This occurred by chance as the 200 trichiasis cases used to determine the control matching characteristics had proportionately more females than in the full group of 1000 trichiasis cases. The trichiasis cases were more likely to be widowed or divorced, be from poorer households, and report other health problem in the past month than controls. For the analysis of socio-economic data we combined the "very poor" with the "poor" group and the "very wealthy" with "wealthy" group because of small numbers at both ends of the SES distribution. Trichiasis cases had substantially lower visual acuity scores (median LogMAR, 0.35; IQR, 0.15 to 0.6) than the controls (median LogMAR, -0.05; IQR, -0.1 to 0.1; Wilcoxon ranksum test, $p<0.0001$). Among trichiasis cases vision in the better eye was 6/18 or better in 63%, and 50% had minor trichiasis. The median duration of trichiasis among the cases was 5 years (IQR, 2–10).

Vision related quality of life

The trichiasis cases had substantially lower VRQoL scores than the controls in all four subscales ($p<0.0001$) (Table 2). The largest differences between cases and controls were found for visual symptoms (mean difference, 51.5; 95%CI, 48.5–54.5) and the smallest in general functioning (mean difference, 24.1; 95%CI, 21.1–27.1). In a sub-group analysis, trichiasis cases with normal vision had significantly lower VRQoL in all subscales than controls with normal vision (Table 3).

The relationship between VRQoL and various demographic and clinical characteristics among individuals with trichiasis are presented in Table 4. VRQoL scores were lower in all domains with increasing age, severity and duration of trichiasis and with decreasing visual acuity and contrast sensitivity scores. Scores were also lower in females, illiterate individuals and in cases with central corneal opacity.

In multivariable analysis, lower overall VRQoL scores were found in those with longer trichiasis duration, central corneal opacity, visual impairment and poor contrast sensitivity (Table 4). In addition to these, older age and female gender were associated with lower VRQoL score in the general functioning subscale. In the model, people with Major Trichiasis had lower

Table 1. Demographic and clinical characteristics of participants.

Variables	Cases		Controls		p-value
	n / 1000	(%)	n / 200	(%)	
Age, mean (SD)	47.3 years	(13.5)	45.9 years	(13.3)	-
Gender, female	765	(76.5)	167	(83.6)	-
Illiterate	886	(88.6)	170	(85.0)	0.005
Marital status					
Married	646	(64.6)	162	(81.0)	0.0001[‡]
Widowed	203	(20.3)	27	(13.5)	
Divorced	119	(11.9)	9	(4.5)	
Single	32	(3.2)	2	(1.0)	
Job[‡]					
Farmer	839	(83.9)	168	(84.0)	0.006[‡]
Employed/self employed	52	(5.2)	17	(8.5)	
Daily labourer	46	(4.6)	4	(2.0)	
No job	63	(6.3)	11	(5.5)	
Self rated wealth*					
Very wealthy/ Wealthy	32	(3.2)	30	(15.0)	<0.0001[†]
Middle	447	(44.7)	135	(67.5)	
Very Poor / Poor	521	(52.1)	35	(17.5)	
Health problem					
No	628	(62.8)	172	(86.0)	<0.0001
Yes	372	(37.2)	28	(14.0)	
Visual Acuity—better eye					
Normal (≥6/18)	638	(63.8)	194	(97.0)	<0.0001[†]
Moderate visual impairment (<6/18 to ≥6/60)	327	(32.7)	4	(2.0)	
Severe visual impairment (<6/60 to ≥3/60)	18	(1.8)	1	(0.5)	
Blind (<3/60)	17	(1.7)	1	(0.5)	
Contrast sensitivity					
1 (Best)	336	(33.6)	142	(71.0)	<0.0001[†]
2	193	(19.3)	33	(16.5)	
3	249	(24.9)	17	(8.5)	
4 (Worst)	222	(22.2)	8	(4.0)	

p-values are calculated using logistic regression and adjusted for age and gender, with the exception for age, which was calculated using linear regression.

‡ Combined p-value from likelihood ratio-test.

† P-value for trend.

* We merged "very wealthy" and "wealthy" and "very poor" and "poor" because of small numbers at the extremes of the distribution, to create three levels of socio-economic status measure to facilitate data modelling.

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VRQoL score in the visual symptom domain after controlling for potential confounders (p = 0.011), however, this is confounded by duration of trichiasis and was therefore dropped from the final model (Table 4).

Health related quality of life

The trichiasis cases had substantially lower overall HRQoL (p<0.0001) and overall self rated health (p<0.0001) scores than the controls (Table 2). Strikingly, 55.4% of trichiasis cases rated

Table 2. Comparison of mean domain scores of VRQoL and HRQoL of trichiasis cases and controls.

Domain	TT Cases		Controls		Mean difference		p-value
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	
VRQoL [a]							
Overall eyesight	45.9	(44.5–47.3)	95.4	(93.2–97.5)	49.5	(46.3–52.7)	<0.0001
Visual symptom	46.0	(44.7–47.3)	97.5	(96.1–98.9)	51.5	(48.5–54.5)	<0.0001
General Functioning	73.7	(72.4–75.0)	97.7	(96.4–99.1)	24.1	(21.1–27.1)	<0.0001
Psychosocial	69.1	(67.4–70.7)	98.1	(96.8–99.5)	29.1	(25.3–32.8)	<0.0001
HRQoL [b]							
General Facet Items							
Overall quality of life	34.5	(33.3–35.7)	64.6	(61.9–67.3)	30.1	(27.2–33.1)	<0.0001
Overall health	38.2	(37.0–39.5)	71.7	(69.5–74.0)	33.5	(30.4–36.5)	<0.0001
Domains							
Physical health	47.4	(46.4–48.3)	79.8	(77.9–81.7)	32.4	(30.1–34.7)	<0.0001
Psychological	58.7	(58.0–59.5)	80.5	(79.0–82.0)	21.8	(20.0–23.7)	<0.0001
Social	51.7	(50.3–53.1)	72.1	(69.7–74.5)	20.4	(17.1–23.7)	<0.0001
Environment	38.7	(38.0–39.4)	62.0	(60.4–63.6)	23.3	(21.6–24.9)	<0.0001

[a] p-values were calculated by linear regression and adjusted for age, gender and self-rated wealth.

VRQoL = Vision Related Quality of Life

[b] p-values were calculated by linear regression and adjusted for age, gender, self-rated wealth and other health problem in the past month

HRQoL = Health Related Quality of Life

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Table 3. Comparison of mean VRQoL and HRQoL scores of trichiasis cases and controls with normal vision (presenting visual acuity of ≥6/18 in the better eye).

Domain	TT Cases With Normal Vision n = 638		Controls With Normal Vision n = 194		Mean difference		p-value
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	
VRQoL [a]							
Overall eyesight	50.5	(48.8–52.2)	96.9	(95.2–98.6)	46.4	(43.2–49.6)	<0.0001
Visual symptom	49.4	(47.8–51.0)	98.5	(97.5–99.5)	49.0	(46.1–52.0)	<0.0001
General Functioning	79.8	(78.5–81.2)	98.7	(97.8–99.6)	18.9	(16.4–21.4)	<0.0001
Psychosocial	74.1	(72.2–76.1)	98.8	(97.7–99.9)	24.7	(21.1–28.2)	<0.0001
HRQoL [b]							
General Facet Items							
Overall quality of life	37.0	(35.5–38.5)	64.9	(62.2–67.7)	28.0	(24.9–31.0)	<0.0001
Overall health	41.7	(40.2–43.3)	72.2	(70.0–74.3)	30.4	(27.4–33.5)	<0.0001
Domains							
Physical health	51.5	(50.4–52.6)	80.3	(78.5–82.1)	28.9	(26.5–31.0)	<0.0001
Psychological	60.2	(59.2–61.2)	80.9	(79.4–82.3)	20.7	(18.8–22.6)	<0.0001
Social	54.9	(53.2–56.7)	72.5	(70.1–74.9)	17.5	(14.1–20.9)	<0.0001
Environment	39.9	(39.1–40.9)	62.3	(60.7–63.8)	22.3	(20.6–24.1)	<0.0001

[a] p-values were calculated by linear regression and adjusted for age, gender and self-rated wealth.

VRQoL = Vision Related Quality of Life

[b] p-values were calculated by linear regression and adjusted for age, gender, self-rated wealth and other health problem in the past month

HRQoL = Health Related Quality of Life

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Table 4. Univariable[a] and Multivariable[b] associations of VRQoL with demographic and clinical characteristics among trichiasis cases.

Variable	Overall eyesight		Visual symptom		General functioning		Psychosocial	
	Mean	***(95% CI)***	***Mean***	***(95% CI)***	***Mean***	***(95% CI)***	***Mean***	***(95% CI)***
Age Groups (years)								
≤ 29	55.1	(50.8–59.4)	52.5	(48.7–56.4)	83.7	(80.0–87.3)	74.4	(69.4–79.3)
30–39	51.3	(48.2–54.4)	48.2	(45.6–50.9)	81.5	(79.3–83.7)	74.2	(70.7–77.8)
40–49	46.6	(43.9–49.4)	47.1	(44.3–49.8)	75.7	(73.4–78.0)	69.2	(65.7–72.6
50–59	43.0	(40.2–45.8)	42.7	(40.0–45.4)	71.2	(68.4–73.9)	66.8	(63.3–70.3)
60–69	42.5	(39.1–45.9)	46.0	(42.6–49.4)	68.5	(65.0–71.9)	68.7	(64.5–72.9)
≥ 70	32.2	(30.7–39.8)	39.1	(34.6–43.6)	56.8	(51.4–62.1)	58.8	(53.0–64.6)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]		-	0.069		0.010		0.0048	
Gender								
Male	48.2	(45.2–51.2)	49.1	(46.6–51.7)	77.8	(75.2–80.4)	72.7	(69.5–76.0)
Female	45.2	(43.6–46.7)	45.0	(43.5–46.5)	72.4	(70.9–73.9)	67.9	(66.0–69.9)
p-value [a]	0.07		0.008		0.0007		0.02	
p-value [b]		-		-	0.034			-
Literacy								
Literate	52.6	(48.6–56.7)	52.3	(48.8–55.7)	84.2	(81.3–87.20	77.2	(73.1–81.4)
Illiterate	45.0	(43.5–46.5)	45.2	(43.8–46.6)	72.3	(70.9–73.7)	68.0	(66.2–69.8)
p-value [a]	0.0006		0.0006		<0.0001		0.0005	
p-value [b]	0.19			-	0.049			-
Trichiasis severity								
Minor trichiasis (<6 lashes)	47.7	(45.8–49.6)	48.4	(46.5–50.2)	75.8	(74.0–77.6)	71.1	(68.8–73.4)
Major trichiasis (≥6 lashes)	44.0	(42.1–46.0)	43.6	(41.8–45.4)	71.6	(69.6–73.5)	67.0	(64.7–69.4)
p-value [a]	0.009		0.0003		0.002		0.02	
p-value [b]		-		-		-		-
Trichiasis duration in years								
<2	53.8	(50.5–57.1)	57.4	(54.5–60.3)	81.5	(78.4–84.7)	77.7	(73.8–81.5)
2–4	46.9	(44.4–49.4)	46.5	(44.2–48.8)	74.9	(72.6–77.1)	68.8	(65.8–71.8)
5–9	44.9	(42.1–47.7)	44.3	(41.7–46.9)	73.5	(70.8–76.1)	68.7	(65.4–72.0)
10–15	42.0	(38.2–45.7)	40.7	(37.3–44.1)	70.6	(67.4–73.9)	65.0	(60.5–69.4)
≥15	40.4	(36.9–43.9)	40.0	(66.7–43.3)	66.1	(62.4–69.9)	64.4	(60.0–68.7
p-value [a †]	*<0.0001*		*<0.0001*		*<0.0001*		*<0.0001*	
p-value [b †]	<0.0001		<0.0001		<0.0001		0.0004	
Corneal opacity								
No/peripheral opacity	50.2	(48.4–52.0)	49.2	(47.5–50.9)	78.0	(76.4–79.5)	73.9	(71.8–76.0)
Opacity involving the visual axis	40.4	(38.4–42.4)	41.9	(40.0–43.8)	68.3	(66.1–70.4)	62.9	(60.4–65.5)
p-value [a]	*<0.0001*		*<0.0001*		*<0.0001*		*<0.0001*	
p-value [b]	0.0002		0.0023		0.0077		0.0002	
Presenting VA in the better eye								
Normal (≥6/18)	50.5	(48.8–52.2)	49.4	(47.8–51.0)	79.8	(78.5–81.2)	74.1	(72.2–76.1)
Moderate visual impairment (<6/18 to ≥6/60)	39.7	(37.5–41.8)	40.9	(38.8–43.1)	65.3	(62.9–67.6)	62.3	(59.5–65.2)
Severe visual impairment (<6/60 to ≥3/60)	23.6	(15.7–31.6)	35.6	(26.0–45.3)	46.1	(36.0–56.1)	45.1	(32.7–57.6)
Blind (<3/60)	14.7	(5.6–23.9)	26.0	(16.5–35.4)	33.7	(18.9–48.7)	33.8	(18.3–49.4)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	<0.0001		0.0002		<0.0001		<0.0001	

(*Continued*)

Table 4. (*Continued*)

Variable	Overall eyesight		Visual symptom		General functioning		Psychosocial	
	Mean	***(95% CI)***	***Mean***	***(95% CI)***	***Mean***	***(95% CI)***	***Mean***	***(95% CI)***
Contrast sensitivity								
4 (Best score)	54.2	(51.8–56.6	52.1	(49.9–54.2)	83.6	(81.9–85.3)	78.3	(75.8–80.7)
3	46.8	(43.8–49.8)	46.8	(43.9–49.7)	75.4	(72.9–77.8)	70.0	(66.3–73.7)
2	42.6	(40.1–45.0)	44.2	(41.6–46.8)	71.9	(69.6–74.2)	67.0	(63.9–70.1)
1 (Worst score)	36.1	(33.4–38.9)	38.1	(35.5–40.7)	59.1	(55.8–72.4)	56.6	(52.9–60.4)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	<0.0001		<0.0001		<0.0001		<0.0001	
Self rated wealth								
Very wealthy / Wealthy	53.9	(45.3–62.5)	47.1	(38.9–55.4)	83.5	(76.4–90.7)	80.3	(72.3–88.3)
Middle	48.8	(46.8–50.8)	48.2	(46.4–50.1)	78.3	(76.6–79.9)	72.7	(70.4–75.1)
Poor / Very Poor	42.8	(40.9–44.8)	44.0	(42.2–45.8)	69.1	(67.2–71.1)	65.2	(62.9–67.6)
p-value [a †]	<0.0001		0.0037		<0.0001		<0.0001	
p-value [b †]	0.029		-		0.0001		0.0019	

[a] P-values from univariable analysis.

[b] P-values from multivariable analysis. All p-values are calculated using linear regression. For ordinal exposures with three or more categories the [†]p-values are calculated for trend. Using the Benjamini and Hochberg method, only tests with a p-value below 0.034 have a False Discovery Rate of <5%. Variables with univariable p<0.05 were included in the multivariable model, then those with p>0.2 were excluded (dashed line) from the final model after likelihood ratio- test. VRQoL = Vision related Quality of Life

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their overall QoL "poor" or "very poor" compared to only 9.5% of controls (p<0.0001) and 5.6% of cases rated their overall QoL "good" or "very good" compared to 59.5% of controls (p<0.0001). Across all four domains there were substantial differences in the QoL scores of cases and controls (all p<0.0001, Table 2). The largest difference was seen in the physical health domain (mean difference, 32.4; 95%CI, and 30.1–34.7). Trichiasis cases with normal vision had significantly lower HRQoL in all subscales than controls with normal vision (Table 3).

Among trichiasis cases, overall HRQoL and the four domain scores decreased with increasing age (except for environment domain), decreasing self-rated wealth, visual acuity and contrast sensitivity scores (Table 5). They were also lower in divorced/widowed, illiterate individuals, females and those with other health problems in the past month. Daily labourers, the unemployed and those with central corneal opacity had lower overall QoL and domain scores except for the environment domain. Participants with longer duration trichiasis had lower physical, psychological and social domain scores.

Multivariable analyses identified predictors of HRQoL among trichiasis cases (Table 5). Lower self-rated wealth was associated with lower QoL scores in all domains. Poorer overall QoL was related to not having a marriage partner, visual impairment, being a daily labourer and presence of other health problems. Older participants, females, the unemployed, those with visual impairment, poor contrast sensitivity score and other health problems were associated with lower physical domain scores. Daily labouring, not having a marriage partner and presence of other health problems were associated with lower psychological domain scores.

Impact of trichiasis on daily life

Among the 200 controls, 198 (99%) reported no ocular pain or discomfort. In contrast, among the 1000 trichiasis cases, 143 (14.3%), 281 (28.1%) and 562 (56.2%) reported mild, moderate

Table 5. Univariable[a] and Multivariable[b] associations of HRQoL with demographic and clinical characteristics among trichiasis cases.

Variable	Overall quality of life		Physical domain		Psychological domain		Social domain		Environmental domain	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Age Groups (years)										
≤ 29	38.4	(34.8–42.0)	60.7	(58.2–63.3)	63.4	(61.1–65.6)	61.0	(56.8–65.1)	41.1	(38.9–43.3)
30–39	37.7	(35.0–40.4)	54.3	(52.5–56.1)	60.6	(58.8–62.4)	58.9	(55.9–62.0)	41.5	(39.9–43.0)
40–49	37.9	(35.5–40.2)	49.1	(47.4–50.9)	58.9	(57.4–60.4)	56.6	(53.8–59.4)	38.8	(37.4–40.1)
50–59	32.6	(29.9–35.3)	44.2	(42.3–46.1)	57.6	(56.0–59.2)	46.3	(43.1–49.4)	38.2	(36.7–39.6)
60–69	30.9	(28.0–33.8)	40.7	(36.6–42.8)	56.8	(54.7–58.8)	42.1	(39.0–45.3)	36.4	(34.8–38.0)
≥ 70	26.0	(25.0–30.0)	32.7	(29.8–35.6)	55.4	(52.8–57.9)	42.8	(39.1–46.6)	35.3	(33.2–37.4)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	-		<0.0001		0.13		<0.0001		0.048	
Gender										
Male	36.1	(33.47–38.4)	51.9	(50.0–53.9)	60.1	(58.6–61.5)	57.7	(54.9–60.5)	41.0	(39.6–42.3)
Female	34.0	(32.6–35.4)	46.0	(44.9–47.1)	58.3	(57.4–59.2)	49.8	(48.2–51.4)	38.0	(37.2–38.8)
p-value [a]	0.16		<0.0001		0.06		<0.0001		<0.0001	
p-value [b]	-		<0.0001		-		-		0.024	
Literacy										
Literate	39.9	(36.5–43.3)	56.4	(53.7–59.1)	61.4	(59.1–63.7)	59.3	(55.2–63.3)	42.5	(40.3–44.7)
Illiterate	33.8	(32.5–35.1)	46.2	(45.2–47.2)	58.4	(57.6–59.2)	50.7	(49.2–52.2)	38.2	(37.5–38.9)
p-value [a]	0.0016		<0.0001		0.02		0.0001		<0.0001	
p-value [b]	-		-		-		-		0.19	
Marital status										
Married	39.4	(38.1–40.8)	51.0	(49.9–52.1)	60.9	(60.0–61.7)	60.6	(58.9–62.2)	40.4	(39.6–41.2)
Single	32.0	(23.4–40.7)	53.6	(46.5–60.7)	55.9	(50.1–61.6)	41.4	(34.9–47.9)	37.6	(32.5–42.7)
Divorced/widowed	24.8	(22.7–20.7)	39.4	(37.8–41.1)	54.7	(53.2–56.2)	34.9	(33.2–36.6)	35.4	(34.3–36.5)
p-value [a]										
Married vs. Single	0.03		0.33		0.02		<0.0001		0.14	
Married vs. Divorced/widowed	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	
P value [b]										
Married vs. Single	0.023		0.35		0.023		<0.0001		0.0043	
Married vs. Divorced/widowed	<0.0001		0.18		0.0076		<0.0001		0.77	
Job										
Farmer	36.3	(35.0–37.6)	48.0	(47.0–49.0)	59.5	(58.8–60.3)	53.1	(51.6–54.7)	38.9	(38.2–39.6)
Employed/self-employed	30.3	(24.5–36.0)	51.2	(46.9–55.5	56.9	(53.1–60.7)	45.2	(39.5–50.9)	38.7	(35.8–41.5)
Daily labour	17.9	(12.8–23.0)	43.7	(38.5–48.9)	52.2	(46.3–58.0)	42.6	(35.6–49.6)	37.4	(33.4–41.3)
No job (including students)	26.2	(20.4–32.0)	38.4	(33.4–43.3)	54.6	(50.4–58.9	44.4	(39.0–49.8)	36.7	(33.3–40.1)
p-value [a]										
Farmer vs. Employed/self-employed	0.03		0.14		0.13		0.01		0.89	
Farmer vs. Daily labour	<0.0001		0.06		0.0001		0.002		0.34	
Farmer vs. No job	<0.0001		<0.0001		0.002		0.003		0.12	
p-value [b]										
Farmer vs. Employed/self-employed	0.55		0.030		0.62		-		-	
Farmer vs. Daily labour	<0.0001		0.17		0.0086		-		-	
Farmer vs. No job	0.037		0.0005		0.18		-		-	
Trichiasis severity										
Minor trichiasis (<6 lashes)	35.2	(33.6–36.9)	48.7	(47.4–50.1)	58.9	(57.9–60.0)	53.7	(51.7–55.7)	39.4	(38.5–40.3)
Major trichiasis (≥6 lashes)	33.7	(32.0–35.5)	46.0	(44.6–47.4)	58.3	(57.4–59.7)	49.6	(47.6–51.6)	38.0	(37.0–39.0)

(Continued)

Table 5. (*Continued*)

Variable	Overall quality of life		Physical domain		Psychological domain		Social domain		Environmental domain	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
p-value [a]	0.22		0.005		0.60		0.004		0.05	
p-value [b]	-		-		-		-		-	
Trichiasis duration										
<2	35.0	(32.2–37.8)	50.2	(47.8–52.6)	59.4	(57.6–61.3)	51.4	(47.8–55.0)	39.7	(38.1–41.2)
2–4	34.7	(32.4–37.0)	49.3	(47.6–51.0)	60.1	(58.7–61.4)	54.9	(52.1–57.6)	37.9	(36.6–39.1)
5–9	35.9	(33.5–38.4)	47.6	(45.7–49.5)	58.2	(56.5–59.8)	51.7	(47.8–54.5)	40.0	(38.6–41.4)
10–15	34.7	(31.3–38.1)	46.1	(43.7–48.5)	59.6	(57.5–61.6)	53.4	(49.9–56.9)	39.3	(37.6–41.0)
≥15	31.2	(28.2–34.2)	41.7	(39.1–44.3)	55.8	(53.7–57.9)	45.0	(41.7–48.3)	36.7	(35.0–38.4)
p-value [a †]	0.11		<0.0001		0.005		0.003		0.14	
p-value [b †]	-		-		-		-		-	
Corneal Opacity										
No/peripheral opacity	36.6	(35.0–38.1)	50.3	(49.0–51.5)	59.8	(58.8–60.8)	53.4	(51.5–55.3)	39.3	(38.4–40.2)
Opacity involving the visual axis	31.9	(30.1–33.7)	43.7	(42.3–45.1)	57.4	(56.2–58.6)	49.5	(47.4–51.5)	37.9	(36.9–38.9)
p-value [a]	0.0002		<0.0001		0.003		0.006		0.04	
p-value [b]	-		0.057		-		-		-	
Presenting VA in the better eye										
Normal (≥6/18)	37.0	(33.5–38.4)	51.5	(50.4–52.6)	60.2	(59.2–61.2)	54.9	(53.2–56.7)	39.9	(39.1–40.8)
MVI (<6/18 to ≥6/60)	31.0	(28.9–33.2)	40.8	(39.2–42.4)	56.6	(55.4–57.9)	46.0	(43.6–48.4)	37.0	(35.8–38.1)
SVI (<6/60 to ≥3/60)	23.6	(13.6–33.6)	34.9	(29.0–40.9)	54.9	(48.1–61.6)	46.8	(34.7–58.8)	33.0	(27.6–38.3)
Blind (<3/60)	19.1	(8.4–29.8)	31.1	(21.5–40.7)	49.0	(39.2–58.8)	43.1	(30.3–56.0)	31.4	(24.3–38.5)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	0.068		0.0010		0.054		-		0.17	
Contrast sensitivity										
1 (Best score)	36.5	(36.4–40.5)	55.5	(54.0–57.0)	61.5	(60.2–62.7)	58.1	(55.6–60.4)	41.0	(39.8–42.2)
2	36.9	(34.2–39.6)	46.6	(44.6–48.7)	58.2	(56.5–59.9)	51.9	(48.6–55.2)	40.0	(38.5–41.3)
3	32.0	(29.7–34.4)	45.3	43.6–47.0)	58.5	(57.0–59.9)	49.3	(46.4–52.1)	38.1	(36.9–39.3)
4 (Worst score)	29.2	(26.6–31.7)	38.0	(36.1–39.9)	55.3	(53.5–57.2)	44.5	(41.6–47.4)	34.9	(33.5–36.3)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	-		0.0008		0.15		0.18		0.027	
Other health problems										
No	37.2	(35.8–38.6)	51.8	(50.6–52.9)	60.4	(59.5–61.4)	53.4	(51.6–55.2)	39.8	(39.0–40.7)
Yes	30.0	(27.9–32.1)	40.0	(38.5–41.4)	55.9	(54.6–57.1)	48.7	(46.6–50.9)	36.8	(35.8–37.8)
p-value [a]	<0.0001		<0.0001		<0.0001		0.002		<0.0001	
p-value [b]	0.0018		<0.0001		0.0002		-		0.080	
Self rated wealth										
Very wealthy / Wealthy	54.7	(48.4–60.9)	56.8	(52.0–61.6)	62.8	(57.8–67.7)	59.4	(50.6–68.2)	46.3	(42.4–50.2)
Middle	46.0	(44.6–47.3)	52.4	(51.0–53.7)	62.4	(61.4–63.4)	59.8	(57.9–61.7)	42.7	(41.7–43.6)
Poor / Very Poor	23.4	(22.0–24.8)	42.5	(41.2–43.8)	55.4	(54.3–56.4)	44.2	(42.3–46.1)	34.8	(34.0–35.7)
p-value [a †]	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	
p-value [b †]	<0.0001		<0.0001		<0.0001		<0.0001		<0.0001	

[a] P-values from univariable analysis.

[b] P-values from multivariable analysis. P-values are calculated using linear regression. For ordinal exposures with three or more categories the [†]p-values are calculated for trend. Using the Benjamini and Hochberg method, only tests with a p-value below 0.03 have a False Discovery Rate of <5%. Variables with univariable p<0.05 were included in the multivariable model, then those with p>0.2 were excluded (dashed line) from the final model after likelihood ratio test. MV = Moderate Visual Impairment; SVI = Severe Visual Impairment. HRQoL = Health related Quality of Life.

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and severe ocular pain or discomfort, respectively (p<0.0001). The cases reported the following effects of trichiasis: 596 (59%) felt ashamed or embarrassed; 913 (91.3%) worried that they might lose their remaining eyesight; 70 (7.0%) had been troubled in their marriage and ignored by their marriage partner; 681 (68.1%) reported sleeping problems, largely due to pain (675/681 (67.5%)) from the trichiasis.

Validity and reliability of the QoL Data

Satisfying the known-groups difference criteria, the trichiasis cases had significantly lower VRQoL and HRQoL scores in all domains (p<0.0001) than the controls (Table 2). With respect to convergence validity, worsening visual acuity and contrast sensitivity scores, trichiasis duration and central corneal opacity were significantly associated with lower scores in all four domains of VRQoL (Table 4). The VRQoL data were reliable after being assessed for internal consistency with a Cronbach's alpha: coefficients of >0.80. The overall QoL data showed very high internal consistency with a Cronbach's alpha of 0.90. The physical health, psychological, social and environment domains demonstrated internal consistency with Cronbach's alpha of 0.87, 0.65, 0.47, and 0.64, respectively.

Discussion

Trachomatous trichiasis results in considerable morbidity even before the development of irreversible visual impairment or blindness from corneal opacification. The eyelashes constantly rub the cornea causing irritation and pain [26]. However, despite these important consequences there are surprisingly limited data on the impact of trichiasis on quality of life. Moreover, few studies have investigated the resulting functional physical impairment [27,28]. The psychological and social effects of trichiasis have usually been overlooked. Little information has previously been collected using validated tools. In response, this study was conducted to address these gaps, using standard WHO QoL instruments, and found that trachomatous trichiasis has a very profound impact on both VRQoL and HRQoL, even prior to the development of visual impairment.

Vision related quality of life

Overall, the VRQoL of trichiasis cases was substantially lower in all domains compared to controls. When we restricted the analysis to people with a visual acuity of 6/18 or better, the difference in VRQoL was of a similar magnitude and was highly significant. This is an important observation, which demonstrates that trichiasis reduces VRQoL even before impairment of visual acuity develops.

We found that, of the four sub-scales, the one with the largest difference was the visual symptom subscale. This is a composite of questions about visual functioning, pain/discomfort, glare and light/dark adaption. The general functioning subscale showed the smallest difference compared to controls. This may be because approximately two-thirds of trichiasis cases had normal vision, and this subscale includes items on vision difficulties and role limitation.

Consistent with our study, several other studies have demonstrated the effect trichiasis has on physical functioning [26–28]. A population-based study in Tanzania found trichiasis without visual impairment results in limitation of physical functioning in women that was comparable to limitation associated with visual impairment from other causes [27]. A qualitative study of 23 women with trichiasis in Niger (without a control group for comparison) reported trichiasis had marked effects on the general well-being of these individuals and was linked to physical disability and inability to work and earn an income [26]. In a study conducted in southern Ethiopia, 61% of trichiasis cases reported difficulty in physical functioning including walking, recognizing faces and performing day-to-day farming activities [28].

Among trichiasis cases, VRQoL was significantly lower with central corneal opacity, increasing trichiasis duration and decreasing visual acuity and contrast sensitivity scores. This suggests that trichiasis cases had significantly lower contrast sensitivity than the controls. Other studies have found conditions such as dry eyes and reduced tear break-up time, resulting from progressive conjunctival scarring and ocular epithelial tissues damage, are associated with reduced contrast sensitivity score [29,30]. Impaired contrast sensitivity score can greatly affect the person's ability to recognise objects and perform daily activities under different conditions. A recent study conducted on glaucoma patients revealed that contrast sensitivity plays a major role in daily functioning and VRQoL; and the contrast sensitivity score was correlated with VRQoL indicators such as facial recognition, finding objects, motion detection and general vision [22]. Poor contrast sensitivity has been associated with physical injuries from accidents, suggesting that it would greatly hamper overall well being [31,32]. The association between trichiasis severity and the visual symptom subscale was weakened after including trichiasis duration in the multivariable regression model. Severity and duration are not independent of each other. The general functioning subscale of the VRQoL and physical health domain in HRQoL were lower in females than males. Although the reason is not apparent, a similar finding has been reported in a Tanzanian study: women without visual impairment were more likely to have functional limitation than their male counterparts [27].

Health related quality of life

Trichiasis cases had a poorer HRQoL than controls in all domains, again even without visual impairment. Strikingly, the physical domain in the WHOQOL-BREF, which includes questions on pain and discomfort, had the highest mean score difference between cases and controls, emphasising the suffering trichiasis causes. Among the QoL domains, the environmental domain had the lowest score in both trichiasis cases and controls. This domain is built from items such as satisfaction with financial resources, access to health service, transport, information and leisure activities, which generally have low availability in the communities where this study was conducted. Hence, participants would be anticipated to have a lower rate of satisfaction for these items.

The WHOQOL-BREF has been used to assess HRQoL of entropion patients (with and without trichiasis) [5]. Apart from the environment domain scores of the trichiasis cases, the average QoL scores of trichiasis cases and controls in all domains in the Indian study were generally lower than those we recorded in Ethiopia [5]. This difference could be attributed to two things. Firstly, perceptions towards QoL in Indian and Ethiopian communities could be different. Secondly, in the Indian study, all participants were recruited from hospital, compared to community-based recruitment in our study. Hospital participants might be more likely to report poor QoL than people in the community [14]. In contrast to trichiasis, there is an extensive literature about the impact of cataract on QoL [7,9–11,33]. However, there are fundamental differences between cataract and trichiasis in the nature of visual loss, pain and other symptoms they cause.

Validity and reliability of QoL data

These tools have previously been reported to be valid and reliable in studies conducted in similar settings to this study [9–11,14,18–20]. In this study, both the VRQoL and HRQoL data measured what they were intended to measure (construct validity) by demonstrating significant differences in the scores between groups known to be different; cases and controls had lower and higher scores respectively. The VRQoL data also showed that sub-scales correlate well with measures of similar constructs (convergent validity) such as visual acuity and contras sensitivity where worsening in these measures is associated with lower VRQoL subscale scores. There was evidence of higher homogeneity among the items in each VRQoL subscale (internal consistency) than the generally accepted criteria of >0.70. In the HRQoL data, the overall QoL and the physical health domain items were internally consistent and reliable in measuring the same construct, while the psychological, social relations and environment domains had less internal consistency. Similar psychometric properties have been reported in the field trial results of this tool in other countries [14]. The lower alpha score for the social relationship domain is anticipated as its analysis is based on three items instead of the generally recommended minimum four for evaluating internal consistency [6]. Hence, this domain's results should be interpreted in caution, as there was insufficient evidence that the items in this domain are always measuring the same construct.

Strengths and limitations

This is a large case-control study examining the impact of trichiasis on QoL. We used tools validated in settings similar to this study setting. The VRQoL tool has been validated in Kenya while the HRQoL tool has been tested and used in other studies in Ethiopia. The study has some limitations. Perfect matching was not achieved in terms of gender, resulting in more females in the controls than the trichiasis cases. However, all comparisons between cases and controls were adjusted for gender, age and self-rated wealth. A community-based screening method was employed to identify trichiasis cases. Although we think that this was an efficient and comprehensive approach to finding cases, it is possible that some cases might have been missed, particularly those with mild disease who may be less likely to come forward, which could lead to an overestimation of the QoL scores for trichiasis cases in general. Trichiasis is strongly associated with a poorer QoL, However, the cross-sectional nature of this study precludes us from drawing definite conclusions about causality. This question is being investigated by reassessing this group of people one year after surgery.

Conclusions

In this Ethiopian population, we found that trichiasis cases have significantly lower VRQoL and HRQoL than controls regardless of visual impairment. The results provide solid data for advocacy and encourage programme leaders and funders to secure resources to promote trichiasis intervention. Trichiasis inflicts considerable physical and psychosocial trauma including sleep disturbance, low self-esteem and possibly a less stable marriage. The burden of trichiasis goes beyond visual loss. Timely treatment is needed not only to prevent visual loss but also alleviate physical and psychological suffering and social exclusion of trichiasis patients, thereby improving their physical and psychological health, general functioning and social relations. The comprehensive SAFE strategy is needed to prevent the development of trichiasis. The long-term effect of trichiasis surgery on VRQoL and HRQoL in trichiasis patients needs to be measured in longitudinal studies.

Supporting Information

S1 Checklist. STROBE Checklist.
(DOCX)

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Author Contributions

Conceived and designed the experiments: EH PME HK SP HW MJB. Performed the experiments: EH TW SA ZT MZ ZZ WG MJB. Analyzed the data: EH HAW MJB. Wrote the paper: EH TW SA ZT MZ ZZ WG KC PME HK RLB DCWM SNR SP HAW MJB.

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8. Impact of Trachomatous Trichiasis Surgery on Quality of Life: A Longitudinal Study in Ethiopia

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Section D - Multi-authored Work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper	With senior colleagues I designed the study and prepared the protocol / SOP, led the research project and collected data, analysed data and wrote the first draft of the paper with edits from my supervisor and co-authors.

Student Signature: [signature] Esmael Habtamu Ali Date: 15th December 2016

Supervisor Signature: [signature] Prof. Matthew Burton
Date: 1st December 2016

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RESEARCH ARTICLE

Impact of Trichiasis Surgery on Quality of Life: A Longitudinal Study in Ethiopia

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Abstract

Background

Trachomatous trichiasis significantly reduces vision and health related quality of life (QoL). Although trichiasis surgery is widely performed to treat trichiasis, there is little data on the effect of surgery on QoL. We measured the impact of trichiasis surgery on vision and health related QoL in a longitudinal study from Amhara Region, Ethiopia.

Methodology/Principal Findings

We recruited 1000 adult participants with trichiasis (cases) and 200 comparison participants, matched to every fifth trichiasis case on age (+/- two years), sex and location. Vision-related quality of life (VRQoL) and health-related quality of life (HRQoL) were measured using the WHO/PBD-VF20 and WHOQOL-BREF questionnaires respectively, at enrolment and 12 months after enrolment. All trichiasis cases received free standard trichiasis surgery immediately after enrolment. The mean difference in QoL scores between enrolment and follow-up for cases and comparison participants, and the difference-in-differences by baseline trichiasis status was analysed using random effects linear regression, the later adjusted for age, sex and socioeconomic status. At 12-months follow-up, data was collected from 980 (98%) and 198 (98%) trichiasis cases and comparison participants respectively. At this follow-up visit, VRQoL and HRQoL scores of trichiasis cases improved substantially in all subscales and domains by 19.1–42.0 points ($p<0.0001$) and 4.7–17.2 points ($p<0.0001$), respectively. In contrast, among the comparison participants, there was no evidence of improvement in VRQoL and HRQoL domain scores during follow-up. The improvement in VRQoL and HRQoL in cases was independent of the presence of visual acuity improvement at 12 months.

all the data and had final responsibility for the decision to submit for publication.

Competing Interests: The authors have declared that no competing interests exist.

Conclusions/Significance

Trichiasis surgery substantially improves both VRQoL and HRQoL regardless of visual acuity change. Unprecedented effort is needed to scale-up trichiasis surgical programmes not only to prevent the risk of sight loss but also to improve overall wellbeing and health perception of affected individuals.

Author Summary

We previously reported that Trachomatous Trichiasis (TT) has a profound impact on vision and heath related quality of life (QoL), even when vision is not impaired. The World Health Organization (WHO) recommends corrective eyelid surgery for trichiasis to reduce the risk of vision loss. However, trichiasis surgery may also improve overall well-being. There is very limited evidence on the long-term impact of trichiasis surgery on QoL. We measured vision and health-related quality of life of 1000 TT patients before and one year after receiving TT surgery and compared the QoL scores of these with the baseline and 1 year follow-up QoL score of 200 matched individuals who have never had trichiasis or trichiasis surgery. We found strong evidence that surgery substantially improves both vision and heath related QoL of TT case, even when there is no improvement in vision; while there was no evidence of improvement in the QoL of the trichiasis free participants. The results provide clear evidence that the benefit of trichiasis surgery goes beyond preventing the risk of blindness and improves the overall wellbeing and health perception of affected individuals, indicating the need to provide prompt surgical intervention for affected individuals.

Introduction

Trachoma, an eye disease caused by *Chlamydia trachomatis*, is the leading infectious cause of blindness worldwide [1]. The infection can lead to progressive conjunctival scarring and subsequently trachomatous trichiasis, the in-turning of eyelashes. Trichiasis in turn can cause constant painful abrasion to the cornea, irreversible corneal opacification and ultimately visual impairment and blindness. Approximately 7.3 million people have untreated trichiasis, and 2.4 million people are visually impaired from trachoma worldwide [2,3].

Trachomatous trichiasis is a painful condition, which can have a major impact on the individual's general health and wellbeing, even prior to the development of visual impairment [4]. Moreover, it may have major socioeconomic consequences for affected families and communities [4–6]. We have previously reported that trichiasis adversely impacts vision and health related quality of life (QoL), even before visual impairment develops [7]. Other studies have found trichiasis causes considerable functional and physical impairment, social withdrawal and exclusion, inability to work and earn an income [4,6,8,9].

The World Health Organization (WHO) recommends corrective eyelid surgery for trichiasis, to reduce the risk of sight loss [10]. Limited evidence suggests that the benefits of surgery may go beyond preventing vision loss and in fact help to restore the physical, social, psychological, environmental and economic wellbeing of individuals through improving vision and reducing pain and discomfort [8,11,12]. However, detailed empirical data on the impact of surgery on QoL is lacking. One longitudinal study from Ethiopia assessed the effect of trichiasis surgery on physical functioning of 411 trichiasis patients, six months after trichiasis surgery

[9]. Another study, conducted in India, assessed HRQoL in 60 trachomatous entropion patients before and 1 month after trichiasis surgery and epilation [13]. No studies have measured the long-term overall effect that trichiasis surgery has on the different QoL domains and overall wellbeing.

The WHO has developed and validated several tools for measuring QoL. These include the WHO/PBD-VF20 which is designed to measure vision related quality of life (VRQoL); and the WHOQOL-BREF which measures general health related quality of life [14,15]. We have previously reported a case-control study, which used both of these tools to compare the QoL of individuals with trichiasis to healthy controls, and found substantial differences [7]. Here we report a longitudinal study of these same cases and controls (hereafter referred to as comparison participants), in which we explore the longer-term impact of trichiasis surgery on vision and health-related QoL.

Methods

Ethics Statement

This study was reviewed and approved by the National Health Research Ethics Review Committee of the Ethiopian Ministry of Science and Technology, the London School of Hygiene & Tropical Medicine (LSHTM) Ethics Committee, and Emory University Institutional Review Board. Written informed consent in Amharic was obtained prior to enrolment from participants. It was conducted in accordance with the Declaration of Helsinki. If the participant was unable to read and write, the information sheet and consent form were read to them and their consent recorded by thumbprint. Interviews were conducted privately, paper data were archived in a locked cabinet and electronic data were stored on a password-protected computer isolated from the Internet in a secured dedicated study office. Study participants with identified ocular problems were managed as per local protocol.

Study Design and Participants

This longitudinal study was nested within a clinical trial of two alternative surgical treatments for trichiasis [16]. We recruited 1000 trichiasis cases into the trial, who were also enrolled into this QoL study. The pre-operative baseline data from this study have been previously reported in detail [7]. Cases were defined as individuals with one or more eyelashes touching the eyeball or with evidence of epilation in either or both eyes in association with tarsal conjunctival scarring. People with trichiasis from other causes, recurrent trichiasis and those aged <18 years were excluded. Trichiasis cases were identified mainly through community-based screening [17]. Recruitment was done in three districts of West Gojam Zone, Amhara Region, Ethiopia between February and May 2014. This area has one of the highest burdens of trachoma worldwide [18].

We also recruited 200 comparison participants. These were individuals without clinical evidence or a history of trichiasis (including epilation), who came from households without a family member with trichiasis or a history of trichiasis. Comparison participants were individually matched to every fifth trichiasis case by location, sex and age (+/- two years). The research team visited the sub-village (30–50 households) of the trichiasis case that required a matched control. A list of all potentially eligible people living in the sub-village of the case was compiled with the help of the sub-village administrator. One person was randomly selected from this list using a lottery method, given details of the study and invited to participate if eligible. If a selected individual refused or was ineligible, another was randomly selected from the list. When eligible comparison participants were not identified within the sub-village of the index case, recruitment was done in the nearest neighbouring sub-village, using the same procedures.

Baseline Assessment

Data from trichiasis cases were collected at health facilities at the time of enrolment into the clinical trial, prior to trichiasis surgery. Data from the comparison participants were collected at their homes. Six trained Amharic speaking interviewers collected data from participants using a standardised questionnaire, including socio-demographic variables (age, sex, marital and literacy status), presence of other health problems in the last month and self-rated socio-economic status (SES). For self-rated SES, participants were asked to rate the wealth of their households in relation to other households in their village by choosing one of the following options: (1) very poor, (2) poor, (3) average, (4) wealthy or (5) very wealthy [5].

Quality of life data. VRQoL was measured using the WHO/PBD-VF20 tool [14]. This contains 20 questions sub-divided into three subscales: visual symptom (3 questions), general functioning (12 questions) and psychosocial (4 questions). Each question has a five-point response option: one indicates the highest and five the lowest score. The psychosocial questions assess the frequency of experiencing a specific vision-related problem and the general functioning questions measure the difficulty associated with overall performance. This tool was translated into Amharic by two independent translators. The two translations were compared and differences were discussed and resolved to develop a single, final version.

HRQoL was measured using the WHOQOL-BREF [15]. This contains 26 questions, subdivided into four domains: physical health, psychological, social relationships and environment in the past four weeks [15,19,20]. The first two questions assess general QoL and health. Each item is scored on a five-point scale. We used the Amharic version provided by the WHO, which has been previously validated and used in Ethiopia [21–23].

Clinical data. Presenting LogMAR (Logarithm of the Minimum Angle of Resolution) visual acuity at two metres was measured using "PeekAcuity" software on a Smartphone in a dark room in both cases and controls [24]. We assessed contrast sensitivity with a prototype smartphone based test that presents the individual with calibrated grey scale spots against a white background, which they have to identify by touching the screen (www.peekvision.org). For cases, ophthalmic examination was conducted using a 2.5x binocular magnifying loupe and a bright torch. Clinical signs such as trichiasis severity and corneal opacity were graded using the Detailed WHO FPC Grading System [25].

Surgical Intervention

Immediately after baseline data collection was completed, all cases received trichiasis surgical management. They were randomised to receive either the bilamellar or the posterior lamellar tarsal rotation, which were being compared in the clinical trial [16]. Both surgical procedures involve an incision through the scarred upper eyelid, parallel to and about 3mm above the lid margin, followed by outward rotation and suturing in the corrected position [26]. Six standardised trichiasis surgeons performed the surgery.

Follow-up Assessment

Follow-up was conducted approximately one year after enrolment (minimum 10 and maximum 14 months), during the same season as the baseline. For cases, a reminder was sent to attend the 12-month follow-up. Follow-up data were collected for the majority of cases at a health facility. For cases who could not come to the health facility, data were collected during a home visit. Follow-up data were collected on comparison participants at their homes. Participants were interviewed using the same QoL tools at baseline, and clinical data were collected using the same procedures by the same interviewers and a clinical grader.

Analysis

The sample size of 1000 cases and 200 comparison participants has 94% power to detect an effect size of about 0.27 (standardised mean difference (3/11)) with a Type I error of 5%. Data were double-entered into Access (Microsoft), cleaned in Epidata 3.1 and transferred to Stata 11 (StataCorp) for analysis. Analyses were restricted to participants with both baseline and follow-up data.

Quality of life data analyses. Items within each VRQoL sub-scale were summed to create a total sub-scale score which was then converted into a scaled value out of one hundred, using the formula: ([individual score—lowest possible score]/[highest possible score–lowest possible score]) x 100. Therefore, the person with the lowest possible VRQoL score would receive a scaled value of 0 and the person with the highest possible VRQoL score receives a scaled value of 100 [27]. Item scores were substituted by the mean of the subscale score in two cases with missing item scores in the visual symptom and psychosocial subscales separately.

The HRQoL data were analysed following the WHOQOL protocol [15,20]. Three negatively framed items were reversed into a positive frame so higher scores denote higher QoL. To generate domain scores, questions were grouped into their respective domains and their scores totalled. The mean score of all items included in the domain was calculated and then multiplied by four. These scores were then transformed to a 0 (lowest HRQoL) to 100 (highest HRQoL) scale [20]. Item scores were substituted by the mean of the domain score in cases with missing score in one item in the psychological domain and social domain, and in two items in the environment domain.

Mean change in VRQoL and HRQoL scores between baseline and follow-up was analysed using a random effect linear regression model separately for cases and comparison participants. This was repeated in stratified analysis by vision change at follow-up (better, same, worse) and analysis of variance was employed to test for significant difference in QoL score changes between those with better, same and worse vision. To test the null hypothesis that the difference in each QoL domain score between baseline and 12 month follow-up did not differ by case status, a difference-in-differences analysis was conducted using random effect linear regression with an interaction term included between visit (baseline and 12 month) and case status, adjusted for age, sex and self-rated SES [28]. The effect sizes for change between baseline and follow-up were estimated by dividing the mean score change for each QoL domain by the standard deviation of the baseline score separately for both cases and comparison participants. Effect sizes of <0.5, 0.5–0.79 and ≥ 0.8 were considered as small, moderate and large, respectively [29,30].

All comparisons of cases and comparison participants were adjusted for the matching variables (age and sex), and self-rated SES. Analyses of HRQoL analysis additionally adjusted for presence of other health problems during the previous four weeks, as these factors may confound the association between trachomatous trichiasis and HRQoL. Analysis was not adjusted for location as neighbourhood comparison participants were used. Logistic and linear regression methods adjusted for the matching variables were used for binary and continuous outcome analysis, respectively. P-values were obtained using likelihood ratio-tests.

Finally, we explored socio-economic and clinical predictors of change in VRQoL and HRQoL among cases between baseline and follow up using univariable and multivariable linear regression models. Tests for trend were undertaken in case of ordered categorical independent variables. Variables that were associated with the outcome on univariable analyses at a level of $p<0.05$ were included in the multivariable analysis and then those with $p<0.2$ were retained in the model. To adjust for multiple comparisons, we used the Benjamini and Hochberg method, assuming a false discovery rate (FDR) of 5%.

Clinical data analyses. To analyse vision and contrast sensitivity, the operated eye scores were used in unilateral cases; while the score in the better eye was used in comparison participants and cases with bilateral surgery. For visual acuities of counting fingers or less, LogMAR values were attributed as follows: counting fingers, 2.0; hand movements, 2.5; perception of light, 3.0; no perception of light, 3.5. The LogMAR visual acuity scores were then categorised based on the WHO classifications: Normal vision, >6/18; moderate visual impairment, <6/18 to ≥6/60; severe visual impairment, <6/60 to ≥3/60; and blind, <3/60. Contrast sensitivity scores were grouped into quartiles. The differences between baseline and follow-up scores were used to analyse longitudinal vision change. Participants were grouped into better vision (>0.1 LogMAR), same vision (-0.1 to 0.1 LogMAR) and worse vision (<-0.1 LogMAR) categories in relation to their baseline vision scores. Corneal opacity and trichiasis grading in the more affected eye was used in cases with bilateral surgery; while the operated eye grading was used in cases with unilateral surgery to test the association of these with QoL in trichiasis cases. Corneal opacity grading was categorised as either (i) no opacity/peripheral opacity or (ii) opacity involving the visual axis. Based on their baseline trichiasis severity, cases were categorised into Minor Trichiasis (<6 lashes or evidence of epilation in <1/3rd of the lashes) and Major Trichiasis (≥6 lashes or evidence of epilation in ≥1/3rd of the lashes). Recurrence in either of the operated eyes at 12 month was used to test its association with QoL domains.

Results

Demographic and Clinical Characteristics

At baseline 1000 trachomatous trichiasis cases and 200 comparison participants were recruited. At the 12-month follow-up, complete QoL data were collected from 980 (98%) cases and 198 (98%) comparison participants. Cases and comparison participants had a similar age distribution (mean 47.0 vs 45.7 years), but there were fewer females among the cases than among the comparison participants (76.4% vs 84.3%). This difference occurred by chance, as the randomly selected 200 trichiasis cases used to determine the matching characteristics had a higher proportion of females than the full group of 1000 trichiasis cases, Table 1. After adjusting analyses for age and gender, the trichiasis cases were significantly more likely to be illiterate, widowed or divorced, be from poorer households, and report other health problems in the past month than comparison participants, Table 1.

At baseline almost all comparison participants (97%) had normal vision (≥6/18) compared with about half (52%) of the cases (in the operated eye). Trichiasis cases also had significantly lower contrast sensitivity score than the comparison participants at baseline (P<0.0001), and poorer visual acuity and contrast sensitivity scores at 12-months (Table 1). In contrast, at 12 months follow-up there was strong evidence of an improvement in visual acuity (mean LogMAR change: 0.08; 95%CI: 0.05 to 0.10) and contrast sensitivity scores (mean contrast sensitivity score change: 2.41; 95%CI: 1.48 to 3.35) among trichiasis cases. Moreover, among comparison participants there was a small but significant reduction in visual acuity (mean LogMAR change: -0.04; 95%CI: -0.07 to -0.02) and no evidence of a change in contrast sensitivity scores (mean contrast sensitivity score change: -0.14; 95%CI: -0.40 to 0.13, p = 0.31).

Vision Related Quality Of Life

At baseline, trichiasis cases had substantially lower VRQoL scores than comparison participants in all four subscales (p<0.0001), Table 2. One year after trichiasis surgery the mean VRQoL score of cases had improved substantially in all subscales by 19.1 to 42.3 points (p<0.0001), with large effect sizes in the visual symptom (2.03), overall eyesight (1.57) and psychosocial (0.88) subscales and a moderate effect size in the general functioning (0.67) subscale.

Table 1. Demographic and Clinical characteristics of participants seen at baseline and 12-months.

Variables	Cases		Comparison Participants		p-value
	n / 980	(%)	n / 198	(%)	
Baseline					
Age, mean (SD)	47.0 years	(14.8)	45.7 years	(13.2)	0.55
Gender, female	749	(76.4)	167	(84.3)	0.03
Illiterate	867	(88.5)	168	(84.8)	0.008
Marital status					
Married	641	(65.4)	160	(80.8)	<0.0001‡
Widowed	194	(19.8)	27	(13.6)	
Divorced	114	(11.6)	9	(4.6)	
Single	31	(3.2)	2	(1.0)	
Job					
Farmer	823	(83.9)	166	(83.8)	0.03‡
Employed/self employed	51	(5.2)	17	(8.6)	
Daily labourer	45	(4.6)	4	(2.0)	
No job	61	(6.2)	11	(5.6)	
Self-rated wealth*					
Very wealthy/ Wealthy	32	(3.3)	30	(15.1)	<0.0001†
Middle	442	(45.1)	133	(67.2)	
Very Poor / Poor	506	(51.6)	35	(17.7)	
Health problem					
No	618	(63.1)	172	(86.9)	<0.0001
Yes	362	(36.9)	26	(13.1)	
Visual Acuity [a] –best eye ¶					
Normal (≥6/18)	512	(52.2)	192	(97.0)	<0.0001†
Moderate visual impairment (<6/18 to ≥6/60)	380	(38.8)	4	(2.0)	
Severe visual impairment (<6/60 to ≥3/60)	31	(3.2)	1	(0.5)	
Blind (<3/60)	57	(5.8)	1	(0.5)	
Contrast sensitivity–best eye ¶					
1 (Best)	258	(26.3)	141	(71.2)	<0.0001†
2	396	(40.4)	49	(24.7)	
3	87	(8.9)	1	(0.5)	
4 (Worst)	239	(24.4)	7	(3.5)	
12-months follow-up					
Health problem					
No	553	(56.4)	161	(81.3)	<0.0001
Yes	427	(43.6)	37	(18.7)	
Visual Acuity [b] –best eye ¶					
Normal (≥6/18)	584	(59.7)	187	(94.4)	<0.0001†
Moderate visual impairment (<6/18 to ≥6/60)	336	(34.4)	8	(4.0)	
Severe visual impairment (<6/60 to ≥3/60)	18	(1.8)	1	(0.5)	
Blind (<3/60)	40	(4.1)	2	(1.0)	
Contrast sensitivity [b] –best eye ¶					
1 (Best)	*338*	(34.6)	145	(73.2)	<0.0001†
2	182	(18.6)	23	(11.6)	
3	244	(24.9)	13	(6.6)	

(*Continued*)

Table 1. (*Continued*)

Variables	Cases		Comparison Participants		p-value
	n / 980	(%)	n / 198	(%)	
4 (Worst)	214	(21.9)	17	(8.6)	

p-values are calculated using logistic regression and adjusted for age and gender, with the exception for age, which was calculated using linear regression.

‡ Combined p-value from likelihood ratio-test.

† P-value for trend.

* We merged "very wealthy" and "wealthy"; and "very poor" and "poor" because of small numbers at these extremes of the distribution, to create three levels of socio-economic status measure to facilitate data modelling.

¶ Best eye vision and contrast sensitivity are presented for comparison participants and for cases with bilateral trichiasis surgery; while the operated eye visual acuity and contrast sensitivity are presented for cases with unilateral trichiasis surgery.

[a] No data for 1 person.

[b] Not possible to take visual acuity and contrast sensitivity in two participants.

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In contrast, there was no evidence of a difference between baseline and follow-up VRQoL scores in all subscales scores in the comparison participants and the effect sizes were very small and negative (-0.08 to -0.03), Table 2. The difference-in-differences analysis showed strong evidence that the improvement in mean VRQoL score from baseline to 12-month follow-up was greater for cases than comparison participants in all sub-scales (difference-in-differences score: 18.9 to 42.9 points, p<0.0001), Table 2.

Similar results were seen when analyses were stratified by level of visual acuity change at 12-months, Table 3. VRQoL score among trichiasis cases improved significantly in all subscales, independent of visual changes over 12-months, while the VRQoL scores of comparison participants remained the same (Table 3). The largest VRQoL change was observed in trichiasis cases with visual improvement, Table 3. In addition, among trichiasis cases, VRQoL improved in all subscales independent of postoperative recurrent trichiasis, although the improvements in the overall eyesight was significantly less in those with recurrent trichiasis than their counterparts. (30.8 vs 35.7; p = 0.04).

Health related quality of life. At baseline, trichiasis cases had substantially lower HRQoL scores than comparison participants in all four domains (p<0.0001), Table 2. One year after trichiasis surgery, the HRQoL scores of trichiasis cases had significantly improved in all four domains (mean improvement: 4.7 to 17.2 points; p<0.0001). In contrast, the HRQoL scores for comparison participants had reduced at 12-months in all four domains. The effect sizes were large for trichiasis cases in the physical health (1.11) psychological (0.87) and environment (0.95) domains and small for the social domain (0.21). In contrast, the effect sizes for comparison participants were negative. The difference-in-differences analysis showed that the change in mean HRQoL score was significantly greater for cases than comparison participants for all four domains (9.58 to 20.8 points, p<0.0001) Table 2.

Results stratified by visual acuity change at 12-months showed that there was significant improvement in HRQoL scores of trichiasis cases in all domains, independent of visual change over 12-months Table 3, but no improvement among the comparison participants Table 3.

Determinants of quality of life change in trichiasis cases. The relationship between socio-demographic and clinical factors and change in VRQoL and HRQoL among trichiasis cases 12 months after surgery are presented in Table 4. In multivariable analysis, greater improvements in all VRQoL subscales were independently associated with longer trichiasis

Table 2. Comparison of mean VRQoL and HRQoL domain score changes and effect size between baseline and 12-months follow-up in trichiasis cases and comparison participants.

Variable	Baseline		Follow-up		Baseline v 12-month				
	Mean	*(95% CI)*	*Mean*	*(95% CI)*	*Difference*	*(95% CI)*	*P-value* [b]	Effect size	*(95% CI)*
VRQoL									
Overall eyesight									
Cases	46.3	(44.9–47.7)	81.3	(79.8–82.8)	35.0	(33.3–36.6)	<0.0001	1.57	(1.50–1.65)
Comparison	95.4	(93.3–97.6)	94.8	(92.6–97.1)	-0.63	(-2.40–1.14)	0.48	-0.04	(-0.16–0.07)
	P<0.0001[a]		P<0.0001[a]		35.6 [d]	(31.8–39.4)	<0.0001		
Visual symptom									
Cases	46.2	(44.9–47.5)	88.5	(87.5–89.6)	42.3	(40.8–43.8)	<0.0001	2.03	(1.96–2.10)
Comparison	97.6	(96.2–98.9)	97.0	(95.7–98.2)	-0.59	(-1.80–0.62)	0.34	-0.06	(-0.18–0.06)
	P<0.0001[a]		P<0.0001[a]		42.9 [d]	(39.6–46.2)	<0.0001		
General functioning									
Cases	74.2	(72.9–75.5)	93.3	(92.4–94.3)	19.1	(17.9–20.3)	<0.0001	0.67	(0.61–0.74)
Comparison	97.7	(96.4–99.1)	97.9	(96.8–99.1)	0.21	(-0.87–1.29)	0.70	-0.08	(-0.21–0.05)
	P<0.0001[a]		P<0.0001[a]		18.9 [d]	(16.2–21.6)	<0.0001		
Psychosocial									
Cases	69.6	(67.9–71.2)	92.9	(91.9–94.0)	23.4	(21.7–25.0)	<0.0001	0.88	(0.81–0.94)
Comparison	98.1	(96.8–99.5)	97.8	(96.4–99.3)	-0.25	(-1.33–0.82)	0.64	-0.03	(-0.14–0.09)
	P<0.0001[a]		P<0.0001[a]		23.6 [d]	(19.9–27.3)	<0.0001		
HRQoL									
Physical health									
Cases	47.8	(46.8–48.7)	64.9	(63.6–66.3)	17.1	(16.0–18.3)	<0.0001	1.11	(1.03–1.18)
Comparison	80.1	(78.3–81.9)	76.5	(74.0–78.9)	-3.61	-5.48 –-1.74)	0.0002	-0.27	(-0.41–-0.13)
	P<0.0001[a]		P<0.0001[a]		20.8 [d]	(18.1–23.4)	<0.0001		
Psychological									
Cases	58.8	(58.0–59.6)	69.6	(68.6–70.6)	10.8	(9.78–11.8)	<0.0001	0.87	(0.79–0.95)
Comparison	80.7	(79.2–82.2)	79.5	(77.9–81.1)	-1.18	(-2.72–0.37)	0.13	-0.11	(-0.25–0.03)
	P<0.0001[a]		P<0.0001[a]		12.0 [d]	(9.58–14.4)	<0.0001		
Social									
Cases	52.0	(50.6–53.4)	56.7	(55.3–58.1)	4.69	(3.29–6.10)	<0.0001	0.21	(0.14–0.27)
Comparison	72.0	(69.6–74.4)	67.2	(64.6–69.7)	-4.88	(-7.20 –-2.57)	<0.0001	-0.29	(-0.42–-0.15)
	P<0.0001[a]		P<0.0001[a]		9.58 [d]	(6.28–12.9)	<0.0001		
Environment									
Cases	38.8	(38.2–39.5)	49.2	(48.3–50.1)	10.3	(9.43–11.2)	<0.0001	0.95	(0.87–1.03)
Comparison	62.1	(60.6–63.7)	55.6	(53.8–57.4)	-6.55	(-8.45 –-4.64)	<0.0001	-0.58	(-0.75–-0.41)
	P<0.0001[a]		P<0.0001[a]		16.8 [d]	(14.7–18.9)	<0.0001		

VRQoL = Vision Related Quality of Life

HRQoL = Health Related Quality of Life

[a] p-values were calculated by linear regression and adjusted for age, gender and self-rated wealth (and other health problem in past month for HRQoL domains) comparing cases and comparison participants QoL scores at baseline and follow-up.

[b] p-values from random effect linear regression adjusted for age, gender and self-rated wealth (and other health problem in past month for HRQoL domains) comparing QoL change between baseline and follow-up separately for case and comparison participants

[d] Difference-in-differences analysis conducted using random effect linear regression with interaction term included between visit (baseline and 12 month) and case/ comparison status and adjusted for age, gender and self-rated wealth (and other health problem in past month for HRQoL domains)

Using the Benjamini and Hochberg method, only tests with a p-value below 0.0003 have a False Discovery Rate of <5%.

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Table 3. Comparison of mean change in VRQoL and HRQoL domain scores between baseline and 12-months in trichiasis cases and comparison participants, stratified by the change in vision between baseline and 12-months (Better, Same and Worse).

Variable	Vision Better			Vision Same			Vision Worse			ANOVA
	Mean change	*(95% CI)*	*P-value* [a]	*Mean change*	*(95% CI)*	*P-value* [a]	*Mean change*	*(95% CI)*	*P-value* [a]	P-value [c]
VRQoL										
Overall eyesight										
Cases	40.1	(37.5–42.7)	<0.0001	33.5	(30.8–36.1)	<0.0001	28.4	(24.9–31.9)	<0.0001	<0.0001
Comparison participants	-2.00	(-8.90–4.89)	0.57	-0.70	(-2.48–1.08)	0.44	0.0	(-3.73–3.73)	1.000	0.83
Difference-in-Differences [b]	42.1	(31.8–52.4)	<0.0001	34.2	(29.1–39.2)	<0.0001	28.4	(21.7–35.0)	<0.0001	
Visual symptom										
Cases	44.7	(42.4–47.1)	<0.0001	41.9	(39.7–44.2)	<0.0001	38.4	(35.2–41.6)	<0.0001	0.0056
Comparison participants	0.33	(-5.20–5.87)	0.91	-0.62	(-1.68–0.43)	0.25	-0.88	(-3.36–1.59)	0.48	0.99
Difference-in-Differences [b]	44.4	(35.1–53.6)	<0.0001	45.6	(38.3–46.9)	<0.0001	39.3	(33.3–45.3)	<0.0001	
General functioning										
Cases	22.5	(20.5–24.4)	<0.0001	17.1	(15.3–18.9)	<0.0001	16.4	(13.9–19.0)	<0.0001	0.033
Comparison participants	1.75	(-5.39–8.89)	0.63	-0.43	(-1.15–0.30)	0.25	0.66	-0.74–2.07)	0.36	0.59
Difference-in-Differences [b]	20.7	(12.8–28.7)	<0.0001	17.5	(14.2–20.8)	<0.0001	15.8	(11.2–20.4)	<0.0001	
Psychosocial										
Cases	25.6	(22.9–28.3)	<0.0001	22.3	(19.7–24.8)	<0.0001	21.1	(17.6–24.6)	<0.0001	0.12
Comparison participants	-1.00	(-6.99–4.99)	0.74	-0.17	(-0.77–0.42)	0.56	-0.09	(-2.22–2.03)	0.93	0.94
Difference-in-Differences [b]	26.6	(16.0–37.1)	<0.0001	22.4	(17.6–27.3)	<0.0001	21.2	(14.8–27.5)	<0.0001	
HRQoL										
Physical health										
Cases	17.1	(15.3–18.9)	<0.0001	18.1	(16.4–19.8)	<0.0001	15.8	(13.3–18.3)	<0.0001	0.62
Comparison participants	0.14	(-5.58–5.86)	0.96	-3.14	(-5.22–1.05)	0.0032	-5.79	(-9.67–-1.90)	0.0035	0.016
Difference-in-Differences [b]	17.0	(9.67–24.2)	<0.0001	21.2	(17.8–24.7)	<0.0001	21.6	(16.6–26.5)	<0.0001	
Psychological										
Cases	10.9	(9.27–12.5)	<0.0001	11.6	(9.93–13.3)	<0.0001	9.36	(7.17–11.5)	<0.0001	0.80
Comparison participants	1.00	(-4.08–6.08)	0.70	-1.13	(-2.95–0.69)	0.22	-2.08	(-5.11–0.94)	0.18	0.06
Difference-in-Differences [e]	9.90	(3.39–16.4)	0.0029	12.8	(9.42–16.1)	<0.0001	11.4	(7.16–15.7)	<0.0001	
Social										
Cases	5.23	(3.02–7.44)	<0.0001	4.76	(2.53–7.00)	<0.0001	3.91	(0.76–7.07)	0.015	0.80
Comparison participants	0.33	(-6.30–7.00)	0.92	-5.84	(-8.92–-2.76)	0.0002	-5.30	(-9.40–-1.23)	0.011	0.06
Difference-in-Differences [b]	4.90	(-3.95–13.7)	0.28	10.6	(6.11–15.1)	<0.0001	9.22	(3.09–15.3)	0.0032	
Environment										
Cases	9.17	(7.82–10.5)	<0.0001	11.8	(10.4–13.2)	<0.0001	9.90	(8.03–11.8)	<0.0001	0.12
Comparison participants	-8.87	(-15.4–-2.35)	0.0077	-6.25	(-8.80–-3.70)	<0.0001	-6.15	(-9.27–-3.04)	0.0001	0.71
Difference-in-Differences [b]	18.0	(12.5–23.6)	<0.0001	18.0	(15.0–21.0)	<0.0001	16.0	(12.3–19.8)	<0.0001	

To analyse vision change, best eye vision and contrast sensitivity were used for comparison participants and for cases with bilateral trichiasis surgery; while the operated eye visual acuity and contrast sensitivity were used for cases with unilateral trichiasis surgery. "Mean" refers to the mean difference between baseline and 12month follow-up QoL scores. VRQoL = Vision Related Quality of Life. HRQoL = Health Related Quality of Life.

[a] p-values from random effect linear regression adjusted for age, gender and self-rated wealth (and other health problem in past month for HRQoL domains) comparing QoL change between baseline and follow-up within each vision change group, separately for case and comparison participants

[b] Difference in differences analysis conducted within each vision change group using random effect linear regression with interaction term included between visit (baseline and 12 month) and case/ comparison status and adjusted for age, gender and self-rated wealth (and other health problem in past month for HRQoL domains)

[c] p-value from ANOVA (controlling for age, gender, self-rated wealth for the VRQoL subscales; and controlling for age, gender, self-rated wealth and other health problem in the past month for the HRQoL domains) to test for a difference of mean change for each domain, between better, same and worse vision groups.

Using the Benjamini and Hochberg method, only tests with a p-value below 0.034have a False Discovery Rate of <5%.

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Table 4. Determinants of VRQoL and HRQoL change between baseline and 12-months after trichiasis surgery.

Variable	VRQoL						HRQoL							
	Visual symptom		General functioning		Psychosocial		Physical		Psychological		Social		Environment	
	Mean change	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*
Age Groups (years)														
≤ 29	43.2	(39.2–47.1)	12.0	(8.1–15.9)	25.1	(20.1–30.0)	21.5	(18.6–24.4)	14.6	(11.9–17.2)	5.1	(0.67–9.6)	14.4	(11.7–17.2)
30–39	44.9	(42.1–47.8)	11.7	(9.1–14.3)	23.9	(20.4–27.4)	22.2	(19.6–24.8)	14.7	(12.4–17.1)	8.5	(5.5–11.4)	13.2	(11.2–15.1)
40–49	43.3	(40.4–46.3)	14.6	(12.0–17.2)	25.7	(22.3–29.1)	17.1	(14.7–19.5)	11.4	(9.5–13.4)	3.4	(0.55–6.3)	10.2	(8.4–12.0)
50–59	43.7	(40.5–46.9)	14.9	(11.8–18.0)	25.5	(22.0–29.0)	14.8	(12.3–17.2)	9.8	(7.6–12.1)	5.9	(2.8–9.0)	8.3	(6.5–10.1)
60–69	36.3	(32.1–40.5)	13.9	(10.0–17.7)	17.7	(13.4–21.9)	13.2	(10.4–16.0)	7.4	(4.6–10.3)	4.2	(0.40–7.9)	8.4	(6.2–10.5)
≥ 70	40.2	(34.6–45.8)	21.4	(16.5–26.2)	19.0	(13.2–24.8)	13.8	(10.4–17.1)	4.3	(0.72–7.9)	-2.5	(-6.6–1.6)	7.5	(4.9–10.0)
p-value [a] †	0.008		0.003		0.01		<0.0001		<0.0001		0.01		<0.0001	
p-value [b] †	0.0001		-		0.0001		<0.0001		<0.0001		0.03		<0.0001	
Gender														
Male	40.7	(37.8–43.5)	11.7	(9.2–14.3)	19.8	(16.6–23.0)	18.7	(16.5–21.0)	14.8	(12.8–16.8)	4.4	(1.1–7.6)	12.7	(11.0–14.4)
Female	42.8	(41.1–44.5)	15.1	(13.5–16.7)	24.5	(22.6–26.4)	16.7	(15.4–18.0)	9.6	(8.4–10.8)	4.8	(3.2–6.3)	9.6	(8.6–10.6)
p-value [a]	0.22		0.04		0.02		0.13		<0.0001		0.80		0.003	
p-value [b]	-		0.16		-		-		<0.0001		-		<0.0001	
Trichiasis severity														
Minor trichiasis (<6 lashes)	40.9	(39.0–42.9)	13.0	(11.2–14.9)	21.7	(19.5–23.9)	17.6	(16.1–19.2)	11.9	(10.5–13.2)	4.2	(2.3–6.1)	10.5	(9.3–11.7)
Major trichiasis (≥6 lashes)	43.8	(41.7–46.0)	15.8	(13.8–17.7)	25.2	(22.8–27.6)	16.6	(15.0–18.3)	9.6	(8.1–11.1)	5.3	(3.2–7.3)	10.0	(8.8–11.3)
p-value [a]	0.05		0.04		0.03		0.39		0.03		0.46		0.58	
p-value [b]	-		-		-		-		-		-		-	
Trichiasis duration in years														
<2	32.4	(29.1–35.8)	8.2	(5.1–11.3)	14.4	(10.8–18.8)	16.6	(14.1–19.1)	9.0	(6.4–11.6)	5.5	(2.0–9.0)	8.9	(6.6–11.2)
2–4	43.5	(41.0–46.1)	14.9	(12.5–17.2)	24.9	(21.9–27.9)	17.3	(15.2–19.4)	11.2	(9.5–13.0)	3.7	(1.0–6.5)	11.7	(10.2–13.2)
5–9	44.9	(42.1–47.7)	15.4	(12.7–18.0)	25.1	(21.7–27.5)	17.6	(15.3–19.9)	12.6	(10.5–14.9)	6.3	(3.3–9.3)	9.9	(8.1–11.8)
10–15	43.4	(39.3–47.6)	13.6	(9.8–17.3)	25.8	(21.3–30.2)	15.8	(12.8–18.9)	9.0	(6.3–11.7)	3.0	(0.02–6.0)	9.3	(7.1–11.4)
≥15	45.9	(42.0–49.9)	19.3	(15.3–22.8)	25.6	(21.5–29.8)	17.9	(15.0–20.8)	10.7	(7.8–13.5)	4.5	(1.1–8.0)	10.6	(8.4–12.8)

(*Continued*)

Table 4. (*Continued*)

Variable	VRQoL						HRQoL							
	Visual symptom		General functioning		Psychosocial		Physical		Psychological		Social		Environment	
	Mean change	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*
p-value [a †]	<0.0001		0.0002		0.0007		0.79		0.76		0.76		0.97	
p-value [b †]	<0.0001		0.01		0.0001		-		-		-		-	
Baseline corneal opacity														
No/ peripheral opacity	40.7	(39.0–42.5)	11.7	(10.2–13.3)	21.4	(19.5–23.3)	16.9	(15.6–18.3)	11.4	(10.1–12.6)	6.0	(4.3–7.8)	10.5	(9.4–11.5)
Opacity involving the visual axis	45.2	(42.6–47.8)	19.1	(16.6–21.6)	27.0	(24.1–30.0)	17.5	(15.5–19.5)	9.7	(7.9–11.6)	2.2	(-0.09–4.4)	10.0	(8.6–11.4)
p-value [a]	0.004		<0.0001		0.001		0.64		0.14		0.01		0.60	
p-value [b]	0.02		0.001		0.0004		-		-		0.04		-	
Baseline presenting VA														
Normal (≥6/18)	42.8	(41.0–44.7)	12.0	(10.4–13.5)	22.2	(20.1–24.3)	18.5	(17.0–20.0)	12.7	(11.4–14.0)	5.8	(3.8–7.8)	12.3	(11.1–13.4)
MVI (<6/18 to ≥6/60)	41.7	(39.1–44.3)	15.6	(13.2–18.0)	24.0	(21.3–26.7)	16.0	(14.2–17.9)	9.0	(7.2–10.7)	3.6	(1.4–5.9)	8.0	(6.6–9.5)
SVI (<6/60 to ≥3/60)	44.3	(35.9–52.8)	23.2	(14.2–32.3)	26.8	(16.6–37.0)	11.4	(4.58–18.2)	5.8	(-0.28–11.8)	-3.8	(-9.7–2.2)	10.2	(5.5–14.9)
Blind (<3/60)	40.9	(33.7–48.1)	22.3	(15.1–29.5)	28.2	(19.1–37.3)	15.6	(10.7–20.4)	8.6	(3.5–13.7)	6.7	(1.1–12.2)	7.5	(4.5–10.5)
p-value [a †]	0.55		<0.0001		0.05		0.02		0.0008		0.28		0.0001	
p-value [b †]	-		-		-		-		-		-		-	
Baseline contrast sensitivity														
4 (Best score)	41.1	(38.5–43.7)	9.4	(7.1–11.7)	19.6	(16.6–22.5)	20.2	(18.1–22.2)	14.4	(12.5–16.3)	7.7	(5.0–10.3)	14.3	(12.5–16.1)
3	44.1	(41.8–46.4)	14.4	(12.4–16.4)	25.5	(22.9–28.0)	16.9	(15.2–18.7)	10.3	(8.7–11.8)	3.1	(0.9–5.4)	9.3	(8.0–10.6)
2	41.2	(36.4–45.9)	13.8	(9.4–18.2)	23.3	(17.9–28.7)	16.3	(12.2–20.3)	10.2	(6.8–13.5)	2.5	(-2.7–7.7)	9.2	(6.5–11.9)
1 (Worst score)	41.1	(37.9–44.3)	19.6	(16.4–22.8)	23.9	(20.4–27.5)	14.5	(12.2–16.9)	8.0	(5.7–10.4)	4.8	(2.1–7.6)	8.0	(6.3–9.7)
p-value [a †]	0.65		<0.0001		0.16		0.0007		0.0001		0.25		<0.0001	
p-value [b †]	-		<0.0001		-		-		0.02		-		-	
Surgery														
Unilateral	40.3	(38.6–42.0)	13.2	(11.6–14.8)	22.0	(20.2–23.9)	17.0	(15.7–18.3)	10.9	(9.7–12.1)	4.6	(3.0–6.2)	9.6	(8.6–10.6)
Bilateral	48.1	(45.4–50.7)	17.5	(14.9–20.2)	27.2	(18.9–28.1)	17.6	(15.3–19.9)	10.5	(8.4–12.6)	5.0	(2.1–7.9)	12.2	(10.5–14.0)
p-value [a †]	<0.0001		0.006		0.0070		0.65		0.73		0.81		0.01	
p-value [b †]	0.0007		0.01		-		-		-		-		0.007	

(*Continued*)

Table 4. (*Continued*)

Variable	VRQoL						HRQoL							
	Visual symptom		General functioning		Psychosocial		Physical		Psychological		Social		Environment	
	Mean change	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*	*Mean change*	*(95% CI)*
Surgical procedure														
PLTR	43.1	(41.0–45.1)	15.3	(13.4–17.2)	24.1	(21.7–26.4)	16.9	(15.3–18.4)	11.2	(9.8–12.7)	4.9	(2.9–6.9)	10.0	(8.8–11.3)
BLTR	41.5	(39.5–43.6)	13.3	(11.4–15.2)	22.7	(20.3–25.0)	17.4	(15.8–19.0)	10.4	(8.8–11.9)	4.5	(2.5–6.5)	10.6	(9.4–11.7)
p-value [a †]	0.31		0.15		0.40		0.63		0.40		0.77		0.56	
p-value [b †]	-		-		-		-		-		-		-	
Vision change at 12 month														
Better	44.7	(42.4–47.1)	16.8	(14.6–19.1)	25.6	(22.9–28.2)	17.1	(15.3–18.9)	10.9	(9.3–12.5)	5.2	(3.0–7.4)	9.2	(7.8–10.5)
Same	41.9	(39.7–44.2)	12.9	(10.8–14.9)	22.3	(19.7–24.8)	18.1	(16.4–19.8)	11.6	(9.9–13.3)	4.8	(2.5–7.0)	11.8	(10.4–13.2)
Worse	38.4	(35.2–41.6)	12.0	(9.2–14.9)	21.1	(17.6–24.6)	15.8	(13.3–18.3)	9.4	(7.2–11.5)	3.9	(0.8–7.1)	9.9	(8.0–11.8)
p-value [a †]	0.001		0.004		0.03		0.53		0.39		0.50		0.28	
p-value [b †]	0.001		0.01		0.05		-		-		-		-	

[a] P-values from univariable analysis.

[b] P-values from multivariable analysis adjusted. All p-values are calculated using linear regression. For ordinal exposures with three or more categories the †p-values are calculated for trend. Using the Benjamini and Hochberg method, only tests with a p-value below 0.020 have a False Discovery Rate of <5%. Variables with univariable p<0.05 were included in the multivariable model, then those with p>0.2 were excluded (dashed line) from the final model after likelihood ratio- test. VRQoL = Vision related Quality of Life.

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duration, central corneal opacity at baseline and improved vision at 12-months. In addition, cases with bilateral trichiasis surgery had greater gains in visual symptom and general functioning subscales scores than those with monocular surgery. Cases with poor contrast sensitivity scores at baseline had significantly greater improvement in general functioning scores than their counterparts. Younger individuals had greater improvement in the visual symptom and psychosocial domain scores; while older individuals had greater improvement in the general functioning subscale score.

For the HRQoL, young age was independently associated with larger improvements in all domains; while males had greater improvement in psychological and environment domain scores than females (Table 4). Cases with better baseline contrast sensitivity; no/peripheral baseline corneal opacity and bilateral surgery had larger psychological, social and environment domain scores improvements than their counterparts' respectively. The type of surgical procedure (PLTR or BLTR) was not associated with differences in either change in vision or health related QoL (Table 4). Hence, all QoL change results are presented combining all operated Trachomatous Trichiasis cases.

Discussion

Trichiasis surgery is primarily performed to reduce the risk of sight loss [10]. Between 2004 and 2013, about 1.2 million operations were performed worldwide, and currently around

200,000 trichiasis cases are treated annually [31]. However, despite this activity, there is very little longitudinal information on the impact of trichiasis surgery on quality of life. Cross-sectional studies, including the baseline report of this study, have shown that trichiasis is associated with a reduced quality of life and causes marked disability [6,7,13]. In this study we measured the vision and health related QoL of trichiasis patients before and one year after trichiasis surgery using standard WHO assessment tools. We also compared these outcomes with the QoL scores of individuals who have never had trichiasis, matched by age, gender and location to the cases. We found strong evidence that trichiasis surgery substantially improves both VRQoL and HRQoL 12-months after treatment, even when there is no improvement in vision; while the scores for the comparison participants were largely unchanged.

Vision Related Quality of Life

For VRQoL, the largest improvement was seen in the visual symptom subscale indicating the major effect that surgery has on relieving pain and discomfort from trichiasis. Trichiasis surgery is also shown to significantly improve visual acuity and contrast sensitivity, which might be related to elimination of the photophobia and tears and restoration of the corneal epithelium as result of the removal of the trichiatic lashes [8,11]. Larger gains in VRQoL were seen in those with improved vision. However, substantial improvement in VRQoL also occurred in patients without visual acuity improvement or even in those with deteriorating vision. This strongly supports the view that trichiasis surgery should be performed not only to save vision but also to treat other debilitating symptoms and improve the VRQoL of affected individuals. In contrast, the comparison participants had no improvement in visual acuity, contrast sensitivity or VRQoL 12-months after enrolment.

There has been no previous longitudinal study quantifying the effect of trichiasis surgery on VRQoL. However, our findings are consistent with a retrospective qualitative study of 13 women with trichiasis in Niger, in which most participants reported that trichiasis surgery markedly improved their quality of life in association with a complete disappearance of the painful physical symptoms [6]. Interestingly, despite a fundamental difference between cataract and trichiasis in the amount of visual loss, the effect size for the improvement in overall eyesight between our study and a study of the impact of cataract surgery in Kenya was comparable (1.6 vs 1.5) and there were large effect sizes (>0.80) in the psychosocial subscales in both studies [30].

Health Related Quality of Life

Among trichiasis cases, there was marked improvement in HRQoL one year after trichiasis surgery, independent of change in vision. The largest improvement was seen in the physical health domain indicating that trichiasis surgery considerably improves work capacity and ability to function without pain. Similar findings have been reported in the Niger qualitative study [6]. In contrast, there was either reduction or no change in the HRQoL of comparison participants one year after enrolment.

The results of our study were consistent with the only longitudinal study on HRQoL and trichiasis, conducted in India, which assessed HRQoL in patients before and one month after trichiasis surgery for trachomatous entropion (n = 41) and 15 days after epilation for minor trichiasis cases (n = 19). In the Indian study, HRQoL significantly improved after treatment of patients with normal and poor vision in the physical health, psychological and environment domains, while there was no significant improvement in the social domain. Consistent with our study, the greatest and least improvements were seen in the physical health (mean 21.3 to 23.1 points) and social domains (2.0 to 3.3 points), respectively. The social domain is a composite of social support and personal relationships, which may be less altered by trichiasis surgery.

The QoL improvement in our study was larger in the three HRQoL domains except the physical domain, than reported in the Indian study. These two studies have the following differences that might explain the differences in HRQoL gains. Firstly, most of the cases (67%) in the Indian study had entropion without trichiasis while all had trachomatous trichiasis in our study. Secondly, 19 cases with minor trichiasis received epilation (rather than surgery) while everyone in our study underwent trichiasis surgery. Thirdly, there was less than one month of follow-up in the Indian study during which the surgical wound healing process might influence QoL results [13].

Predictors of Change in Quality of Life of Trichiasis Cases

Longer trichiasis duration and central corneal opacity at baseline predict larger VRQoL gains in all subscales. This suggests that cases with severe disease probably benefit more in terms of improved VRQoL following trichiasis surgery. The results also suggest that bilateral cases benefit more from bilateral surgery to restore their functioning. Older trichiasis cases had greater improvement in the general functioning subscale than younger cases, while younger cases showed greater improvement in the psychosocial scores. Older individuals had more difficulty in general functioning in relation to distance and near vision difficulties at baseline, hence should benefit more from trichiasis surgery in improving their vision and thereby participation in day to day activities. Younger cases may be more likely to be embarrassed, worry about losing eyesight and hesitate to participate in social activities due to their trichiasis than older cases, which may be the reason for younger trichiasis cases to having greater improvement in the psychosocial subscale than older people one year after trichiasis surgery.

Strengths and Limitations

This is the first large longitudinal study to measure VRQoL and HRQoL change after trichiasis surgery using validated WHO tools. The same interviewers collected data at both baseline and follow-up to ensure questionnaires were administered in a standard way at baseline and follow-up. The study used comparison participants. Absence of significant improvement in QoL among the comparison participants compared to the cases lends weight to the view that the positive QoL change observed is attributable to trichiasis surgery. The study has a number of limitations. The interviewers were not masked in the trichiasis status of the participants and we cannot rule out the possibility of response bias with cases providing a positive answer to satisfy the interviewers regardless of real change or improvement. To limit these, participants were asked to provide honest answers and reassured that their answers would not affect their treatment in any way. In addition, knowledge of trichiasis status by the interviewers might possibly introduced bias in the outcome assessment. Although the improved QoL probably is largely related to vision improvement, less pain and irritation after the surgery, it is difficult to rule out the possibility that the extent of positive change observed among cases might have been related to the effect of just receiving a health intervention rather than solely attributed to the effect of trichiasis surgery. This possibly would explain the 28.4 score improvement in the overall eyesight subscale in those with vision deterioration one year after trichiasis surgery.

Conclusions

Overall this study demonstrated that trichiasis surgery substantially improves both vision and health related QoL regardless of the visual acuity improvement, suggesting that the effect of trichiasis surgery goes beyond preventing the risk of blindness and improves the overall wellbeing and health perception of affected individuals. Unprecedented effort is needed to scale-up trichiasis surgical programmes and provide prompt surgical intervention to improve overall well-being of affected individuals.

Supporting Information

S1 Checklist. STROBE checklist.
(DOCX)

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Author Contributions

Conceived and designed the experiments: EH PME HK SP HAW MJB. Performed the experiments: EH TW SA ZT MZ AM ZZ MJB. Analyzed the data: EH HAW MJB. Wrote the paper: EH TW SA ZT MZ AM ZZ KC PME HK RLB DCWM SNR SP HAW MJB.

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9. Impact of Trichiasis Surgery on Daily Living: A Longitudinal Study in Ethiopia

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Impact of Trichiasis Surgery on Daily Living: a longitudinal study in Ethiopia

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Abstract

Background

Trachomatous Trichiasis (TT) may lead to disability, impeding engagement with productive activities, resulting in loss of income, even prior to the development of visual impairment. This longitudinal comparative study was conducted to determine if trichiasis surgery improves participation in productive and leisure activities, and ability to perform activities without difficulty or assistance.

Methods/Principal Findings

We recruited 1000 adult participants with trichiasis (cases) and 200 comparison participants, matched to every fifth trichiasis case on age (+/- two years), sex and location. The 'Stylised Activity List' tool developed for the World Bank Living Standard Measurement Survey was adapted to collect data on activity in the last week (participation in activity, difficulty with activity, requirement of assistance for activity), at baseline and 12 months later. All trichiasis cases received free standard trichiasis surgery at baseline. A two-sample test of proportion was employed for differences, and random effect logistic regression was used to compare cases and comparison participants. At 12-months follow-up, data was collected from 980 (98%) trichiasis cases and 198 (99%) comparison participants. There was strong evidence that trichiasis surgery substantially improves the ability of trichiasis cases to perform all the productive and leisure activities investigated without difficulty, with large increases in processing agricultural products from 21.1% to 87.0% ($p<0.0001$), farming from 19.1% to 82.4% ($p<0.0001$) and fetching wood from 25.3% to 86.0% ($p<0.0001$). Similarly, there was a significant increase in the proportion of cases who could perform activities without assistance with the largest increases observed in animal rearing 54.2% to 92.0% ($p<0.0001$) and farming 73.2% to 96.4% ($p<0.0001$). In contrast, there was no change in the proportion of comparison participants performing activities without difficulty or assistance. The change in most of the activities in cases was independent of visual acuity improvement at 12 months. One year after trichiasis surgery the proportion of cases reporting ocular pain reduced from 98.9% to 33.7% ($p<0.0001$).

Conclusions/Significance

Corrective eyelid surgery for TT improves functional capabilities of affected individuals regardless of vision gains. These data lend strong support to the view that TT surgery improves function and contributes to improved household income and wealth.

Author Summary

In trachoma endemic settings, employment opportunities are often limited and household income is mainly generated through engagement of family members in agricultural activities. Trachomatous Trichiasis (TT) limits engagement with productive activities and may result in loss of income. We have previously reported that TT significantly reduces an individual's participation in productive and leisure activities, and their ability to perform activity without difficulty and assistance. However, data on the long-term effect of TT surgery on engagement in and execution of activities are limited. We measured the long-term impact of TT surgery on productive and leisure activity participation and ability to perform activities without difficulty or assistance in 1000 TT cases, and compared to 200 matched individuals who have never had TT. We found strong evidence of substantial improvement in the ability of TT cases to perform all the productive and leisure activities investigated without difficulty and assistance one year after TT surgery, while there was no evidence of change in the TT free participants. These data lend strong support to the view that TT surgery improves functional capabilities, and could therefore contribute to improved household income and wealth.

Introduction

Trachomatous trichiasis (TT) is the in-turning of the eyelashes towards the eye, which results from progressive conjunctival scarring caused by recurrent infection with *Chlamydia trachomatis.* Trichiasis causes painful abrasion of the cornea, leading to corneal opacification and usually irreversible visual impairment. Approximately 3.2 million people have un-treated trichiasis, and 2.4 million people are visually impaired from trachoma worldwide of whom 1.2 million are estimated to be irreversibly blind, making trachoma the leading infectious cause of blindness worldwide [1-3].

The pain and photophobia from trichiasis may also lead to disability, limiting engagement with productive household and agricultural activities even prior to the development of visual impairment. This can result in loss of income and additional economic pressure on often already deprived households. We have previously reported that TT significantly reduces participation in productive household, outdoor, agricultural and leisure activities, even prior to the development of visual impairment [4]. Moreover, we found that TT cases experienced considerably more difficulty in performing tasks and required extra assistance, compared to their neighbours without TT [4]. Other studies have shown that trichiasis causes considerable functional and physical impairment, inability to work and earn an income[5-7].

The economic impact of TT affects not just the individual but potentially the whole family. In most trachoma endemic settings, employment opportunities are often limited and household income is mainly generated from agricultural activities. These are carried out by all family members regardless of age and gender. For instance women, who are more frequently affected by TT than men, usually participate in both household and agricultural activities, including caring for family members, cooking, farming and processing agricultural products [8]. In Sub-Saharan Africa, agriculture accounts for nearly 60% of employment of women [9].

Trachomatous trichiasis is usually treated with corrective eyelid surgery to stop the abrasive damage to the cornea with the aim of reducing the risk of sight loss [10]. However, the surgery also improves overall wellbeing and the individual's capacity to engage in household and agricultural activities by effectively treating the pain and discomfort from the trichiasis [11]. A longitudinal study in Ethiopia assessed the six-month effect of trichiasis surgery on physical functioning using a locally appropriate questionnaire. This study found that trichiasis surgery increased the proportion of trichiasis patients performing physical activities without difficulty [7]. Other than this, there are no other longitudinal studies measuring the long-term effect TT surgery has on engagement and execution of activities.

The 'stylised activity list' was developed for the World Bank's Living Standards Measurement Survey (LSMS) to assess participation in various productive and leisure activities before and after interventions [12]. We have previously reported a case-control study, which adapted this tool to compare a subset of TT cases to controls without TT [4]. This additional longitudinal comparative study was undertaken to explore the long-term impact of trichiasis surgery on productive and leisure activity participation, difficulty and required assistance in TT cases, and compare this with the same controls used in the baseline paper (hereafter referred to as comparison participants).

Methods

Ethics Statement

This study was reviewed and approved by the National Health Research Ethics Review Committee of the Ethiopian Ministry of Science and Technology, the London School of Hygiene & Tropical Medicine (LSHTM) Ethics Committee, and Emory University Institutional Review Board. Written informed consent in Amharic was obtained prior to enrolment from participants. It was conducted in accordance with the Declaration of Helsinki. If the participant was unable to read and write, the information sheet and consent form were read to them and their consent recorded by thumbprint. Interviews were conducted privately, paper data were archived in a locked cabinet and electronic data were stored on a password-protected computer isolated from the Internet in a secure dedicated study office. Study participants with identified ocular problems were managed as per local protocol.

Study Design and Participants

This longitudinal study was nested within a clinical trial of two alternative surgical treatments for TT [13]. The study design and participants in this study has been described previously. In summary, we recruited 1000 TT cases into the trial, who were also enrolled into this impact study. Cases were defined as individuals with one or more eyelashes touching the eyeball or with evidence of epilation in either or both eyes in association with tarsal conjunctival scarring. They were identified mainly through community-based screening [14]. Recruitment was done in three districts of West Gojam Zone, Amhara Region, Ethiopia between February and May 2014.

We also recruited 200 comparison participants. These were individuals without clinical evidence or a history of trichiasis (including epilation), who came from households without a family member with trichiasis or a history of trichiasis. Comparison participants were individually matched to every fifth trichiasis case by location, sex and age (+/- two years). The research team visited the sub-village (30–50 households) of the trichiasis case that required a matched control. A list of all potentially eligible people living in the sub-village of the case was compiled with the help of the sub-village administrator. One person was randomly selected from this list using a lottery method, given details of the study and invited to participate if eligible. If a selected individual refused or was ineligible, another was randomly selected from the list. When eligible comparison participants were not identified within the sub-village of the index case, recruitment was done in the nearest neighbouring sub-village, using the same procedures.

Baseline Assessment

Data from TT cases were collected at health facilities at the time of enrolment into the clinical trial, prior to trichiasis surgery. Data from the comparison participants were collected at their homes. Six trained Amharic speaking interviewers collected data from participants using a standardised questionnaire, including socio-demographic variables (age, sex, marital and literacy status), presence of any other health problems in the last month and self-rated socioeconomic status (SES). For self-rated SES, participants were asked to rate the wealth of their household in relation to other households in their village by choosing one of the following options: (1) very poor, (2) poor, (3) average, (4) wealthy or (5) very wealthy [4].

Activity Participation Data

The 'Stylised Activity List' tool developed for the World Bank Living Standard Measurement Survey was used to collect activity participation data [12]. This tool contains a list of common activities in different subgroups: household activities, paid work, work for own use, leisure activities and personal activities. Participants were asked if they had participated in each of the activities in the subgroups in the last week. If they had undertaken a specific activity in the last week, they were asked the question *"How much difficulty did you have in doing [Activity] in the last week?"* and asked to choose one of the following options: (0) extreme/not able to do, (1) a lot of difficulty, (2) some difficulty, (3) little difficulty, (4) no difficulty; and another question whether they have done the activity: (1) fully assisted, (2) with some assistance, (3) with no assistance.

Ocular pain impact data

Data on the impact of ocular pain on daily living were collected through a locally relevant structured questionnaire. This was developed through a focus group discussion with community based TT case screeners (Eye Ambassadors) and then was piloted in two surgical outreaches. Both cases and comparison participants were asked the question: "How often have you experienced eye pain in the last month?", then they were asked to choose an option from a four point scale: "Never", "Occasionally", "Often", "Constantly". Those who reported experiencing any pain in the last month were asked the following five questions, using the same four point scale options (above): *" (1) how often has eye pain interfered with your personal care such as bathing, eating, and dressing?"; "(2) how often has eye pain disturbed your sleep?"; "(3) how often has eye pain interfered with your household work such as cooking, house cleaning, washing clothes, fetching water, fetching firewood, caring for other family members?"; "(4) how often has eye pain affected your agricultural or paid work?", "(5) how often has eye pain affected your participation in social activities such as attending weddings, social meetings, and funerals?"*

Clinical data

Presenting LogMAR (Logarithm of the Minimum Angle of Resolution) visual acuity at two metres was measured using "PeekAcuity" software on a Smartphone in a dark room for both cases and comparison participants [15]. An ophthalmic examination was conducted using a 2.5x binocular magnifying loupe and a bright torch.

Surgical Intervention

Immediately after baseline data collection was completed, all cases received trichiasis surgical management. They were randomised to receive either the bilamellar or the posterior lamellar tarsal rotation, which were being compared in the clinical trial [13]. Both surgical procedures involve an incision through the scarred upper eyelid, parallel to and about 3mm above the lid margin, followed by outward rotation and suturing in the corrected position [16]. Six standardised trichiasis surgeons performed the surgery.

Follow-up Assessment

Follow-up was conducted approximately one year after enrolment (minimum 10 and maximum 14 months), during the same season as the baseline assessment. For cases, a short reminder letter was sent to attend the 12-month follow-up. Follow-up data were collected for the majority of cases at a health facility. For cases that could not come to the health facility, data were collected during a home visit. Follow-up data were collected on comparison participants at their homes. Participants were interviewed using the same 'Stylised Activity List' and ocular pain impact tool as at baseline, and clinical data were collected using the same procedures by the same interviewers and clinical grader.

Analysis

Sample size determination has been reported previously.[11,17] Data were double entered into Access (Microsoft), cleaned in Epidata 3.1 and transferred to Stata 11 (StataCorp) for analysis. Analyses were restricted to participants with both baseline and follow-up data.

The three binary primary outcomes assessed were "participated in activity in last week", "performed activity without difficulty in last week" and "performed activity without any assistance in last week". To generate the latter two outcomes, the "difficulty" and "assistance" question responses were categorised as follows. The "difficulty" question responses were dichotomized into "performed activity with difficulty" (if the participant was not able to do it, had a lot of difficulty, or some difficulty in doing the activity in the last week); and "performed activity without any difficulty" (if the participant had no difficulty in doing the activity in the last week). The "assistance" question responses were dichotomized as "performed activity with assistance" (if the participant performed activity with some assistance or was fully assisted in the last week) and "performed activity without any assistance" (if the participant performed the activity without any assistance).

For ease of presentation, activities were regrouped into productive household activities (cooking and cleaning dishes, house cleaning, washing clothing and looking after family members), productive outdoor activities (animal rearing, farming, processing agricultural products, fetching wood, fetching water, shopping/marketing, travelling), paid work (daily laboring and self employment activities), leisure activities (making social or family visits, attending ceremonies, attending social meetings, engagement in relaxing activities such as reading, watching TV, listening to the radio or chatting with friends), and daily activities (eating, bathing, dressing and sleeping). For the combined analysis of these activities in their subgroups, participation was determined by whether an individual participated in at least one of the activities in the subgroup during the last week. Being without difficulty or not requiring assistance was determined at the subgroup level by whether an individual could perform at least one task within the subgroup without reported difficulty or without assistance.

The vision data analyses have been reported previously in detail [11]. Participants were grouped into better vision (improvement of >0.1 LogMAR), same vision (-0.1 to 0.1 LogMAR) and worse vision (deterioration of >0.1 LogMAR) categories in relation to their baseline vision scores. Based on their baseline trichiasis severity, cases were categorized into Minor Trichiasis (<6 lashes or evidence of epilation in <1/3rd of the lashes) and Major Trichiasis (≥ 6 lashes or evidence of epilation in ≥ 1/3rd of the lashes).

To quantify the difference in the proportion of cases who participate in an activity at baseline and the proportion at follow up, a two-sample test of proportion was employed, providing an estimate of the differences in proportion with a 95% confidence interval. This was also performed separately for the comparison group. The same procedure was also applied to compare the proportions of participants with difficulty and requiring assistance at baseline and follow up, among those who report participation in the activity in the last week.

To test whether the increase/decrease in proportion of participants from baseline to follow up in the three outcome measures differed in the cases and comparison group, a random effect logistic regression model was used, with case/non-case status and time point (baseline or follow up) as exposure variables. This model was adjusted for the matching variables (age and sex), and presence of another health problem during the last month, as these factors may confound activity participation, difficulty and assistance requirements. The analysis was not adjusted for village, as neighbourhood comparison participants were used, and it was assumed that village would not affect participation, difficulty and assistance in activities.

An interaction was included between case status and time point, with the p-value for that interaction reported to provide the strength of evidence that the odds ratio relating the odds of participation, doing activity without difficulty and assistance between baseline and follow-up differed between cases and non-cases. These tests of interaction between case/comparison status and time point in the difficulty and assistance data were not possible to analyse in all activities, as some of the proportion changes (between baseline and follow-up) in the comparison participants have inadequate variability. Therefore, in such activities, data analysis was restricted to within the cases to show if any increases or decreases in proportion of cases doing an activity without difficulty and assistance differ between baseline and follow-up. In a further stratified analysis, p-values for interaction between visit and vision change at 12 month follow-up in cases alone were generated to show if any increase or decrease in proportion of cases performing an activity without difficulty and assistance show a trend across the three group of vision change classifications: better, same and worse.

A similar two-sample test of proportion analysis was performed to examine whether there was a significant change in the proportion of cases and comparison participants with ocular pain, and its impact on personal care, sleep, household, paid, agricultural and social activities. For this analysis among the four response options in the ocular pain impact data; “occasionally”, “often” and “constantly” were combined to create a binary variable with the “Never” option. Random effect ordinal logistic regression model was used to show if there is a trend of increase or decrease in the proportion of cases and comparison participants (separately) with negative reported impact of ocular pain (ordered variable as none, occasionally, often and constantly) on daily living between baseline and follow-up. Then p-values for interaction between visit and case/comparison status were calculated to show if any increase or decrease in proportion of participants with no pain or no negative impact of ocular pain on daily living between baseline and follow-up significantly differ between cases and comparison participants.

Results

Demographic and clinical characteristics

At baseline, 1000 TT cases and 200 comparison participants were recruited. At the 12-month follow-up, complete activity participation data were collected from 980 (98%) cases and 198 (98%) comparison participants. The baseline demographic and clinical characteristics of cases and comparison participants seen at 12-months have been reported previously [11]. In summary, cases and comparison participants were adequately matched for age, but there were significantly more females among the comparison participants (84.3%) than the cases (76.4%, p=0.02). Compared to the comparison participants, the trichiasis cases were more likely to be illiterate (p=0.008), widowed or divorced (p<0.0001), be from poorer households (p<0.0001), and report another health problem in the past month (p<0.0001). The majority of the comparison participants (97%) had normal vision (≥6/18) while about 36% of cases had visual impairment (<6/18) and significantly lower contrast sensitivity score (P<0.0001).

Activity participation

Between baseline and one year after surgery there was a significant increase in the proportion of cases participating in activities during the previous week for five of the seven productive outdoor activities assessed: farming by 5.7% (95% CI, 1.3%–10.3%; p=0.01), processing agricultural products by 18.1% (95% CI, 13.7%–22.4%; p<0.0001), fetching wood by 23.6% (95% CI, 19.3%–27.9%; p<0.0001), fetching water by 5.4% (95% CI, 1.6%–9.3%; p=0.006) and traveling by 9.5% (95% CI, 5.1%–13.8%, p<0.0001). The only other activity that showed a marked increase in participation among cases was the leisure activity attending ceremonies, which increased by 27.5% (95% CI, 23.4%–31.6%; p<0.0001).

However, when the relative changes in activity participation among the cases and the comparison participants are compared, there are few marked differences (Table 1). To analyse this we tested the relative likelihood of cases and comparison participants who did not participate in a specific activity at baseline subsequently participating in the activity at 12-months. For most activities there was no difference (p values in Table 1). The exceptions were firstly fetching wood which was slightly more frequent among the cases (borderline significance, p=0.06); secondly, processing agricultural products (p=0.02), looking after a family member (p=0.0002) and making social visits (p=0.0002) were relatively more frequent in the comparison participants at 12-months (Table 1).

Performing activity without difficulty

The proportion of participants performing the different activities without any difficulty at baseline and at 12-months, and the change between the two time points are presented in Table 2. At baseline, the proportion of cases performing activities without difficulty was low for productive household activities (range 16.1–55.1%), productive outdoor activities (range 19.1%–31.6%), and paid work (range 25.5%–27.2%). The exception was leisure activities (range 46.8%–73.7%), Table 2. However, there was strong evidence that trichiasis surgery improves the ability of trichiasis cases to perform all the activities investigated without difficulty. The increases for productive activities ranged from 33.1% to 65.9%, for paid work they ranged from 58.2% to 61.3% and for leisure activities they ranged from 22.5% to 41.3%. The largest increases were observed in productive outdoor activities: processing agricultural products increased by 65.9% (95% CI, 61.4%–70.5%; p<0.0001), farming by 63.3% (95% CI, 58.4%–68.1%; p<0.0001) and fetching wood by 60.7% (95% CI, 55.5%–65.9%; p<0.0001), Table 2. In contrast, the comparison participants reported very little change in their ability to perform activities without difficulty. The analysis for interaction between visit and case/comparison participant status showed that for nearly all investigated activities cases experienced a substantial reduction in difficulty one year after trichiasis surgery, relative to the comparison participants, Table 2.

In a combined subgroup analysis of activities, there was a significant increase in the proportion of trichiasis cases performing productive household activities (37.4%. 95% CI, 33.4%–41.4%; p=0.0007), productive outdoor activities (45.6%, 95% CI 41.8%– 49.5%, p<0.0001), paid work (57.5%, 95% CI, 49.5%–65.5%, p<0.0001), and leisure activities (25.1%, 95% CI, 21.5%–28.7%, p=0.0008) without any difficulty one year after trichiasis surgery.

Performing activity without assistance

At baseline, trichiasis cases were less likely to perform activities without assistance, than the comparison participants, Table 3. However, one year after TT surgery, there was a significant increase in the proportion of cases who could perform activities without assistance with the increases ranging from 6.4% to 7.5% for paid work, 1.4% to 37.8% for productive activities and 0.1% to 3.8% for leisure activities. The largest increases observed were in animal rearing 37.8% (95% CI, 33.5%–42.1%; p<0.0001) and farming 23.2% (95% CI, 18.8%–27.5%; p<0.0001), Table 3. The comparison participants reported very little change in their ability to perform activities without assistance. The analysis for interaction between visit and case/comparison participant status showed that for nearly all investigated activities cases experienced a substantial reduction in need for assistance one year after trichiasis surgery, relative to the comparison participants, Table 3.

In a combined subgroup analysis of activities, there was an increase one year after trichiasis surgery in the proportion of trichiasis cases performing productive household activities (5.7%, 95% CI, 3.7%–7.6%1, p<0.0001), productive outdoor activities (5.8%, 95% CI, 3.9%–7.6%, p<0.0001), paid work (6.6%, 95% CI 2.2%–11.0%, p=0.03), and leisure activities (1.9%, 95% CI, 0.6%–3.1%, p=0.02) without assistance.

Effect of vision change on difficulty and assistance

We examined whether the increase in proportion of case performing an activity without difficulty or assistance showed a trend across the three groups of vision changes, Table 4. The improvement in processing agricultural products (p=0.006), cooking and cleaning dishes (p=0.03), animal rearing (p=0.02) and making social visits (p=0.03) without difficulty was significantly greater among people who experienced improvement in their visual acuity, compared to those with unchanged or worse vision. For most other activities the proportion of cases performing the activity without difficulty and their ability to perform an activity without assistance, improved by similar degrees for all three vision change groups (p-value for trend >0.10), Table 4.

Ocular pain, trichiasis surgery and its impact on daily living

At baseline 968/980 (98.8%) of the trichiasis cases seen again at the 12-month follow-up had ocular pain. Of these, 61% felt it often or constantly. In a multivariable analysis, baseline major trichiasis (OR, 1.54; 95%CI, 1.21–1.95; p=0.0004), female gender (OR, 1.63; 95%CI, 1.22–2.19; p=0.0011), and reports of other health problem in the last month (OR, 2.27; 95%CI, 1.77–2.92; p<0.0001), were significantly associated with increased frequency of ocular pain in trichiasis cases. In addition, cases with major TT at baseline were more likely to report ocular pain interfering with participation in productive household (OR, 1.65; 95%CI, 1.30–2.10; p<0.0001), paid or agricultural (OR, 1.48; 95%CI, 1.16–1.88; p=0.0015), and social activities (OR, 1.29; 95%CI, 1.01–1.64; p=0.043), than cases with minor TT.

One year after trichiasis surgery the proportion of cases experiencing ocular pain reduced from 98.9% to 33.7% (Proportion difference, 65.2%; 95% CI, 62.1%–68.1%; p<0.0001). In contrast, the proportion of comparison participants with ocular pain increased by 7.6% (95% CI, 3.4%–11.7%; p<0.0001) at follow-up. At baseline a considerable number of trichiasis cases reported that ocular pain interfered with personal care (31.2%), sleep (70.0%), participation in productive household activities (78.9%), paid or agricultural work (83.4%) and social activities (53.1%), Table 5. However, one year after trichiasis surgery the proportion experiencing interfering pain dropped substantially (Table 5). There were very significant decreasing trends in the frequency of ocular pain and its interference with sleep, engagement in personal care, productive household, paid or agricultural and social activities among TT cases, Table 5. In multivariable analysis, recurrent TT during the 12-month period was strongly associated with increased likelihood of ocular pain at 12-months (OR, 1.83; 95%CI, 1.30–2.56; p=0.0005) and increasing frequency of ocular pain was strongly associated with reduced participation in productive household activities (OR, 1.84; 95%CI, 1.15–2.97; p=0.012) in TT cases.

Table 1: Change in activity participation of cases and comparison participants between baseline and 12-month follow-up

Activity	Performed Activity in the last week						
	Baseline		*Follow-up*				
	n	*(%)*	*n*	*(%)*	*Diff*	*(95% CI)*	*P-value* [a]
Productive household activities							
Cooking and cleaning dishes							
Cases	740	(75.5)	714	(72.9)	-2.6	(-6.53 – 1.22)	0.95
CPs	168	(84.8)	165	(83.3)	-1.5	(-0.87 – 5.67)	
House cleaning							
Cases	708	(72.2)	707	(72.1)	-0.1	(-0.40 – 0.39)	-
CPs	167	(84.3)	165	(83.3)	-0.1	(-0.83 – 0.62)	
Washing clothing							
Cases	382	(39.0)	373	(38.1)	-0.9	(-5.22 – 3.39)	0.05
CPs	129	(65.1)	109	(55.0)	-10.1	(-19.7, -0.51)	
Looking after family member							
Cases	673	(68.7)	706	(72.0)	3.3	(-0.67 – 7.41)	0.0002
CPs	136	(68.7)	170	(85.9)	17.2	(9.09 – 25.2)	
Productive outdoor activities							
Animal rearing							
Cases	675	(68.9)	666	(68.0)	-0.9	(-5.03 – 3.20)	0.80
CPs	163	(82.3)	163	(82.3)	0.0	-	
Farming							
Cases	466	(47.6)	522	(53.3)	5.7	(1.29 – 10.3)	-
CPs	118	(59.6)	162	(81.8)	22.2	(13.5 – 30.9)	
Processing agricultural products							
Cases	455	(46.4)	632	(64.5)	18.1	(13.7 – 22.4)	0.02
CPs	159	(80.3)	190	(96.0)	15.7	(9.47 – 21.8)	
Fetching wood							
Cases	376	(38.4)	607	(61.9)	23.6	(19.3 – 27.9)	0.06
CPs	152	(76.8)	168	(84.8)	8.0	(3.64 – 15.8)	
Fetching water							
Cases	703	(71.7)	756	(77.1)	5.4	(1.55 – 9.26)	0.08
CPs	170	(85.9)	185	(93.4)	7.5	(1.62 – 13.5)	
Shopping/marketing							
Cases	563	(57.4)	534	(54.5)	-2.9	(-7.53 – 1.43)	0.70
CPs	151	(76.3)	143	(72.2)	-4.1	(-12.6 – 4.56)	
Travelling							
Cases	365	(37.2)	458	(46.7)	9.5	(5.14 – 13.8)	0.52
CPs	116	(58.6)	140	(70.7)	12.1	(2.78 – 21.5)	
Paid work							
Daily labouring							
Cases	47	(4.80)	38	(3.88)	-0.92	(-2.72 – 0.88)	0.27
CPs	4	(2.02)	1	(0.51)	-1.5	(-3.71 – 0.68)	
Self employment [†]							
Cases	147	(15.0)	151	(15.4)	0.4	(-2.77 – 3.59)	0.80
CPs	25	(12.6)	27	(13.6)	1.0	(-5.64 – 7.66)	
Leisure activities							
Social visits							
Cases	683	(69.7)	702	(71.6)	1.9	(-2.09 – 5.97)	0.0002
CPs	148	(74.7)	181	(91.4)	16.7	(9.47 – 23.9)	
Attending ceremonies							
Cases	235	(24.0)	504	(51.5)	27.5	(23.4 – 31.6)	0.24
CPs	59	(29.8)	103	(52.0)	22.2	(12.8 – 31.7)	
Attending social meetings							
Cases	107	(10.9)	131	(13.4)	2.5	(-0.44 – 5.34)	0.32
CPs	31	(15.7)	30	(15.2)	-0.5	(-7.62 – 6.61)	
Relaxing activities [b]							
Cases	186	(19.0)	210	(21.4)	2.4	(-1.10 – 6.00)	0.37
CPs	64	(32.3)	63	(31.8)	-0.5	(-9.70 – 8.69)	

CPs = Comparison Participants
Diff = Difference of proportions between 12 month follow-up and baseline, calculated using two sample test of proportions

[a] p-values for interaction between visit and case/comparison status; calculated using random effect logistic regression model by including interaction term between cases/comparison status and time point, and adjusted for age, gender and self reported health problem in the last month to show whether non-active cases at baseline are more or less likely to become active at follow-up than comparison participant who were non-active at baseline.

[b] Listening to radio, Reading, Watching TV .
[†] Selling Goods

Table 2: Change in performing activities without difficulty between baseline and 12 month follow-up in cases and comparison participants

Activity	Baseline n/N	Baseline (%)	Follow-up n/N	Follow-up (%)	Diff	(95% CI)	P-value [a]
	Performed Activity Without Difficulty						
Productive household activities							
Cooking and cleaning dishes							
Cases	119/740	(16.1)	485/714	(67.9)	51.8	(47.5 – 56.2)	<0.0001
CPs	164/168	(97.6)	157/165	(95.2)	-2.4	(-6.47 – 1.54)	
House cleaning							
Cases	155/708	(21.9)	550/707	(77.8)	55.9	(51.6 – 60.2)	<0.0001
CPs	164/167	(98.2)	159/165	(96.4)	-1.8	(-5.33 – 1.65)	
Washing clothing							
Cases	133/382	(34.8)	320/375	(85.3)	50.5	(44.5 – 56.5)	<0.0001 [c]
CPs	128/129	(99.2)	110/110	(100)	0.8	(-0.84 – 2.29)	
Looking after family member							
Cases	371/673	(55.1)	623/706	(88.2)	33.1	(28.7 – 37.6)	0.02
CPs	135/136	(99.3)	168/170	(98.8)	-0.5	(-2.61 – 1.72)	
Productive outdoor activities							
Animal rearing							
Cases	204/675	(30.2)	553/666	(83.0)	52.8	(48.3 – 57.3)	<0.0001
CPs	159/163	(97.5)	157/163	(96.3)	-1.2	(-4.97 – 2.51)	
Farming							
Cases	89/466	(19.1)	430/522	(82.4)	63.3	(58.4 – 68.1)	<0.0001 [c]
CPs	118/118	(100)	153/162	(94.4)	-5.6	(-9.08 - -2.20)	
Processing agricultural products							
Cases	96/455	(21.1)	551/633	(87.0)	65.9	(61.4 – 70.5)	<0.0001
CPs	158/159	(99.4)	182/190	(95.8)	-3.6	(-6.69 - -0.47)	
Fetching wood							
Cases	95/376	(25.3)	522/607	(86.0)	60.7	(55.5 – 65.9)	<0.0001
CPs	148/152	(97.4)	161/168	(95.8)	-1.6	(-5.49 – 2.41)	
Fetching water							
Cases	222/703	(31.6)	612/756	(80.9)	49.3	(44.9 – 53.8)	<0.0001
CPs	165/170	(97.1)	176/185	(95.1)	-2.0	(-5.93 – 2.08)	
Shopping/Marketing							
Cases	145/563	(25.7)	427/536	(79.7)	54.0	(48.9 – 58.9)	<0.0001
CPs	147/151	(97.3)	138/143	(96.5)	-0.8	(-4.80 – 3.10)	
Travelling							
Cases	93/365	(25.5)	367/458	(80.1)	54.6	(48.9 – 60.4)	0.0001
CPs	114/116	(98.3)	135/140	(96.4)	-1.9	(-5.73 – 0.20)	
Paid work							
Daily labouring							
Cases	12/47	(25.5)	33/38	(86.8)	61.3	(44.8 – 77.8)	0.34 [c]
CPs	4/4	(100)	1/1	(100)	0.0	-	
Self employment [†]							
Cases	40/147	27.2	129/151	85.4	58.2	(49.1 – 67.3)	0.0001 [c]
CPs	24/25	(96.0)	27/27	(100)	0.4	(-3.68 – 11.7)	
Leisure activities							
Social visits							
Cases	441/683	(64.6)	644/703	(91.6)	27.0	(22.9 – 31.2)	0.0006
CPs	146/148	(98.6)	175/181	(96.7)	-1.9	(-5.17 – 1.24)	
Attending ceremonies							
Cases	110/235	(46.8)	445/505	(88.1)	41.3	(34.3 – 48.3)	<0.0001 [c]
CPs	59/59	(100)	101/103	(98.1)	-1.9	(-4.61 – 0.72)	
Attending social meetings							
Cases	65/107	(57.9)	126/131	(96.2)	38.3	(28.3 – 48.1)	0.0005 [c]
CPs	31/31	(100)	30/30	(100)	0.0	-	
Relaxing activities [b]							
Cases	137/186	(73.7)	203/211	(96.2)	22.5	(15.7 – 29.4)	0.23
CPs	62/64	(96.9)	62/63	(98.4)	1.5	(-3.72 – 6.80)	
Daily activities							
Cases	665/980	(67.9)	925/980	(94.4)	26.5	(23.3 – 29.8)	0.005
CPs	196/198	(99.0)	195/198	(98.5)	-0.5	(-2.70 – 1.69)	

CPs = Comparison Participants

Diff = Difference of proportions between 12 month follow-up and baseline, calculated using two sample test of proportions.

[a] p-values for interaction between time point and case/comparison status; calculated using random effect logistic regression model adjusted for age, gender and self reported health problem in the last one month to show if any increase or decrease in performing an activity without difficulty from baseline to follow-up differ between cases and comparison participants. [b] Listening to radio, Reading, Watching TV . [†] Selling Goods. b[c] p-values calculated using random effect logistic regression model to show if any increase or decrease in proportion of cases doing an activity without difficulty differ between baseline and follow-up after adjusting for potential confounders: age, gender and self reported health problem in the last one month. This analysis is used for variables with inadequate variability in the proportion of comparison participants for interaction analysis between time point and case/comparison status.

Table 3: Change in performing activities without assistance between baseline and 12 month follow-up in cases and comparison participants

Activity	*Performed Activity Without Assistance*						
	Baseline		*Follow-up*				
	n	(%)	n	(%)	*Diff*	*(95% CI)*	*P-value* [a]
Productive household activities							
Cooking and cleaning dishes							
Cases	642/740	(86.8)	680/714	(95.2)	8.4	(5.58 – 11.4)	<0.0001
CPs	167/168	(99.4)	165/165	(100)	0.6	(-0.57 – 1.76)	
House cleaning							
Cases	629/708	(88.8)	695/707	(98.3)	9.5	(6.95 – 12.0)	<0.0001
CPs	166/167	(99.4)	165/165	(100)	0.6	(-0.57 – 1.76)	
Washing clothing							
Cases	344/382	(90.0)	363/375	(96.8)	6.8	(3.26 – 10.2)	0.001
CPs	129/129	(100)	110/110	(100)	0.0	-	
Looking after family member							
Cases	564/673	(83.8)	686/706	(97.2)	13.4	(10.3 – 16.4)	<0.0001
CPs	135/136	(99.3)	170/170	(100)	0.7	(-0.70 – 2.17)	
Productive outdoor activities							
Animal rearing							
Cases	366/675	(54.2)	613/666	(92.0)	37.8	(33.5 – 42.1)	<0.0001
CPs	144/163	(88.3)	162/163	(99.4)	11.1	(5.97 – 16.1)	
Farming							
Cases	341/466	(73.2)	503/522	(96.4)	23.2	(18.8 – 27.5)	<0.0001
CPs	116/118	(98.3)	162/162	(100)	1.7	(-0.63 – 4.02)	
Processing agricultural products							
Cases	401/455	(88.1)	626/633	(98.9)	10.8	(7.68 – 13.8)	<0.0001
CPs	159/159	(100)	190/190	(100)	0	-	
Fetching wood							
Cases	345/376	(91.8)	602/607	(99.2)	7.4	(4.55 – 10.3)	<0.0001
CPs	150/152	(98.7)	168/168	(100)	1.3	(-0.50 – 3.13)	
Fetching water							
Cases	599/703	(85.2)	734/756	(97.1)	11.9	(9.00 – 14.8)	<0.0001
CPs	169/170	(99.4)	185/185	(100)	0.6	(-0.56 – 1.74)	
Shopping/Marketing							
Cases	546/563	(96.9)	527/536	(98.3)	1.4	(-0.44 – 3.12)	0.19
CPs	150/151	(99.3)	143/143	(100)	0.7	(-0.63 – 1.96)	
Travelling							
Cases	342/365	(93.7)	448/457	(98.0)	4.3	(1.53 – 7.13)	0.02
CPs	115/116	(99.1)	140/140	(100)	0.9	(-0.82 – 2.54)	
Paid work							
Daily labouring							
Cases	44/47	(93.6)	39/39	(100)	6.4	(-0.61 – 13.4)	-
CPs	4/4	(100.0)	1/1	(100)	0.0	-	
Self employment [†]							
Cases	132/147	(89.8)	147/151	(97.3)	7.5	(2.03 – 13.1)	0.03
CPs	25/25	(100)	27/27	(100)	0.0	-	
Leisure activities							
Social visits							
Cases	664/683	(97.2)	697/703	(99.1)	1.9	(0.52 – 3.34)	0.02
CPs	148/148	(100)	181/181	(100)	0.0	-	
Attending ceremonies							
Cases	226/235	(96.2)	497/505	(98.4)	2.25	(-0.44 – 4.93)	0.33
CPs	59/59	(100)	103/103	(100)	0.0	-	
Attending social meetings							
Cases	106/107	(99.1)	130/131	(99.2)	0.1	(-2.18 – 2.53)	0.91
CPs	31/31	(100)	30/30	(100)	0.0	-	
Relaxing activities [b]							
Cases	178/186	(95.7)	209/210	(99.5)	3.8	(0.76 – 6.89)	0.04
CPs	63/64	(98.4)	62/63	(98.4)	0.0	-	
Daily activities							
Cases	955/980	(97.4)	969/980	(98.9)	1.5	(0.24 – 2.62)	0.02
CPs	198/198	(100)	198/198	(100)	0.0	-	

CPs = Comparison Participants

Diff = Difference of proportions between 12 month follow-up and baseline, calculated using two sample test of proportions.

[a] p-values calculated using random effect logistic regression model to show if any increase or decrease in proportion of cases doing an activity without assistance differ between baseline and follow-up after adjusting for potential confounders: age, gender and self reported health problem in the last one month. This analysis is chosen as the change in assistance (between baseline and follow-up) data in the comparison participants have inadequate variability for interaction analysis between time point and case/comparison status. [b] Listening to radio, Reading, Watching TV . [†] Selling Goods

Table 4: Change in performing activities without difficulty and assistance in cases by vision change at 12 month

Activity	Performed Activity Without Difficulty							Performed Activity Without Assistance						
	Vision Better		Vision Same		Vision Worse		*P-value* [a]	Vision Better		Vision Same		Vision Worse		*P-value* [a]
	Diff	*95% CI*	*Diff*	*95% CI*	*Diff*	*95% CI*		*Diff*	*95% CI*	*Diff*	*95% CI*	*Diff*	*95% CI*	
Productive household activities														
Cooking and cleaning dishes	55.2	(48.1 – 62.3)	53.1	(46.8 – 29.4)	41.8	(31.2 – 52.4)	0.03	9.7	(4.31 – 15.1)	6.9	(3.20- 10.6)	9.5	(2.19 – 16.8)	0.91
House cleaning	60.1	(53.5 – 67.7)	54.0	(47.9 – 60.6)	51.0	(40.9 – 61.4)	0.09	10.9	(6.41 – 15.4)	7.9	(4.44 – 11.2)	10.9	(4.70 – 17.2)	0.70
Washing clothing	55.1	(44.3 – 65.9)	44.9	(36.3 – 53.6)	58.5	(46.1 – 70.9)	0.70	8.0	(1.95 – 14.0)	5.3	(0.48 – 10.2)	9.8	(1.56 – 18.1)	0.85
Looking after family member	40.3	(32.4 – 48.3)	29.0	(22.9 – 35.1)	31.3	(20.8 – 41.7)	0.11	14.8	(9.08 – 20.5)	11.0	(7.06 – 14.8)	16.7	(9.11 – 24.3)	0.95
Productive outdoor activities														
Animal raring	59.3	51.7 – 66.9)	51.5	(45.1 – 57.9)	45.2	(34.2 – 55.9)	0.03	38.3	(30.4 – 46.2)	39.3	(33.4 – 45.2)	33.7	(23.8 – 43.7)	0.90
Farming	57.0	(48.0 – 66.1)	67.4	(60.9 – 74.1)	63.6	(52.6 – 74.6)	-	24.2	(16.1 – 32.3)	24.8	(18.8 – 30.8)	17.8	(8.06 – 27.6)	0.83
Processing agricultural products	74.7	(68.8 – 81.6)	63.3	(56.4 – 70.2)	57.4	(46.4 – 68.3)	0.006	16.2	(9.89 – 22.5)	7.0	(3.24 – 10.7)	10.6	(3.67 – 14.4)	0.42
Fetching wood	63.8	(55.1 – 72.4)	63.4	(56.1 – 70.8)	49.8	(37.0 – 62.7)	0.12	7.8	(2.69 – 12.9)	5.4	(1.76 – 9.03)	12.2	(40.5 – 20.3	0.74
Fetching water	53.9	(46.4 – 61.4)	48.4	(42.0 – 54.8)	43.7	(33.4 – 54.0)	0.05	15.3	(9.63 – 21.0)	7.6	(4.27 – 11.0)	15.6	(8.35 – 22.8)	0.85
Shopping/Marketing	55.2	(46.3 – 64.0)	53.5	(46.5 – 60.5)	53.2	(42.1 – 64.3)	0.78	3.6	(-0.90 – 8.06)	0.3	(-0.92 – 1.60)	0.2	(-4.07 – 4.52	0.33
Travelling	53.4	(43.7 – 63.1)	56.6	(48.1 – 65.0)	50.4	(36.8 – 64.1)	0.56	5.3	(0.15 – 10.4)	3.1	(0.43 – 5.82)	3.5	(-4.99 – 12.1)	0.27
Paid work														
Daily labouring	80.6	(54.7 – 1.06)	59.3	(39.1 – 79.4)	52.4	(12.1 – 92.6)	0.27	16.7	(-4.42 – 37.7	3.6	(-3.30 – 10.4)	0	-	-
Self employment [†]	55.0	(36.1 – 73.9)	59.8	(47.8 – 71.7)	55.8	(33.7 – 77.8)	0.88	6.8	(-6.03 – 19.6)	6.5	(0.25 – 12.7)	10.4	(-4.48 – 25.4)	0.73
Leisure activities														
Social visits	32.9	(25.6 – 40.2)	27.4	(21.8 – 33.1)	18.0	(8.44 – 27.5)	0.03	3.4	(0.61 – 6.23)	0.33	(-1.1 – 1.75)	3.0	(-0.41 – 6.34)	0.77
Attending ceremonies	43.2	(30.5 – 55.9)	39.3	(29.2 – 49.4)	41.6	(28.8 – 26.4)	0.96	1.7	(-2.52 – 5.91)	3.0	(1.32 – 7.32)	1.3	(-4.21 – 6.85)	0.75
Attending social meetings	40.4	(20.2 – 60.5)	31.8	(18.9 – 44.7)	49.7	(28.6 – 70.9)	0.91	3.6	(-3.30 – 10.4)	-1.5	(-4.46 – 1.43)	0	-	-
Relaxing activities [e]	23.6	(11.5 – 35.6)	20.9	(11.3 – 30.4)	23.5	(7.58 – 39.4)	0.42	7.2	(-1.23 – 15.6)	0	-	5.0	(-1.75 – 11.7)	-
Daily activities	27.5	(21.6 – 33.2)	24.9	(20.3 – 29.6)	28.4	(21.0 – 35.8)	0.71	2.4	(0.08 – 4.75)	1.3	(-0.03 – 2.71)	0	-	0.20

Diff = Difference of proportions between 12 month follow-up and baseline, calculated using two sample test of proportions.
[a] p-values for interaction between time point and vision change at 12-month follow-up in cases alone; calculated using random effect logistic regression model adjusted for age, gender and self reported health problem in the last one month to show if any increase or decrease in performing an activity without difficulty/ assistance among the cases show a trend across the three group of vision changes: better, same and worse. P values particularly indicate if there is a trend of a larger difference with worse vision.
[e] Listening to radio, Reading, Watching TV . [†] Selling Goods. Dashed lines indicate that the proportion variability in the data is inadequate for such analysis.

Table 5: Change in impact of ocular pain on daily living between baseline and 12 months after trachomatous trichiasis surgery in cases and comparison participants

Activity	Cases							Comparison Participants							*P value* [b]
	Baseline N=1000		*12 Months N=980*		*Diff* [†]	*95% CI*	*P value* [a]	*Baseline N= 200*		*12 Months N=198*		*Diff* [†]	*95% CI*	*P value* [a]	
	n	*(%)*	*n*	*(%)*				*n*	*(%)*	*n*	*(%)*				
Ocular pain															
No	12	(1.22)	650	(66.3)	-65.0	(-68.1 – -62.1)	<0.0001	196	(99.0)	181	(91.4)	7.56	(3.43 – 11.7)	0.0004	<0.0001
Occasionally	369	(37.6)	261	(26.6)				2	(1.0)	15	(7.6)				
Often	343	(35.0)	54	(5.5)				0	(0.0)	1	(1.0)				
Constantly	256	(26.1)	15	(1.5)				0	(0.0)	0	(0.0)				
Ocular pain interfered personal care															
No	688	(68.8)	962	(98.2)	-28.6	(-31.6 – -25.6)	<0.0001	198	(99.0)	198	(100)	-0.1	(-2.4 – 0.38)	-	-
Occasionally	207	(20.7)	10	(1.0)				2	(1.0)	0	(0.0)				
Often	70	(7.0)	7	(0.71)				0	(0.0)	0	(0.0)				
Constantly	35	(3.5)	1	(0.1)					(0.0)	0	(0.0)				
Ocular pain disturbed sleep															
No	300	(30.0)	909	(92.8)	-63.0	(-66.0 – -59.4)	<0.0001	198	(99.0)	196	(99.0)	0.0	-	-	0.0001
Occasionally	332	(32.2)	57	(5.8)				1	(0.5)	2	(1.0)				
Often	301	(30.1)	14	(1.4)				0	(0.0)	0	(0.0)				
Constantly	67	(6.7)	0	(0.0)				1	(0.5)	0	(0.0)				
Ocular pain interfered productive household activities															
No	208	(20.8)	862	(88.0)	-66.9	(-70.2 – -63.7)	<0.0001	198	(99.0)	197	(99.5)	-0.5	(-2.21 – 1.20)	-	0.02
Occasionally	426	(42.6)	90	(9.2)				0	(0.0)	1	(0.5)				
Often	290	(29.0)	23	(2.3)				0	(0.0)	0	(0.0)				
Constantly	76	(7.6)	5	(0.3)				2	(1.0)	0	(0.0)				
Ocular pain interfered paid or agricultural work															
No	164	(16.4)	891	(90.9)	-74.3	(-77.2 – -71.3)	<0.0001	198	(99.0)	198	(100)	-1.0	(-2.4 – 0.38)	-	-
Occasionally	502	(50.2)	66	(6.7)				0	(0.0)	0	(0.0)				
Often	248	(24.8)	18	(1.8)				1	(0.5)	0	(0.0)				
Constantly	86	(8.6)	5	(0.5)				1	(0.5)	0	(0.0)				

Activity	Cases							Comparison Participants							P value [b]
	Baseline N=1000		*12 Months N=980*		*Diff* [†]	*95% CI*	*P value* [a]	*Baseline N= 200*		*12 Months N=198*		*Diff* [†]	*95% CI*	*P value* [a]	
	n	*(%)*	*n*	*(%)*				*n*	*(%)*	*n*	*(%)*				
Ocular pain interfered social activities															
No	464	(46.4)	944	(96.3)	-49.4	(-52.7 – -46.0)	<0.0001	198	(99.0)	197	(99.5)	-0.5	(-2.21 – 1.20)	-	0.02
Occasionally	385	(38.5)	25	(2.56				0	(0.0)	1	(0.5)				
Often	94	(9.4)	7	(0.7)				1	(0.5)	0	(0.0)				
Constantly	57	(5.7)	4	(0.4)				1	(0.5)	0	(0.0)				

[†] Diff = proportion difference from two sample test of proportions of those with any level of problem secondary to ocular pain between baseline and 12 month follow-up; creating binary variable after combining those with "occasionally", "often" and "constantly" responses.
[a] p-values calculated using random effect ordinal logistic regression model adjusted for age, gender and self reported health problem in the last one month to show if there is a trend in decrease in proportion of cases and comparison participants (separately) with negative impact of ocular pain on daily living between baseline and follow-up.
[b] p-values for interaction between time point and case/comparison status; calculated using random effect ordinal logistic regression model by including interaction term between cases/comparison status and visit; and adjusted for age, gender and self reported health problem in the last one month to show if any increase or decrease in proportion of cases and comparison participants with no pain or no negative impact of ocular pain on daily living between baseline and follow-up significantly differ between cases and comparison participants. Dashed lines indicate that the proportion variability in the data is inadequate for such analysis.

Discussion

The relationship between trachoma and poverty is likely to be bidirectional, with poverty being both a cause and consequence of trachoma [4]. Trichiasis can cause pain and visual impairment, which may limit participation in productive activity and execution of tasks, resulting in disability. In settings similar to this study, engagement in non-paid household, outdoor and agricultural activities make a substantial economic contribution to household wealth. In fact, participation in non-paid or non-monetized household and outdoor activities is estimated to make a $16 trillion "invisible" monetary contribution to global economic output and between 20% and 60% of national GDP in some regions [9,18]. Women, who are three times more affected by TT than men, undertake most of the unpaid household and care work [8]. Here we explored whether TT surgery improves participation in and performance of activities.

Overall, there was little evidence of a major change in the proportion of people participating in a wide range of daily task and social activities. This might be anticipated for a number of reasons. Firstly, most of these activities are necessary for and intrinsic to life in the communities from which the participants live. People with trichiasis still need to do most of these activities, despite their disability. Secondly, within a household a particular activity might be the responsibility of specific family members. Therefore, the TT case that had not being doing that particular activity at baseline might not necessarily take over that task from someone else after surgery.

The key changes we found were in how able they were to perform the activities they were already engaged in. Performing productive activities without difficulty or assistance increases independence and productivity, which will potentially have a considerable social return and reduce financial strains on the household, through increased contributions. We found strong evidence that trichiasis surgery, regardless of change in vision, could have a major effect on improving functioning and performance in productive and leisure activities.

Firstly, trichiasis surgery significantly improved the ability of trichiasis cases to perform productive activities without difficulty. At baseline, the proportion of cases performing paid work, productive household and outdoor agricultural activities without any difficulty ranged between 16% and 51%. These increased by between 33% and 66% one year after trichiasis surgery. In contrast, comparison participants reported little difficulty with tasks, and this proportion was largely unchanged.

Although the greatest increase in some of the activities was reported by those with improved vision, the improvement in executing most of the productive tasks without difficulty was apparent even among trichiasis cases who had not experienced an improvement in vision, suggesting that treating the pain caused by trichiasis through surgery can improve the ability to perform tasks. The largest improvements were seen in the ability to execute agricultural activities such as processing agricultural products (66%) and farming (63%). Increased capacity to perform agricultural activities can increase agricultural productivity, which is a major driver for improved food security and human development in sub-Saharan Africa [19]. Our study findings were consistent with findings of a study conducted in Southern Ethiopia which measured the physical functioning of trichiasis patients before and six months after surgery [7]. In this earlier study, at baseline 61.1% of trichiasis cases reported difficulty in physical functioning including performing day-to-day farming activities. However, six months after trichiasis surgery the percentage of participants reporting difficulty in physical functioning reduced by 32.6%.

Moreover, executing an activity without difficulty is critical, as it has a positive effect on both physical and mental wellbeing, thereby improving quality of life [9]. A qualitative study in Niger found that women affected by TT were not able to help or care for their families and have diminished spirit and social status [20]. However, TT surgery substantially improved their quality of life and social reintegration [20]. In our study, the proportion of trichiasis cases attending ceremonies, social meetings and relaxing activities without any difficulty increased by more than 22%, indicating the holistic positive effect trichiasis surgery has on the social integration and the day to day lives of people affected by trichiasis. This in turn would have a broader positive impact in building self-esteem or a sense of dignity through engagement in society and income generating activities.

Secondly, we found that trichiasis surgery improved the ability of operated individuals to perform productive activities without assistance. One year after trichiasis surgery, the proportion of trichiasis cases performing productive activities without assistance significantly improved by about 6% to 17% from the baseline. The proportion of TT cases who could execute productive activities such as animal rearing and farming without any kind of assistance increased by 38% and 23%, respectively. This increment was found even without improved visual acuity. The reduced need for assistance would be expected to lead to increased productivity of the individuals as well as less time spent by other household members supporting them, leading to time being released to engage with other activities. Both elements are anticipated to contribute to a reduction in household poverty.

Thirdly, there is evidence that reducing ocular pain through trichiasis surgery improves engagement in productive paid and agricultural activities. At baseline we found that trichiasis cases suffered from ocular pain, which was reported to interfere with their personal care, sleep and social participation. It also affected perceived involvement in productive household, paid or agricultural activities suggesting that trichiasis pain contributes to disability and impedes productivity. One year after trichiasis surgery, the frequency of ocular pain interfering in productive activities markedly reduced, and the proportion of trichiasis cases that reported ocular pain interfering with productive activities significantly reduced by more than two thirds. Similar results have been reported in a longitudinal study, in which the proportion of trichiasis cases with pain and discomfort reduced by more than 90% six months after trichiasis surgery [7]. Higher frequency of reported pain and increasing interference in productive and social activities was significantly associated with baseline TT severity. Similarly, recurrent TT was associated with persistent ocular pain and less participation in productive activities following surgery. These data together suggest that prompt and high quality TT surgery provides considerable economic and social benefits to patients with severe TT.

This study is the first large comparative longitudinal study to measure impact of trichiasis surgery on participation, difficulty and assistance needs of people living with trichiasis on a wide range of productive and leisure activities. The same interviewers collected data at both baseline and follow-up to ensure questionnaires were administered in a standard way at baseline and follow-up. The study has a number of limitations. The interviewers were not masked to the trichiasis status of the participants. We cannot exclude the possibility of response bias. In an earlier report, more than 90% of the cases in this study reported satisfaction with the outcomes of TT surgery [13]. In low-income settings such as this study's area, participation in productive activities would be affected by seasonality of activities. The baseline and 1-year follow-up data were collected during the same time of the year: the dry season when communities are less engaged in productive activities and more engaged in leisure activities compared to other times of the year. This might explain the lack of difference in the proportion of both cases and comparison participants engaged in most of the productive activities between baseline and follow-up. Activity participation, difficulty and assistance were measured through self-report. Time spent in different activities was not measured, as pilot studies demonstrated difficulty estimating and recalling this. The pain impact questionnaire was not a standardized tool, but was developed to be locally relevant through community focus group discussion.

Conclusions

There was strong evidence that TT surgery improves the ability of TT cases in executing productive and leisure activities. TT surgery substantially increased the proportion of patients who perform productive and leisure activities without difficulty and assistance. Trichiasis surgery effectively treated ocular pain and discomfort, which in turn improved engagement in productive paid and agricultural activities. These data together suggest that trichiasis surgery could have a major effect in improving productivity and contributing to household income and wealth. An unprecedented effort is under way to scale-up trichiasis surgical programmes. Providing prompt surgical intervention to prevent visual loss will also improve overall socio-economic engagement of affected individuals and contribute to the wealth of affected communities.

Supporting Information

S1 Checklist: STROBE Checklist

Acknowledgments

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10. General Discussion

10.1. Implications for Programme and Recommendations

10.1.1. Which Surgical Procedure?

The BLTR has been favoured by WHO for the management of TT following the two Oman trials about 25 years ago, which found the BLTR was more successful than the other surgical procedures compared.[98,128] These two trials, however, did not include the PLTR as one of the procedures being compared. The only trial that has attempted to examine this question was insufficiently powered and only had three months follow-up.[152] Despite this lack of head to head comparison with the BLTR and being initially "overlooked", the PLTR has been used for the management of TT in many African countries, mostly in francophone Africa. Results from studies conducted using the PLTR showed that it may not give inferior outcomes to the BLTR.[4,33,40,152,164] In Ethiopia, both surgical procedures have been used just based on personal preference of surgical trainers and programmers. There has been confusion among new programmes on which surgical procedure to use.

A major global effort is being undertaken to clear the 3.2 million TT surgical backlog with in the coming few years.[43] This raised the need to identify the better of the two most commonly used surgical procedures, in terms of clinical outcomes and patient acceptance.

In our clinical trial, we found that the posterior lamellar tarsal rotation (PLTR) surgery was superior to the bilamellar tarsal rotation surgery (BLTR) in terms of lower rates of postoperative TT and surgical complications.

With respect to postoperative TT, the PLTR had about 13% postoperative TT by one year compared to 22% following the BLTR surgery. This gives a highly significant 9% risk difference in postoperative TT between the two surgical procedures. This is a break through result in the fight against blinding trachoma, indicating that if the PLTR surgical procedure is used instead of the BLTR surgery from now on wards, about 300,000 people will avoid having postoperative trachomatous trichiasis. This would have huge physical and psychological implications for TT affected communities as well service acceptance and financial implications to programmes.

It was previously suggested that, no single surgical procedure is effective against the wide range of severity of trichiasis.[25,105,113] However, in trachoma endemic settings, there is a wide spectrum of disease severity. Therefore, it would be programmatically difficult to implement different types of surgical procedures for the different stages of the disease in such settings. This would require training more highly qualified surgeons in more than one procedure and in how to select the right operation for the patient. This is resource intensive and impractical, given the current huge TT backlog that needs to be addressed within short period of time.

Evidences suggest that in cases with severe scaring and lid retraction, surgical procedures concentrating on the posterior lamella must be used to minimise failure.[25,113,117,123] In fact one of the surgical procedures recommended for cases with lid retraction and severe entropion secondary to excessive tarsal conjunctival scarring is the PLTR procedure, which would effectively correct the severe entropion with 180^0 rotation to the distal tarso-conjunctiva; while on the other hand the BLTR was considered more effective to relatively less severe cases.[25,113,117,123]

A recent article on the use of clamp for BLTR surgery suggested that the BLTR is not successful "for very severe cases with total in-turning of lashes", and suggested that the PLTR procedure is needed for such cases.[113] Our trial results support these assumptions with the PLTR more effectively treating the full spectrum of TT severity than the BLTR. The PLTR out performed the BLTR on severe cases and had lower postoperative trichiasis rate among cases with minor TT (10% vs 14%), major TT (16% vs 31%), or mild entropion (11% vs 31%), moderate entropion (12% vs 18%), severe entropion (19% vs 31%). In addition, the BLTR had more under correction than the PLTR one year after surgery. This is consistent with the findings of a prospective cohort study where BLTR tended to have more under correction and higher entropion recurrence than the PLTR procedure.[117] These results suggest that the PLTR is preferable for use in programmatic situations in trachoma endemic settings, where there are varied phenotypes of TT and where non-physician cadres with limited training perform the surgeries.

Some people think that the PLTR is more difficult to perform than the BLTR surgery, assuming everting the eyelid, using a traction suture to perform the half thickness incision and then lamellar dissection is relatively difficult in patients with severely scared and contracted eyelids, compared to the BLTR in which a full thickness incision is made from the skin after fixing the eyelid using the clamp. This view is, however, not supported by available evidence, and thousands of non-physician cadres around the world are performing the PLTR surgery successfully. On the contrary, the PLTR surgical procedure is probably the first surgical procedure, which was conducted successfully by lower level cadres in trachoma endemic countries. In 1949, dressers (the lowest level health professionals) were trained and performed TT surgery using the PLTR surgery in Ethiopia, long before the WHO recommendation for task shifting of TT surgery to midlevel health workers.[118]

The PLTR is probably the safest surgical procedure in trachoma endemic settings, with lower rates of surgical complication than the BLTR. Excessive bleeding was higher among patients operated with BLTR, probably because of the full thickness incision involving the vascular anterior lamella. Excessive bleeding could be difficult to manage in remote lower level health facilities by eye care workers or IECWs with relatively little training. In addition, despite the provision of tetracycline eye ointment, the BLTR had more infection than the PLTR, probably related to the external incision exposed to dust and pathogens postoperatively. Infections may not only influence surgical outcomes but also would create distress among patients and these might not be easy to treat in such remote settings with limited access to antibiotics. Patients operated using the BLTR surgery reported more pain after surgery than those operated with the PLTR, suggesting the acceptance rate of the BLTR among communities might go down through time, which would greatly hamper uptake of surgical services. Fear of surgical pain, has been among the most consistently reported barriers for TT surgical service uptake.[29,91,261]

There was higher rate of granuloma and mild, clinically non-significant eyelid contour abnormality (ECA) among patients treated with the PLTR. These are however less of an issue from programmatic point of view. Firstly, the granuloma can resolve by itself or can be removed with simple shave, requiring no particular expertise to manage. The mild ECA is <1mm vertical deviation from the lid margin. Generally these do not need any treatment and do not give cosmetic concerns to the patients. In fact, despite the higher rate of <1mm eyelid contour deviation in the PLTR, 97% of the patients operated in the PLTR reported satisfaction on the cosmetic appearance of the eyelid, compared to 96% in the BLTR operated patients. Kenya has switched from using BLTR to PLTR in response to patient dissatisfaction on the appearance of the eyelid after BLTR surgery. In the PLTR, we found suture distance asymmetry of >2mm between sutures predicted ECA in the PLTR surgery, which is the probably associated with the relatively higher rate of mild ECA. The clinically significant ECA (moderate or severe) rate between the two surgical procedures was comparable, suggesting both surgical procedures have their limitations in this regard, indicating the need for further study to explore why.

Overall, in trachoma endemic areas, where there is a wide spectrum severity of TT, the PLTR surgical procedure should be the procedure of choice for the management of TT. New surgical trainees in both new and established programmes should be trained in the PLTR surgical procedure. We have taken great care to ensure that the previous PLTR practicing trichiasis surgeons operated in this trial performed the BLTR procedure to the same standard and proficiency as PLTR surgery, based on to what has been described in the WHO training manual.

There was no evidence that this has been an issue on influencing results of this trial. However, further research could be done to investigate if the outcome of these would be different if BLTR trained surgeons are retrained to do the surgery using the PLTR procedure.

10.1.2. Optimising Surgical Outcomes

Unfavourable surgical outcomes such as postoperative TT, ECA and granuloma have become a major challenge for most trachoma control programmes. The consequences of such outcomes are huge ranging from psychological and physical consequences deterring patients from accepting surgery to adding extra burden to surgical programmes. We found some interesting findings that would help maximise surgical outcomes in programmatic settings using both the PLTR and BLTR surgical procedures.

Performing medial and lateral dissections to increase the length of incision reduced the rate of postoperative TT in both PLTR and BLTR surgeries. This correlates well to the fact that peripheral and mixed location lashes tend to recur more often than central lashes, probably due to inadequate incision and dissection of the periphery of the eyelid. Incision height of ≥4mm did not improve surgical outcomes particularly in the BLTR procedure. Similarly another prospective cohort study results showed that a BLTR procedure performed with an incision at about 5mm-6mm distance from the lid margin did not give better results than a PLTR procedure performed with incision at around 3mm distance. These results indicate that the current WHO guide of making incision at 3mm distance from the lid margin should be maintained.

We have found suture distance asymmetry of >2mm was associated with ECA in PLTR surgery. In addition, irregular suture tensions tended to cause ECA and granuloma in both PLTR and BLTR procedures; while using four sutures as compared to three tended to prevent ECA particularly in BLTR surgery. Great care should be taken to insert sutures with equal separation and tension; and probably the use of four mattress sutures might reduce, tissue defect and the chance of uneven placement of sutures and provide regular suture tension across the eyelid. Further studies are needed to elucidate the effect of using four mattress sutures in TT surgical outcomes.

In PLTR surgery, the smooth insertion of the cut edge of the upper tarsal portion into the pocket between the anterior and posterior lamella of the distal lid margin probably plays a major role in promoting eversion as well as improving the cosmetic appearance of the eyelid.

In addition, a regular and smooth incision on the posterior lamella probably would reduce granuloma formation.

Overall, surgical programmes should emphasise in their initial and subsequent on the job training that making adequate peripheral incisions and dissections, regular and smooth incisions, adequate and smooth tucking of the tarsus, and symmetric insertion and tension of mattress sutures are crucial in determining the outcome of surgery. Preoperative major trichiasis and old age are consistent predictors of postoperative TT in this and other studies.[4,5,40,154,159,160,164,166,167] In areas where both PLTR and BLTR surgeries are performed, PLTR surgery should be used to operate on major TT cases. In addition, more experienced and skilled surgeon in the programme should operate on cases above the age of 60 and those with major TT.

Finally, monitoring surgical services should be an integral part of all surgical programmes. This requires conducting frequent and regular supportive supervision and the active follow-up of patients on the next postoperative day and several months after their surgery to look at the results. There should be a system to identify and manage poor surgical outcomes such as postoperative TT, ECA and granuloma that could negatively impact patients and programmes. The consistent finding of such outcomes should alert the programme to the need to look carefully at the quality of the surgery being performed and address technical errors. TT surgeons with poor surgical outcomes should be identified and the reasons for the poor outcomes of their surgeries should be studied in-depth.

10.1.3. The Economic Case of Trachomatous Trichiasis

Our studies demonstrated that a strong association exists between long-term household poverty and TT. Although trachoma has been linked with poverty, there were no adequate data that quantitatively measured this association. The TT cases were from significantly poorer households than their non-trichiatic neighbourhood controls in all three economic measures employed in our study. TT cases were less likely to participate in productive activities, and more likely to report difficulty and needing assistance in performing productive activities than the controls. These results suggest a bidirectional association: long-term household poverty predisposing to TT and TT contributing to household poverty.

Long-term household poverty increases vulnerability of families to *Ct* infection. Poor families are more likely to live in conditions that are believed to transmit chlamydia infection. Various studies have shown that children with active infection were more likely to be from poorer households.[46,219,228] Poorer households are less likely to seek treatment and are probably more prone to long-term frequent re-infection and inflammation that would lead to scarring of the conjunctiva and trichiasis. The trichiasis in turn may result in loss of productivity from the disability caused by the pain, photophobia and visual impairment; which in turn results in loss of income that would exacerbate the pre-existing poverty.[237,238]

These data provide strong support for advocacy to secure resources for trachoma control. In addition to its health related benefits, spending money for TT treatment means spending to alleviate poverty in poor resource communities. Trachoma can be used as a proxy for inequality within communities and would help to target and evaluate health and poverty alleviation programs.

10.1.4. TT Surgery, Quality of Life and Functioning

In low-income settings the participation of all members of a household hugely contributes to household income or wealth. As discussed above, TT significantly reduces the individual's capacity to engage and execute productive and leisure activities, hence negatively impacting on household productivity and income. Prior to our study, the impact that TT surgery has on productivity has not been explored in detail. We found strong evidence that trichiasis surgery substantially improves the functional ability of TT cases to perform productive and leisure activities without difficulty and assistance, even just by reducing ocular pain and discomfort, independent of vision improvement. This increases the independence and productivity of the individual, which would have a considerable social return and reduce financial strains through increased contributions to the household income or wealth.

We have found strong evidence that TT substantially reduces vision and health related QoL, even without visual impairment indicating that the burden of TT goes beyond vision loss. We then, in a longitudinal study, examined if TT surgery improves QoL of TT patients. This found strong evidence that TT surgery dramatically improves vision and health related QoL of TT patients, even without visual improvement. This suggests that the effect of trichiasis surgery goes beyond preventing the risk of blindness and improves the overall wellbeing and health perception of affected individuals.

These data together support the unprecedented effort to scale-up TT surgical programmes and provide prompt surgical interventions for people suffering from TT, not only to reducing the risk of blindness but also to improve socioeconomic and wealth contribution of affected individuals and then to alleviate household poverty; and improve overall wellbeing of affected individuals. These data can be used to support advocacy in securing international and national funds and resources for TT surgery. Studies are needed to directly quantify the impact of TT surgery on productivity.

10.2. Future work

Currently, there is a large international effort to improve TT surgery productivity and quality. The work from this project as well as the evidences from the literature indicate that that the outcome of TT surgery can still be improved to the level that can give satisfactory results. Further studies are needed to explore ways of maximizing TT surgical quality and quantity in programmatic settings. Below is a list of studies that could be conducted to improve the surgical management of TT in trachoma endemic settings.

1) There is global interest to see the long-term outcome of the two surgical procedures compared in this project. In the short term, from the cohort of the trial participants, we would like to answer questions such as, what are the results of PLTR and BLTR surgical procedures 4 years after surgery? Do they give different results from what has been found at 1 year? What are the factors influencing long-term outcomes in PLTR and BLTR surgery. In addition, there is generally a thought that ECA particularly mild ECA, might get better or resolve through time. We would like to explore if this is the case from our cohort.

2) We would like to conduct further research to investigate if the outcome of the two surgical procedures would be different if BLTR practicing surgeons are retrained to do the surgery using the PLTR procedure.

3) It is clear that poor quality surgeries would result in surgical failure. Limited evidence suggests that immediate postoperative outcomes determine long-term surgical outcomes. On the other hand, there are assumptions that despite satisfactory immediate postoperative outcomes, long-term surgical outcomes such as recurrence and ECA are probably influenced by other factors that may occur during the wound healing process or at later stage. The relationship between the immediate post-operative appearance at the end of surgery and the development of recurrence or ECA is not understood. We do not know what proportion of surgeries considered to have a

"good immediate postoperative outcome" develop poor surgical outcomes such as recurrence or ECA at later stage and why? In addition, no studies have been conducted to measure the effect of immediate correction of poor surgical outcomes on long-term surgical outcomes. We would explore these in a trial.

4) Despite the inevitable increase in the number of cases of postoperative TT in recent years with the ongoing scale up of surgery, there is little information on how to manage postoperative TT in trachoma endemic settings. The current WHO guideline is to refer such patients to "the most experienced or skilled surgeon available". In remote trachoma control programmes this "experienced or skilled surgeon" is usually the IECW, or an ophthalmic nurse or, rarely an ophthalmologist that would mostly repeat the initial operation. Unpublished data show that repeat TT surgery by nurses using the same procedure used during the initial operation provided unsatisfactory results. In patients with postoperative TT it is likely that the eyelid would be relatively shortened or contracted in relation to the initial surgery. This might require slightly different surgical procedures to the commonly used surgical procedures to treat TT. In addition the relative effectiveness of repeat surgery to different approaches such as, epilation and electrolysis need to be thought about and investigated in a randomised controlled trial. There is a need to develop a guidance about which type of postoperative TT cases require surgery and what type of surgery; and which ones require a different approach, such as epilation.

5) There is greater awareness of the problem of ECA in areas where large volume community based TT surgical services are delivered. Patients often complain how the trichiasis surgery left their eyes disfigured; and is considered one of the factors deterring TT patients from accepting surgery. However, typical programmes do not have many staff skilled in handling such cases. In Amhara Region trachoma control programme, one of the oldest and most productive trachoma programmes worldwide, the guideline is to refer patients with ECA to an ophthalmologist. However, ophthalmologists often do not know how to manage these cases. The current management practice for ECA is repeating the same trichiasis surgery used to correct the trichiasis during the first surgery. As discussed in earlier sections, the tarsal advance variant procedures have been used to correct eyelid closure defects. However, these were not successful. Therefore, the type of surgical procedure to be used for the management of significant ECA is still unknown. There is a need to

identify or develop a relatively easy and practical surgical procedure to treat ECA for use in trachoma endemic settings.

6) There is a concern by some people that the newly growing lashes after epilation are more likely to be "stiff" and damaging to the cornea than the original trichiatic lashes. There is also an assumption among patients and some programme coordinators that epilation 'would make few trichiatic lashes grow in large numbers'. There is no evidence either to support or challenge these assumptions. Prospective cohort studies are needed to understand the nature (quality and quantity) of post epilation lashes and their visual significance.

7) We will conduct a programme evaluation on the role of supportive supervision in improving surgical productivity and quality.

8) No studies have been conducted to directly quantify the impact of TT surgery on productivity. We would like to quantitatively measure how much TT surgery improves productivity. We will measure the productively of TT patients using quantitative measures before TT surgery and then measure the change after surgery.

9) In the long term, we have a plan to build a comprehensive, not-for-profit, eye care and research institution in Amhara Region, Ethiopia; that will help alleviate the huge burden of avoidable blindness.

Appendices

Appendix I: Interventions for Trachoma Trichiasis (Review)

Interventions for trachoma trichiasis (Review)

Burton M, Habtamu E, Ho D, Gower EW

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[Intervention Review]

Interventions for trachoma trichiasis

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ABSTRACT

Background

Trachoma is the leading infectious cause of blindness. The World Health Organization (WHO) recommends eliminating trachomatous blindness through the SAFE strategy: Surgery for trichiasis, Antibiotic treatment, Facial cleanliness and Environmental hygiene. This is an update of a Cochrane review first published in 2003, and previously updated in 2006.

Objectives

To assess the effects of interventions for trachomatous trichiasis for people living in endemic settings.

Search methods

We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (2015, Issue 4), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to May 2015), EMBASE (January 1980 to May 2015), the ISRCTN registry (www.isrctn.com/editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 7 May 2015. We searched the reference lists of included studies to identify further potentially relevant studies. We also contacted authors for details of other relevant studies.

Selection criteria

We included randomised trials of any intervention intended to treat trachomatous trichiasis.

Data collection and analysis

Three review authors independently selected and assessed the trials, including the risk of bias. We contacted trial authors for missing data when necessary. Our primary outcome was post-operative trichiasis which was defined as any lash touching the globe at three months, one year or two years after surgery.

Main results

Thirteen studies met the inclusion criteria with 8586 participants. Most of the studies were conducted in sub-Saharan Africa. The majority of the studies were of a low or unclear risk of bias.

Five studies compared different surgical interventions. Most surgical interventions were performed by non-physician technicians. These trials suggest the most effective surgery is full-thickness incision of the tarsal plate and rotation of the terminal tarsal strip. Pooled data from two studies suggested that the bilamellar rotation was more effective than unilamellar rotation (OR 0.29, 95% CI 0.16 to 0.50). Use of a lid clamp reduced lid contour abnormalities (OR 0.65, 95% CI 0.44 to 0.98) and granuloma formation (OR 0.67, 95% CI 0.46 to 0.97). Absorbable sutures gave comparable outcomes to silk sutures (OR 0.90, 95% CI 0.68 to 1.20) and were associated with less frequent granuloma formation (OR 0.63, 95% CI 0.40 to 0.99). Epilation was less effective at preventing eyelashes from touching the globe than surgery for mild trichiasis, but had comparable results for vision and corneal change. Peri-operative azithromycin reduced post-operative trichiasis; however, the estimate of effect was imprecise and compatible with no effect or increased trichiasis (OR 0.85, 95% CI 0.63 to 1.14; 1954 eyes; 3 studies). Community-based surgery when compared to health centres increased uptake with comparable outcomes. Surgery performed by ophthalmologists and integrated eye care workers was comparable. Adverse events were typically infrequent or mild and included rare postoperative infections, eyelid contour abnormalities and conjunctival granulomas.

Authors' conclusions

No trials were designed to evaluate whether the interventions for trichiasis prevent blindness as an outcome; however, several found modest improvement in vision following intervention. Certain interventions have been shown to be more effective at eliminating trichiasis. Full-thickness incision of the tarsal plate and rotation of the lash-bearing lid margin was found to be the best technique and is preferably delivered in the community. Surgery may be carried out by an ophthalmologist or a trained ophthalmic assistant. Surgery performed with silk or absorbable sutures gave comparable results. Post-operative azithromycin was found to improve outcomes where overall recurrence was low.

PLAIN LANGUAGE SUMMARY

Interventions for trachomatous trichiasis

Review question

This review addressed the question: "Which interventions improve the results of the treatment for trichiasis (in-turned eyelashes) caused by trachoma?"

Background

Trachoma is the commonest infectious cause of blindness in the world. It is caused by a bacterium called *Chlamydia trachomatis*. This infection causes inflammation and scarring of the surface of the eye, which results in the eyelid turning in (entropion) so that the eyelashes touch the eyeball. This is known as trachomatous trichiasis. The lashes can scratch the corneal surface, leading directly or indirectly (from secondary infections) to corneal opacity. Surgery to correct the eyelid deformity is the main treatment for the late stages of the disease. Most cases of trachomatous trichiasis occur in sub-Saharan Africa. They are generally treated by nurses with limited surgical training. Unfortunately the results of the surgery can be quite variable, with frequent post-operative trichiasis reported. Therefore, we wanted to find out what types of surgery and other interventions give the best results in treating this condition.

Study characteristics

We identified 13 randomised controlled trials. They were all conducted in trachoma-endemic countries (mostly in sub-Saharan Africa) with surgical interventions carried out by non-physician surgeons. Five studies compared different surgical treatments. Three studies investigated whether azithromycin antibiotic treatment after surgery improves the results. One study compared different types of sutures. One study compared surgery to the pulling out of eyelashes (epilation). One study compared the outcomes of treatments provided in the community with hospital care. One study compared the results of surgery performed by eye doctors with those of non-specialist technicians. The evidence is current to May 2015. Most studies were funded by government research councils or charitable foundations.

Key results

These trials suggested that the most effective surgery requires full-thickness incision of the tarsal plate and rotation of the edge of the eyelid. The use of a surgical lid clamp improves eyelid contour outcomes and reduces granuloma formation. Silk and absorbable sutures give comparable results. The addition of azithromycin treatment at the time of surgery may reduce post-operative trichiasis under certain conditions. Epilation is less effective than surgery at treating trichiasis, but has comparable results for vision and corneal change two years after intervention. Community-based surgery was more convenient for patients by reducing the time and expense of travelling to a conventional hospital, and it did not increase the risk of complications or recurrence. Surgery performed by ophthalmologists and by integrated eye care workers were both similarly effective. Destroying the lash roots by freezing or electrical ablation appeared to have low success rates and the equipment required is costly and can be difficult to maintain.

Quality of the evidence

The quality of the evidence from these randomised controlled trials was variable. Most were of a high quality. However, several were relatively small in size and several had potential bias problems due to the method of randomisation and masking.

BACKGROUND

Description of the condition

Clinical Features

Trachoma is a form of chronic conjunctivitis caused by *Chlamydia trachomatis*. Following repeated infections, the upper tarsal conjunctiva becomes scarred. As the scar tissue contracts, it shortens the posterior lamella (inner surface) of the upper lid causing the eyelashes to turn in (entropion) and rub against the transparent cornea. This contact between one or more lashes and the surface of the eye is called trichiasis. Trichiasis due to trachoma has a wide spectrum of severity from a single lash touching the eye through to the entire upper lid being rolled in (Rajak 2011). It may result from misdirected or metaplastic eyelashes, in the absence of frank entropion (Rajak 2011). Corneal opacification and the resulting blindness probably develop primarily as a result of this trauma and secondary bacterial corneal infection.

Epidemiology

The most recent World Health Organization (WHO) estimates suggest that about 40 million people have active trachoma and about 8.2 million have trichiasis (Mariotti 2009). The signs of active trachoma are usually most frequently found in young children, with males and females equally affected. The scarring complications become evident in later life. Women are usually more frequently affected by trichiasis than men (West 1991). The rate at which the scarring complications of the disease progress varies, possibly reflecting variation in the pressure of *C. trachomatis* infection and immunogenetic predisposition of different populations (Hu 2013). Trachoma is most prevalent in hot, dry areas and is associated with poverty (Emerson 2000). The greatest burden of disease is in sub-Saharan Africa.

Description of the intervention

Trachoma control

The eradication of blinding trachoma is one of the objectives of the global Vision 2020 programme to eliminate avoidable blindness, led by the WHO and the International Agency for the Prevention of Blindness. In 1997 the WHO launched an initiative on trachoma control based on the 'SAFE' strategy. SAFE stands for Surgery for trichiasis, Antibiotics, Facial cleanliness, and Environmental improvement. Improved facial cleanliness and environmental hygiene are effective at reducing transmission by removing the conditions that promote spread of the disease. Antibiotics reduce the risk of disease transmission by treating the infectious agent. Surgery to correct the lid deformity is the only treatment that is likely to be beneficial in the late stages of the disease; however, once corneal opacification has occurred, management options are very limited. Cochrane reviews of the optimum antibiotic regimen for trachoma (Evans 2011), environmental sanitation (Rabiu 2012), and face-washing promotion (Ejere 2015), are published on the Cochrane Library.

Trichiasis treatment options

The primary aim of treatment for trichiasis is to prevent blindness due to trauma from the lashes abrading the cornea (Rajak 2012). Treatments may be divided into non-surgical treatments and surgical treatments:

Non-surgical treatments

- epilation (manual removal of eyelashes, usually with forceps);
- eyelid-taping (to force eyelashes back to correct position)

Surgical treatments

Surgical procedures for lash ablation or removal:

- electrolysis (fine needle used to pass electric current to base of lash follicle);
- cryotherapy (freezing treatment to the lash follicles)
- excision of lash-bearing tissue

A wide variety of surgical options are available for the treatment of upper lid entropion (Rajak 2012), and it is likely that certain operations are more successful than others. In trachoma-endemic countries the most commonly used procedures are:

- bilamellar tarsal rotation (BLTR): full-thickness incision through the eyelid, including the scarred tarsal plate, orbicularis oculi and the skin, fixation with everting sutures;

- posterior lamellar tarsal rotation (PLTR)/Trabut: incision through the scarred tarsal plate and conjunctiva only, leaving the skin and orbicularis oculi intact, fixation with everting sutures;

- tarsal advance and rotation: incision of the tarsal plate and rotation of the terminal portion. The upper part of the tarsus is separated from the anterior lamellar, advanced and fixed with sutures.

These techniques are illustrated in the WHO's publication - Trichiasis surgery for trachoma (WHO 2013).

How the intervention might work

The lash treatments directly remove or ablate the follicles. They do not correct any underlying anatomical abnormality such as entropion and are, therefore, generally not suitable if there is a significant degree of entropion. The lid rotation procedures correct the underlying entropion by an incision through the scarred tissue, outward turning of the lid and fixation with sutures. Generally, this will correct the trichiasis in most cases, although in more severe cases this might be insufficient. Post-operative trichiasis can occur either through inadequate surgery or progressive scarring disease.

Why it is important to do this review

Evidence from case series and randomised controlled trials suggests that upper lid surgery can be successful at abolishing trichiasis; however, typically 20% to 40% of eyelids suffer from post-operative trichiasis by one year (Bog 1993; Bowman 2000; Burton 2005b; Rajak 2011b; Reacher 1990; Reacher 1992; Ward 2005; West 2005); and up to 60% at three years (Khandekar 2001). Therefore, it is important to understand the determinants of a good treatment outcome and identify strategies that lead to this.
Risk factors associated with post-operative trichiasis include the severity of pre-operative trichiasis (Alemayehu 2004; Burton 2005a; Rajak 2013); chlamydial infection (Zhang 2004); inflammation of the tarsal conjunctiva (Burton 2005a; Burton 2005b; Ward 2005); bacterial infection (Burton 2005a); and left eyes (Merbs 2005; West 2005).
The choice of treatment will depend on factors such as available resources and expertise, location (opportunity for follow up) and how advanced the disease is. The WHO strategy for the control of blinding trachoma calls for lid surgery to be delivered by ophthalmic assistants as well as ophthalmologists (Habtamu 2011), because the numbers of ophthalmologists are insufficient to provide the service. Ophthalmic assistants are usually taught to perform only one type of operation so it is important to ensure that the operation they use is known to be effective.
Although surgery generally produces good results, in many settings only a minority of patients with trichiasis will attend for surgery (Bowman 2002; Courtright 1994; West 1994). Delivery of surgery in the community or non-surgical management of trichiasis may be more acceptable than surgery in a conventional hospital setting (Bowman 2000; Graz 1999; Rajak 2011a).

OBJECTIVES

To assess the effects of interventions for trachomatous trichiasis for people living in endemic settings.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials of interventions for trachomatous trichiasis. The unit of randomisation was individuals or clusters, depending on the design of the study.

Types of participants

Participants in the trials were people with trachomatous trichiasis, defined as one or more eye lashes touching the globe when looking straight ahead.

Types of interventions

We included trials in which any intervention intended to prevent corneal opacification from prolonged lash-globe contact was compared to another intervention or to no treatment. Surgical interventions were procedures to correct entropion or ablate the lash roots and non-surgical interventions were taping of the lid margin or manual removal of the eyelashes (epilation). We included trials that compared:

- different surgical or non-surgical interventions;
- medication to reduce post-operative trichiasis;
- any intervention delivered in a hospital setting to the same intervention in a community setting;
- the same intervention delivered by different types of health care professionals.

Types of outcome measures

Primary outcomes

The primary outcome measure for this review was post-operative trichiasis. This dichotomous outcome was defined as any lash touching the globe in the primary position. The critical points for follow-up were three months, one year, and two years after treatment.

Secondary outcomes

Secondary measures were:

Visual acuity change

Measured by Snellen or logMAR visual acuity charts at one year and two years after treatment.

Corneal opacification change

Measured by clinical examination or photographic comparisons at one year and two years after treatment.

Acceptance of treatment

As measured by uptake/attendance for treatment.

Adverse effects

Any adverse effects, whether minor or severe, were recorded.

Quality of life

Any qualitative measures of discomfort/patient satisfaction were noted.

Economic evaluation

Where any cost data for interventions were available this was noted and commented on in the context of cost-effectiveness. No formal cost-effectiveness evaluation was planned.

Search methods for identification of studies

Electronic searches

We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (2015, Issue 4), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to May 2015), EMBASE (January 1980 to May 2015), the ISRCTN registry (www.isrctn.com/editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 7 May 2015.
See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), ISRCTN (Appendix 4), ClinicalTrials.gov (Appendix 5) and the ICTRP (Appendix 6).

Searching other resources

We contacted experts and researchers in the field to ask them for details of published, unpublished or ongoing trials. We searched the reference lists of relevant trials.

Data collection and analysis

Selection of studies

Two review authors assessed the titles and abstracts resulting from the searches and selected all titles that referred to treatment for trachomatous trichiasis. Copies of possibly relevant trials were obtained and independently assessed by three review authors according to the 'Criteria for considering studies for this review'. Trials meeting these criteria were also assessed for quality.

Data extraction and management

We recorded data from included studies in a table under the following headings:

- methods - including randomisation, intention-to-treat analysis;

- participants - including cluster or individual, country, number; losses to follow up;
- interventions - including types of surgery or other intervention, setting of intervention (community or clinic);
- outcomes - including definitions of success or failure, visual acuity change, adverse effects.

Authors independently extracted outcome data. One author entered data into RevMan 5, which was checked by a second author.

Assessment of risk of bias in included studies

Three review authors assessed trial quality according to methods set out in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) using the Cochrane Eyes and Vision Group Review Development Guidelines. In particular, random sequence generation, allocation concealment, performance bias, detection bias (masking of outcome graders to initial treatment), attrition bias (adequacy of follow up) and reporting bias were assessed. Risk of bias was graded as "Low Risk", "High Risk" and "Unclear Risk", according to the guidelines in Section 8 of the Handbook. We resolved disagreements between the authors by discussion.

Measures of treatment effect

The treatment effects were measured by calculating the odds ratio and 95% confidence interval for these.

Unit of analysis issues

The unit of analysis was generally the individual patient, with the exception of one cluster randomised trial.

Dealing with missing data

Studies were assessed for missing data and whether missing data were "missing at random". In one instance, data were found to be systematically excluded from the analysis of the primary outcome in the original report (recurrence occurring by three months after surgery). As sufficient information was presented in the report it was possible to reintroduce these primary outcome events here.

Assessment of heterogeneity

Heterogeneity between studies was assessed for those investigating the use of post-operative antibiotic. Heterogeneity was considered in several categories: clinical, methodological and statistical.

Assessment of reporting biases

The studies were assessed in terms of the completeness of data presented.

Data synthesis

The interventions tested were varied and there was considerable heterogeneity. We present a descriptive summary of the results rather than a single summary statistic. Where the unit of randomisation was a cluster rather than an individual, data were analysed by cluster. The principal outcome measure was post-operative trichiasis, which was defined as any lash touching the globe in the primary position. Odds ratios were calculated for the different interventions. Visual acuity data were presented as dichotomous data-statistically significant improvement or no improvement from pre-to post-intervention. Data on adverse effects and acceptance of surgery were also presented as dichotomous data. The exception to this was the three studies examining the effect of azithromycin on the outcome of surgery. A meta-analysis was performed for the dichotomous outcome of post-operative trichiasis using a Mantel-Haenszel, random-effects model. For trials where there were more than two arms these were considered separately in relation to the reference intervention where appropriate, such as different surgical options. However, if two arms utilised the same intervention, they were combined.

Subgroup analysis and investigation of heterogeneity

No sub-group analysis was performed.

Sensitivity analysis

No sensitivity analysis was performed.

RESULTS

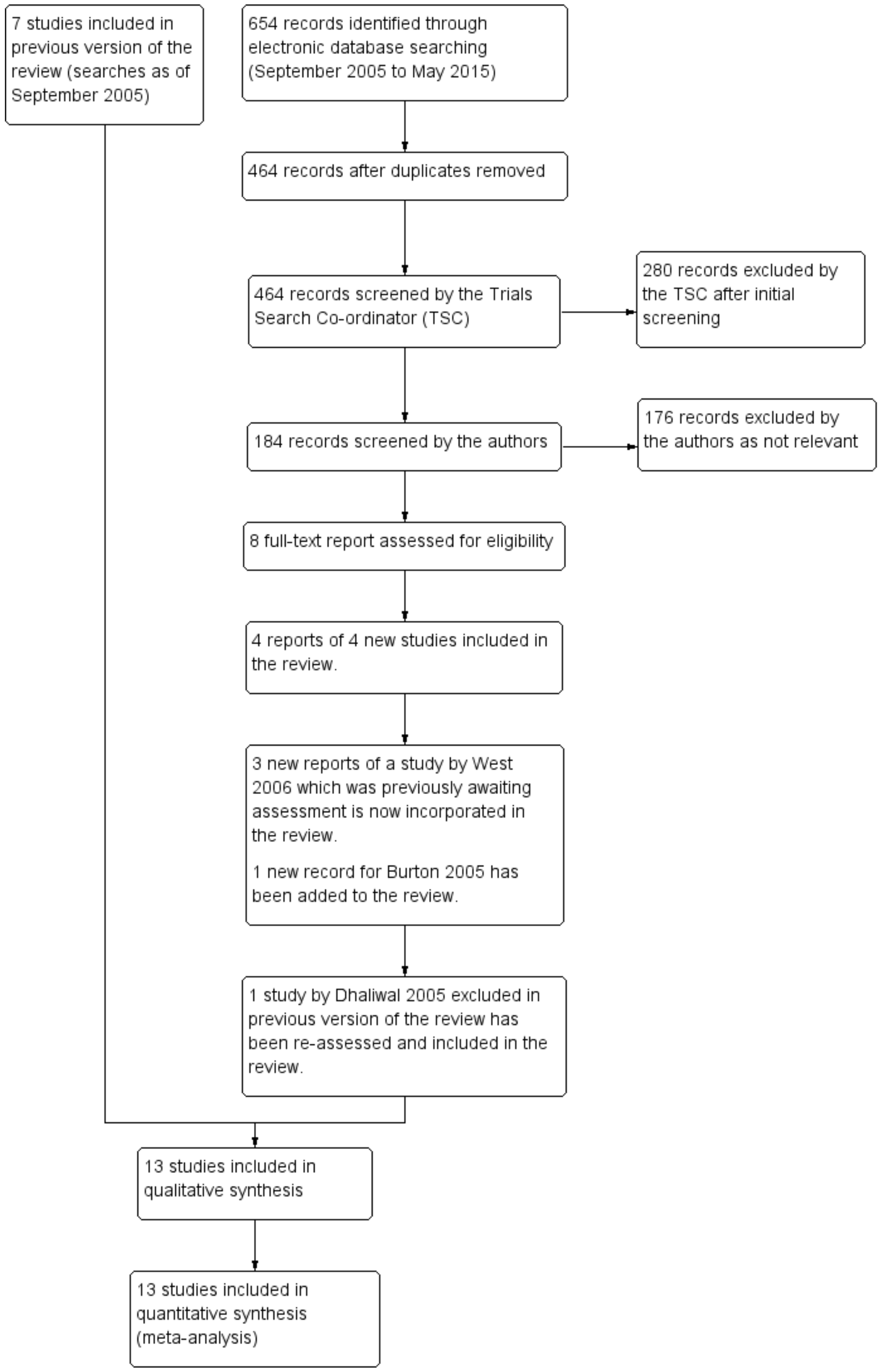
Description of studies

Results of the search

The search of electronic databases revealed a total of 656 reports. We retrieved nine papers for further assessment. All of these were randomised trials of interventions for trachoma trichiasis (Adamu 2002; Alemayehu 2004; Bowman 2000; Burton 2005a; Dhaliwal 2005; Graz 1999; Reacher 1990; Reacher 1992; West 2006).
An update search run in May 2015 identified 654 new records (Figure 1). The Trials Search Co-ordinator removed 190 duplicate records, screened 464 records and removed 280 references that were not relevant to the scope of the review. We screened the remaining 184 references and discarded 176 reports as not relevant. We obtained eight full-text reports of trials for assessment. We included four reports of four new studies (Gower 2013; Rajak 2011a; Rajak 2011b; Zhang 2006); and added a new report to

Burton 2005a. Previously a study by West 2006 was awaiting assessment: this study has now been included and three new reports of the trial have been added to the review. In the previous version of this review Dhaliwal 2005 was excluded; however we have reassessed this study and have now included it in the review.

Figure 1. Study flow diagram.



Included studies

In some of the included studies, participants with bilateral disease were randomised by eye rather than by individual participant (details below); these studies were included on the basis that the majority of participants were randomised individually. Details of the included studies can be found in the 'Characteristics of included studies' table.

For ease of interpretation, studies have been grouped according to the aspect of trichiasis management they address:

- Surgical technique: Adamu 2002, Dhaliwal 2005, Gower 2013, Reacher 1990 and Reacher 1992 compared different surgical interventions.
- Epilation: Rajak 2011a compared epilation to surgery
- Lid taping: Graz 1999 examined lid taping versus epilation for managing trichiasis.
- Antibiotic treatment: Burton 2005a, West 2006 and Zhang 2006 examined whether peri-operative azithromycin treatment reduced post-operative trichiasis versus another or no treatment.
- Alternative suture materials: Rajak 2011b compared absorbable to non-absorbable sutures.
- Surgery setting: Bowman 2000 investigated alternative settings for conducting surgery (health centre versus village).
- Personnel performing surgery: Alemayehu 2004 compared the outcome of surgery performed by different types of health care personnel.

Types of interventions

Surgical technique

Five studies compared different surgical interventions for trichiasis: Adamu 2002; Dhaliwal 2005; Gower 2013; Reacher 1990 and Reacher 1992.

Reacher 1990 randomly allocated individuals with major trichiasis (six or more lashes touching) to one of five operations: (1) bilamellar tarsal rotation; (2) tarsal advance and rotation; (3) eversion splinting; (4) tarsal advance; or (5) tarsal grooving. Minor trichiasis cases were excluded. Eyes with defective lid closure were also excluded from the study and all received a tarsal advance procedure. Surgery was performed by one of three surgeons.

In the Reacher 1992 study participants were again grouped (stratified) according to severity and then randomly allocated:

- Minor trichiasis - allocated to (1) electrolysis; (2) cryotherapy; or (3) bilamellar tarsal rotation.
- Major trichiasis - allocation to either (1) bilamellar tarsal rotation; or (2) tarsal advance and rotation.
- Defective lid closure - allocation to (1) tarsal advance and rotation; or (2) tarsal advance with buccal mucosal membrane graft.

Adamu 2002 compared bilamellar tarsal rotation and posterior lamellar tarsal rotation in patients with minor trichiasis, major trichiasis or defective lid closure with trichiasis. Surgery was performed by second-year ophthalmic residents according to standardised procedures.

Dhaliwal 2005 compared three operations: (1) terminal tarsal rotation (a variant of the posterior tarsal rotation); (2) tarsal advance and rotation; and (3) tarsal grooving. One surgeon performed all of the procedures.

Gower 2013 compared standard bilamellar tarsal rotation surgery to the same procedure performed using an eyelid clamp. Surgery was performed by 18 surgical technicians, who were trained and certified to perform only one form of the operation. Patients were randomly allocated to the surgeon.

Epilation

Rajak 2011ainvestigated whether epilation was non-inferior to posterior lamellar rotation surgery for minor trichiasis. Patients with minor trichiasis were randomised to either immediate surgery or repeated epilation with manufactured epilating forceps.

Lid taping

Graz 1999 compared manual removal of eyelashes (epilation) with the use of a double-sided sticking plaster to force eyelashes away from contact with the globe: both interventions were undertaken prior to lid surgery. There were three groups: (1) epilation alone; (2) sticking plaster alone; and (3) sticking plaster for eight weeks then crossover to epilation.

Antibiotic treatment

Three separate trials have examined whether post-operative oral azithromycin can reduce post-operative trichiasis in three different countries: (1) The Gambia (Burton 2005a; (2) Ethiopia (West 2006); and (3) Nepal (Zhang 2006).

In the Gambian study all participants underwent posterior lamellar tarsal rotation and were prescribed tetracycline eye ointment twice daily for two weeks (Burton 2005a). Those randomised to the intervention group received a 1 g dose of azithromycin at the time of surgery; adults and children in these households were also given a single dose of azithromycin (adults 1 g and children 20 mg/kg) to reduce the risk of re-infection. This medication was re-administered at six months.

In the Ethiopian study, participants all underwent bilamellar tarsal rotation surgery (West 2006). They were then randomised to one of three intervention arms: (1) 1g dose of azithromycin for the patient alone; (2) 1 g dose of azithromycin for the patient and single-dose azithromycin treatment for household members; (3) topical tetracycline (twice per day for six weeks).
In the Nepal study, participants all received bilamellar tarsal rotation surgery (Zhang 2006). At the end of surgery they were alternately given either azithromycin or a placebo.

Alternative suture materials

Rajak 2011b compared posterior lamellar rotation performed with silk sutures to the same procedure performed with absorbable polyglactin-910 sutures.

Surgery setting

Bowman 2000 compared providing surgery in the participants' own village to surgery provided at the nearest health centre. Posterior lamellar tarsal rotation surgery was performed on all participants by one of five trained nurses or an ophthalmic assistant.

Personnel performing surgery

Alemayehu 2004 compared post-operative trichiasis rates following surgery by ophthalmologists and non-ophthalmologist integrated eye care workers (IECW) in Ethiopia. Subjects with trachomatous trichiasis (TT) were randomised to surgery by either an ophthalmologist or an IECW. Both groups used the bilamellar tarsal rotation procedure.

Types of participants

Surgical technique

Participants in the Reacher 1990 study were 165 adult Omanis with TT. Participants were grouped according to severity: minor trichiasis, major trichiasis or defective lid closure as defined above. Only those with major trichiasis were eligible for randomisation. Participants who had undergone previous treatment were included.
Reacher 1992 recruited 367 individuals diagnosed with TT by the Oman Prevention of Blindness Program. Trichiasis was graded as for the Reacher 1990 paper, and participants were grouped as minor trichiasis, major trichiasis or defective lid closure. Participants who had undergone previous treatment were included.
In the study by Adamu 2002, participants were 153 consecutive patients with TT presenting at a teaching hospital in Addis Ababa. Eight children (< 15 years) were included. All participants were graded pre-operatively as having minor trichiasis, major trichiasis or defective lid closure. Previously operated eyes were excluded from the study.
Dhaliwal 2005 recruited 77 consecutive patients (90 eyes) in an eye clinic in India.
In Gower 2013, which was conducted in Tanzania, 1917 participants were enrolled through screening campaigns. Participants were at least 18 years old, had previously unoperated trichiasis and did not plan to move within 2 years. All degrees of trichiasis severity were eligible.

Epilation

Rajak 2011awas conducted in Ethiopia. Only adults (> 18 years) with minor trichiasis were eligible. 1300 individuals were identified and recruited through community outreach campaigns; 66% were female. At baseline by chance there was slightly more corneal disease in the epilation arm.

Lid taping

Graz 1999randomised a total of 57 consecutive adult patients attending a hospital clinic: n = 21 randomised to sticking tape; n = 18 to epilation; n = 18 to sticking tape followed by epilation. Baseline characteristics were comparable except that five lids (number of participants not stated) in the sticking tape group had trichiasis due to a cause other than trachoma.

Antibiotic treatment

In Burton 2005a 451 participants with major trichiasis were enrolled; 70% were female. Baseline characteristics were similar between the two randomisation groups for age, ethnicity and severity of trichiasis.
In West 2006 1452 individuals with any degree of TT were recruited; 77% were female. The three arms were balanced in terms of baseline characteristics.
Zhang 2006 randomised 109 individuals with TT (both major and minor trichiasis); 73% were female. The baseline characteristics of the two arms were comparable.

Alternative Suture Materials

Rajak 2011b recruited 1300 adults with major TT; 78% were female. They were identified through community outreach campaigns.

Surgery setting

Bowman 2000 selected five districts in The Gambia that were known to have high levels of trichiasis and where village-based surgery previously had not been available. The districts were subdivided to form eight pairs of village clusters. Within each pair, one cluster of villages was randomised to village-based surgery and the other cluster of villages to health centre-based surgery. Screening was undertaken by trained ophthalmic nurses. Only participants with major trichiasis (at least five in-turned lashes) were eligible for inclusion, in accordance with the Gambian national guidelines for surgery. Participants ineligible for village-based surgery for medical reasons were excluded from the trial and referred for health centre-based surgery. In all 158 individuals with major trichiasis were recruited.

Personnel performing surgery

Alemayehu 2004 recruited 982 people with TT; 77% were female and 3% were children. Baseline characteristics of the randomised groups are not described.

Types of outcomes

In all but one of the studies a successful outcome included the absence of post-operative trichiasis; this is usually defined as no lashes touching the eye. Specific outcomes for each study are described below.

Surgical technique

In the Reacher 1990 study a successful outcome was defined as no post-operative trichiasis (no lashes in contact with the globe after surgery) and complete gentle closure of eyelids. There was no pre-defined outcome point, and in the group with major trichiasis follow-up varied from 5 to 11 months.

Reacher 1992 defined a successful surgical outcome as no post-operative trichiasis, no further epilation/surgery during follow up period, complete lid closure, no over-correction of lid margin, acceptable appearance to patient and examiner, and no onset of phthisis. They also examined the effect on visual acuity and the complication rate. Follow-up points were not defined in the methodology, but occurred (on average) at 9 and 21 months.

Adamu 2002 defined success as no eyelash-eyeball contact, complete lid closure and no over- or under-correction. Recurrence was defined as eyelash-eyeball contact in all positions of gaze or inward rotation of the lid margin. Visual acuity was measured pre- and post-operatively. Final follow up was planned at three months.

Dhaliwal 2005 used several outcome measures at six months: trichiasis and/or entropion recurrence, palpebral aperture, an acceptable cosmetic appearance.

In Gower 2013, the primary outcome was the presence of one or more of the following unfavourable outcomes: post-operative trichiasis; eyelid contour abnormality; or granuloma formation. Participants were re-examined at six weeks, 12 months and 24 months. Both eyes in bilateral cases were included in the analysis, with an appropriate adjustment.

Epilation

In Rajak 2011a, the primary outcome measure was "failure" which was defined as either (1) five or more eyelashes touching the globe; or (2) a history of surgery performed in the trial eye at any point during the two-year follow-up period (in the case of the surgical arm this would be repeat surgery). Participants were re-examined every six months for two years.

Lid taping

Graz 1999 collected data at 1, 4 and 12 weeks and recorded recurrence of trichiasis, visual acuity, patient discomfort and any adverse events.

Antibiotic treatment

Outcomes in the Burton 2005a study were assessed at 6 and 12 months post-operatively. The primary outcome was post-operative trichiasis. Secondary outcomes included visual acuity and patient perception of improvement by asking whether vision and pain was 'worse', 'same' or 'better'.

In West 2006 the primary outcome was post-operative trichiasis. This was assessed at 2 weeks, 6 weeks, 6 months, and 12 months. Patients were examined again at 2 and 3 years.

Zhang 2006 evaluated three outcomes: post-operative trichiasis; chlamydial infection; and active trachoma. Participants were re-examined at 3, 6 and 12 months post-operatively. If the participant developed "surgical failure", which was defined as five or more lashes touching the eye by three months, they were excluded from the analysis.

Alternative Suture Materials

Rajak 2011b The primary outcome measure was the proportion of those individuals seen at the 12-month follow-up who were found to have either (1) post-operative trichiasis; or (2) a history of repeat TT surgery during the first year. Participants were re-examined every six months for two years.

Surgery setting

There were three main outcomes in the Bowman 2000 study: (1) uptake of treatment in the local village compared to the health centre; (2) post-operative trichiasis); (3) complication rate. Other parameters measured included time taken by the patient to travel to the operating room and cost implications associated with presenting for surgery.

Personnel performing surgery

The first follow-up in the Alemayehu 2004 study was at seven days post-operatively: those with post-operative trichiasis at this assessment were deemed surgical failures and were excluded from the primary analysis; the main outcome was post-operative trichiasis rate at three and six months. Those with post-operative trichiasis at three months were excluded from the six-month assessment. Analysis was by randomised group and also by presenting severity.

Risk of bias in included studies

There are potential biases in several of the studies. These are considered under the following headings: allocation, blinding, incomplete data, and selective reporting. See Figure 2; Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

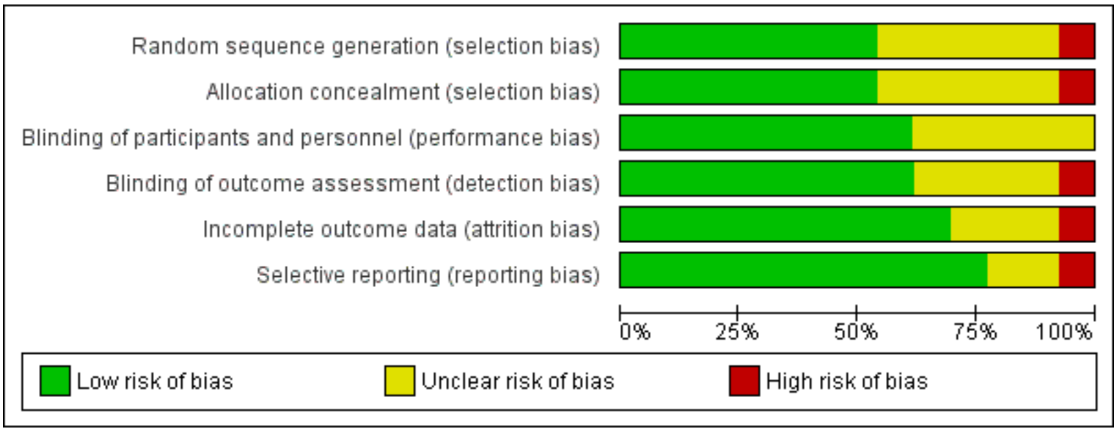
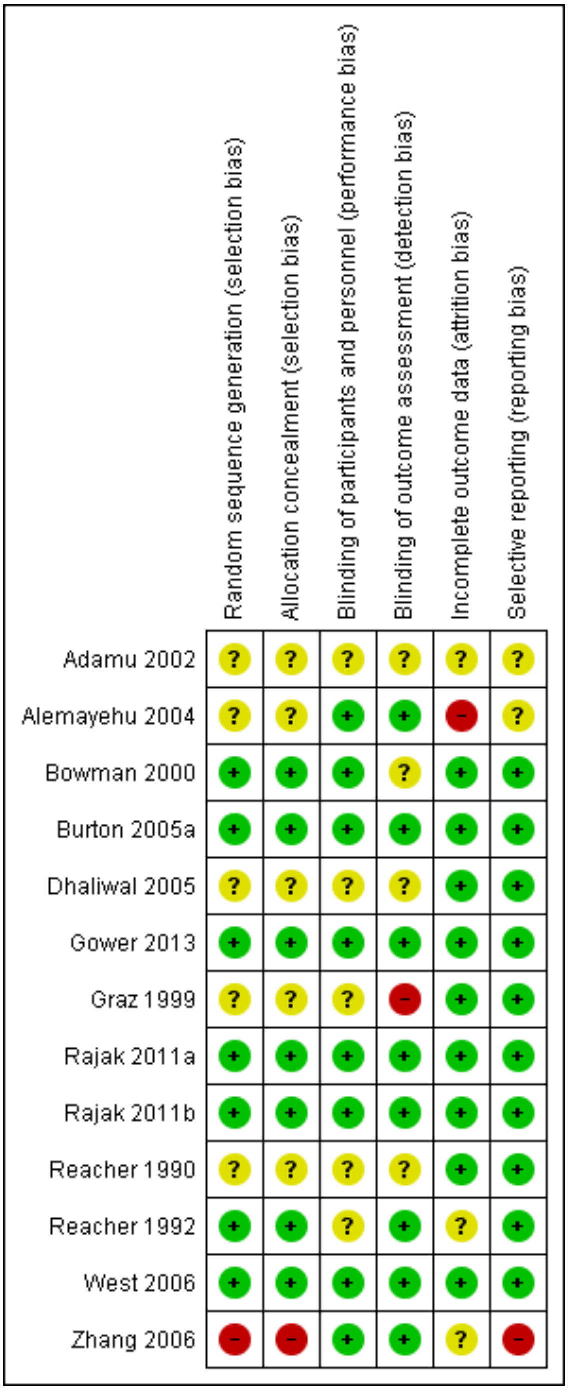


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Surgical technique

Adamu 2002 used an unspecified 'Lottery method' for randomisation. In bilateral cases the left eye always received the opposite treatment to that randomly allocated to the right eye, with no analytic adjustment for bilateral cases reported. The risk of bias is unclear given the limited details reported. In Gower 2013 randomisation assignments were created using permuted block sizes of 6 to 12 and placed in opaque envelopes; hence, the risk of bias is expected to be low. Reacher 1990 randomly allocated procedures using random number tables. Limited information is provided on the process and no details are provided on concealment; thus, the risk of bias is unclear. In the Reacher 1992 study, participants were randomly allocated using a computer-generated sequence; assignments were concealed in opaque envelopes. Risk of bias is expected to be low. Dhaliwal 2005 randomised the study eye by a computer-generated sequence. However, if a second eye was operated one of the other two options was used. The details are limited and, therefore, the risk of allocation bias is unclear.

Epilation

In Rajak 2011a participants were allocated to arm by a computer-generated randomisation sequence and assignments were kept in sealed, opaque envelopes, leading to a low risk of bias.

Lid Taping

Graz 1999 provide no description of the randomisation process.

Antibiotic treatment

In Burton 2005a separate randomisation sequences were generated for each surgeon using random number tables and blocked in groups of four, and assignments were kept in sequential sealed envelopes, leading to a low risk of allocation bias. In West 2006, participants were randomly assigned to one of three intervention arms using a computer-generated sequence with a variable block size, and assignments were kept in opaque containers until needed, leading to a low risk of bias. In Zhang 2006 participants all received bilamellar tarsal rotation surgery, and at the end of surgery they were alternately given either azithromycin or a placebo. This randomisation method makes the next assignment predictable, and hence makes the risk of allocation bias high.

Alternative Suture Materials

In Rajak 2011b the risk of allocation bias is expected to be low since people were allocated to arm by a computer-generated randomisation sequence and assignments were maintained in opaque envelopes.

Surgery setting

In Bowman 2000, a cluster randomised trial, the communities were paired and randomly allocated before the numbers of TT patients was known, so risk of allocation bias low.

Personnel performing surgery

Alemayehu 2004 do not provide any details of the randomisation or concealment methods employed; hence, risk of bias is unknown.

Blinding

Surgical technique

Adamu 2002 provides no description of methods to mask either the participants or those performing the follow-up examinations. In Gower 2013 randomisation assignments were placed in opaque envelopes and stored in a locked office until distribution and outcomes were assessed by a masked examiner. Reacher 1990 provides no information on the concealment of treatment allocation sequences. The follow-up examinations were by a single observer, but it is unclear if he was masked to the allocation. In Reacher 1992 the allocation sequence was concealed in opaque envelopes. Follow-up examinations were performed by a single masked observer. Dhaliwal 2005 provide no details about masking of the allocation prior to administration or during follow-up; it is unclear if the observations were made by the same clinician who performed surgery or by a separate clinician. Therefore the risk of bias is unclear.

Epilation

In Rajak 2011a the randomisation sequence was concealed in opaque envelopes. Observers were independent of, and masked to, the allocation.

Lid taping

In Graz 1999 masking of the observers was not possible.

Antibiotic treatment

In Burton 2005a allocation was contained in opaque sequentially-numbered envelopes and administered immediately following surgery by a nurse not involved in surgery or follow-up assessment. Pre-operative assessments and the 12-month follow-up assessments were made by the same observer. Assessments at six months were by a different observer. Both observers were masked to treatment allocation. Surgery was performed prior to the randomisation. In West 2006 the random treatment allocation was concealed in sequential opaque envelopes. In Zhang 2006 participants and observers were masked to whether they had received azithromycin or a placebo; however, this was on an alternating basis, rather than random allocation.

Alternative suture materials

In Rajak 2011b the randomisation sequence was concealed in opaque envelopes. Observers were independent of, and masked to, the allocation.

Surgery setting

In Bowman 2000 it would have been impossible to mask the patients or personnel to the location of surgery.

Personnel performing surgery

In Alemayehu 2004 the patients and the surgeons were not masked to the allocation. The follow-up observations were made by ophthalmologists masked to the allocation.

Incomplete outcome data

Surgical technique

The studies by Adamu 2002, Gower 2013, Dhaliwal 2005, Reacher 1990 and Reacher 1992 all present a complete data set with high rates of follow-up.

Epilation

Rajak 2011a presents a complete data set with high rates of follow-up.

Lid taping

Graz 1999 presents a complete data set with high rates of follow-up.

Antibiotic treatment

Burton 2005a presents a complete data set with high follow-up. A geographically defined sub-set of the original trial subjects was followed up to 4 years, with 94% follow-up of those alive at 4 years. West 2006 presents a complete data set with high follow-up. Similarly Zhang 2006 reports a complete data set with high follow-up rate.

Alternative Suture Materials

Rajak 2011b presents a complete data set with high rates of follow-up.

Surgery setting

Bowman 2000 presents complete outcome data.

Personnel performing surgery

Alemayehu 2004 had moderate loss to follow-up. No comparative data on those lost to follow-up are provided to determine risk of attrition bias.

Selective reporting

Surgical technique

Adamu 2002 provides limited information of their analytical protocol; therefore, risk of bias is unclear. The studies by Gower 2013, Reacher 1990 and Reacher 1992 all report a clear analytical approach which was followed in the results.

Epilation

The protocol for Rajak 2011a is published online and was followed.

Lid taping

Graz 1999 reports a clear analytical approach which was followed in the results.

Antibiotic treatment

Burton 2005a reports a clear analytical approach which was followed in the results. The protocol for West 2006 is published separately. Zhang 2006 excluded "surgical failures" from the analysis, defined as five or more lashes touching the globe at 3 months.

Alternative suture materials

The protocol for Rajak 2011b is published online and was followed.

Surgery setting

Bowman 2000 reports a clear analytical approach.

Personnel performing surgery

Alemayehu 2004 provides limited information on the analytical protocol; however, all participants seen at follow-up were included in the analyses.

Other potential sources of bias

None identified.

Effects of interventions

Surgical interventions

1. Bilamellar tarsal rotation surgery compared to tarsal advance and rotation

Two studies reported this comparison. In Reacher 1990 the mean months of follow-up per group ranged from 7.4 to 8.8 months (total range 5 to 11 months); in Reacher 1992 this was reported at 9 and 21 months after surgery.

1.1 Post-operative trichiasis

Eyes receiving bilamellar tarsal rotation surgery had lower odds of post-operative trichiasis compared to eyes receiving tarsal advance and rotation (OR 0.29, 95% CI 0.16 to 0.50, 260 eyes, $I^2 = 0\%$) (Analysis 1.1).

1.2 Visual acuity change

Visual acuity was not reported in Reacher 1990.
In Reacher 1992 eyes receiving surgery for major trichiasis on average had half a line improvement in Snellen acuity ($P < 0.001$) but the difference between the intervention groups (if any) was not clearly reported.

1.3 Corneal opacification change

Not reported.

1.4 Acceptance of treatment

This was not reported in Reacher 1990.
In Reacher 1992 38 people refused their random allocation but it was not reported which groups they were allocated to.

1.5 Adverse effects

Bilamellar tarsal rotation surgery was associated with more overcorrection of the entropion but the estimate was imprecise with very wide confidence intervals compatible with no effect, or more overcorrection in the tarsal advance group (OR 2.57, 95% CI 0.28 to 23.25, 312 eyes, $I^2 = 0\%$) (Analysis 1.2). There were only 3 cases of overcorrection in the two trials but they were all in the bilamellar group.
Defective lid closure was also more common in the bilamellar group but again occurred rarely and the estimate of effect was very imprecise (OR 1.90, 95% CI 0.29 to 12.37, 312 eyes, $I^2 = 0\%$). (Analysis 1.3).

1.6 Quality of life

Not reported.

2. Bilamellar tarsal rotation compared to techniques that do not create a full-thickness incision of the tarsal plate and complete rotation of the lash-bearing tissue

Only one study reported these comparisons (Reacher 1990). The mean months of follow-up per group ranged from 7.4 to 8.8 months (total range 5 to 11 months)

2.1 Post-operative trichiasis

Bilamellar tarsal rotation was more effective than techniques that do not create a full-thickness incision of the tarsal plate and complete rotation of the lash-bearing tissue such as tarsal grooving and eversion splinting, and a non-significant trend in the comparison with the tarsal advance procedure (Table 1).
None of the other review outcomes were reported.

3. Bilamellar tarsal rotation surgery compared to posterior lamellar tarsal rotation

One study reported this comparison (Adamu 2002). 256 upper eyelids of 153 people with trichiasis were randomly allocated to bilamellar tarsal rotation (n = 124) or posterior lamellar tarsal rotation (n = 132) and followed up to 3 months.

3.1 Post-operative trichiasis

After three months there was less post-operative trichiasis in the bilamellar tarsal rotation group but the confidence intervals were wide and compatible with no effect, or more trichiasis (Table 2).

3.2 Visual acuity change

The authors stated that there was an improvement in vision after surgery but the data were not reported and it was of borderline statistical significance (P = 0.0515).

3.3 Corneal opacification change

Not reported.

3.4 Acceptance of treatment

Not reported.

3.5 Adverse events

Lid-notching and pyogenic granuloma were more common in the bilamellar than the posterior lamellar tarsal rotation operations (Chi² 9.54, P = 0.002) but no data were reported.

3.6 Quality of life

Not reported.

4. Terminal tarsal rotation compared to tarsal advance and rotation and tarsal grooving

One study reported these comparisons (Dhaliwal 2005). The study randomised 77 participants (90 eyes); all 77 participants had six-month follow-up data. Pre-operatively entropion was found to be moderate in 65 eyes and severe in 25 eyes (although these terms were not defined). No eyes had defective lid closure. Bilateral TT was present in 13 people.

4.1 Post-operative trichiasis

After six months there was no significant difference in the rate of post-operative trichiasis between the three procedures; however, the sample size in each group was insufficient to detect a statistically significant difference at a meaningful level.

4.2 Visual acuity change

Not reported.

4.3 Corneal opacification change

Not reported.

4.4 Acceptance of treatment

Not reported.

4.5 Adverse effects

Lid-notching: (1) terminal tarsal rotation 9 (30%); (2) tarsal advance and rotation 6 (20%); and (3) tarsal grooving 10 (33%)
Pyogenic granuloma: (1) terminal tarsal rotation 3 (10%); (2) tarsal advance and rotation 5 (17%); and (3) tarsal grooving 3 (10%)

4.6 Quality of life

There was no difference between the three groups in terms of the proportion of patients who were satisfied with the cosmetic appearance following surgery: (1) terminal tarsal rotation 28 (93%); (2) tarsal advance and rotation 27 (90%); and (3) tarsal grooving 27 (90%).

5. Bilamellar tarsal rotation with a clamp compared to bilamellar tarsal rotation without a clamp

One study (Gower 2013) reported this comparison. The study randomised 1917 participants (3345 eyes) and followed up to two years.

5.1 Post-operative trichiasis

There was more post-operative trichiasis in the clamp surgery group at two years. After adjustment for correlation between eyes and for surgeon, age, sex and baseline TT severity the adjusted OR was 1.36, 95% CI 0.96 to 1.93. The lower confidence interval includes, but is fairly close to 1 (no effect).

5.2 Visual acuity change

Not reported.

5.3 Corneal opacification change

Not reported.

5.4 Acceptance of treatment

Not reported.

5.5 Adverse effects

Eyelid contour abnormalities were less frequent in the clamp surgery group (adjusted OR 0.65, 95% CI 0.44 to 0.98, 3343 eyes).
Granulomas were less frequent in the clamp surgery group (adjusted OR 0.67, 95% CI 0.46 to 0.97, 3343 eyes).

5.6 Quality of life

Not reported.

6. Bilamellar tarsal rotation surgery compared to cryotherapy or electrolysis

6.1 Post-operative trichiasis

Post-operative trichiasis in 166 eyes with minor trichiasis was reported by Reacher 1992; follow-up ranged from 1 to 21 months. Bilamellar tarsal rotation was more effective than destruction of the lashes by cryotherapy or electrolysis (Table 3).

6.2 Visual acuity change

Treatment of minor trichiasis was not associated with any improvement in vision but the differential effect of treatment, if any, was not clearly reported.

6.3 Corneal opacification change

Not reported.

6.4 Acceptance of treatment

Not reported.

6.5 Adverse effects

Not reported.

6.6 Quality of life

Not reported.

7. Posterior lamellar tarsal rotation surgery compared to epilation

One trial reported this comparison (Rajak 2011a). At baseline 1300 participants with minor trichiasis were randomised to surgery or epilation and followed up for two years.

7.1 Post-operative trichiasis

Trichiasis defined as one or more lashes touching the globe or repeat surgery was less frequent in the surgery group over two years (Table 4).

7.2 Visual acuity change

There was no evidence of a difference between the two groups in deterioration in visual acuity between baseline and one year or two years; however the confidence intervals include 1, therefore they are consistent with no effect (Table 4).

7.3 Corneal opacification change

Progression in corneal opacification was infrequent in both groups at one and two years. There was a non-significant trend to less deterioration in corneal opacification between baseline and one or two years in the surgery group; however the wide confidence intervals mean we cannot exclude the possibility that there is less deterioration in the epilation group or no difference between procedures (Table 4).

7.4 Acceptance of treatment

All participants accepted their initial randomisation allocation. At two years 185/593 (31%) of individuals who were still epilating accepted the offer of free community-based surgery.

7.5 Adverse effects

In the surgery arm, by two years, 105 (16%) of eyes had developed recurrent trichiasis, granulomas developed in 18 (2.9%) and eyelid contour abnormalities were reported in 29 (4.7%).

7.6 Quality of life

At 12 months 43% of participants in the surgery arm recalled "severe" treatment pain compared to 27% of people in the epilation group. More people in the surgery groups reported better subjective improvement in vision at 12 months (78%) compared to 33% of the epilation group, and less eye pain (44% compared to 70%), and eye watering (51% compared to 63%). All these differences were statistically significant.

8. Absorbable (polyglactin-910) compared to non-absorbable (silk) sutures

One trial investigated this comparison (Rajak 2011b). 1300 participants with major trichiasis were randomised to absorbable polyglactin-910 sutures or silk sutures and followed-up at one year and two years.

8.1 Post-operative trichiasis

Post-operative trichiasis at one year and two years was similar between the two groups (Table 5).

8.2 Visual acuity change

Change (deterioration of one or more lines) in visual acuity between baseline and two years was similar in the two groups (Table 5).

8.3 Corneal opacification change

There was less deterioration in corneal opacification between baseline and one year in the absorbable sutures group and more at two years but the confidence intervals were wide and compatible with no effect (Table 5).

8.4 Acceptance of treatment

Not reported.

8.5 Adverse effects

Fewer granulomas were found in the absorbable sutures group at six months (OR 0.63, 95% CI 0.40 to 0.99, 1187 eyes).

8.6 Quality of life

Not reported.

Non-surgical interventions

9. Sticking tape compared to epilation

One study reported this comparison and followed up to 3 months (Graz 1999). The study randomised 57 participants.

9.1 Post-operative trichiasis

The use of sticking tape alone was significantly more effective at preventing eyelashes from touching the eye compared to epilation alone at three months (Table 6).

9.2 Visual acuity change

Snellen visual acuity was measured using the 'E' optotype, but outcomes were not reported.

9.3 Corneal opacification change

Not reported.

9.4 Acceptance of treatment

Attendance for treatment was not recorded but it was mentioned in the discussion that there may have been compliance issues.

9.5 Adverse effects

Not reported.

9.6 Quality of life

A patient questionnaire of six closed-response questions was used to measure levels of discomfort; results were summarised as 'complaint' versus 'no complaint'. Patients found the less successful treatment of epilation significantly more uncomfortable than the sticking tape (P = 0.002); this was only reported on those with unilateral trichiasis.

10. Azithromycin compared to no azithromycin

Three studies reported this comparison (Burton 2005a; West 2006; Zhang 2006).

Burton 2005a randomised 451 people with major trichiasis only to receive azithromycin or no azithromycin at time of surgery; household members were also treated.

West 2006 (STAR trial) randomised participants to three groups: azithromycin to patient only (483); azithromycin to patient and household (485); or tetracycline (484).

Zhang 2006 randomised 109 people (148 eyes) with either minor and major trichiasis to azithromycin or placebo at time of surgery.

10.1 Post-operative trichiasis

There was heterogeneity between the trials in terms of postoperative trichiasis. West 2006 found a lower recurrence with azithromycin, while Burton 2005a and Zhang 2006 did not find a significant difference. In combining the data from the three trials, overall there was less post-operative trichiasis at one year in people given azithromycin; however the combined result effect was uncertain as the confidence intervals include 1 (OR 0.85, 95% CI 0.63 to 1.14, 1954 eyes, 3 studies) (Analysis 2.1).

At three years in the STAR trial (West 2006) there was less post-operative trichiasis but again the overall effect was uncertain. A similar pattern was seen at four years follow-up in Burton 2005a (Analysis 2.2).

10.2 Visual acuity change

In Burton 2005a visual acuity improved in 57.6% of eyes by 12 months. There was an overall improvement of 0.14 logMAR ($P < 0.0001$). Data were not reported by randomised groups.

In the STAR trial (West 2006) a comparison of the change in visual acuity between baseline and six months on a consecutive subset of 439 study subjects did not find a significant difference in visual acuity outcomes between the azithromycin and control groups but data were not reported.

10.3 Corneal opacification change

Not reported.

10.4 Acceptance of treatment

In Burton 2005a all study participants accepted their allocated treatment.
In the STAR trial (West 2006) and Zhang 2006 this was not reported.

10.5 Adverse effects

In Burton 2005a one participant had a post-operative skin infection that settled on oral antibiotics. Two individuals had defective lid closure of less than 2 mm lagophthalmos.
In West 2006 there was a similar rate of adverse events in the azithromycin and control groups with a rate per 100 person of adverse events (death/illness/ocular) at 6 weeks of 2.90 (1.93-4.19) in the azithromycin group and 3.10 (1.73-5.11) in the tetracycline group.
Adverse effects were not reported in Zhang 2006.

10.6 Quality of life

In Burton 2005a 77% reported improvement in vision and 94.3% felt the operated eye was more comfortable but this was not analysed by randomised groups.
In West 2006 trichiasis surgery had a marked benefit on physical functioning in a sub-group analysis (Wolle 2011), but this was not analysed by groups allocated to azithromycin or control.
Quality of life was not reported in Zhang 2006.

Settings and personnel

11. Community-based compared to health centre-based surgery

One study reported this comparison (Bowman 2000). This was a cluster-randomised trial. Eight paired clusters of villages were randomised to community or village-based surgery (86 participants) or health centre-based surgery (72 participants).

11.1 Post-operative trichiasis

More people in the village-based surgery group had post-operative trichiasis at 3 months compared to the health centre-based surgery group but the confidence intervals were wide and compatible with no effect or less trichiasis (OR 1.44, 95% CI 0.26 to 7.90).

11.2 Visual acuity change

Not reported.

11.3 Corneal opacification change

Not reported.

11.4 Acceptance of treatment

In six of the eight pairs of clusters surgical uptake was higher for village-based surgery; however, this difference might have occurred by chance (difference 20%, 95% CI −9% to 49%). Analysed by individual, 57/86 (66%) in the village-based clusters attended for surgery compared to 32/72 (44%) in the health centre-based group (OR 2.46, 95% CI 1.29 to 4.68).

11.5 Adverse effects

A total of four events are reported but there was said to be no difference between groups (data not reported).

11.6 Quality of life

Not reported.

11.7 Cost

The cost of travel was significantly less in the clusters randomised to community-based surgery (difference between means 10.5 Dalasi, 95% CI 6.07 to 14.93). Journey time to village-based surgery was significantly less (difference between means 36 minutes, 95% CI 15.37 to 56.63).

12. Ophthalmologist compared to integrated eye care worker (IECW)

One study reported this comparison (Alemayehu 2004). Of the 982 randomised, 713 (73%) attended the three-month outcome assessment: 370/713 (52%) ophthalmologist group; 343/713 (48%) IECW group.
This study reported a linear trend for increased risk of recurrence with increasing severity of pre-operative entropion (X^2 22, $P < 0.001$). Randomisation was not stratified according to severity. Data on pre-operative disease severity is not presented by the two randomisation groups. It is possible that either group may have treated a higher proportion of patients with severe disease, which could influence the outcome. A seven-day post-operative check was planned to identify surgical failures (which were then excluded from further analysis) but the outcomes from this assessment were not reported. If there was a significant difference in the number of failures between the groups at that stage, it would affect the interpretation of the results.

12.1 Post-operative trichiasis

There was more post-operative trichiasis in the ophthalmologist group at 3 months but the confidence intervals were wide and compatible with no effect or less trichiasis (OR 1.32, 95% CI 0.83 to 2.11, 713 eyes).

There was a difference in the success rates of the two IECWs: one operated on 184 of whom 12 (6.5%) developed recurrence, the other operated on 159 of whom 22 (13.8%) developed recurrence (OR 2.3, 95% CI 1.1 to 4.8).

None of the other review outcomes were reported.

DISCUSSION

Summary of main results

Trachomatous trichiasis is a significant ophthalmic public health problem in several regions of the world, particularly in sub-Saharan Africa. The evidence identified in this review serves to highlight not only what is currently known about the effectiveness of treatment for this condition but also the challenges involved in delivering the necessary care and achieving good long-term outcomes to prevent blindness.

Surgical interventions

Detailed descriptions of the different surgical procedures are provided elsewhere (Rajak 2012). Some evidence suggests that operations in which the full-thickness of the tarsal plate is incised and the terminal lash-bearing tarsus is rotated so that the lid margin is everted are more effective than procedures that do not involve this (Reacher 1990). It was possible to pool the results of Reacher 1990 and Reacher 1992, which found evidence that bilamellar tarsal rotation has lower post-operative trichiasis rates than tarsal advance and rotation. This unilamellar procedure was performed by placing the sutures through the marginal strip of the tarsal plate and a second set from the upper end of the tarsal plate into the anterior lamella. In Adamu 2002 a variant of the bilamellar tarsal rotation was compared to the posterior lamellar tarsal rotation (also known as the Trabut procedure), in which the sutures were placed above the lashes, similar to the bilamellar technique. The same unilamellar technique as that used by Adamu 2002 was used in a case series in East Africa with similar anatomical success (Bog 1993). It is possible that the difference in results reflects the difference in technique, but the studies also had differing follow-up periods (times of assessment), which may have influenced the outcomes.

At present both the bilamellar and posterior lamellar tarsal rotation operations are both extensively used in trachoma-endemic countries. There is currently no conclusive evidence that bilamellar surgery is superior to the posterior lamellar operation. Although cases of overcorrection and exposure were more common following bilamellar lid surgery, the risk was very low and the difference was not statistically significant in any study. It appears that both bilamellar and posterior lamellar tarsal rotation procedures are safe operations. The only common complication was post-operative trichiasis.

The use of a lid clamp in the bilamellar tarsal rotation procedure did not reduce post-operative trichiasis but was associated with better eyelid contour outcomes and fewer granulomas (Gower 2013).

Both lid rotation operations are relatively simple and require little equipment. Ophthalmologists, nurses, ophthalmology trainees and IECWs undertook the surgery in the included studies. It is possible that certain types of surgery are more effective than other types in specific situations. To our knowledge this has not yet been tested in any trial.

Interventions to treat minor trichiasis by destroying the lashes, such as cryotherapy and electrolysis, appear to have low success rates in preventing recurrent trichiasis compared to bilamellar tarsal rotation surgery (Reacher 1992). As the equipment required is costly and can be difficult to maintain, this strategy is not recommended.

Epilation

Epilation is widely practised in most regions that have a high prevalence of trichiasis and it may have a role in the management of minor trichiasis where there are only a few peripheral lashes and a patient declines surgery. The study that investigated this was a non-inferiority trial comparing enhanced epilation (high-quality forceps and training) to posterior lamellar tarsal rotation surgery for minor trichiasis cases only (Rajak 2011a). The primary endpoint in that trial was progression to major trichiasis with a prespecified non-inferiority margin of 10%. The cumulative risk of failure was 13.2% in the epilation group and 2.2% in the surgical group, with a risk difference of 11% (95% CI 8.1% to 13.9%, which includes the 10% non-inferiority margin). Therefore, the trial provided an inconclusive result relative to the predefined 10% non-inferiority margin. The proportion having any degree of trichiasis during follow-up was significantly higher in the epilation group. However, over a two-year period the important secondary outcome measures of change in visual acuity and corneal opacity showed no significant difference. It is notable that at two years only 31% of those still epilating accepted the offer of surgery.

Lid-taping

Double-sided sticking plaster requires replacement of the plaster every week. As a temporary measure, however, the use of sticking plaster to evert the lashes is useful and in the study by Graz 1999 was superior to, and more comfortable than, epilation.

Antibiotic treatment

Post-operative trichiasis was observed more often when the tarsal conjunctiva was inflamed (Burton 2005a; Burton 2005b; Rajak 2011b; West 2005). This clinically apparent inflammatory reaction could arise for a number of reasons: a smouldering immunologically driven process, infection with chlamydia or other bacteria, or mechanical irritation from the lashes (Burton 2010; Burton 2012). It is likely that chronic inflammation is the basis of progressive conjunctival scarring. Adjuvant therapy may reduce the risk of recurrent scarring and trichiasis.

Three studies with heterogeneous designs, populations and study participants have investigated whether azithromycin can reduce trichiasis recurrence. Azithromycin is a broad spectrum antibiotic with some anti-inflammatory properties. The first study was conducted in a programmatic context where many different surgeons were operating in The Gambia, a country with a very low prevalence of chlamydial infection, and recruited only major trichiasis cases (Burton 2005a). This study did not find an effect from azithromycin at one or four years, and overall recurrence rates were relatively high with significant inter-surgeon heterogeneity. The second (and largest) study, which included both major and minor trichiasis from an area of Ethiopia with high chlamydial infection rates and a limited number of surgeons, found a significantly lower trichiasis recurrence rate in the azithromycin arm at one year, but not at three years (West 2006). The third study, from Nepal, did not find an overall significant difference at one year (Zhang 2006). A sub-group analysis suggested a possible effect for major trichiasis cumulatively to one year. None of the other sub-groups showed a significant effect. It is not possible to draw a definite conclusion about the impact of azithromycin on post-operative trichiasis due to the study heterogeneity. The pooled analysis did not find a significant reduction in post-operative trichiasis. It appears that where post-operative trichiasis rates are low, there may be some benefit of azithromycin treatment; however, under operational/programmatic conditions with higher overall post-operative trichiasis rates there was no observed effect. Non-chlamydial bacteria have been frequently cultured from the conjunctiva of people with trichiasis (Burton 2005a).

Alternative suture materials

The study comparing silk with absorbable sutures found no difference in the recurrence rates at one or two years (Rajak 2011b). In many settings patients with trichiasis have to travel long distances to obtain surgical services. The typical practice is to use silk sutures, which have to be removed a week to 10 days post-operatively. This incurs additional transport and time for both the patient and surgical team, adding to the overall cost of surgery. However, in many settings absorbable sutures are substantially more expensive than silk sutures. Occasionally silk sutures are not removed, which can cause granuloma formation and serious complications for the cornea if left in long-term. Therefore, the use of absorbable sutures may be preferable for cost reasons where these can be afforded; a formal cost benefit analysis is needed to answer this question.

Surgery setting

The uptake of trichiasis surgery is often low (Courtright 1994; West 1994); strategies that increase the proportion of patients who attend for surgery need to be developed. Bowman 2000 showed that it was less costly, and took less time, for participants to attend surgery in the community and that community-based surgery was as safe and as effective as surgery in a health centre. However the uptake of surgery was only 20% better for village-based surgery than for health centre-based surgery (when analysed by cluster). It is not mentioned whether the resource implications for setting up village-based surgery were greater than those required for health centre-based surgery and it may be that this needs to be considered in the light of the reasonably small improvement in uptake. The village-based approach to delivering surgery may work better in certain environments than others and should be considered along with other strategies for further research.

Personnel performing surgery

Most regions where trichiasis is prevalent have few ophthalmologists, and other health workers need to be trained to undertake the surgery in order to provide an adequate level of service. The evidence from the Alemayehu 2004 study suggests that surgery performed by a specially-trained integrated eye worker is as successful as that undertaken by an ophthalmologist. Some caution needs to be applied in interpreting this result as the early recurrences (occurring by seven days) were excluded from the analysis. While this is very encouraging in terms of providing not only manpower but also a high-quality service, care needs to be taken to ensure appropriate specialist training is in place. Multiple studies have shown that success rates vary across surgeons (Burton 2005a; West 2005). This finding probably reflects varying levels of training, innate skill and experience, and serves to highlight the need not only for a high standard of basic training but also for ongoing monitoring and support.

Secondary outcome measures

Improvement in visual acuity or prevention of visual acuity deterioration is the primary long-term aim of treating trachomatous trichiasis. However, this requires long-term studies and therefore such evidence would be very difficult to obtain. The studies included here do not provide the opportunity to evaluate whether trichiasis surgery prevents long-term loss of vision, because surgery has never been compared directly with no treatment. However, several studies have found modest but significant improvement in vision following surgery (Burton 2005a; Rajak 2011b; Reacher 1992; West 2006). Some of the visual impairment prior to surgery may be due to photophobia, lacrimation or irritation, or combinations of these three factors, caused by trichiatic lashes. Correction of the trichiasis should relieve these symptoms. Corneal scarring generally does not improve following surgery, although one study which compared corneal photographs before surgery to those at 2 years did find a degree of improvement in a minority of people (Rajak 2011b).

Some trials have reported relatively high rates of eyelid contour abnormalities, which were less frequent with the use of a lid clamp (Rajak 2011b, Gower 2013). Other factors that are likely to affect patient satisfaction with surgery are comfort and appearance. Despite a lack of evidence for improvement or preservation of vision, Bowman 2002 reported 85% of operated patients were pleased with the outcome of surgery and 94% would recommend the operation to others. In the Burton 2005a study, 94% of patients said they were more comfortable a year after surgery, compared to their pre-operative condition. Careful study of these important subjective factors may help provide a more complete picture of successful treatment and maybe even identify motivators for attendance.

Quality of the evidence

It is important to recognise the real difficulties of conducting studies in areas where resources and access to health care are limited, but there are several quality issues that must be highlighted in order for the studies to be interpreted appropriately. The grade of the evidence presented by many of the thirteen studies was high; however, there was some variability in the quality either due to small sample size or unclear or sub-optimal methodology.

For several the sample size was relatively low and probably insufficient to address the question (Dhaliwal 2005; Graz 1999; Reacher 1990; Zhang 2006).

Most studies randomised participants; for several, however, sufficient information is not provided to determine the risk of bias associated with randomization (Adamu 2002; Alemayehu 2004; Graz 1999; Reacher 1990). In one study patients were assigned on an alternating basis (Zhang 2006), and this approach is vulnerable to bias because the assignment coordinator could adjust the enrolment order based on his/her preferences or beliefs.

Participant masking to intervention was not possible in most studies and would not be expected to influence the outcome, since typically an independent observer evaluated a non-subjective outcome (presence of lashes touching the eye). Masking of outcome assessors is more crucial for unbiased reporting; however, in four studies it is unclear whether masking was done (Adamu 2002; Bowman 2000; Graz 1999; Reacher 1990). While this must be considered a quality concern, the reality may have been that researchers were working with a limited number of eye care professionals and did not have the resources to exclude some staff from delivery of care in order to ensure adequate masking.

The length of follow-up in many of the included trials is quite short, limiting information regarding the long-term effectiveness of the treatments. Long-term follow-up studies indicate that trichiasis continues to return after several years, but at a slower rate than during the first year post-operatively (Rajak 2013; West 2006). With the exception of Reacher 1992, Burton 2005a, West 2006, Rajak 2011a, Rajak 2011b and Gower 2013, all studies had less than 12 months of follow-up. Many areas where trachomatous trichiasis remains a significant public health problem are isolated and poor, and some of the population may be semi-nomadic, making longer follow-up difficult to achieve. The relatively short duration of follow-up did, however, mean there were generally high levels of follow-up.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence summarised in this review provides some indication of the basis for practice but one must remember that there are weaknesses in some of the data that may make the results unreliable.

There is less risk of recurrence if the full thickness of the tarsal plate is incised and the lash-bearing tissue is rotated away from the globe to evert the lid margin compared to procedures that do not involve a full-thickness tarsotomy. This can be achieved by either unilamellar or bilamellar lid surgery. Operations such as tarsal grooving, tarsal advance and eversion splinting are less effective. The bilamellar tarsal rotation is better than either cryotherapy or electrolysis in rendering a patient trichiasis-free.

The optimal management of minor trichiasis remains uncertain. However, for patients with minor trichiasis who refuse surgery or where surgery is unavailable, epilation is a generally acceptable second-line alternative treatment with comparable visual outcomes.

Post-operative azithromycin may be associated with reduced risk of post-operative trichiasis; however, this effect is less certain under programmatic conditions than under high-quality surgery by a few highly-skilled integrated eye care workers.

Silk and absorbable sutures have comparable outcomes. However, absorbable sutures have practical operational advantages in settings where they are affordable.

Local health workers (nurses, medical assistants or non-ophthalmologist doctors) may be trained to a level where they can perform trichiasis surgery as effectively as an ophthalmologist; however, it is essential that local health workers receive good training, surgical certification and follow-up supportive supervision in order to help ensure high-quality surgery is maintained.

If uptake for trichiasis surgery is low in central settings, consideration should be given to providing it in patients' own communities.

Implications for research

Recurrent trichiasis: the recurrence rate of trichiasis following surgery remains high in most programmatic settings, regardless of the intervention used. Recurrence is strongly associated with tarsal conjunctival inflammation, the cause of which is not well understood. Research is needed to improve understanding of the reasons why trichiasis recurs and to investigate targets for possible adjuvant therapy. Further trials are needed to compare the long-term results of bilamellar and posterior lamellar tarsal rotation surgery, the two most commonly used operations. Since it is now known that the risk of recurrence is influenced by entropion severity, this must be taken into account in the design of future trials.

Acceptability of treatment: a major obstacle to successful trichiasis surgery is failure to attend for an operation. Further research is required to identify other means of increasing the proportion of people who attend for surgery. It may be possible to identify the perceived benefits of lid surgery to the patient-such as free transport or improved cosmesis-and to use these perceived benefits to persuade others to attend.

Pattern of surgical provision: we do not yet know the most effective way of delivering trichiasis surgery: is it through a high-volume surgical camp, or through a single surgeon working long-term in a specific district? Further studies are required to determine not only which method will give the best uptake, but also which is most cost effective and is associated with the lowest recurrence rate.

Quality of surgery: there is a need for research to understand the determinants of a successful surgical training programme. There is a need to assess methods to audit the outcome of surgery by individual surgeons. This information then needs to be fed back to improve training programmes.

Quality of life: although it has been shown that most trichiasis patients are happy with the results of their surgery the impact of surgery on quality of life and what might enhance this is a neglected area of research,

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adamu 2002

Methods	Study Design: parallel group randomised trial of different operations for trichiasis Eyes: for cases who only had trichiasis affecting one eye only that eye was included. In bilateral cases both eyes were included: surgery type was allocated randomly for the right eye and then the left eye was allocated to the other procedure. Analysis was not adjusted for bilateral cases
Participants	Country: Ethiopia Setting: teaching hospital Number of participants: 153 patients, 256 eyes Lost to follow up: 19 Male: 32, Female: 109 (gender unknown for 19 not followed up)
Interventions	(1) Bilamellar tarsal rotation (2) Posterior lamellar tarsal rotation
Outcomes	Primary outcome: recurrent trichiasis (one or more lashes touching eye) Secondary outcomes: overcorrection; complications Follow up: 3 months Reported improvement in vision, but no details given
Notes	The unilamellar operation is different to the one described in Reacher 1990 and Reacher 1992 Funder: not specified

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	An unspecified 'Lottery method' used. In bilateral cases the left eye always received the opposite treatment to that randomly allocated to the right eye
Allocation concealment (selection bias)	Unclear risk	No description.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description.

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No description of the individuals lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	No study protocol available. Limited information on analytical protocol in methods

Alemayehu 2004

Methods	Study Design: parallel group randomised trial of different levels of surgical training and background for surgeons performing trichiasis surgery Eyes: in bilateral cases both eyes were included. No adjustment was made in the analysis
Participants	Country: Ethiopia Setting: unclear Number of participants: 982 patients (1750 eyes) Lost to follow up: 464 eyes Female: 77.2% (absolute numbers not provided)
Interventions	(1) Bilamellar tarsal rotation carried out by ophthalmologist (2) Bilamellar tarsal rotation carried out by integrated eye worker
Outcomes	Primary outcome: recurrent trichiasis (one or more lashes touching eye) Secondary outcomes: severity of recurrence Follow up: 3 months
Notes	Funder: not specified

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description: "were randomised" but no further details provided
Allocation concealment (selection bias)	Unclear risk	No description.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No masking of participants or surgical personnel, but unlikely to have influenced the outcome
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Follow-up by ophthalmologists who were not involved in the surgery and masked to the allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Participants were excluded post-randomisation if surgery failed. 269 patients were lost to follow-up at 3 months.

Selective reporting (reporting bias)	Unclear risk	No study protocol available. Limited information on analytical protocol in methods

Bowman 2000

Methods	Study Design: cluster randomised study of surgery provided in the patients' village compared to surgery provided at a local health centre Eyes: unclear how bilateral cases were analysed.
Participants	Country: The Gambia Setting: village and health centre-based surgery Number of participants: 8 pairs of villages (156 participants) Lost to follow up: 0 All participants had major trichiasis pre-operatively
Interventions	(1) Posterior lamellar tarsal rotation surgery in village (2) Posterior lamellar tarsal rotation surgery in health centre
Outcomes	Primary Outcome: surgical uptake Secondary Outcomes: recurrent trichiasis, time taken from home to surgery, cost, complications Follow up: 1 week and 3 months
Notes	Funder: Sight Savers International

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Clusters were paired by district or geographical proximity. One cluster from each pair was randomly allocated to receive village-based surgery and the other, health centre-based surgery." Method of sequence generation not specified
Allocation concealment (selection bias)	Low risk	All clusters randomly allocated at baseline, before the TT patients were identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and personnel not masked to community allocation. Unlikely to have influenced the outcome
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description.

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data complete.
Selective reporting (reporting bias)	Low risk	No study protocol available. Clear analytical approach in methods

Burton 2005a

Methods	Study Design: parallel group randomised trial of peri-operative azithromycin treatment Eyes: only one eye per participant was included in the analysis. In bilateral cases, the eye with more severe baseline trichiasis was included
Participants	Country: The Gambia Setting: health centres Number of participants: 451 Lost to follow up: 25 Male: 133, Female: 318 A consecutive, geographically defined sub-set of the original participants was followed-up at 4 years Number of participants: 356 Lost to follow up: 90 Male: 103, Female: 253 Major trichiasis cases only
Interventions	(1) Posterior lamellar tarsal rotation surgery (no placebo) (2) Posterior lamellar tarsal rotation surgery followed by single-dose azithromycin treatment at baseline and 6 months, administered to the patient and the members of their household
Outcomes	Primary Outcome: recurrent trichiasis by one year Secondary Outcomes: visual acuity by reduced LogMAR chart, conjunctival infection, corneal opacification Follow up: 12 months and 4 years (subset)
Notes	Funder: International Trachoma Initiative

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Separate randomisation sequences were generated for each surgeon from random number tables and blocked in groups of four"
Allocation concealment (selection bias)	Low risk	Quote "Treatment allocations were concealed in opaque sequentially numbered envelopes"

Burton 2005a (*Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote "Immediately following surgery a nurse not involved in clinical assessments or surgery administered the randomly allocated treatment." Participants were not masked to allocation, as no placebo was used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Examiners were "blinded" to treatment allocation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	98% follow-up of those still alive at 1 year. At 4 years 94% of the surviving patients were re-examined
Selective reporting (reporting bias)	Low risk	Clear analytical approach in methods.

Dhaliwal 2005

Methods	Study Design: parallel groups randomised to one of three procedures Eyes: in bilateral cases both eyes were separately randomised. No adjustment was made for this in the analysis
Participants	Country: India Setting: hospital ophthalmology department Number of participants: 77 patients (90 eyes) Lost to follow up: 0 eyes Female: unclear as % is provided by eye and not person
Interventions	(1) Terminal tarsotomy and rotation (2) Tarsal advance and rotation (3) Tarsal grooving
Outcomes	Post-opearative trichiasis and/or entropion at 6 months
Notes	Terminal tarsotomy and rotation is different from the PLTR/Trabut Funder: not specified

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method for the allocation for the second eye is unclear and excluded the method used on the first eye to be operated
Allocation concealment (selection bias)	Unclear risk	No description.

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description.
Incomplete outcome data (attrition bias) All outcomes	Low risk	High follow-up.
Selective reporting (reporting bias)	Low risk	No study protocol available. Clear analytical approach in methods

Gower 2013

Methods	Study Design: parallel group randomised controlled trial bilamellar tarsal rotation surgery with or without a TT clamp Eyes: both eyes of bilateral cases were included in the analysis. Appropriate adjustment was made in the analysis for bilateral cases
Participants	Country: Tanzania Setting: health centres Number of participants: 1917 Number of Eyes: 3345 Lost to follow up: 51 Male: 490, Female: 1427
Interventions	(1) Standard bilamellar tarsal rotation (2) Bilamellar tarsal rotation performed with a TT clamp
Outcomes	Primary Outcome: was defined as one or more of the following: recurrent trichiasis, eyelid contour abnormality or granuloma Secondary outcomes: post-operative trichiasis, eyelid contour abnormality or granuloma individually Follow-up: 6 weeks, 12 months, 24 months.
Notes	18 different surgical technicians performed the surgery. Surgeons were randomly allocated at the outset to only perform one of the two types of operation. Each recruitment day there were 4 surgical technicians operating - 2 standard procedure and 2 with the TT clamp. Patients with TT were randomly allocated to one of the 4 surgical technicians operating Funder: Bill and Melinda Gates Foundation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Quote "Randomization assignments were created using permuted block sizes of 6 to 12"
Allocation concealment (selection bias)	Low risk	Quote "Randomization assignments were placed in opaque envelopes and stored in a locked office until distribution"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and surgical technicians were not masked to the allocation; however, this is unlikely to have affected the outcome measure
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Examinations were conducted by a single trained examiner who was not involved in enrolment, randomization, or surgical procedures"
Incomplete outcome data (attrition bias) All outcomes	Low risk	98% follow-up rate.
Selective reporting (reporting bias)	Low risk	No study protocol available. Clear analytical approach in methods

Graz 1999

Methods	Study Design: parallel group randomised trial of epilation versus sticking tape Eyes: in bilateral cases both eyes were treated the same way and the data from both included in the analysis. The authors combined the data from both eyes to give a single 'clinical status' outcome
Participants	Country: China Setting: hospital and home Number of participants: 57 (68 eyes) Lost to follow up: 0 Male: 20, Female: 37
Interventions	(1) Epilation alone for 12 weeks (2) Sticking plaster for 12 weeks (3) Sticking plaster for 8 weeks, followed by cross-over to epilation
Outcomes	Successful outcome: no lashes touching the eye. Secondary outcomes: visual acuity by Snellen E-chart, corneal status, patient-reported symptoms by questionnaire. Follow up: 3 months
Notes	The group that had sticking plaster for 8 weeks followed by epilation has been excluded from our analysis as this group received both interventions

	Funder: Swiss Agency for Development and Cooperation	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No description.
Allocation concealment (selection bias)	Unclear risk	No description.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Personnel not masked; performance risk possible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Observer not masked. Quote "A blinded design was not possible for obvious reasons, but data entry and analysis were blinded."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data complete.
Selective reporting (reporting bias)	Low risk	Data complete.

Rajak 2011a

Methods	Study Design: parallel group randomised trial of epilation versus surgery for minor trichiasis. Non-inferiority trial Eyes: only one eye per participant was included in the analysis. In bilateral cases, one eye was randomly assigned to be the 'study eye', although both eyes were treated, if indicated
Participants	Country: Ethiopia Setting: health centres Number of participants: 1300 Lost to follow up: 81 Male: 537, Female: 863 Minor trichiasis cases only
Interventions	(1) Posterior lamellar tarsal rotation (2) Epilation with new forceps and training
Outcomes	Primary Outcome: proportion of individuals at any follow-up who had "failed" defined as either (1) five or more eyelashes touching the globe or (2) a history of surgery performed in the trial eye at any point during the follow-up period (in the case of the surgical arm this would be repeat surgery). A pre-specified non-inferiority margin was 10% Secondary Outcomes: corneal opacity change, visual acuity by LogMAR E-chart, entropion, conjunctival inflammation and symptoms by questionnaire Follow up at 6, 12, 18 and 24 months.

Notes	Funder: Band Aid Foundation and The Wellcome Trust. Johnson & Johnson donated all sutures. Tweezerman donated all forceps

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Participants were randomly allocated to the epilation or surgery groups using a 1:1 allocation ratio for each surgeon, using a computer-generated randomisation sequence with random block sizes. Randomisation was stratified by surgeon because of possible intersurgeon variability."
Allocation concealment (selection bias)	Low risk	Quote "The random allocation sequences for each surgeon were concealed in sequentially numbered, sealed, opaque envelopes, which were colour coded for surgeon and placed in separate containers for each surgeon. The person who prepared these envelopes was independent of all other aspects of the trial."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were not masked to their allocation, as they either received surgery or practiced epilation. Other than the surgeons performing the operation and the epilation trainer, all other personnel were masked to the allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "The two individuals responsible for all the clinical outcome measurements were masked to the allocation. At follow-up, the trichiasis and corneal examination was performed and recorded before the eyelid was everted, so that the examiner was masked to whether surgery had been performed on the tarsal conjunctiva."
Incomplete outcome data (attrition bias) All outcomes	Low risk	93.5% follow-up at 24 months.
Selective reporting (reporting bias)	Low risk	Study protocol published online.

Rajak 2011b

Methods	Study Design: parallel group randomised trial of absorbable versus silk sutures for major trichiasis Eyes: only one eye per participant was included in the analysis. In bilateral cases, one eye was randomly assigned to be the 'study eye', although both eyes were treated, if indicated
Participants	Country: Ethiopia Setting: health centres Number of participants: 1300 Lost to follow up: 82 Male: 285, Female: 1015
Interventions	(1) Posterior lamellar tarsal rotation with absorbable sutures (2) Posterior lamellar tarsal rotation with silk sutures
Outcomes	Primary Outcome: proportion of those individuals seen at the 12-month follow-up who were found to have either (1) recurrent trichiasis, defined as one or more lashes touching the eye or clinical evidence of epilation; or (2) a history of repeat TT surgery during the first year Secondary Outcomes: corneal opacity change, visual acuity by LogMAR E-chart, entropion, conjunctival inflammation and symptoms by questionnaire Follow up at 6, 12, 18 and 24 months.
Notes	Funder: Band Aid Foundation and The Wellcome Trust. Johnson & Johnson donated all sutures

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Participants were randomly allocated to the silk or polyglactin-910 suture arms using a 1:1 allocation ratio for each surgeon, using a computer-generated randomisation sequence with random block sizes. Randomisation was stratified by surgeon because of possible inter-surgeon variability."
Allocation concealment (selection bias)	Low risk	Quote "The random allocation sequences for each surgeon were concealed in sequentially numbered, sealed, opaque envelopes, which were placed in separate containers for each surgeon; a person independent of all other aspects of the trial prepared these envelopes."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote "Participants and surgeons were aware of the suture allocation." Other personnel involved in the study were masked

		to the allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "The two individuals who were responsible for all the clinical observations in this trial were masked to the allocation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	95.1% follow-up at 12 months.
Selective reporting (reporting bias)	Low risk	Study protocol published online.

Reacher 1990

Methods	Study Design: parallel group randomised trial of five different operations for trachomatous trichiasis Eyes: only one eye per participant was included in the analysis. Unclear how lids were selected in bilateral cases
Participants	Country: Oman Setting: not specified Number of participants: 165 (165 eyes) Lost to follow-up: 12 Gender: not specified
Interventions	(1) Bilamellar tarsal rotation (2) Tarsal advance and rotation (3) Eversion splinting (4) Tarsal advance (5) Tarsal grooving
Outcomes	Primary outcome: "treatment success" defined as no eyelash/eyeball contact in the primary position and complete eyelid closure. Mean follow up: 7.9 months. A follow-up schedule is not specified beyond 14 days
Notes	Three surgeons performed the surgery, with two surgeons performing relatively few of the operations Funder: not specified

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Limited information. Quote "operations allocated by random number tables"
Allocation concealment (selection bias)	Unclear risk	No comment on concealment of the random sequence.

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants and surgeon were not masked to the allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not specified.
Incomplete outcome data (attrition bias) All outcomes	Low risk	93% follow-up rate.
Selective reporting (reporting bias)	Low risk	No study protocol available. Clear analytical approach in methods

Reacher 1992

Methods	Study Design: three separate parallel group trials for minor trichiasis, major trichiasis and defective lid closure
Participants	Country: Oman Setting: hospital or health centre Number of participants: 367 (172 eyes with minor trichiasis, 200 eyes with major trichiasis, 21 eyes with lid closure defect) Lost to follow up: 24
Interventions	Minor trichiasis: (1) Bilamellar tarsal rotation (2) Electrolysis (3) Cryotherapy Major trichiasis: (1) Bilamellar tarsal rotation (2) Tarsal advance and rotation Defective lid closure: (1) Tarsal advance and rotation (2) Tarsal advance with graft
Outcomes	Primary outcome: "Successful outcome" defined as no eyelash/eyeball contact in the primary position, complete eyelid closure, no overcorrection and a cosmetically acceptable outcome
Notes	The group with lid closure defects was too small to be analysed separately and has been excluded from the analysis Funder: Edna McConnell Clarke Foundation and National Institutes of Health

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Low risk	Quote: "Allocation was made by opening a sequence of sealed envelopes specific for lid grade that contained one of a random series of operations generated by computer. "
Allocation concealment (selection bias)	Low risk	Quote: "Allocation was made by opening a sequence of sealed envelopes specific for lid grade that contained one of a random series of operations generated by computer. "
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants and surgeons were not masked to the allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Masked independent assessor.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	96% follow-up, but very variable time frames (1.2 to 25 months)
Selective reporting (reporting bias)	Low risk	No study protocol available. Clear analytical approach in methods

West 2006

Methods	Design: parallel group randomised trial of peri-operative azithromycin treatment Eyes: only one eye per participant was included in the analysis. In bilateral cases, the study eye was determined by the study number (left eye if an odd number)
Participants	Country: Ethiopia Setting: health centres Number of participants: 1452 Lost to follow-up: participants were followed until they developed recurrence or until 1 year post-operatively, whichever came first. 98% of eligible subjects were followed at 1 year Male: 331, Female: 1121 Number of participants: 1452 Lost to follow-up: 30 Male: 331, Female: 1121
Interventions	(1) Bilamellar tarsal rotation with tetracycline eye ointment (2) Bilamellar tarsal rotation with azithromycin to the patient only (3) Bilamellar tarsal rotation with azithromycin to the patient and their family

Outcomes	Primary Outcome: post-operative trichiasis 1 year and 3 years after surgery Secondary Outcomes: visual acuity reported in a subset of the trial participants
Notes	Funder: National Eye Institute.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence, with variable block size.
Allocation concealment (selection bias)	Low risk	Allocation concealed in envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were not blinded to the allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments were performed by a masked grader.
Incomplete outcome data (attrition bias) All outcomes	Low risk	98% follow-up at one year; 91.1% follow-up at three years.
Selective reporting (reporting bias)	Low risk	Study protocol published and no evidence of selective reporting of outcomes

Zhang 2006

Methods	Design: parallel group randomised trial of peri-operative azithromycin treatment Eyes: bilateral cases both eyes included.
Participants	Country: Nepal Setting: field camps Number of participants: 109 (148 eyes operated) Lost to follow-up: uncertain, as reported by eye rather than person Male: 29, Female: 80
Interventions	(1) Bilamellar tarsal rotation with placebo (2) Bilamellar tarsal rotation with azithromycin, single dose
Outcomes	Primary outcome: recurrent trichiasis (1+ lash touching the eye)
Notes	Funder: Fight for Sight, International Trachoma Initiative, National Institutes of Health

Risk of bias

Zhang 2006 (*Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No random sequence. Patients allocated to azithromycin and placebo on an alternating basis
Allocation concealment (selection bias)	High risk	No concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo used.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Examinations by masked graders.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some minor internal inconsistencies data.
Selective reporting (reporting bias)	High risk	Excluded "surgical failures" from the analysis, defined as five+ lashes touching the globe at 3 months

TT = trachomatous trichiasis

DATA AND ANALYSES

Comparison 1. Bilamellar tarsal rotation versus tarsal advance and rotation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 One or more lashes touching globe at nine months	2	260	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.16, 0.50]
2 Overcorrection following surgery	2	312	Odds Ratio (M-H, Fixed, 95% CI)	2.57 [0.28, 23.25]
3 Defective lid closure following surgery	2	312	Odds Ratio (M-H, Fixed, 95% CI)	1.90 [0.29, 12.37]

Comparison 2. Peri-operative azithromycin versus no azithromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 One or more lashes touching the globe at one year	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2 One or more lashes touching the globe at longer follow-up	2	1589	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.60, 1.05]
2.1 Three years	1	1322	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.54, 1.07]
2.2 Four years	1	267	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.53, 1.41]

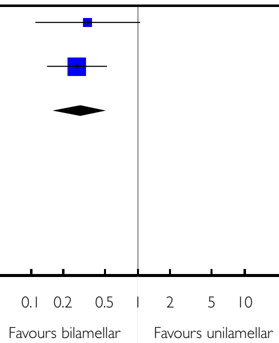
Analysis 1.1. Comparison 1 Bilamellar tarsal rotation versus tarsal advance and rotation, Outcome 1 One or more lashes touching globe at nine months.

Review: Interventions for trachoma trichiasis

Comparison: 1 Bilamellar tarsal rotation versus tarsal advance and rotation

Outcome: 1 One or more lashes touching globe at nine months

Study or subgroup	Bilamellar n/N	Unilamellar n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Reacher 1990	10/39	11/22		22.0 %	0.34 [0.11, 1.04]
Reacher 1992	18/98	46/101		78.0 %	0.27 [0.14, 0.51]
Total (95% CI)	**137**	**123**		**100.0 %**	**0.29 [0.16, 0.50]**



Total events: 28 (Bilamellar), 57 (Unilamellar)

Heterogeneity: $Chi^2 = 0.15$, df = 1 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 4.42 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Bilamellar tarsal rotation versus tarsal advance and rotation, Outcome 2 Overcorrection following surgery.

Review: Interventions for trachoma trichiasis

Comparison: 1 Bilamellar tarsal rotation versus tarsal advance and rotation

Outcome: 2 Overcorrection following surgery

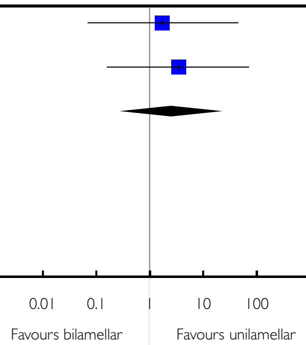
Study or subgroup	Bilamellar n/N	Unilamellar n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Reacher 1990	1/39	0/22		51.0 %	1.75 [0.07, 44.88]
Reacher 1992	2/150	0/101		49.0 %	3.42 [0.16, 71.93]
Total (95% CI)	**189**	**123**		**100.0 %**	**2.57 [0.28, 23.25]**

Total events: 3 (Bilamellar), 0 (Unilamellar)

Heterogeneity: $Chi^2 = 0.09$, df = 1 (P = 0.77); $I^2 = 0.0\%$

Test for overall effect: Z = 0.84 (P = 0.40)

Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1 Bilamellar tarsal rotation versus tarsal advance and rotation, Outcome 3 Defective lid closure following surgery.

Review: Interventions for trachoma trichiasis

Comparison: 1 Bilamellar tarsal rotation versus tarsal advance and rotation

Outcome: 3 Defective lid closure following surgery

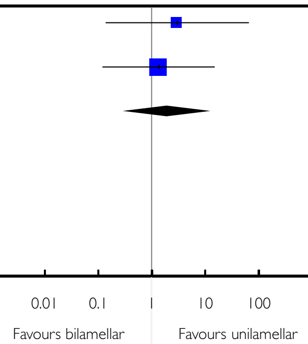
Study or subgroup	Bilamellar n/N	Unilamellar n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Reacher 1990	2/39	0/22		33.5 %	3.00 [0.14, 65.34]
Reacher 1992	2/150	1/101		66.5 %	1.35 [0.12, 15.10]
Total (95% CI)	**189**	**123**		**100.0 %**	**1.90 [0.29, 12.37]**

Total events: 4 (Bilamellar), 1 (Unilamellar)

Heterogeneity: $Chi^2 = 0.16$, df = 1 (P = 0.69); I^2 =0.0%

Test for overall effect: Z = 0.67 (P = 0.50)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 Peri-operative azithromycin versus no azithromycin, Outcome 1 One or more lashes touching the globe at one year.

Review: Interventions for trachoma trichiasis

Comparison: 2 Peri-operative azithromycin versus no azithromycin

Outcome: 1 One or more lashes touching the globe at one year

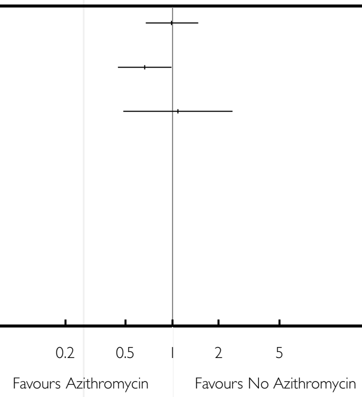
Study or subgroup	Azithromycin n/N	No azithromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Burton 2005a	84/204	92/222			0.99 [0.67, 1.46]
West 2006 (1)	62/944	45/470			0.66 [0.44, 0.99]
Zhang 2006	17/57	16/57			1.09 [0.48, 2.45]
Subtotal (95% CI)	**0**	**0**			**0.0 [0.0, 0.0]**

Total events: 163 (Azithromycin), 153 (No azithromycin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); I^2 =0.0%

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



(1) Compared to tetracycline

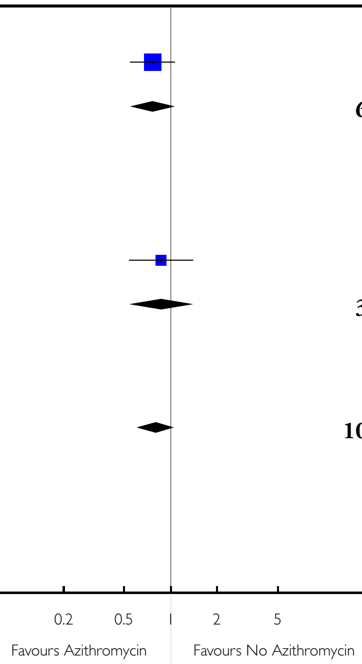
Analysis 2.2. Comparison 2 Peri-operative azithromycin versus no azithromycin, Outcome 2 One or more lashes touching the globe at longer follow-up.

Review: Interventions for trachoma trichiasis

Comparison: 2 Peri-operative azithromycin versus no azithromycin

Outcome: 2 One or more lashes touching the globe at longer follow-up

Study or subgroup	Azithromycin n/N	No azithromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 Three years					
West 2006 (1)	99/884	62/438		67.3 %	0.76 [0.54, 1.07]
Subtotal (95% CI)	**884**	**438**		**67.3 %**	**0.76 [0.54, 1.07]**
Total events: 99 (Azithromycin), 62 (No azithromycin)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.54 (P = 0.12)					
2 Four years					
Burton 2005a	50/127	60/140		32.7 %	0.87 [0.53, 1.41]
Subtotal (95% CI)	**127**	**140**		**32.7 %**	**0.87 [0.53, 1.41]**
Total events: 50 (Azithromycin), 60 (No azithromycin)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.58 (P = 0.56)					
Total (95% CI)	**1011**	**578**		**100.0 %**	**0.80 [0.60, 1.05]**
Total events: 149 (Azithromycin), 122 (No azithromycin)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.17$, df = 1 (P = 0.68); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.60 (P = 0.11)					
Test for subgroup differences: $Chi^2 = 0.17$, df = 1 (P = 0.68), $I^2 = 0.0\%$					



(1) Compared to tetracycline

ADDITIONAL TABLES

Table 1. Bilamellar tarsal rotation compared to techniques that do not create a full-thickness incision of the tarsal plate and complete rotation of the lash-bearing tissue

Outcome	Other technique Follow-up range 5 to 11 months	Bilamellar tarsal rotation n/N	Other technique n/N	Odds ratio (95% CI)
Post-operative trichiasis	Tarsal grooving	10/39	29/33	0.05 (0.01, 0.17)
	Eversion splinting	10/39	14/21	0.17 (0.05, 0.55)
	Tarsal advance	10/39	17/38	0.43 (0.16, 1.11)

Data from Reacher 1990.
n = number of eyes with outcome; N = total number of eyes followed up

Table 2. Bilamellar tarsal rotation surgery compared to posterior lamellar tarsal rotation

Outcome	Follow-up	Bilamellar tarsal rotation n/N	Posterior lamellar tarsal rotation n/N	Odds ratio (95% CI)
Post-operative trichiasis	3 months	12/124	15/132	0.84 (0.37, 1.86)

Data from Adamu 2002
n = number of eyes with outcome; N = total number of eyes followed up

Table 3. Bilamellar tarsal rotation surgery compared to cryotherapy or electrolysis

Outcome	Other technique Follow-up range 1 to 21 months	Bilamellar tarsal rotation n/N	Other technique n/N	Odds ratio (95% CI)
Post-operative trichiasis	Cryotherapy	6/52	41/57	0.05 (0.02, 0.14)
	Electrolysis	6/52	30/57	0.12 (0.04, 0.32)

Data from Reacher 1992
n = number of eyes with outcome; N = total number of eyes followed up

Table 4. Posterior lamellar tarsal rotation surgery compared to epilation

Outcome	Follow-up	Posterior lamellar tarsal rotation surgery n/N	Epilation n/N	Odds ratio (95% CI)
Post-operative trichiasis	Two years	114/637	298/641	0.25 (0.19, 0.32)
Visual acuity change: deterioration of one or more lines of visual acuity	One year	168/620	174/598	0.91 (0.71, 1.16)
	Two years	207/613	224/603	0.86 (0.68, 1.09)
Deterioration in corneal opacification	One year	7/620	12/598	0.56 (0.22, 1.43)
	Two years	25/613	33/603	0.73 (0.43, 1.25)

Data from Rajak 2011a.
n = number of eyes with outcome; N = total number of eyes followed up

Table 5. Absorbable (polyglactin-910) compared to non-absorbable (silk) sutures

Outcome	Follow-up	Absorbable sutures n/N	Silk sutures n/N	Odds ratio (95% CI)
Post-operative trichiasis	One year	114/608	120/628	0.98 (0.73, 1.30))
	Two years	117/609	118/609	0.99 (0.75, 1.32)
Visual acuity change: deterioration of one or more lines	One year	167/608	146/628	1.25 (0.97, 1.62)
	Two years	191/609	198/609	0.95 (0.75, 1.21)
Deterioration in corneal opacification	One year	6/608	11/628	0.56 (0.21, 1.52)
	Two years	24/609	18/609	1.35 (0.72, 2.51)

Data from Rajak 2011b.
n = number of eyes with outcome; N = total number of eyes followed up

Table 6. Sticking tape compared to epilation

Outcome	Follow-up	Sticking tape n/N	Epilation n/N	Odds ratio (95% CI)
Post-operative trichiasis	3 months	6/21	18/18	0.01 (0, 0.22)

Data from Graz 1999.

n = number of eyes with outcome; N = total number of eyes followed up

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Trachoma] explode all trees
#2 MeSH descriptor: [Trichiasis] this term only
#3 MeSH descriptor: [Chlamydia trachomatis] explode all trees
#4 MeSH descriptor: [Eye] explode all trees
#5 #3 and #4
#6 trachoma* or tracoma* or trichiasis
#7 MeSH descriptor: [Entropion] explode all trees
#8 entropion
#9 #6 or #7 or #8
#10 #1 or #2 or #5 or #9
#11 MeSH descriptor: [Ophthalmologic Surgical Procedures] explode all trees
#12 MeSH descriptor: [Eyelids] explode all trees
#13 MeSH descriptor: [Eyelid Diseases] explode all trees
#14 surg* or operat* or incis*
#15 tars* near/3 rotat*
#16 tars* near/3 plat*
#17 tarsotom* or trabut or ballen or streatfield
#18 epilat$ or electrolysis or cryo*
#19 (tap* or plaster*) near (eye*)
#20 (tap* or plaster*) near (lid*)
#21 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20
#22 #10 and #21

Appendix 2. MEDLINE (Ovid) search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. exp trachoma/
14. trichiasis/
15. exp chlamydia-trachomatis/
16. exp eye/

17. 15 and 16
18. (trachoma$ or tracoma$ or trichiasis).tw.
19. exp entropion/
20. entropion.tw.
21. or/18-20
22. 13 or 14 or 17 or 21
23. exp ophthalmologic surgical procedures/
24. exp eyelids/
25. exp eyelid diseases/
26. (surg$ or operat$ or incis$).tw.
27. (tars$ adj3 rotat$).tw.
28. (tars$ adj3 plate).tw.
29. (tarsotom$ or trabut or ballen or streatfield).tw.
30. (epilat$ or electrolysis or cryo$).tw.
31. ((tap$ or plaster$) adj5 eye$).tw.
32. ((tap$ or plaster$) adj5 lid$).tw.
33. or/23-32
34. 22 and 33
35. 12 and 34
36. (201307$ or 201308$ or 201309$ or 201310$ or 201311$ or 201312$ or 2014$ or 2015$).ed.
37. 35 and 36

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville (Glanville 2006).

Appendix 3. EMBASE (Ovid) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin$ adj3 trial$).tw.
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/

28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10

Appendix 4. ISRCTN search strategy

(Trachoma OR Tracoma OR Trichiasis)

Appendix 5. ClinicalTrials.gov search strategy

(Trachoma OR Tracoma OR Trichiasis)

Appendix 6. ICTRP search strategy

Trachoma OR Tracoma OR Trichiasis

WHAT'S NEW

Last assessed as up-to-date: 7 May 2015.

Date	Event	Description
19 May 2015	New search has been performed	Issue 11, 2015: Electronic searches have been updated
19 May 2015	New citation required and conclusions have changed	Issue 11, 2015: 6 studies (4 new: Gower 2013; Rajak 2011a; Rajak 2011b; Zhang 2006 and 2 from previous searches: Dhaliwal 2005; West 2006) have been included in this update

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 3, 2006

Date	Event	Description
29 October 2008	Amended	Converted to new review format.
1 March 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Conceiving the review: DY

Designing the review: MB

Screening search results: MB

Organising retrieval of papers: MB/DH

Screening retrieved papers against inclusion criteria: MB/EH/DH/EG

Appraising quality of papers: MB/EH/DH/EG

Abstracting data from papers: MB/DH/EG

Writing to authors of papers for additional information: MB

Obtaining and screening data on unpublished studies: MB

Data management for the review: MB

Entering data into RevMan: MB

Analysis of data: MB/EG

Interpretation of data: MB/EH/DH/EG

Writing the review: MB/EH/DH/EG

DECLARATIONS OF INTEREST

MJB was an investigator on three of the trials: Burton 2005a; Rajak 2011a; Rajak 2011b

EH was an investigator on two of the trials: Rajak 2011a; Rajak 2011b

EWG was an investigator on two of the trials: West 2006; Gower 2013

SOURCES OF SUPPORT

Internal sources

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External sources

- MJB is supported by the Wellcome Trust, UK.
- National Institute for Health Research (NIHR), UK.
- Richard Wormald, Co-ordinating Editor for the Cochrane Eyes and Vision Group (CEVG) acknowledges financial support for his CEVG research sessions from the Department of Health through the award made by the National Institute for Health Research to Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology for a Specialist Biomedical Research Centre for Ophthalmology.
- The NIHR also funds the CEVG Editorial Base in London.

The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS, or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The protocol for this review was originally published in 2003 (Yorston 2003). Since that time Cochrane methods have changed and we have incorporated these changes, in particular assessment of risk of bias in included studies.

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [therapeutic use]; Chlamydia trachomatis; Entropion [surgery]; Eyelid Diseases [surgery; *therapy]; Hair Removal [methods]; Randomized Controlled Trials as Topic; Trachoma [surgery; *therapy]

MeSH check words

Humans

Appendix II: Epilation for Minor TT: Four Year Results of a RCT

No funding bodies had any role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

Conclusions/ Significance

Most minor TT participants randomised to the epilation arm continued epilating and controlled their TT. Change in vision and corneal opacity was comparable between surgery and epilation-only participants. This suggests that good quality epilation with regular follow-up is a reasonable second-line alternative to surgery for minor TT for individuals who either decline surgery or do not have immediate access to surgical treatment.

Author Summary

Trachoma causes visual impairment through the effect of in-turned eyelashes (trichiasis) on the surface of the eye. Epilation is a common traditional practice of intermittent plucking of lashes touching the eye, however, its long-term effectiveness in preventing visual impairment is unknown. We conducted a randomized controlled trial of epilation versus eyelid surgery (the main treatment option) in 1300 people with mild trichiasis in Ethiopia. We defined mild trichiasis as fewer than six lashes touching the eye. We have previously reported results to two years and have now re-assessed these individuals at four years. Overall, we found no difference between the epilation and surgery groups in terms of change in vision and corneal opacity between baseline and four years. Most mild trichiasis participants randomised to the epilation arm continued epilating and controlled their trichiasis. This suggests that good quality epilation is a reasonable second-line alternative to surgery for mild trichiasis for individuals who either decline surgery or do not have immediate access to surgical treatment.

Introduction

Trachoma is the leading infectious cause of blindness worldwide [1]. Trachomatous trichiasis (TT) is the late stage scarring sequelae of repeated conjunctival *Chlamydia trachomatis* infection and inflammation in which the upper eyelid is distorted and rolled inwards (entropion) and the eyelashes turn towards the eye [2]. Trachoma leads to visual impairment through the damaging effect of trichiasis on the cornea. The risk of sight loss is directly correlated with disease severity, becoming more frequent with increasing severity of trichiasis [3–6]. The clinical phenotype ranges from a single aberrant eyelash touching the eye (without entropion) to the whole eyelid rolled inwards [7]. Some lashes may scratch the cornea directly while others are peripheral. Trichiasis is usually grouped, based on the number of eyelashes touching the eye into minor TT (1–5 lashes touching the eye) and major TT (>5 lashes touching the eye) [5,8]. Globally, the most recent World Health Organisation (WHO) estimate suggested 8 million people had trichiasis in 2009 [1]. Updated disease estimates will become available in the next few years from the Global Trachoma Mapping Programme.

Eyelid surgery is performed to correct the anatomical abnormality, in the expectation that this reduces the risk of sight loss [4,9]. The WHO advises that "all patients should be offered surgery for entropion trichiasis" [9]. However, up to half of the individuals with trachomatous trichiasis may not have significant entropion [7]. Therefore, there is a degree of ambiguity about how programmes should manage patients with non-entropic trichiasis, particularly those with only a few lashes touching the eye.

Despite considerable efforts to scale-up surgery programmes only around 150,000 people per year have been reported as treated surgically in recent years worldwide [10]. It has been estimated at the current rate the trichiasis backlog (ignoring incident cases) would not be dealt with until 2032, twelve years after the 2020 target for controlling trachoma [11]. Given the current surgical rate in Ethiopia, the country with the greatest burden of trichiasis, it will take more than 10 years to clear the backlog [12].

Many individuals with trichiasis, particularly those with mild disease, decline surgery, even when this is provided free and close to home [13–16]. Lack of time and fear of surgery are leading reasons for poor surgical uptake, suggesting a need for non-surgical, community-based management strategies for those declining surgery [8,13,17]. Poor surgical outcomes (recurrent trichiasis or an unsatisfactory cosmetic appearance) may also deter people from accepting surgery [5,18–20].

Epilation is a widespread traditional practice in many trachoma endemic societies, with up to 70% of people with trichiasis using this treatment strategy [3,6,13,21]. It involves the repeated plucking of lashes touching the eye with forceps [3,4,8]. Many individuals who decline surgical treatment consider epilation an acceptable alternative [13]. In view of the problems in delivering the necessary volume of surgery, the high rate of refusals in some areas and concerns about the quality of programmatic surgical outcomes, we conducted a randomized controlled non-inferiority trial of epilation versus surgery for minor trichiasis in Ethiopia; the two-year follow-up results have been reported [22]. With respect to the primary outcome of progression to major trichiasis there was an inconclusive result, relative to the predetermined non-inferiority margin of 10%. However, at two years there was no difference in the change in visual acuity or change in corneal disease between the two groups. At the two-year time-point all individuals who had been randomized at baseline to epilation were offered free surgery, however, only one third accepted. Here we report the four-year outcomes of study participants.

Methods

Ethics statement

This study was approved by the National Health Research Ethics Review Committee (NHRERC) of the Ethiopian Ministry of Science and Technology, the London School of Hygiene and Tropical Medicine Ethics Committee and Emory University Institutional Review Board. Potential participants were provided with both written and oral information in Amharic about the trial. For those agreeing to participate, written informed consent in Amharic was required prior to enrolment. If the participant was unable to read and write, the information sheet and consent form were read to them and their consent recoded by witnessed thumbprint. The detailed Trial Protocol is described in S1 Text and the CONSORT statement in Text S2 of the report of the two-year results [22].

Trial summary: baseline to two-years

The trial methods and results up to two-years have been published previously [22]. Briefly, 1300 individuals aged 18 years or over with previously un-operated minor trichiasis were recruited in West Gojjam, Amhara Region, Ethiopia from March to June 2008. At baseline, unaided and pinhole LogMAR visual acuities were measured at 4 metres using an ETDRS equivalent Tumbling-E LogMAR chart and the eyes were examined using 2.5x magnification loupes by a single ophthalmologist (SR), and graded according to the detailed WHO FPC Trachoma grading system. Standardised high-resolution digital photographs were taken of each of the clinical features. In individuals with bilateral trichiasis one eye was randomly designated as the "study eye" although both eyes were treated. Following baseline assessment, participants were randomised to one of two intervention groups: (1) posterior lamella tarsal rotation surgery, or (2) repeated epilation using high quality, machine-manufactured epilation forceps (Tweezerman). Surgery was performed by five experienced Integrated Eye Care Workers (IECWs), chosen on the basis of the quality of their surgery. The surgeons received refresher training and underwent a standardisation process. Individuals randomised to the epilation group were each given two pairs of epilation forceps; the participant and an accompanying adult ("epilator") with good near vision were trained to perform epilation. The procedure was explained and demonstrated to them by a field worker, who then in turn watched and checked the technique of the relative / patient in performing epilation.

Participants were followed-up at 6, 12, 18 and 24 months and re-assessed using the same protocol. Participants who showed evidence of disease progression during the follow-up period, defined as five or more lashes touching the eye or corneal changes related to observed lashes, were immediately offered primary surgery (epilation arm) or repeat surgery (surgery arm) to be performed by a senior surgeon. New epilating forceps were provided for epilation arm participants as required. Individuals with other ophthalmic pathology (e.g. cataract) were referred to the regional ophthalmic service in Bahirdar. At the end of the trial at two-years all epilation arm participants were offered free trichiasis surgery in the community. Some individuals accepted this, but the majority chose to continue epilating.

Four-year follow-up assessment

About four years after enrolment participants were invited for a follow-up assessment (March to August 2012). They were notified by a letter sent out through the village administration teams, which explained the purpose, date and place of follow-up assessment. People not able to come to the health facilities for assessment were assessed in their homes. Reasons for loss to follow-up were identified and documented. Participants were interviewed in Amharic about their vision, ocular symptoms, epilation forceps retention and history of epilation and/or surgery since the two-year follow-up. Individuals were considered to be "frequent epilators" if they performed epilation at least once in two months. Participants enrolled into the epilation arm were asked about their views on epilation and epilation practices.

Unaided and pinhole LogMAR visual acuities were measured at 4 metres. Ophthalmic examinations were conducted in the same manner as the previous follow-ups by a single observer (EH) who had also conducted the 6 and 18-month follow-ups. Grades of trichiasis, entropion, and corneal opacity were documented and the eyes were photographed. The examiner was masked to the intervention allocation. The treatment allocation code had been previously broken for the two year analysis. Recurrent trichiasis was defined as one or more lashes touching the eye or evidence of epilation or repeat surgery. Clinical evidence of epilation was identified by the presence of broken or newly growing lashes, or areas of absent lashes. Change in corneal opacity was assessed by direct comparison of the baseline and four-year cornea photographs. Photographs were viewed on a computer screen at about 10x magnification by a single masked ophthalmologist (MJB). These were graded as improved, no change, or worse.

Statistical analysis

Patients initially randomised to epilation were sub-divided according to whether or not they had surgery during the four-year follow-up period. These are subsequently referred to as epilation-to-surgery and epilation-only groups, respectively. Baseline and four-year follow-up demographic and clinical characteristics, and the change in clinical phenotypes during follow-up were compared between the surgery-only, epilation-only and epilation-to-surgery participants using X^2 tests. The Wilcoxon rank-sum test was used to test for significant differences in number of lashes. Logistic regression was used to assess factors associated with trichiasis progression within the epilation-only group, to identify predictors of surgery uptake in all epilation arm participants and corneal opacity deterioration in all study participants. Ordinal logistic regression was used to assess factors associated with reduction in visual acuity by four-years in all study participants. Variables that were associated with the outcome on univariable analyses at a level of $p<0.05$ were retained in the multivariable logistic regression models.

Results

Participants and baseline characteristics

At baseline, 1300 individuals were recruited, of whom 650 were randomised to immediate surgery and 650 to epilation (Fig. 1). The baseline demographic and clinical characteristics of all 1300 participants have been previously described along with the results up to two-years follow-up [22]. At four-years 1151 (88.5%) were re-examined: 579 (89%) participants from the surgery arm and 572 (88%) from the epilation arm. The baseline demographic and clinical characteristics of these individuals are shown in Table 1 (columns A and B). They were all Amharan with an average age of 50.3 years (SD 14.4; range 18–95) at baseline. The majority were female (767, 66.6%) and illiterate (1034, 89.8%). Of those initially randomised to the epilation arm, 189 (33%) had undergone trichiasis surgery by the four-years follow-up, while the other 383 (67%) were still epilating only (Fig. 1).

There were 149 participants who were not re-examined at four-years. The reasons for not being re-examined are shown in Fig. 1. In summary, at baseline this group was slightly older ($p<0.001$), had worse presenting LogMAR visual acuity ($p<0.001$) and had slightly more corneal opacification ($p = 0.04$) than the 1151 re-examined at four-years. Other variables such as sex, literacy and other baseline clinical characteristics including trichiasis severity and corneal opacity were comparable between those re-examined and not re-examined at four-years.

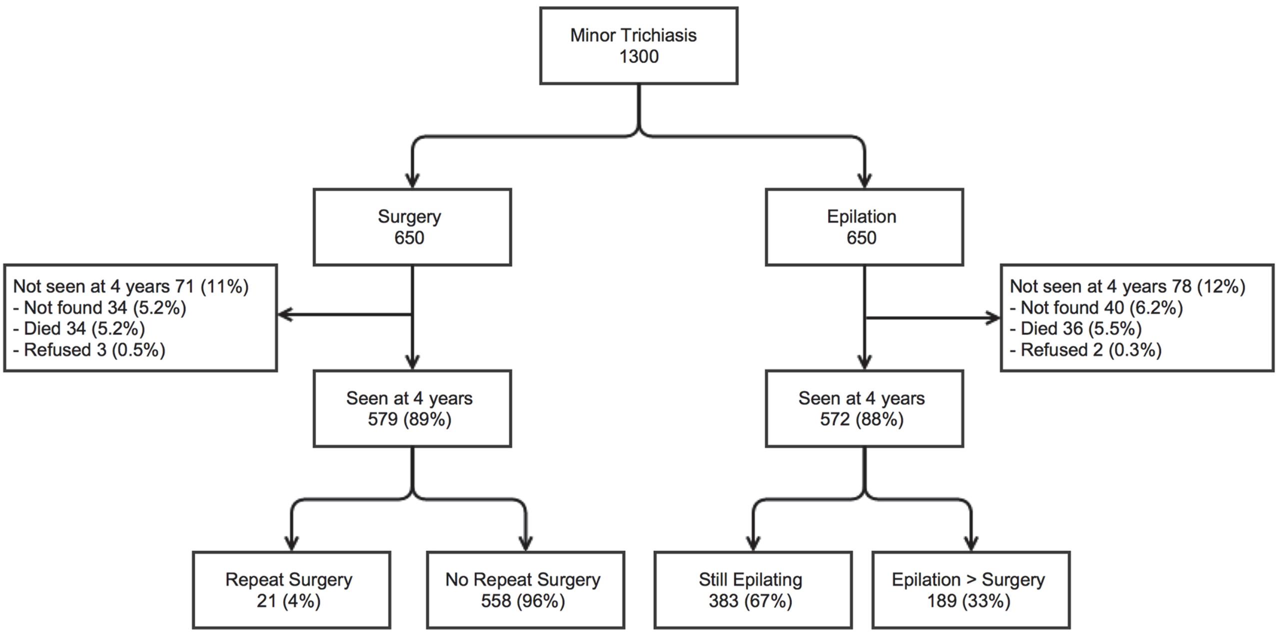

Fig 1. Study participant flow diagram.

doi:10.1371/journal.pntd.0003558.g001

Amongst those re-examined at four-years, there were more female participants randomised to surgery compared to those randomisation to epilation (p = 0.03), however, there was no difference in age or literacy status (Table 1). Baseline clinical characteristics were balanced between the randomisation arms (Table 1), with the exception of central corneal opacity (CC2/CC3), which was more frequent in the epilation group (128; 22.4%) than the surgery group (95; 16.4%).

The 383 epilation arm participants who were still only epilating at four-years (epilation-only) were slightly older than both the 579 surgery arm and 189 epilation-to-surgery participants (mean ages 50.0, 49.0 and 46.4 years respectively; $p<0.002$, Table 1). Within the epilation arm, the epilation-only group had slightly less baseline trichiasis than the epilation-to-surgery group ($p<0.001$). The epilation-only group had slightly less baseline entropion than both the surgery arm (p = 0.02) and epilation-to-surgery participants (p = 0.001). The baseline LogMAR visual acuity of the epilation-only group was slightly worse than both the surgery-arm (p = 0.007) and the epilation-to-surgery arm (p = 0.02), Table 1.

Trichiasis status at four-years

During the four-year period, recurrent trichiasis developed in 122 (21.1%) of the 579 participants randomised to surgery. Of these 122, 61 (50.0%) were practicing epilation at four years. Twenty-one (3.6%) had undergone repeat surgery during the four years. Among the 189 epilation-to-surgery participants, 42 (22.2%) had failed surgery (recurrent trichiasis), of whom 27 (64.2%) were epilating.

At four-years, among the 383 epilation-only participants, 207 (54.1%) were successfully epilating (had no lashes touching the eye), 166 (43.3%) had minor trichiasis (<6 lashes) and 10 (2.6%) had major trichiasis (>5 lashes). Overall, the epilation-only group had more trichiasis, entropion and lid margin conjunctivalisation than either the surgery arm or the epilation-to-surgery group (Table 2).

Changes in clinical phenotype between baseline and four-years are shown in Table 3. The outcomes of surgery in terms of trichiasis, entropion and conjunctivalisation were mostly very good. In the epilation-only group, the number of lashes touching the eye increased in 82 (21.5%), however, this was mostly a minor increase, with progression from minor to major trichiasis in six (1.6%) of the 383 epilation only patients. The majority of individuals had less or the same level of trichiasis. Independent risk factors for 5+ lashes touching were baseline age ≥50 years, ≥3 lashes at baseline, and infrequent epilation (Table 4).

Visual acuity at four-years

At four-years the surgery arm and epilation-to-surgery participants had slightly better LogMAR visual acuity than the epilation-only group (Table 2). However, this difference is attributable to the pre-existing difference in baseline vision (reported above, Table 1), as there was no difference between the different groups in terms of change in visual acuity between baseline and four-years (Table 3). Age ≥50 years, male gender, detection of other visually impairing conditions (e.g. cataract), baseline corneal opacification (CC2/CC3) and incident/progressive corneal opacification were independently associated with deterioration in visual acuity (Table 5).

Corneal opacification at four-years

Overall, few individuals had a change in corneal opacification, determined by the comparison of baseline and four-year photographs (Table 3). There was no difference in change of corneal opacification between the surgery arm and the epilation-only group or the epilation-to-surgery

Table 1. Baseline demographic and clinical characteristics of participants seen at four years.

Characteristics	(A) Surgery Arm (579)		(B) Epilation Arm (572)		(C) Epilation-Only (383)		(D) Epilation-to-Surgery (189)		A v B	A v C	C v D
	n	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*p-value*	*p-value*	*p-value*
Gender. female	403	(69.6%)	364	(63.6%)	243	(63.2%)	122	(64.6%)	0.032	0.038	0.750
Age, mean years (SD)	49.0	(14.0)	50.0	(13.9)	51.8	(13.5)	46.4	(14.1)	0.219	0.002	<0.001
Illiterate	517	(89.3%)	517	(90.4%)	344	(89.8%)	173	(91.5%)	0.540	0.795	0.512
Lash Number											
Median (IQR)	1.0	(1–2)	1.0	(1–2)	1.0	(1–2)	1.0	(1–3)	0.376	0.709	0.008
Trichiasis Distribution											
None (epilating)	106	(18.3%)	101	(17.7%)	67	(17.5%)	34	(18.0%)	0.632	0.481	<0.001
1–2 lashes	360	(62.2%)	346	(60.5%)	251	(65.5%)	95	(50.3%)			
3–4 lashes	94	(16.2%)	109	(19.1%)	58	(15.1%)	51	(27.0%)			
5 lashes	19	(3.3%)	16	(2.8%)	7	(1.8%)	9	(4.8%)			
Lash Location											
No lashes	106	(18.3%)	101	(17.7%)	67	(17.5%)	34	(18.0%)	0.564	0.064	0.005
Corneal ± Peripheral	422	(72.9%)	410	(71.7%)	264	(68.9%)	146	(77.2%)			
Peripheral	51	(8.8%)	61	(10.7%)	52	(13.6%)	9	(4.8%)			
Entropion Grade											
0	244	(42.1%)	265	(46.3%)	200	(52.2%)	65	(34.4%)	0.340	0.020	0.001
1	226	(39.0%)	216	(37.8%)	128	(33.4%)	88	(46.6%)			
2	106	(18.3%)	90	(15.7%)	54	(14.1%)	36	(19.0%)			
3	3	(0.5%)	1	(0.2%)	1	(0.3%)	0	-			
4	0	-	0	-	0	-	0	-			
Conjunctivalisation											
0	5	(0.9%)	5	(0.9%)	5	(1.3%)	0	-	0.455	0.311	0.288
1	15	(2.6%)	22	(3.8%)	17	(4.4%)	5	(2.7%)			
2	148	(25.7%)	129	(22.5%)	87	(22.6%)	42	(22.2%)			
3	411	(70.9%)	416	(72.7%)	274	(72.7%)	142	(75.1%)			
Visual Acuity											
-0.2–0.3	224	(38.9%)	192	(33.6%)	115	(30.0%)	77	(41.0%)	0.126	0.007	0.024
0.3–0.7	245	(42.5%)	243	(42.6%)	166	(43.3%)	77	(41.0%)			
0.7–1.1	66	(11.5%)	74	(13.0%)	54	(14.1%)	20	(10.6%)			
1.1–2.0	15	(2.6%)	23	(4.0%)	15	(3.9%)	8	(4.3%)			
CF/HM/PL/NPL	26	(4.5%)	39	(6.8%)	33	(8.6%)	6	(3.2%)			
Not measurable[a]	3	-	1	-	0	-	1	-			
Corneal opacity											
CC0	357	(61.7%)	311	(54.4%)	213	(55.6%)	98	(51.9%)	0.008	0.025	0.724
CC1	127	(21.9%)	133	(23.3%)	84	(21.9%)	49	(25.9%)			
CC2	85	(14.7%)	123	(21.5%)	83	(21.7%)	40	(21.2%)			
CC3	10	(1.7%)	5	(0.9%)	3	(0.8%)	2	(1.1%)			

The participants were subdivided into the following groups: (A) Surgery Arm, (B) Epilation Arm, (C) Epilation-Only, and (D) Epilation-to-Surgery. The following comparisons were made: Surgery Arm to Epilation Arm (A v B), Surgery Arm to Epilation-Only (A v C) and Epilation-Only to Epilation-to-Surgery (C v D).

P-values were calculated by X^2, with the exception of those for age and lash number differences, which were calculated by t-test and Wilcoxon rank-sum test, respectively.

CF, count fingers; HM, hand movements; PL, perception of light; NPL, no perception of light. CC0 to CC3: WHO Detailed Trachoma Grading System for corneal opacification.

[a] Baseline VA was not measured in 2 people from those not seen at 4 years and 4 people from those seen at 4 years.

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Table 2. Four-year clinical characteristics of participants.

Characteristics	(A) Surgery Arm (579)		(B) Epilation Arm (572)		(C) Epilation-Only (383)		(D) Epilation-to-Surgery (189)		A v C	C v D
	n	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*p-value*	*p-value*
Lash Number										
Median (IQR)	0	(0–0)	0	(0–1)	0	(0–2)	0	(0–0)	<0.001	<0.001
Trichiasis Distribution										
None	548	(94.7%)	371	(64.9%)	207	(54.0%)	164	(86.8%)	<0.001	<0.001
1–2 lashes	27	(4.7%)	133	(23.3%)	113	(29.5%)	20	(10.6%)		
3–4 lashes	4	(0.7%)	41	(7.2%)	37	(9.7%)	4	(2.1%)		
5+ lashes	0	-	27	(4.7%)	26	(6.8%)	1	(0.5%)		
Lash Location										
No lashes	548	(94.7%)	371	(64.9%)	207	(54.0%)	164	(86.8%)	<0.001	<0.001
Corneal±Peripheral	21	(3.6%)	185	(32.3%)	162	(42.3%)	23	(12.2%)		
Peripheral	10	(1.7%)	16	(2.8%)	14	(3.7%)	2	(1.0%)		
Entropion Grade										
0	559	(96.6%)	332	(58.0%)	159	(41.5%)	173	(91.5%)	<0.001	<0.001
1	14	(2.4%)	144	(25.2%)	133	(34.7%)	11	(5.8%)		
2	6	(1.0%)	92	(16.1%)	89	(22.7%)	5	(2.7%)		
3	0	-	4	(0.7%)	4	(1.0%)	0	-		
4	0	-	0	-	0	-	0	-		
Conjunctivalisation										
0	192	(33.2%)	61	(10.7%)	16	(4.2%)	45	(23.9%)	<0.001	<0.001
1	71	(12.3%)	25	(4.4%)	6	(1.6%)	19	(10.1%)		
2	130	(22.5%)	53	(9.3%)	15	(3.9%)	38	(20.2%)		
3	186	(32.1%)	432	(75.7%)	346	(90.3%)	86	(45.7%)		
Visual Acuity										
-0.2–0.3	229	(39.6%)	200	(35.0%)	118	(30.9%)	82	(43.4%)	0.006	0.028
0.3–0.7	223	(38.6%)	201	(35.2%)	142	(37.2%)	59	(31.2%)		
0.7–1.1	49	(8.5%)	68	(11.9%)	52	(13.6%)	16	(8.5%)		
1.1–2.0	13	(2.2%)	15	(2.6%)	12	(3.1%)	3	(1.6%)		
CF/HM/PL/NPL	64	(11.1%)	87	(15.2%)	58	(15.2%)	29	(15.3%)		
Not measurable	1	-	1	-	1	-	0	-		
Corneal Opacity										
CC0	293	(51.1%)	273	(48.2%)	177	(46.8%)	96	(51.1%)	0.065	0.746
CC1	203	(35.4%)	185	(32.7%)	125	(33.1%)	60	(31.9%)		
CC2	71	(12.4%)	100	(17.7%)	70	(18.5%)	30	(16.0%)		
CC3	7	(1.2%)	8	(1.4%)	6	(1.6%)	2	(1.1%)		

The participants were subdivided into the following groups: (A) Surgery Arm, (B) Epilation Arm, (C) Epilation-Only and (D) Epilation-to-Surgery. The following comparisons were made: Surgery Arm to Epilation-Only (A v C) and Epilation-Only to Epilation-to-Surgery (C v D).
P-values were calculated by X^2, with the exception of those for the lash number differences, which were calculated by the Wilcoxon rank-sum test. CF, count fingers; HM, hand movements; PL, perception of light; NPL, no perception of light. CC0 to CC3: WHO Detailed Trachoma Grading System for corneal opacification.

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group (Table 3). Incident or progressive corneal opacification was independently associated with age ≥50 years and the presence of some baseline corneal opacification (CC2/CC3), Table 6.

Table 3. Change in clinical phenotype between baseline and four-years.

Characteristics	(A) Surgery Arm (579)		(B) Epilation Arm (572)		(C) Epilation-Only (383)		(D) Epilation-to-Surgery (189)		A v B	A v C	C v D
	n	(%)	n	(%)	n	(%)	n	(%)	*p-value*	*p-value*	*p-value*
Trichiasis											
≥5 lashes more	0	-	6	(1.1%)	6	(1.6%)	0	-	<0.001	<0.001	<0.001
3–4 lashes more	0	-	21	(3.7%)	21	(5.5%)	0	-			
1–2 lashes more	5	(0.9%)	63	(11.0%)	55	(14.4%)	8	(4.2%)			
No change	120	(20.7%)	138	(24.1%)	101	(26.4%)	37	(19.6%)			
1–2 lashes less	346	(59.8%)	262	(45.8%)	172	(44.9%)	90	(47.6%)			
3–4 lashes less	92	(15.9%)	73	(12.8%)	25	(6.5%)	48	(25.4%)			
≥5 lashes less	16	(2.8%)	9	(1.6%)	3	(0.8%)	6	(3.2%)			
Entropion											
>1 grade worse	5	(0.9%)	32	(5.6%)	31	(8.1%)	1	(0.5%)	<0.001	<0.001	<0.001
1 grade worse	2	(0.3%)	116	(2.3%)	109	(28.5%)	7	(3.7%)			
No change	243	(42.0%)	234	(40.9%)	166	(43.3%)	68	(36.0%)			
1 grade better	227	(39.2%)	140	(24.5%)	62	(16.2%)	78	(41.3%)			
>1grade better	102	(17.6%)	50	(8.7%)	15	(3.9%)	35	(18.5%)			
Conjunctivalisation											
>1 grade worse	5	(0.9%)	10	(1.8%)	10	(2.6%)	0	-	<0.001	<0.001	<0.001
1 grade worse	26	(4.5%)	93	(16.3%)	79	(20.6%)	14	(7.4%)			
No change	190	(32.8%)	356	(62.3%)	271	(70.8%)	85	(45.2%)			
1 grade better	131	(22.6%)	46	(8.1%)	12	(3.1%)	34	(18.1%)			
>1 grade better	227	(39.2%)	66	(11.7%)	11	(2.9%)	55	(29.3%)			
Visual Acuity [a]											
>-0.3 much worse	83	(14.4%)	102	(17.9%)	63	(16.5%)	39	(20.9%)	0.271	0.892	0.219
-0.1 to -0.3 worse	109	(19.0%)	118	(20.7%)	75	(19.6%)	43	(23.0%)			
Within 0.1 (same)	240	(41.7%)	205	(36.0%)	150	(39.2%)	55	(29.4%)			
0.1 to 0.3 better	98	(17.0%)	102	(17.9%)	66	(17.5%)	36	(18.7%)			
>0.3 much better	45	(7.8%)	43	(7.5%)	28	(7.3%)	15	(8.0%)			
Corneal Opacification [b]											
More opacity	8	(1.4%)	13	(2.3%)	9	(2.4%)	4	(2.1%)	0.467	0.377	0.668
No Change	558	(97.2%)	548	(96.7%)	367	(96.8%)	181	(96.3%)			
Less opacity	8	(1.4%)	6	(1.1%)	3	(0.8%)	3	(1.6%)			

The clinical assessment included a change in trichiasis, entropion, conjunctivalisation, visual acuity and corneal opacification. The following comparisons were made: Surgery Arm to Epilation Arm (A v B), Surgery Arm to Epilation-Only (A v C) and Epilation-Only to Epilation-to-Surgery (C v D).
P-values were calculated by X^2.

[a] Four individuals in the surgery arm and two individuals in the epilation arm did not have visual acuity measured at both baseline and four years.

[b] Ten individuals did not have paired corneal photographs from both baseline and four years.

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Epilation practice at four-years

Among the epilation-only group 259 (67.6%) were "frequent epilators" (at least once in two months) between the two and four-year follow-ups. They were asked about their experience: 185 (72%) reported "no problem", 37 (14.3%) did not always find the trained epilators when needed, 17 (6.6%) had found epilation uncomfortable, the trained epilators of 9 (3.5%) reported difficulty epilating, and 7 (2.7%) had found people unwilling to epilate them. Among the 124 who were not frequently epilating, 119 (96%) did not have a specific reason for not

Table 4. Univariable and multivariable associations with the presence of 5+ lashes in Epilation-Only patients at four-years.

Variable	OR	95% CI	p-value
Univariable analysis			
Age, ≥50 years	3.04	(1.12–8.25)	0.029
Gender, Female	1.63	(0.67–3.98)	0.283
Baseline lash number ≥ 3 lashes	3.43	(1.48–7.96)	0.004
Entropion progression	1.09	(0.48–2.48)	0.834
Not Epilating frequently at 4 years	2.65	(1.04–6.75)	0.042
Multivariable logistic regression model			
Age, ≥50 years	2.97	(1.09–8.18)	0.035
Baseline lash number ≥ 3 lashes	3.51	(1.49–8.29)	0.004
Not Epilating frequently at 4 years	2.54	(0.98–6.59)	0.054

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epilating other than not needing to; the other five had nobody to perform epilation. Epilation frequency was not associated either with age (p = 0.31) or gender (p = 0.60). Compared to the "infrequent epilators", the "frequent epilators" had a slightly higher lash burden at baseline (Median: 1 vs 1, Wilcoxon rank-sum test, p = 0.19), but lower lash burden at four-years (Median: 0 vs 1, Wilcoxon rank-sum test, p = 0.073).

The epilation-only group were asked if they had tried to obtain trichiasis surgery at any time between the two and four-year follow-up: 352 (92%) replied "Never" and 325 (85%) reported that they were happy epilating. There was no statistically significant difference in the average lash burden at four-years between those who were happy epilating and those that were not (1.11 v 1.31, p = 0.30). Participants who were not happy epilating were more likely to have tried to obtain surgical treatment for their trichiasis between two and four-year follow-ups (Fisher's exact test, p = <0.001).

Table 5. Univariable and multivariable associations with visual acuity deterioration by four-years, amongst all individuals seen at four years (surgery and epilation arms).

Variable	OR	95% CI	p-value
Univariable analysis			
Age, ≥50 years	1.81	(1.47–2.24)	<0.001
Sex, Female	0.59	(0.47–0.74)	<0.001
Treatment Arm, Epilation	1.14	(0.93–1.41)	0.217
Lash number at 4 years ≥ 3 lashes	1.33	(0.86–2.06)	0.207
Other visually impairing conditions identified*	5.41	(2.71–10.8)	<0.001
Baseline corneal opacity (CC2/CC3)	1.68	(1.27–2.23)	<0.001
Incident or progressive corneal opacity at 4 years	3.60	(1.50–8.64)	0.004
Multivariable ordinal logistic regression			
Age, ≥50 years	1.45	(1.16–1.82)	0.001
Sex, Female	0.67	(0.53–0.85)	0.001
Other visually impairing conditions identified*	4.68	(2.27–9.64)	<0.001
Baseline corneal opacity (CC2/CC3)	1.40	(1.05–1.87)	0.021
Incident or progressive corneal opacity at 4 years	2.70	(1.11–6.60)	0.029

* 25 people had other visually impairing conditions identified: 20 cataract, 2 glaucoma, 1 Aphakic, 1 Evisceration, 1 corneal ulcer

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Table 6. Univariable and multivariable associations with corneal opacity deterioration (incident and progressive) by four-years, amongst all individuals seen at four years (surgery and epilation arms).

Variable	OR	95% CI	p-value
Univariable analysis			
Age, ≥50 years	4.43	(1.29–15.1)	0.017
Sex, Female	0.45	(0.19–1.07)	0.069
Treatment Arm, Epilation	1.66	(0.68–4.04)	0.263
Lash number at 4 years ≥ 3 lashes	0.74	(0.10–5.58)	0.769
Baseline corneal opacity (CC2/CC3)	3.19	(1.33–7.68)	0.009
Multivariable logistic regression			
Age, ≥50 years	3.85	(1.11–13.3)	0.033
Baseline corneal opacity (CC2/CC3)	2.67	(1.10–6.47)	0.030

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At the two-year follow-up, 589 / 603 (98%) of epilation arm participants still had their epilation forceps. At the four-year follow-up, 351 / 383 (92%) of the epilation-only group had retained at least one pair of epilation forceps. Females were more likely to have retained their forceps than males (OR 2.38; 95%CI 1.15–4.96; p = 0.020). At four-years, new forceps were provided to those who had lost their forceps, and did not want surgery.

Surgery uptake by the epilation arm participants

Univariate and multivariable associations with having surgery in epilation arm participants at any point during the four years of follow-up are shown in Table 7. Having surgery was independently associated with age less than 50 years, ≥3 lashes or corneal lashes at baseline, and frequent baseline epilation.

Management at four-years

At the four-year follow-up, all participants with recurrent trichiasis in the surgery arm and all participants in the epilation arm who had not previously had surgery were offered free surgery: only 17 / 383 (4.4%) of the epilation only participants accepted surgery, the remaining 366 (95.6%) preferred to continue epilating.

Table 7. Univariable and multivariable associations with accepting trichiasis surgery by four-years in all participants randomised to the epilation arm.

Variable	OR	95% CI	p-value
Univariable analysis			
Age, ≥50 years	0.53	(0.37–0.75)	<0.001
Sex, Female	1.06	(0.74–1.53)	0.750
Baseline lash number ≥ 3 lashes	2.27	(1.52–3.42)	<0.001
Baseline lash location (Corneal lashes)	3.19	(1.53–6.67)	0.002
Epilating frequently at baseline	2.32	(1.60–3.38)	<0.001
Multivariable logistic regression			
Age (≥50 years)	0.52	(0.34–0.78)	0.001
Baseline lash number ≥ 3 lashes	2.17	(1.40–3.39)	<0.001
Baseline lash location (Corneal lashes)	2.83	(1.33–6.05)	0.006
Epilating frequently at baseline	2.39	(1.57–3.63)	<0.001

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Discussion

Trachomatous trichiasis has a wide disease spectrum, with many individuals having relatively few lashes touching the eye [4,7]. This may partly explain the observation in this study that at two-years, despite being offered surgery free of charge and close to home, more than two-thirds of people practicing epilation declined surgery. Most (92%) of the epilation-only patients had not sought trichiasis surgery during the two to four-year follow-up period, and the majority (85%) reported that they were still happy epilating. This was also reflected in 96% of the epilation-only patients declining the offer of free community-based surgery at the time of the four-year follow-up. This finding is consistent with two Gambian cohort studies, in which 50–70% of individuals with major trichiasis declined trichiasis surgery [8,13]. Presence of symptoms interfering with work was a predictor for accepting surgery [13]. In our study, younger patients and those with higher baseline lash burden, corneal lashes and frequent epilation at baseline were more likely to accept surgery. It seems likely that these individuals are more symptomatic and therefore more motivated to find a potential long-term solution in surgery. It is encouraging to note that patients with corneal lashes and higher lash burden are more willing to accept surgical management, as these are strong indications for surgery.

In this study, surgery was better than epilation at correcting entropion and controlling trichiasis. However, it should be noted that at four-years 76.2% of the epilation-only participants had mild or no entropion, and 63.4% had no entropion progression. The epilation-only group generally controlled their trichiasis well by epilation, with only a few showing signs of significant progression. At four-years 2.6% of this group had major trichiasis (>5 lashes), which is low compared to the Gambian longitudinal study, in which 37% of the eyes progressed from minor to major trichiasis over four years [8]. However, in the Gambian study participants used low quality traditional epilation forceps without training. In our original trial analysis with follow-up to two-years, the primary endpoint was the presence of 5+ lashes touching or a history of surgery. At four-years only 6.8% of the epilation only group had 5+ lashes. This is somewhat less that the cumulative total of 13.9% individuals who had reached the primary endpoint by two-years, many of whom had accepted surgery at two years.

The proportion of participants in the surgery arm with recurrent trichiasis at four-years was relatively low compared to other trials and longitudinal studies [18,23,24]. This is because the risk of recurrence is heavily influenced by pre-operative disease severity; all the participants in our study had minor trichiasis at baseline; other studies have enrolled patients with more severe disease [5,22,25,26].

The epilation-only group had poorer baseline visual acuity compared to both the surgical arm participants and the epilation-to-surgery group. However, there was no difference in visual acuity change (baseline to four-years) between the epilating and surgery groups, which is similar to what we reported at two-years [22]. Several studies have reported an overall improvement in visual acuity after trichiasis surgery [5,27]. However, participants in these studies, unlike those in our present study, had a wider range of baseline trichiasis severity and were therefore more likely to have an improvement in vision following trichiasis surgery. Consistent with other studies, older age, presence of other blinding conditions, baseline corneal opacity and progressive corneal opacification were associated with deterioration of vision [8]. It is likely that much of the reduction in visual acuity over the four years is due to age related changes such as cataract. Interestingly, we found that female participants had 33% less risk of loss of vision than males. The explanation for this is unknown. The proportion of participants with visual impairment and blindness increased markedly at four-years in all groups, pointing to a major burden of blindness in the study area from other causes such as cataract in this older group of people.

The epilation arm as a whole and the epilation-only sub-group had more baseline corneal opacity than the surgery arm participants. However, there was no significant difference in change of corneal opacity between the different groups at four-years. This result is consistent with our findings at two-years and a report from a longitudinal study in The Gambia, which compared change in corneal opacity in individuals with minor trichiasis who had undergone surgery with those who had declined surgery and practiced epilation [8]. In farming communities, corneal opacity can occur from other causes such as corneal infections and injuries. Similarly, new corneal opacity has been reported after surgery without the presence of recurrent trichiasis [18]. Corneal opacity development or progression was associated with old age and the presence of some pre-existing opacification, similar to other studies [5,6].

More than two-thirds of the epilation-only participants reported frequent epilation. Most reported no problems. Difficulty of getting the trained epilator when they needed help was cited as the main problem, encountered by 14%. However, this could be addressed by training more than one family member. The high retention rate of forceps in this study is encouraging, suggesting that the forceps are valued.

This study has a number of limitations. This four-year follow-up and analysis was not pre-specified in the original trial protocol, which covered the period up to the two-year follow-up. The study ceased to have a fully randomised treatment allocation at two-years when all the epilation arm participants were offered free surgery, and hence we have adjusted follow-up outcomes for baseline imbalances. Those not examined at four-years were older and had worse baseline presenting visual acuity than those seen at four-years. This could have underestimated change in vision over time as older age is associated with greater visual impairment. However, this is unlikely to introduce bias in vision change between the surgery arm and epilation only group as those lost to follow-up were equally distributed between these groups.

We found that surgery was more effective for controlling trichiasis than epilation; however there was no difference in change in visual acuity and corneal opacity. The progression of minor trichiasis can be effectively mitigated with frequent epilation. We found low rates of surgery uptake among people with mild disease, even with free community-based surgery. There is a need for clear guidelines on how programmes should manage patients with a few non-entropic lashes who refuse surgery. Trichiasis in general and particularly major trichiasis warrants surgical treatment. However, the results of this study and the reality of low surgical uptake in many regions, suggest that good quality epilation, in the context of regular follow-up by a service that can provide surgery if subsequently needed, is a reasonable second-line alternative to surgery for minor trichiasis for individuals who either decline surgery or do not have immediate access to surgical treatment.

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Author Contributions

Conceived and designed the experiments: MJB SNR EH DCWM PTK KC HAW PME AB TG. Performed the experiments: EH SNR ZT TW MZ BG TG ABK PME MJB. Analyzed the data: EH MJB HAW SR. Wrote the paper: EH SNR ZT TW MZ BG TG ABK KC DCWM PTK CEG HAW PME MJB.

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Appendix III: Baseline Data Record Form

1.	**Demographic Data**	
1.1.	Study Reference Number	
1.2.	Matched to control: write reference number or 99	
1.3.	Recruitment Location	
1.4.	Recruitment Date	
1.5.	First Name	
1.6.	Father's Name	
1.7.	Grandfather's Name	
1.8.	Household Head's Name	
1.9.	Husband's Name (if female + married)	
1.10.	Name of Well Known Neighbour	
1.11.	Gott	
1.12.	Kabele	
1.13.	Woredah	
1.14.	Telephone number (if possible)	
1.15.	Who's tel is this	
1.16.	Other demographic notes	

		Answer Options	**Answer**
1.17.	Sex	1 = Male 2 = Female	
1.18.	Age	Years	
1.19.	Marital Status	*0 = Single* *1 = Married* *2 = Divorced* *3 = Widowed*	
1.20.	Ethnic Group	*1 = Amhara* *2 = Agew* *3 = Tigrie* *4 = Oromo* *77 = Other (describe)*	
1.21.	Literacy	0 = Illiterate 1 = Able to read Amharic a little 2 = Able to read Amharic well 4 = Able to read English and Amharic 77 = Other (specify)	
1.22.	Level of education achieved?	0 = No formal education 1 = Primary school (Grade 1-6) 2 = Junior secondary school (7-8) 3 = High school (9-10) 4 = Preparatory (11-12) 5 = Certificate 6 = 10+3 Diploma	

		7 = Degree and above	
1.23.	Your occupation	0 = No job 1 = Mainly farmer 2 = Mainly employed (manual) 3 = Mainly employed (non-manual) 4 = Mainly self employed (own business, merchant) 5 = Mainly daily labourer 6 = Retired 7 = Student 77 = Other (specify)	
1.24.	Total number of household members?	*Write number*	
1.25.	Members of the household under 16 years of age?	*Write number*	
1.26.	Members of the household between 16 and 60 years of age?	*Write number*	
1.27.	Members of the household above 60 years of age??	*Write number*	
1.28.	How many under 16 year's member of the household went to school?	*Write number*	
1.29.	How many adult members of the household (≥16 years of age) are "literate"?	*Write number*	
1.30.	The highest level of education achieved in the household	0 = No formal education 1 = Primary school (Grade 1-6) 2 = Junior secondary school (7-8) 3 = High school (9-10) 4 = Preparatory (11-12) 5 = Certificate 6 = 10+3 Diploma 7 = Degree and above	
1.31.	What is the highest status occupation with in the household	1 = Farming 2 = Manual employment 3 = Non –manual employment 4 = Self employment 5 = Daily labour 77 = Other (specify)	
1.32.	In the last month, have you had a job other than working in the field/shop owned or rented by the household?	0 = No 1 = Yes	
1.33.	Have you had any health problem during the past one month?	0 = No 1 = Yes	
1.34.	If yes, what kind of health problem did you have?	*Describe*	
1.35.	Have you ever been depressed or stressed during the last one month?	*0=No* *1=Yes*	
1.36.	Are you the household head? *If the answer is "No" Ask question 1.37 to 1.39 and If the Answer is "Yes", enter "99" to those three questions and go to section 2.*	0 = No 1 = Yes	
1.37.	What is the literacy level of the household head?	0 = Illiterate 1 = Able to read Amharic a little 2 = Able to read Amharic well 3 = Able to read English and Amharic 77 = Other (specify) 99 =NA	
1.38.	What is educational level of the household head?	0 = No formal education 1 = Primary school (Grade 1-6) 2 = Junior secondary school (7-8) 3 = High school (9-10) 4 = Preparatory (11-12) 5 = Certificate 6 = 10+3 Diploma 7 = Degree and above	
1.39.	Occupation of the household head?	0 = No job 1 = Mainly farmer 2 = Mainly employed (manual) 3 = Mainly employed (non-manual)	

		4 = Mainly self employed (own business, merchant) 5 = Mainly daily labourer 6 = Retired 7 = Student 77 = Other (specify) 99=NA	

2.	**Quality of Life Questionnaire**					
The following questions ask how you feel about your quality of life, health, or other areas of your life. I will read out each question to you, along with the response options. **Please choose the answer that appears most appropriate.** If you are unsure about which response to give to a question, the first response you think of is often the best one.						
Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last four weeks.**						
		Very poor	Poor	Neither poor nor good	Good	Very good
2.1.	How would you rate your quality of life?	1	2	3	4	5
		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.2.	How satisfied are you with your health?	1	2	3	4	5
The following questions ask about **how much** you have experienced certain things in the last four weeks.						
		Not at all	A little	A moderate amount	Very much	An extreme amount
2.3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
2.4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
2.5.	How much do you enjoy life?	1	2	3	4	5
2.6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5
		Not at all	A little	A moderate amount	Very much	Extremely
2.7.	How well are you able to concentrate?	1	2	3	4	5
2.8.	How safe do you feel in your daily life?	1	2	3	4	5
2.9.	How healthy is your physical environment?	1	2	3	4	5
The following questions ask about how completely you experience or were able to do certain things in the last four weeks.						
		Not at all	A little	Moderately	Mostly	Completely
2.10.	Do you have enough energy for everyday life?	1	2	3	4	5
2.11.	Are you able to accept your bodily appearance?	1	2	3	4	5
2.12.	Have you enough money to meet your needs?	1	2	3	4	5
2.13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
2.14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5
		Very poor	Poor	Neither poor nor good	Good	Very good
2.15.	How well are you able to get around?	1	2	3	4	5
		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.16.	How satisfied are you with your sleep?	1	2	3	4	5
2.17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
2.18.	How satisfied are you with your capacity for work?	1	2	3	4	5
2.19.	How satisfied are you with yourself?	1	2	3	4	5

2.20.	How satisfied are you with your personal relationships?	1	2	3	4	5
2.21.	How satisfied are you with your sex life?	1	2	3	4	5
2.22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
2.23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
2.24.	How satisfied are you with your access to health services?	1	2	3	4	5
2.25.	How satisfied are you with your transport?	1	2	3	4	5
The following question refers to how often you have felt or experienced certain things in the last four weeks.						
		Never	Seldom	Quite often	Very often	Always
2.26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

3.	**Visual Functioning Questionnaire**					
The first two questions are about your overall eyesight. I will read out a choice of five answers and you will choose the one that describes you best.						
	Question	**Answer options** (Please circle the number which corresponds to the answer)				
3.1.	Overall, how would you rate your eyesight using both eyes – with glasses or contact lenses if you wear them?	1.V.good	2. Good	3. Moderate	4. Bad	5. V.bad
		1	2	3	4	5
3.2.	How much pain or discomfort do you have in your eyes (e.g. burning, itching, aching)?	1. None	2. Mild	3. Moderate	4. Severe	5. Extreme
		1	2	3	4	5
In the next section, I am going to ask you how much difficulty, if any, you have doing certain activities. I will read out choice of five answers and you will choose the one that describes you best.						
		1. None	2. Mild	3.Moderate	4. Severe	5. Extreme/ Cannot do
3.3.	Because of your eyesight, how much difficulty do you have in going down steps/stairs/ steep slopes?	1	2	3	4	5
3.4.	How much difficulty do you have in noticing obstacles while you are walking alone (e.g. animals or vehicles)?	1	2	3	4	5
3.5.	How much difficulty do you have in seeing because of glare from bright lights	1	2	3	4	5
3.6.	Because of your eyesight, how much difficulty do you have in searching for something on a crowed shelf?	1	2	3	4	5
3.7.	How much difficulty do you have in seeing differences in colours?	1	2	3	4	5
3.8.	Because of your eyesight, how much difficulty do you have in recognizing the face of a person standing near you?	1	2	3	4	5
3.9.	How much difficulty do you have in seeing the level in a container when pouring?	1	2	3	4	5
3.10.	Because of your eyesight, how much difficulty do you have in going to activities outside of the house on your own (e.g. sporting events, shopping, religious events)?	1	2	3	4	5
3.11.	Because of your eyesight, how much difficulty do you have in recognizing people you know from a distance of 20 metres? (e.g. from that building/tree – give marker of 20 meters**)**	1	2	3	4	5
3.12.	How much difficulty do you have in seeing close objects (e.g. making out differences in coins or notes, reading newsprint)?	1	2	3	4	5
3.13.	How much difficulty do you have in seeing irregularities in the path when walking (e.g. potholes)?	1	2	3	4	5
3.14.	How much difficulty do you have in seeing after a few moments when coming inside after being in bright sunlight?	1	2	3	4	5
3.15.	How much difficulty do you have in doing activities that require you to see well close up (e.g. sewing – not including threading the needle, using hand tools)?	1	2	3	4	5
3.16.	Because of your eyesight, how much difficulty do you have in carrying out your usual work?	1	2	3	4	5
In the next section, I am going to ask you how you feel because of your vision problem. I will read out a choice of five answers and you will choose the one that describes you best.						
		1. Never	2. Rarely	3. Sometimes	4.Often	5. Very often
3.17.	Because of your eyesight, how often have you been hesitant to participate in social functions?	1	2	3	4	5
3.18.	Because of your eyesight, how often have you found that you are ashamed or embarrassed?	1	2	3	4	5
3.19.	Because of your eyesight, how often have you felt that you are a burden on others?	1	2	3	4	5
3.20.	Because of your eyesight, how often do you worry that you may lose your remaining eyesight?	1	2	3	4	5

3.21.	Does your *vision problem affect your life in ways we have not mentioned? If YES, describe how*	
	Record as fully as possible the answer given	

4.	**Activity and Participation**																
		Were you involved in [activity] in the last week?		Why have you not done [Activity]? 0= Not able to do it 1=There was no need to do the activity/was not available 2= The activity was not my responsibility 99=NA				How much difficulty did you have in doing [Activity] in the last week? 0 = Extreme /not able to do 1= A lot of difficulty 2= Some difficulty 3= Little difficulty 4= No difficulty 99=NA						Did you do this activity: 1 = fully assisted 2 =with some assistance 3 = with no assistance 99 = NA			
		0=No	1=Yes														
Household/Family																	
4.1.	Cooking/washing dishes	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.2.	House cleaning	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.3.	Washing clothes	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.4.	Shopping	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.5.	Looking after children	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.6.	Looking after elderly/sick	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.7.	Travel (any purpose)	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.8.	Other Specify:………	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
	Paid work																
4.9.	Paid employment	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.10.	Commission work	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.11.	Daily labour	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.12.	Self employed/own business	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.13.	Other paid work: Specify……………………	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
	Work for own use																
4.14.	Farming	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.15.	Animal rearing	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.16.	Fetching firewood/charcoal	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.17.	Fetching water	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.18.	Processing agricultural products/food	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.19.	Other production own use:Specify:…………	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
	Leisure																
4.20.	Social visits	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99

4.21.	Attending ceremonies	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.22.	Attending meetings	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.23.	Reading, listening to radio, watching TV, games etc	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.24.	Chatting, relaxing with friends/family	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
4.25.	Other activities, specify	0	1	0	1	2	99	0	1	2	3	4	99	1	2	3	99
	Personal activities																
4.26.	Eating, Bathing, Dressing, sleeping	-	-	-	-	-	-	0	1	2	3	4	99	1	2	3	99

5.	**Pain Impact Questionnaire**				
		Never	Occasionally	Often	Constantly
5.1.	How often have you experienced eye pain in the last month?	1	2	3	4
5.2.	In the last month, how often has eye pain interfered with your personal care such as bathing, eating, and dressing?	1	2	3	4
5.3.	In the last month, how often has eye pain disturbed your sleep?	1	2	3	4
5.4.	In the last month, how often has eye pain interfered with your household work such as cooking, house cleaning, washing cloth, fetching water, fetching firewood, caring to other family members?	1	2	3	4
5.5.	In the last month, how often has eye pain affected your agricultural or paid work?	1	2	3	4
5.6.	In the last month, how often has eye pain affected your participation in social activities such as attending weddings, social meetings, and funerals?	1	2	3	4

6.	**Self Rated Wealth**		
6.1.	How well-off do you think your household is in relation to the other households in the village?	1 = Very poor 2 = Poor 3 = Average (neither poor nor wealthy) 4 = Wealthy 5 = Very wealthy	

7.	**Ophthalmic Questionnaire**		
	Question	***Answer option***	**Answer**
7.1.	How many months/years since you have the trichiasis?	*Write duration in months*	
7.2.	Do you epilate?	0 = No 1 = Yes	
7.3.	How often do you epilate?	0 = Do not epilate 1 = More than once a week 2 = once/week to once/month 3 = Less than once a month	
7.4.	Does any other member of the household has/had trichiasis?	0 = No 1 = Yes	
7.5.	Do you feel ashamed or embarrassed due to the trichiasis?	*0 = No* *1 = Yes*	
7.6.	Do you worry that you may lose your remaining eyesight due to the trichiasis?	*0 = No* *1 = Yes*	
7.7.	Does your husband/wife/family member ignore you due to the trichiasis?	*0 = No* *1 = Yes*	
7.8.	Do you have sleeping problem? (If No, enter "99" to the next two questions and go to Q 6.11.)	*0 = No* *1 = Yes*	
7.9.	If yes, do you think your sleeping problem is related with the trichiasis?	*0 = No* *1 = Yes* *99 = NA*	
7.10.	How do you think your sleeping problem is related to the trichiasis?	*1 = Related to the pain* *2 = Psychological (frustration, low self esteem, poor functioning ...)* *77 = Other (Describe)* *99 = NA*	
7.11.	Dose the trichiasis restricts you from doing/participating in productive activities or earn an income?	*0 = No* *1 = Mildly (A little bit)* *2 = Moderately (Some restriction)* *3 = Severely (a lot of restriction)* *4 = Extremely/not able to do/participate)*	
7.12.	Does the trichiasis affect your life in any way? For instance in physical functioning, social functioning/relationship, marriage...etc	*0 = No* *1 = Yes*	
7.13.	If yes, in what ways? describe		

8.	**Visual Function Tests**					
8.1.						
	LogMAR Distance Visual Acuity using Peek	**Options**	**Right**		**Left**	
			LogMar Score	Dist	LogMar Score	Dist
		Presenting vision				
8.2.	Contrast Sensitivity (using Peek)	Perecentage of gray identified				
8.3	Near Vision Score from 40 CM					

9.	**Pre OP Ophthalmic Examination**			
		Answer Option	*Answer*	
9.1.	Eye being treated	1=Right 2=Left 3=Bilateral		
		Answer Option	*Right*	*Left*
9.2.	Primary Outcome			
9.3.	No. of medial globe lashes			
9.4.	No. of lateral globe lashes			
9.5.	No. of corneal lashes			
9.6.	Trichiasis grade	T 0,1,2,3		
9.7.	Number of metaplastic lashes			
9.8.	Number of misdirected lashes			
9.9.	Lower lid trichiasis	0= No 1= Yes		
9.10.	Entropion grade	E 0,1,2,3,4		
9.11.	Epilation	0= No 1= Yes		
9.12.	How much epilation	0 = none 2 = $1/3^{rd}$-$2/3^{rd}$ 1 = $<1/3^{rd}$ 3 = >2/3rd		
9.13.	Photo TT	*Number / date. month*		
9.14.	Ocular discharge	0= No 1= Serous (watery) 2= Purulent 3=Foamy 77= Other (describe)		
9.15.	Corneal scar grade	CO 1,2a,2b,2c,2d,3,4		
9.16.	Photo cornea	*Number / date. month*		
9.17.	Lagophthalmos	0= No 1= Yes		
9.18.	Conjunctivilisation of margin grade	CM 0,1,2,3		
9.19.	Papillary grade	P 0,1,2,3		
9.20.	Follicle grade	F 0, 1, 2, 3		
9.21.	Conj scar grade	C 0,1,2,3,6(n/a)		
9.22.	Conj scar grade if prev surgery	SC 0,1,2,3,4,5,6(n/a)		
9.23.	Tarsal plate photo	*Number / date. month*		
9.24.	Other examination Notes	*Describe*		

10.	**Intra and Immediate Post OP Ophthalmic Examination for Operated Eyes Only**					
		Answer Option	***Right***		***Left***	
Please first reset the stop watch and START the stop watch when the patients inters the surgery room after the randomisation is completed						
10.1.	Once ready to operate ask the surgeon to measure the distance between the lachrymal punctum medially and the lateral canthus and **STOP** the stop watch when he/she starts measuring	*Write in mm or circle 99 if NA*		99		99
Please* RESTART *the stop watch when the surgeon starts to injecting the lidocaine						
10.2.	Time the surgeon started injecting lidocaine	*Minute/Second*	/	99	/	99
10.3.	Time the surgeon started placing the lid clamp /everting suture is started	*Minute/Second*	/	99	/	99
10.4.	Time the first incision is made	*Minute/Second*	/	99	/	99
10.5.	Number of passes made with blade	*Write in number or circle 99 if NA*		99		99
10.6.	Number of cuts made with scissor to complete the incision	*Write in number or circle 99 if NA*		99		99
Once the surgeon has completed the incisions, STOP the watch ask the surgeon to measure the incision (Q10.5 – Q10.8)						
10.7.	Incision length in mm	*Write in mm or circle 99 if NA*		99		99
10.8.	Incision distance from the lid margin	*Write in mm or enter 99 if NA*	L		L	
			C		C	
			M		M	
RESTART the clock watch again once the surgeon completed measuring the incision						
10.9.	Was the incision parallel to the lid margin?	0 = No 1 = Yes 99 = NA	L		L	
			C		C	
			M		M	
10.10.	Bleeding	1 = Mild 2 = Moderate 3 = Excessive 99 = NA				
10.11.	Time suturing started	*Minute/Second*	/	99	/	99
10.12.	Time suturing completed/traction suture removed	*Minute/Second*	/	99	/	99
STOP the watch at this point and collect data on Q 10.14 – 10.24 before dressing is started						
10.13.	Number of sutures (knots)	*Write number or "99" if NA*				
10.14.	Sutures position in relation to the lashline	1= Suture positioned below to the lash line 2= Suture positioned right on the lash line 3= Suture positioned 1mm above the lashline 4= Suture positioned >1mm above the lash line 99=NA	L		L	
			C		C	
			M		M	
10.15.	Edge of the incion included in the suture?	*1 = ≤2mm of the incision not included* *2 = >2mm of the incision not included* *99 = NA*	L		L	
			M		M	
10.16.	Distance between suture knots (symmetry)	0 = Spaced within ≤2mm symmetry 1 = Spaced within >2mm symmetry 99 = NA				

		Answer Options	Right		Left	
10.17.	Suture tension/firmness	1 = Less firm/not sufficiently tight 2 = Sufficiently tight 3 = High tension/ extremely tight 99 = NA	L		L	
			C		C	
			M		M	
10.18.	Complications occurred	Describe				
Please examine the operated lid immediately after the surgery is completed and fill-in in the following						
10.19.	Level of eversion/entropion/	1=Extra eversion 2=Lid margin eversion 3=Partial lid margin entropion 4=Total lid margin entropion 99 =NA	Right		Left	
			L		L	
			C		C	
			M		M	
10.20.	Number of touching lashes	*Write number or "99" if NA*	L		L	
			C		C	
			M		M	
10.21.	Eye lid contour irregularity	0 = No 1 = Yes 99 = NA				
Take photo on primary gaze (looking straight up to the roof) and eye looking backward						
RESET the stop watch again and START it once photography is completed and allow the surgeon to do dressing and provide postop advice and recording						
10.22.	Time the patient is leaving the surgery room after post-op advise and recording is completed	*Minute/Second*	/			
Ask the patient the following question						
10.23.	How much pain have you experienced during the surgery (after the anaesthesia is injected)?	*0= None* *1= Mild* *2= Moderate* *3= Severe* *99=NA*				

COMPLETENESS CHECK

The field coordinator, Consent & Questionnaire field workers and the household data collectors are to make sure that each questionnaire is completed (tick box). Ensure that appropriate coding has been used and that all questions are answered and legible.													
Date	Dem	VF	QoL	A&P	PIQ	S.rated wealth	Oph. Q	V test	PreoP Exam	PostoP Exam	Asset	PRW
Name and Sig of Consent & Questionnaire field worker												
Name and Sig of VA measuring field worker												
Name and Sig of Examiner												
Name and Sig of Intra operative data collector												
Name and Sig of Coordinator												

To be completed by visiting the participant's house and village, if the participant is selected as a comparison case for the impact study

11.	**Peer Rated Wealth**				
	Please randomly select three village members of the participant and ask the following question on the wealth status of the household understudy		**Peer 1**	**Peer 2**	**Peer 3**
11.1.	How well-off do you think the household of [Household head] in relation to the other households in the village?	1 = Very poor 2 = Poor 3 = Average (neither poor nor			

		wealthy) 4 = Wealthy 5 = Very wealthy			

12.	Asset (Welath Indicators)		
Please observe and record the following about the main building in the household			
	Question	**Answer options**	**Answer**
12.1.	What is the major construction material of the external walls?	1 = Brick 2 = Concrete blocks 3 = Sand and Cement 4 = Wood, logs 5 = Tin 6 = Mud 7 = Sticks and leafs 8 = Wood and mud 9 = Wood and animal faeces 10 = Sticks and Animal faeces 11 = Sticks and plastics 12 = Rock 77 = Other (specify)	
12.2.	What is the major material of the roof?	1 = Concrete 2 = Tin (metal sheets) 3 = Cereals Straw or grass 4 = Plastic sheath 5 = Wood 6 = Wood and mud 77 = Other (specify)	
12.3.	Number of tin the house is made	Write number	
12.4.	Does the house has a Cornish	0 = No 1 = Yes, Plastic 2 = Yes, Nylon 3 = Yes, Cloth 4 = Yes, Wood 77 = Other (specify)	
12.5.	What is the primary material of the floor	1 = Tile 2 = Concrete 3 = clay/earthen floor 77 = Other (specify)	
12.6.	How many rooms do the members of your household occupy, including bedrooms, living rooms and rooms used for household enterprises (do not include bathrooms, kitchens, balconies and corridors)	Write number of rooms	
12.7.	Location of domestic animals (cattles) dwelling	0 = No cattles 1 = Within the main house 2 = Outside the main house	
12.8.	Kitchen location	1 = Within the main house 2 = Outside the main house	
12.9.	How many houses are there other than the main house (excluding, cattle dwelling and kitchen)	Write number of houses	
12.10.	What is the type of toilet that is used in your household	0 = No latrine 1 = Traditional latrine 2 = Improved pit latrine with ventilation (VIPL) 3 = Flush toilet 77 = Other (specify)	
12.11.	Where is the toilet located	1 = Inside dwelling 2 = Outside dwelling – in compound 3 = Outside dwelling – outside compound 99 = NA	
12.12.	Is this dwelling owned or rented?	1 = Owned 2 = Rented (go to question 5.9)	

12.13.	Please estimate the amount of money you could receive as rent per month if you let this dwelling to another person	Write in Birr or NA			
12.14.	If rented, what is the value paid per month?	Write in Birr or NA			
12.15.	Dose the household has Electric (solar) light	0 = No 1 = Yes			
12.16.	Dose the household own the following materials?		*0 = No*	*1 = Yes*	*Amount*
		Radio/HiFi stereo	*0*	*1*	
		TV/VCD/DVD	*0*	*1*	
		Fridge/Freezer	*0*	*1*	
		Electric stove	*0*	*1*	
		Telephone/Cellular Phone	*0*	*1*	
		Cupboard	*0*	*1*	
		Sofa set	*0*	*1*	
		Table small	*0*	*1*	
		Table medium	*0*	*1*	
		Table large	*0*	*1*	
		Traditional Bed	*0*	*1*	
		Metal bed	*0*	*1*	
		Wood/spring bed	*0*	*1*	
		Chair	*0*	*1*	
		Bench	*0*	*1*	
		Stool/small chair	*0*	*1*	
		Showcase large	*0*	*1*	
		Showcase medium	*0*	*1*	
		Showcase small	*0*	*1*	
		Clock	*0*	*1*	
		Bicycle	*0*	*1*	
		Water pump/generator	*0*	*1*	
		Vehicle, including Bajaj	*0*	*1*	
		Motorbike	*0*	*1*	
		Mule/donkey cart	*0*	*1*	
12.17.	Dose the household own the following? (If Land, enter response by changing in to Hectar)	*Mango Tree*	*0*	*1*	
		Avocado Tree	*0*	*1*	
		Guava Tree	*0*	*1*	
		Lemon Tree	*0*	*1*	
		Orange Tree	*0*	*1*	
		Banana Tree	*0*	*1*	
		Gesho Tree	*0*	*1*	
		Sugarcane land in Hectar	*0*	*1*	
		Chat land in Hectar	*0*	*1*	
		Ecualiptous tree land in Hectar	*0*	*1*	
		Coffee land in Hectar	*0*	*1*	
		Vegtable land in Hectar	*0*	*1*	
		Teff and other cereals land in Hectar	*0*	*1*	
		Town land in Hectar	*0*	*1*	
12.18.	How much amount of land does the family own?	*Write total amount of land in Hectar*			
12.19.	How many Oxes does this household own in total?				
12.20.	How many cows does this household own in total?				
12.21.	How many calfs does this household own in total?				
12.22.	How many goats does this household own in total?	*Write number*			
12.23.	How many sheep does this household own in total?	*Write number*			
12.24.	How many chickens/ does this household own in total?	*Write number*			
12.25.	How many donkey/mule does this household own in total?	*Write number*			
12.26.	How many horses does this household own in total				

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