Diabetic Retinopathy in Kenya: assessment of services and interventions to improve access

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Declaration

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

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With my supervisors, Prof Allen Foster(right) and Dr Covadonga Bascaran(left)

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Left to right: Prof Allen Foster, Prof Colin Cook, Dr Nyawira Mwangi, Dr Edward Fottrell, Dr Covadonga Bascaran at the London School of Hygiene and Tropical Medicine, just after the PhD examination

Dedication

This thesis is dedicated to my maternal grandmother Mrs Phoebe Wangechi Kimburi, and to the memory of my late paternal grandmother Mrs Mary Wothaya Ngumo (I did not get a chance to meet my grandfathers).

You didn't have a chance to attend school, due to the barriers to entry to education for people in your circumstances. Nevertheless, you passionately encouraged me to p ursue education diligently.

Like you, many persons living with diabetes do not have access to the services that they need.

We have shown that we can break the barriers to get them to attend screening for diabetic retinopathy as a way of preventing vision loss and blindness.

This thesis is also dedicated to my parents Mr and Mrs Mwangi Ngumo in recognition that you gave my siblings and I everything you could to enable us obtain education. You gave us opportunities you did not have yourselves.

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Abstract

Background

The majority of the estimated 425 million people living with diabetes (PLWD) reside in low and middle-income countries. An estimated 35% of PLWD have diabetic retinopathy (DR) and 10% have vision threatening retinopathy (VTDR) requiring urgent treatment. There is a high unmet need for DR services in many of these countries, which highlights the need to strengthen health systems. The purpose of this PhD is to provide evidence on the factors and interventions for promoting access and utilisation of services for DR. The study setting is Kenya, which has adopted Universal Health Coverage (UHC) as a target for 2030. The specific objectives were: i) To synthesise the literature on the magnitude, needs and priorities for diabetic retinopathy services; ii)To conduct an assessment of the health system for PLWD and diabetic retinopathy in Kenya; iii) To use the evidence from the literature and evidence from the health system assessment as a platform for health system strengthening; and iv) To develop and test an intervention through a randomized clinical trial to improve uptake of eye care services for PLWD in Kenya.

Methods

The first objective was achieved through a literature review. For the second objective, a health system assessment for diabetes and DR was conducted, based on the World Health Organization's framework for health systems building blocks and the tracer condition approach. For the third objective, as part of health system strengthening, national guidelines for DR and a short online course for health care workers were developed. For the fourth objective, using the evidence from the health system assessment, we designed and implemented a two arm (1:1) pragmatic

cluster randomized controlled trial to test whether a peer-supporter-led package of interventions can increase uptake of DR screening among members of diabetes support groups who have never had screening. The primary outcome measure was attendance at DR screening in the 14 clusters and 734 participants followed up over six months.

Results

A review of the literature on the epidemiology and interventions for diabetes and DR, identified that the key priorities of health systems in reducing the incidence of DR-related blindness are: (1) control of diabetes (2) early detection of DR and (3) appropriate treatment of DR. However, most of the available evidence is from high-income countries. The health system assessment for diabetes and DR in Kenya identified a high unmet need for DR screening, and uptake of screening was the bottleneck to entry to DR services. The barriers were lack of referral and inadequate knowledge of diabetes eye health. The lack of clinical guidelines and inadequate opportunities for continuous professional development limit the availability of DR services. To address this barrier, national clinical guidelines were developed through a process of adaptation from generic guidelines. The scope of the guidelines is screening, diagnosis, treatment and follow-up for DR. In addition, an online training course on the control of DR has been developed using the theories of adult learning and instructional design. The results of the cluster-randomized trial indicate that the peer-led interventions are acceptable and reach the population most vulnerable to DR. One in two of the participants in the intervention arm compared to one in ten in the control arm attended DR screening. We also found that most of the effect occurs early—within the first month of the intervention.

Conclusions

This thesis provides evidence about how national DR guidelines and online training programmes for health workers can be developed to strengthen health systems and improve eye services for PLWD. The thesis also provides evidence that the uptake of DR screening by PLWD can be significantly increased through a community based intervention utilising diabetes support groups and peer-supporters. This can lead to earlier diagnosis of DR and the prevention of blindness.

Acronyms

$	US dollar
ADDIE	Analysis, Design, Development, Implementation, Evaluation Framework
AGREE	Appraisal of Guidelines, Research and Evaluation
AI	Artificial Intelligence
AMREF	African Medical Research Foundation
Anti-VEGF	Anti-vascular Endothelial Growth Factor
BMC	Biomed Central
BMI	Body Mass Index
CCM	Chronic Care Model
CD	Communicable Disease
CEA	Cost-Effectiveness Analysis
CHEW	Community Health Extension Worker
CHV	Community Health Volunteer
CI	Confidence Interval
CIFR	Consolidated Framework for Implementation Research
CONSORT	Consolidated Standards of Reporting Trials
CPD	Continuous Professional Development
cRCT	Cluster Randomized Controlled Trial
CSME	Clinically Significant Macula Oedema
DALY	Disability Adjusted Life Years
DCCT	Diabetes Control and Complications Trial
DED	Diabetic Eye Disease
DM	Diabetes Mellitus
DMO	Diabetic Macula Oedema
DR	Diabetic Retinopathy
DRS	Diabetic Retinopathy Screening
DSG(s)	Diabetes Support Group(s)
DTA	Diagnostic Test Accuracy
DURE	Uptake of Retinal Examination in Diabetes Study
EHSA	Eye Health System Assessment
EMR	Electronic Medical Records
EPICOT	Evidence, Population, Intervention, Comparator, Outcome, Timeline
ETDRS	Early Treatment Diabetic Retinopathy Study
FGD	Focus Group Discussion
GDP	Gross Domestic Product
HSA	Health System Assessment
Hb	Haemoglobin
HbA1c	Glycated Haemoglobin
HMIS	Health Management Information System
HSS	Health System Strengthening
ICD	International Classification of Diseases

IDF	International Diabetes Federation
INGO	International Non-Governmental Organization
Intl$	International Dollar
KDDA	Kenya Defeat Diabetes Association
KDHS	Kenya Demographic and Health Survey
Ksh	Kenya shilling
LMIC	Low and Middle Income County
LSHTM	London School of Hygiene & Tropical Medicine
Mg/dl	Milligrams per Decilitre
Mmol/l	Millimole per Litre
MOH	Ministry of Health
mol	Mole
MRC	Medical Research Council
NCD	Non-Communicable Disease
NGO	Non-Governmental Organization
NHIF	National Hospital Insurance Fund
NHS	National Health Service
OCO	Ophthalmic Clinical Officer
OCT	Optical Coherence Tomography
OEU	Operation Eyesight Universal
OGTT	Oral Glucose Tolerance Test
ON	Ophthalmic Nurse
OOP	Out of Pocket
OR	Odds Ratio
PDR	Proliferative Diabetic Retinopathy
PhD	Doctor of Philosophy
PI	Principal Investigator
PICO	Population, Intervention, Comparator and Outcome
PLWD	People Living With Diabetes
PPP	Public Private Partnership
PS	Peer-supporter
PSED	Posterior Segment Eye Diseases
Q	Quarter
QALY	Quality Adjusted Life Year
RCT	Randomized Controlled Trial
SDG	Sustainable Development Goals
SE	Self-Efficacy
SMS	Short Message Service
STDR	Sight-Threatening Diabetic Retinopathy
STEPS	STEPwise Survey for Surveillance
UHC	Universal Health Coverage
UKPDS	United Kingdom Prospective Diabetic Retinopathy Study
UN	United Nations
UNESCO	United Nations Educational, Scientific and Cultural Organization
US	United States
VEGF	Vascular Endothelial Growth Factor

VI	Visual Impairment
VR	Vitreo-Retinal Service
VTDR	Vision-Threatening Diabetic Retinopathy
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy
WHO	World Health Organization

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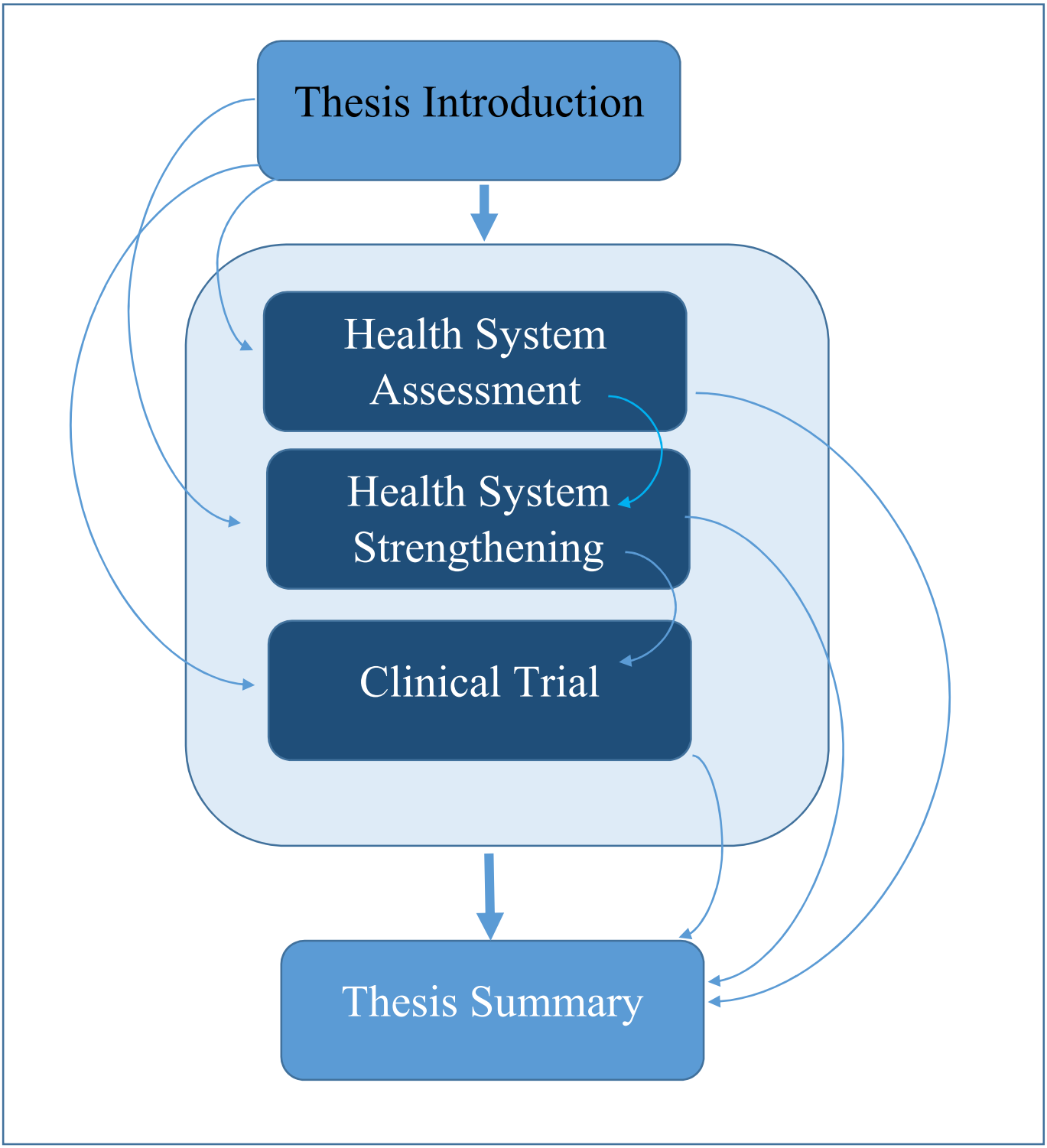
Thesis Introduction
Health System Assessment
Health System Strengthening
Clinical Trial
Thesis Summary

Section A

"You think you understand two because you understand one and one. But you must also understand 'and'."

— Mawlana Jalal-al-Din Rumi

13th century Persian poet (1207-1273)

Finalists for the Three Minute Thesis competition at the London School of Hygiene and Tropical Medicine, May 2017; Nyawira Mwangi is 2nd left.

Chapter 1- Introduction

1.0 Overview

This chapter presents an overview of the research described in this thesis through a brief description of: definition of key terms; research domain; purpose; impetus; rationale; aims and objectives; structure of the thesis and the role of the candidate in the research.

1.1 Definition of key terms

Diabetes

Diabetes mellitus (herein referred to as diabetes) is a group of metabolic diseases characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.[1] The World Health Organization (WHO) diagnostic criteria for diabetes is based on any of the following parameters: fasting plasma glucose of ≥ 126 mg/dl (7.0 mmol/L); plasma glucose after 2-h oral glucose tolerance test (OGTT) ≥ 200 mg/dl (11.1 mmol/L); glycated haemoglobin (HbA1c) ≥ 6.5% (48 mmol/mol Hb) or a random plasma glucose of ≥ 200 mg/dl (11.1 mmol/L) along with symptoms of hyperglycaemia.[2]

Diabetic retinopathy

Diabetic retinopathy (DR), a common ocular complication of diabetes, refers to progressive pathology of the retinal microvasculature (capillaries, arterioles and venules) with subsequent leakage or occlusion of the vessels, and retinal ischaemia.[3] The Early Treatment Diabetic Retinopathy Study (ETDRS) described the vascular lesions in DR, of which the microaneurysm is the hallmark.[4] DR is a key cause of visual impairment and blindness in the working age population.[5]

Screening for diabetic retinopathy

Screening refers to the application of tests for detection of DR in persons with diabetes who have no symptoms of DR. The methods for screening include dilated fundus examination and retinal photography.

Health system and health system strengthening

A health system comprises all the activities, institutions, organizations and resources whose primary purpose is to promote, restore or maintain health.[6, 7] It includes broad categories such as formal health care services (public or private), informal care (home care, herbal and alternative medicine), screening programs, disease control campaigns, health policies, and organizations involved in health insurance, research, training and service delivery organizations.

Health system strengthening (HSS) refers to 'purposeful and significant efforts or actions to improve the performance of the health system'.[7] HSS is often needed to facilitate progress towards desired targets, for example universal health coverage (UHC) and better population health.

Universal Health Coverage

The WHO defines UHC as *"*access to key promotive, preventive, curative and rehabilitative health interventions for all at an affordable cost, thereby achieving equity in access."[8] UHC is a multi-dimensional concept, operationalized in terms of population coverage, financial protection, and access to quality health care according to need, pursued within the framework of legal right to health.[9]

Visual impairment

The International Classification of Diseases 11 (2018) defines visual impairment (VI) as reduction in visual acuity and classifies it as follows: (A) distance VI can be mild

(presenting visual acuity worse than 6/12), moderate (presenting visual acuity worse than 6/18), severe (presenting visual acuity worse than 6/60) and blindness (presenting visual acuity worse than 3/60). (B) Near VI is defined as presenting near visual acuity worse than N6 or M.08 with existing correction.[10]

1.2 Research domain

Epidemiologic evidence indicates that the prevalence of diabetes has increased internationally over the last four decades, with a more pronounced rise in low and middle-income countries (LMICs).[11-13] In 2017, the global prevalence was estimated at 8.8%, affecting 415 million people aged 20-79 years.[12, 14] The majority of people living with diabetes (PLWD) live in LMICs and are predominantly below the age of 65 (88%).[12, 14-16]

Diabetic retinopathy is the most common ocular complication of diabetes and a major cause of visual impairment in PLWD, especially when there are no screening programs.[17-20] Poor vision is associated with reduced quality of life, increased risk of fall-related injuries, cognitive decline, poor mental health, decreased independence, difficulties in managing comorbidities, and increased health expenditure.[21]

All persons living with any type of diabetes are at risk of DR. Poor control and increasing duration of diabetes are key risk factors for DR. Good management of diabetes is therefore important for the prevention of DR-related vision loss. Yau and colleagues in 2012 in a global review of the literature reported that 34.6% of PLWD at any given time have DR, while 10.2% have vision-threatening DR.[22] Over the past few decades, major advances have been made in the management of DR to reduce associated vision loss. There is evidence that screening, early detection and prompt treatment of vision-threatening DR (VTDR) prevents or delays diabetes-related VI.[23-25] However, evidence on how to make these interventions work in different income,

geography or health system contexts is lacking.[26] Resource constraints,[27] differences in prevalence of DR,[19] and health system barriers[28] contribute to the increasing importance of DR as a cause of avoidable VI.

In LMICs, there are more PLWD, often at a younger age, who are at risk of visual impairment. To address this public health challenge, health systems need to be ready to deliver an increasing volume and quality of services, commensurate to the predicted increase in need. Universal health coverage has become a central theme of global health efforts to provide health care for all people that is effective and sustainable. To achieve this, there is a need to strengthen health systems to address the public health needs of specific populations and specific disease conditions. How can LMICs ensure that all PLWD receive all the services that they need, e.g. eye care services for DR? As LMICs face many health system barriers, it is important to understand how relevant innovations to address DR can be effectively introduced. The work in this thesis focuses on assessing and improving services for DR in Kenya.

1.3 Impetus for the research

The PhD was inspired by observation of the Kenyan health system, where I work at the intersection of ophthalmology, public health and health systems. The research questions have been generated from looking at Kenya's health system through that lens. This research is bidirectional because the health system provided the research questions, and in turn the research has provided ways to strengthen the health system, some of which are already being implemented. During my practice, I have noted that PLWD often fall through the care net. The typical patient with DR presents to the eye clinic with advanced disease already causing VI or blindness, despite having been in contact with the health system often for many years for routine diabetes management. The results of treatment at this stage are less than optimal

and the cost of treatment is often high with most patients not having health insurance. The aspirations of universal eye health, (as part of UHC, which Kenya has adopted) cannot be achieved with this status quo. There is a need to find the right policies and interventions for PLWD to prevent visual loss from DR.

An important window of opportunity to implement change at scale in Kenya is presented by the upcoming development of a new national eye health plan. However, eye health plans need to be informed by evidence regarding interventions that can improve eye health services for PLWD.[29] Towards this, it is important to synthesize evidence from the literature, test hypotheses, and provide local evidence. Given that interventions require considerable investment, it is also essential to understand the context and consider the practical ways in which the health system might work differently. Drawing on the literature review in section A and the health system assessment in section B, I present the need for knowledge translation, which underpins the interventions in section C, in addition to the strategic use of existing resources and the empowerment of PLWD, which underpin the interventions described in section D.

Perhaps because of my medical background, or because the late presentation of PLWD with DR was the most visible gap, I originally thought the main need was to improve treatment services. Therefore, at entry to the PhD my intention was to develop interventions to improve treatment. However, after assessing the health system I found that the main bottleneck was the lack of access of PLWD to regular eye screening. A cluster randomized controlled trial has therefore tested an intervention to improve access to screening, and I present the evidence for its effectiveness in chapters 9 and 10.

Reflecting on what I have learnt through the PhD, at the end of chapter 11, I revisit the question of the priority challenges facing the health system. I conclude that the main challenge to preventing visual loss from DR in PLWD in Kenya (and any LMIC) is broader than either screening or treatment, but that access to screening supported by good treatment services is a starting point. Given that there are no simple solutions to address the diabetes epidemic and its effects,[13] evidence -based health system strengthening (HSS) has a critical role in the pursuit of UHC for PLWD.[29-32] Such HSS requires the engagement of multiple actors and actions in the health system. The work described in this thesis has provided an opportunity to consider the unique contribution that researchers can bring to this agenda.

1.4 Purpose of the research

The purpose of the research is to contribute to improvement of DR services and prevention of vision loss in PLWD. In order to inform practice in the real world settings, a pragmatic approach is adopted.

1.5 Rationale

The number of people affected by VI and blindness from DR increased worldwide between 1990 and 2015.[33] This is avoidable vision loss because DR can be prevented and treated. Of the 415 million PLWD (20-79 years) in 2017, it is estimated that 145 million have DR and 45million have vision-threatening DR (VTDR).[34] Predictions suggest that by 2040, 642 million adults will be living with diabetes, 224 million will have some form of DR and 70 million will have VTDR.[34] There is evidence that appropriate treatment can delay the onset and slow the progression of DR.[35, 36] Thus eye health services for PLWD are important in reducing the incidence of vision loss from DR.

In sub-Saharan Africa (SSA) in particular, investments in health system strengthening may forestall the increase in vision loss from DR.[30, 34, 37] This region is at the beginning of the diabetes and DR epidemic, and although data is limited, there is evidence that health systems can be strengthened to make control of diabetes and DR accessible, affordable and sustainable.[38] SSA can apply existing tools for planning DR services, and learn from DR screening programs in other countries.[39]

Although PLWD have frequent contact with health services, eye care for PLWD is not routinely provided in many situations.[40] This contributes to the risk of vision loss from DR, and increases the cost of care, since patients with DR are often identified in advanced stages. Investing resources on effective eye health services for PLWD can reduce the extra morbidity of vision loss in PLWD. As a starting point, there is a need to identify the current gaps in DR services and provide evidence on well-defined interventions to address these gaps.

1.6 Aim and objectives

1.6.1 Aim

To provide evidence to improve eye care services for PLWD in Kenya in order to reduce vision loss in PLWD.

1.6.2 Specific objectives

1. To synthesise the literature on the magnitude, needs and priorities for diabetic retinopathy services (Chapter 2)
2. To conduct an assessment of the health system for PLWD and diabetic retinopathy in Kenya (Chapter 3 and 4)
3. To use the evidence from the literature and evidence from the health system assessment as a platform for health system strengthening (Chapter 5 and 6)

4. To develop and test an intervention through a randomized clinical trial to improve eye care services for PLWD in Kenya (Chapter 7-10)

1.7 Thesis structure

The thesis is organised in five sections (A, B, C, D and E), each of which has two or more chapters, Figure 1-1.

Section A is the general introduction and consists of two chapters. Chapter 1 gives the background and general direction of the thesis. It provides an overview of the research area, how the research ideas developed and the purpose of the research. Chapter 2 is a synthesis of the published evidence. As diabetes and DR are the subject of independent literature, the literature is analysed to identify the priorities and challenges in global health for eye care for PLWD, particularly in LMICs.

Section B is the health system assessment. In Chapter 3, I discuss the different frameworks for health system assessment and describe the approach for assessing the health system for PLWD and DR in Kenya. This assessment is of interest on its own, because it provided useful evidence on the strengths and weaknesses of the system. This evidence will be useful to policy-makers and implementers. In addition, it provided evidence for developing interventions to improve eye services for PLWD, which were tested in the randomized trial. Chapter 4 consists of two research papers discussing results from the health system assessment —the predictors of uptake of retinal screening and the rationale for integration of diabetes and DR services.

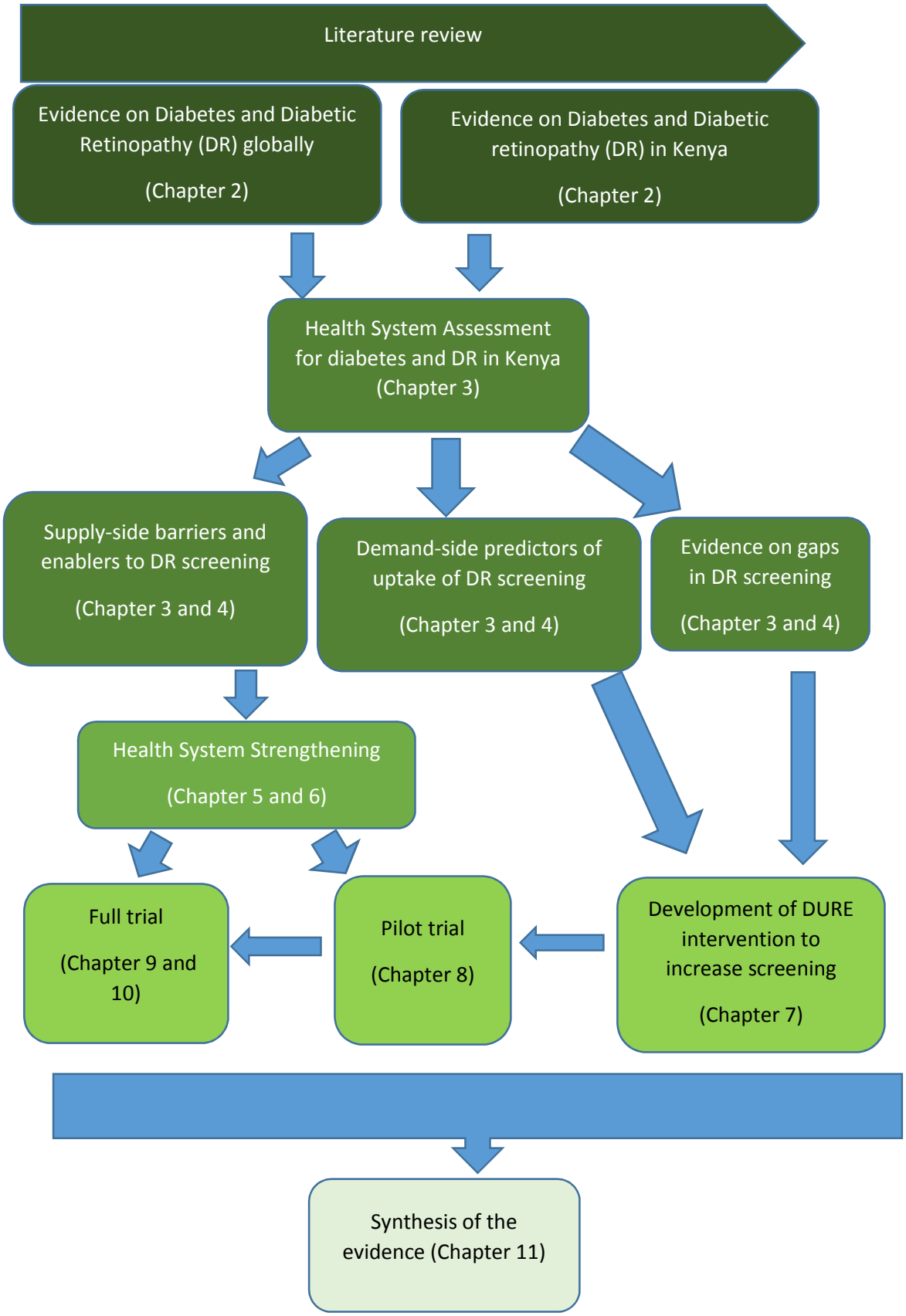

Figure 1-1: Schema of the thesis

Section C provides a discussion on health system strengthening – its importance in this study and how we applied it. The content includes technical and methodological contributions on developing clinical guidelines and a training course about DR, which might be useful to other LMICs wanting to undertake these activities. Chapter 5 consists of two papers on guidelines development process and outputs. Chapter 6 describes the development of an open online course on control of DR.

Section D describes the DURE (uptake of retinal examination in diabetes) intervention to improve access to DR services, developed in accordance to the four phases of the Medical Research Council's (MRC) framework for developing complex interventions. Chapter 7 describes the intervention development and includes the published trial protocol. Chapter 8 describes the pilot and feasibility trial, in a research paper. Chapter 9 describes the process evaluation of the full trial while chapter 10 describes the outcome evaluation of the trial. The four chapters provide evidence for the application of the MRC framework in DR research in a LMIC setting.

Section E comprises Chapter 11, which is the thesis summary consisting of the discussion, conclusions and next steps. It ends with a personal reflection on my learning from the PhD.

The content of the research papers in each section are outlined below:

Section	Paper	What the paper describes
Section B	Paper 1 (published)	Results of health system assessment (Predictors of uptake of retinal examination)
	Paper 2 (submitted)	Results of health system assessment (Rationale for integration of diabetes and DR services)
Section C	Paper 3 (published)	Process of adapting clinical guidelines for DR in Kenya (process and outputs)
	Paper 4 (published)	A summary of the recommendations in the clinical guidelines
Section D	Paper 5 (published)	Protocol for cluster randomized controlled trial
	Paper 6 (submitted)	Results: Pilot trial
	Paper 7 (submitted)	Results: Process evaluation of the trial
	Paper 8 (submitted)	Results: Outcome evaluation of the trial

1.8 Roles of the candidate in the research

I have carried out the work described in all the sections of this thesis, guided by my supervisors and advisory committee. Some of the specific roles are highlighted below:

Before the research	Applying for a grant
	Conceptualizing the study
During the research	Taking the necessary courses (Listed in Appendix 1)
	Managing the grant
	Engaging stakeholders to determine priorities, plan and implement the study
Section A	Conducting the literature review
Section B	Writing the protocol

	Obtaining ethics approval
	Developing research tools
	Training research assistants
	Conducting fieldwork
	Data analysis
	Dissemination of findings
Section C	Conducting literature review specific to guideline development
	Coordinating the guideline development team
	Writing the outputs
	Dissemination
	Developing the training program through mentorship
Section D	Obtaining ethics approval
	Developing protocol
	Developing peer training materials
	Developing questionnaires
	Training research team
	Coordinating field work
	Mixed methods process evaluation
	Data analysis
	Dissemination
Section E	Interpreting the evidence from the PhD
After the research	Synthesis, writing up, Identifying next steps

1.9 Study timelines

The timeframe for the study activities are shown in Appendix 2.

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Chapter Two: Diabetes, Diabetic retinopathy and Visual Impairment – A synthesis of the literature

2.0. Overview

This chapter addresses the first objective of the thesis and follows a narrative structure. Section 2.1 describes the epidemiology of diabetes. Section 2.2 describes the care model for diabetes. Section 2.3 discusses peer support for diabetes. Section 2.4 discusses diabetic retinopathy (DR), visual impairment from DR, including the epidemiology, the impact, and the control measures. The concluding section (2.5) summarizes the priority needs in DR control within a non-communicable disease (NCD), Universal Health Coverage (UHC) and health systems agenda.

2.1 The epidemiology of diabetes

2.1.1 Diabetes globally

The prevalence of diabetes and the number of people living with diabetes (PLWD) has been rising steadily over the past four decades[1].The International Diabetes Federation (IDF) estimates that among adults aged 20–79 years in 2017 there was an estimated 415 million PLWD with a global prevalence of diabetes of 8.8%. This is about a fourfold increase from the number of PLWD in 1980, which the World Health Organization (WHO) estimated to be 108 million, with a global prevalence of 4.7%. [2, 3] There are regional disparities in the prevalence: in 2017, North America and the Caribbean region had the highest prevalence (11%) while Africa had the lowest prevalence (4.2%), as shown in Figure 2-1. We can expect the number of PLWD to continue to increase in the next two decades. There is also a high level of undiagnosed diabetes in all regions, at 37.6% in North America and the Caribbean and 69.2% in Africa in 2017.[4]

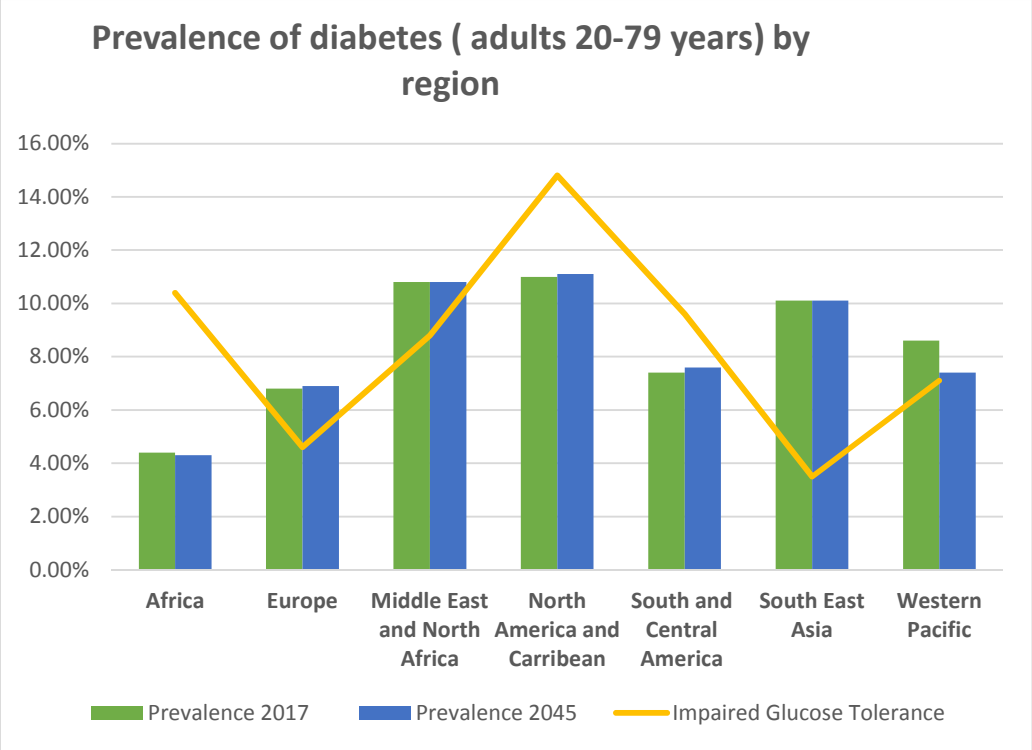


Figure 2-1: Prevalence of diabetes in different regions in 2017 and 2015 (data from the IDF Diabetes Atlas 8th edition)

There are three main types of diabetes (Type 1, 2 and gestational diabetes), all of which are treatable, with the goal of achieving normal levels of glucose. Type 2 diabetes is largely preventable but it accounts for 90% of the diabetes prevalence, and the majority of undiagnosed diabetes. [4, 5] People with impaired glucose tolerance are at high risk of developing Type 2 diabetes and are classified as pre-diabetes. For PLWD in the different regions, whether diagnosed or not, access to diabetes services is a priority. This includes health education, self-management, treatment and interventions for diabetes complications. In order to reduce the prevalence of diabetes it is also crucial to reduce the risk factors for diabetes in the general population.

Given the escalating number of PLWD, diabetes is not only a global health concern, but also an economic and social burden. Individual PLWD, their families, health

systems and countries face a large, growing and long-term economic burden. This includes indirect costs due to disability, loss of productivity and premature mortality, besides the direct costs, particularly treatment costs. The loss in workplace productivity due to diabetes and its complications is considerable because 72% PLWD worldwide are within the working age bracket (20-64 years).[4] This reduction in productivity has an adverse impact in all regions.[6]

The direct annual cost of diabetes in the world is estimated at Intl$ 825 billion, and a significant proportion of these costs are paid out-of-pocket, especially in LMICs, where out of pocket payment accounts for 25-80 % of this health expenditure.[2, 6, 7] The presence of diabetes complications such as visual impairment and blindness from DR significantly increases the direct costs. PLWD and governments struggle to meet these costs, and the protection offered by health insurance is often incomplete.[4] As an example, the health care costs of people with diabetes in the United States (US) are nearly two and a half times of those without diabetes within the same sociodemographic bracket.[8] Jaspers and colleagues in their systematic review on the global impact of non-communicable diseases (NCDs) on households found that financial catastrophe due to NCDs, including diabetes, was seen in all countries and at all income levels, but with a higher proportion of households affected in lower income areas.[9] When the costs of diabetes treatment lead to financial hardship, they are drivers for impoverishment. In turn, poverty is a driver for poor compliance with treatment, poor control of diabetes and the development of complications of diabetes.

The rising magnitude and the high cost of diabetes point to the need for cost-effective control measures. The WHO has identified proven, priority cost-effective interventions 'best buys' for diabetes that can be implemented in all regions. These

are effective glycaemic control, preventive foot care for PLWD, DR screening for all PLWD and laser photocoagulation for prevention of blindness. [10] These 'best buys' may result in social, health and economic benefits by delaying complications and hence preserving health, quality of life and productivity. They are also potentially cost-saving on the treatment costs for these complications. Failure to implement proven interventions will increase health care costs and is therefore counterproductive.

The recognition of the global impact of diabetes has led to several global commitments to catalyse action. In 2011, the Political Declaration on the Prevention and Control of NCDs at the 66th General Assembly of the United Nations (UN) identified diabetes as one of four priority NCDs that constitute the largest NCD burden and are largely preventable.[11] To generate global, regional and national momentum for action on these NCDs, the World Health Assembly in 2013 adopted the WHO Global Action Plan for the prevention and control of NCDs, which included targets for the control of diabetes and its risk factors.[3, 12] Further, in 2015, all UN member states committed to the 2030 Sustainable Development Goals agenda which includes targets to reduce NCD-related premature mortality, achieve UHC and increase access to affordable treatment for these conditions.[13] These commitments have been instrumental in raising awareness of the urgent need to place NCDs on the agenda of governments.[7] Diabetes can be used as a tracer condition for examining the progress towards UHC [14, 15] and also for assessing health systems.[16]

What does UHC mean for PLWD globally? With UHC, all PLWD should obtain the services they need without suffering financial hardship. Many high-income countries such as those of Western Europe, and some middle-income countries such as Thailand, Brazil and Mexico have some form of UHC. For example, in Thailand, a country that has had UHC since 2002, PLWD can access a comprehensive package of

services with financial protection.[17] We highlight some of the lessons the country has to offer to other countries below. One lesson is that not only does Thailand have UHC, but also importantly, the UHC package includes the diabetes services. In many countries, UHC packages exclude even basic diabetes care components, such as HbA1c testing or DR screening, because they are perceived as expensive. Thus having UHC does not necessarily guarantee universal access to diabetes services. Without UHC, PLWD often receive inadequate services. Many undiagnosed PLWD are uninsured, yet health insurance is significantly associated with the likelihood of timely diagnoses, improved diagnosis and control of diabetes.[18] For these reasons, although health-financing schemes cannot cover all possible interventions, it is of utmost importance to ensure that UHC packages address the needs of PLWD.

Many PLWD, especially among poor, rural, less educated and other vulnerable or disadvantaged populations have been 'left behind', and do not access health services. Applying an equity lens to UHC can help to address this modifiable gap, by developing UHC packages that target these people without excluding the rest of the population.[19] This approach has been useful in some Latin American countries, such as Costa Rica.[20] Reaching the disadvantaged populations may be facilitated through investment in primary care, and the use of community volunteers as in the case of Thailand—another lesson from this country.[17] Rwanda, an LMIC that has made significant progress to UHC, has also strengthened primary care through community health volunteers.[21] In addition, Costa Rica and the National Health Service (NHS) in England have implemented UHC through strengthening primary care, where regular assessment of body mass index (BMI), HbA1c and foot examinations are provided to PLWD.[20, 22]

Health system strengthening (HSS), such as better trained health workforce and improved infrastructure as well as addressing the other health system building blocks is critical if PLWD are to access good health services.[17, 22] Ong and colleagues in their systematic review identified several health system factors that influence the response to the diabetes epidemic.[23] They found removal of out of pocket payments and integrated diabetes models enabled the health system to address diabetes. Additional HSS interventions that have been found useful for diabetes services in the literature include: training multidisciplinary health professionals in primary care about diabetes and its complications; avoiding stock-out of supplies; providing essential technologies, such as blood glucose measurement and engaging pharmacists in diabetes care [4, 23-25]. The adoption of national guidelines for care of patients with diabetes, hypertension, and dyslipidaemia in Costa Rica [20] and incentive schemes for primary care providers in the NHS[22] are further examples.

2.1.2 Diabetes in LMICs

The prevalence of diabetes is increasing disproportionately faster in resource-poor regions.[26-28] As in other parts of the world, the rise is mainly for Type 2 diabetes. The risk factors for diabetes, such as sedentary lifestyle, high BMI and impaired glucose tolerance often go unrecognized, leading to a huge unmet need for prevention.[29] The surge in incidence and prevalence of diabetes is driven by increasing population growth and life expectancy, industrialization, urbanisation, lifestyle changes such as the nutrition transition (shift in dietary patterns) and physical inactivity.[1, 2, 4, 25, 30] An estimated 79% of PLWD live in LMICs, and these countries also have the highest proportion of undiagnosed diabetes in the world.[4, 28] Notably, PLWD in LMICs are predominantly below the age of 65 years, experience a large unmet need for

treatment and have inadequate glycaemic control.[24, 31] These are important risk factors for the development of complications such as retinopathy.

In sub-Saharan Africa (SSA), where many of the LMICS are located, public health strategies to manage the diabetes epidemic are known to be inadequate.[32, 33] The priorities for health systems have hitherto been maternal and child health, and communicable diseases that require acute care. In contrast, PLWD require regular and lifelong engagement with the health system, which should mainly be at the primary care level. This is challenging for health systems that are oriented to acute care instead of overall health system development, and which are also fragile particularly at primary care.[34] As an example, large losses to care for PLWD occur at each stage of the diabetes care cascade (testing, diagnosis, treatment, glycaemic control).[24] Only an estimated 11% of PLWD (range 7-33%) are retained throughout the care cascade.[35] In addition, in LMICs, younger PLWD are more likely to fall off the diabetes cascade than the older PLWD.[24] As noted earlier, PLWD in LMICs are on average younger than PLWD in other regions. As they are 'left behind' in access to care, they are at greater risk of complications, with a high social and economic impact.

The ongoing epidemiological transition between communicable diseases and non-communicable diseases (NCDs) presents an opportunity to orient health systems to NCD-relevant responses. This includes health system changes at community level, primary care and secondary care, including referral systems (such as for DR screening) and follow-up mechanisms. As described earlier, effective interventions such as the best buys for diabetes proposed by the WHO exist. Cost-effectiveness analysis (CEA) for these best buys has shown that the cost of implementation is approximately 1$ per disability-adjusted life year (DALY) averted in LMICs.[10] This suggests that with a modest increase in investment, the best buys are feasible for implementation even in

low-resource settings where resources are limited. Despite this evidence, there is very low coverage of these interventions in most LMICs. Given the scarcity of evidence about the best ways to improve coverage of these interventions within health systems, there is a need for robust implementation research that can inform strategies to improve coverage.

The majority of diabetes-related premature mortality, disability and loss of productivity occurs in LMICs, leading to very high indirect costs of diabetes [2, 31]. The direct costs of diabetes treatment are largely borne by PLWD and their families, rather than governments or insurance schemes.[35, 36] This is likely to be a driver for disparities in access. In addition, those who fall out of care are likely to present with complications whose treatment will incur much higher costs. Although countries in the African region spend an average 6% of the national health budget on diabetes, the mean expenditure per PLWD per year is only Intl$ 444 (compared to 3132 and 8396 Intl$ in Europe and North America respectively), and is inadequate to provide the required interventions.[4, 31] The only option available, therefore, is to prioritize a core set of evidence-based interventions, particularly those that can reduce the cost of treating complications. The implementation of the best buys described above should therefore be a priority.

2.1.3 Diabetes in Kenya

The population of Kenya (Fig 2-2) in 2019 is estimated at 52.6 million, with a 2.3% annual rate of population increase, life expectancy at birth of 66 years and 60% of the population being under 25 years.[37] This is a relatively young population, of whom 73% reside in rural areas. Responsibilities for health care in Kenya are shared between the national government and the 47 semi-autonomous county governments. The county level is responsible for essential health service delivery while the national level is

responsible for health policy and regulation, technical assistance to counties and management of national referral hospitals. Achoki and colleagues have recently discussed the gradual escalation in the relative contribution of NCDs to the disease burden at subnational level (epidemiological transition), and the challenge it poses to UHC.[38]

Figure 2-2: Kenya on the world map

Both public and private sectors provide service delivery, with the private sector providing about 49% of services. [39] Health insurance coverage for the population is low, at about 19%.[40] Within this, the national health insurance fund (NHIF), a public corporation, is the largest provider of health insurance, covering 16% of Kenyans. In addition, the NHIF's contracted facility network is only 40% of the health care facilities in the country; hence, services obtained outside this network are not covered. Though NHIF has a comprehensive benefit package, covering the costs of many medicines, laboratory and radiologic tests in the public sector, some of these services are not

available in these facilities. [40] Not all costs in the private sector are covered, therefore even patients who are covered still incur out of pocket expenses.[41]

The Kenya Health Policy 2014-2030 elaborates the commitment to achieve UHC by scaling up health services to populations in need.[42] The policy defines four levels of care within public health services: community level, primary care, county level and national level. The primary care level is the first contact with the health system, which comprises dispensaries, health centres, maternity units and nursing homes. In practice, primary care level often concentrates on acute episodic care and defers chronic disease to county hospitals.

The county level consists of hospitals that complement the primary level and provide secondary and tertiary care. Diabetes clinics and general medical clinics at county level provide the diabetes services. The national level consists of highly specialized tertiary hospitals. Services for diabetes testing, diagnosis and treatment should be available at all the four levels, though not all the laboratory tests and medication are available at all the facilities.[43] Specialist clinics at county and national hospitals provide screening for complications. As there is no gate-keeping mechanism, PLWD are allowed frequent engagement with any level of the services.

At the community level, under the community health strategy, health services are organized around community units of about 5000 people.[44] Each unit has 50 community health volunteers (CHVs, also called community health workers), each responsible for 20 households.[45] The strategy specifies the roles of the CHVs, which include visiting households on a door-to-door basis to identify health problems, provide some interventions related to disease prevention, maternal and newborn care, home-based care, observe treatment and some curative tasks. They are also responsible for community mobilisation and linking the community to the primary

health facility. The CHVs receive an initial 10 days training with regular refreshers and have a kit of supplies. A community health extension worker (CHEW), who is a trained government health worker, provides support and supervision to the CHV. Two CHEWS are responsible for each community unit. A community health committee, consisting of community members, participates in the governance of this level. [44, 45]

The success of implementation of the community level of health care varies at subnational levels. Some of the challenges faced are high attrition of CHVs and conflict of workload for CHEWs.[45, 46] Diabetes services are generally not available at this level, but health promotion around the NCD risk factors may be provided. There is potential to leverage CHVs and CHEWs to deliver NCD interventions with diabetes as an entry point, such as regular BMI measurement or blood sugar testing for adults on a door-to-door basis.

At the community level, there are diabetes support groups (DSGs) for PLWD in many of the counties.[47] The Kenya Defeat Diabetes Association, a civil organization, is the umbrella body for these groups. The groups have monthly meetings where they engage in peer-to-peer support, group education, monitoring BMI and metabolic control. They also engage in advocacy with the government and NGOs, and conduct community diabetes screening camps. These groups have links with the CVs and the primary health facilities. As this peer support resource is known to be useful in the management of diabetes,[48, 49] its role is discussed in detail in subsequent sections.

Evidence from the Global Burden of Disease Study and country-level evidence shows an increase in NCDs over time,[38, 50, 51]with disparities across counties.[38] Kenya has an NCD division within the Ministry of Health, and an NCD strategy to halt and reverse this rising burden of NCDs.[42] However, the NCD program faces challenges due to workforce shortages, frequent stock-outs of medicines in public-sector pharmacies,

and problems guaranteeing the quality of medicines.[52, 53] The Kenya Service Availability and Readiness Assessment Mapping (SARAM) in 2014 showed that only 5% of all facilities offered all NCD services defined in the Kenya Essential Package of Health (KEPH) and only 25% of health facilities had different tracer commodities for NCDs with huge regional variation.[54] The most available services related to health promotion, while the least available services were screening and rehabilitation.[54] Many people obtain the NCD diagnosis in the public sector but buy their drugs in the private sector, and these out-of-pocket payments can be high.[53, 55]

The Lancet Diabetes and Endocrinology Commission on diabetes in sub-Saharan Africa underscored the need for locally derived epidemiologic evidence on diabetes at country level.[35] Such evidence is important because it allows for contextual analysis, identifies opportunities for improving outcomes at country level and can reliably inform subsequent policy, practice and research. A nationally representative STEPwise approach to surveillance (STEPS) survey for NCD risk factors in 2015 reported the prevalence of diabetes to be 2% among the age group 18-64 years.[56] The estimates from the IDF were very similar, at 2.2%.[28] This availability of data from a national survey is a significant starting point that allows consideration of some of the public health implications of the findings in the STEPS survey, which are discussed below.

The age-adjusted prevalence of pre-diabetes and diabetes was 3.1% and 2.4% respectively.[57] As the prevalence of pre-diabetes exceeded that of diabetes, the prevalence of diabetes is likely to increase in the medium-term rather than stabilise, through conversion from the large pool of individuals with pre-diabetes. As complications such as DR can occur even in pre-diabetes,[58] there is need for an integrated response that includes prevention, diagnosis, treatment, and regular screening for complications.

The age adjusted prevalence of diabetes was highest among urban (3.4%) compared to rural (1.9%) residents. Similarly, the prevalence was highest in the richest wealth quintiles (5.2%) compared to the poorest wealth quintile (1.6%). Previous population based studies had also identified the urban-rural variation.[59] That diabetes is still more prevalent in the urban and more affluent segments of the population suggests that the epidemic is still in the early stages. However, given that the majority of the population is rural, even a small increase in the prevalence in the rural areas (especially from conversion from the pre-diabetes pool) would have a significant impact. A cohort study of people age 50+ years in Nakuru Kenya found the six-year cumulative incidence of diabetes to be 61 per 1000, equating to about 10 new cases of diabetes per 1000 per year.[60] Assuming 10% of the 53 million is aged 50+, (5.3million) this would be 53,000 additional PLWD every year, excluding the new cases aged <50 years. A large scale up of service provision in the diabetes care cascade will be required.

The odds for diabetes increased with age and the prevalence was highest in 45–59 age category.[57] Given that diabetes affects working-age people, the consequences of diabetes extend beyond the treatment costs. Besides disability and death, other productivity effects have been described, including: absenteeism, presenteeism (the practice of being present at one's place of work for more hours than is required, especially among workers with reduced productivity due to health issues, as a manifestation of insecurity about one's job), unemployment and premature retirement, leading to reduced income and savings, low self-esteem and low quality of life.[61-63] This suggests the need for effective targeted intervention to help workers better manage their disease. Employers need to be engaged as pertinent stakeholders in diabetes control.

The proportion of undiagnosed diabetes in the STEPs survey was 52.8%, which although not surprising, has far-reaching implications for health-care providers in the country, as many currently undiagnosed PLWD carry the risk of advanced diabetic microvascular complications being present by the time they are diagnosed, resulting in kidney failure, retinopathy, neuropathies and diabetic foot. For patients diagnosed at a late stage, the complications are likely to be progressive.

Among the 47% of PLWD who were aware of their diagnosis, only 41% were on treatment, and among those on treatment only 33% had achieved glycaemic control.[57] This means that out of every 100 PLWD, 47 are aware of the diagnosis, 19 are on treatment and only six have glycaemic control; the other 93 do not achieve glycaemic control. In the poorest households, none of the PLWD were on treatment and as expected, none of them had achieved glycaemic control.[57] This combination points to low awareness, poor access, low treatment coverage, inadequate management of diabetes, and loss of PLWD along the diabetes care cascade. People with uncontrolled diabetes are likely to present with complications, especially the microvascular complications. This means that interventions are required at all the four levels of health care, rather than only primary care. Access to treatment should be a priority in order to prevent the development of complications. Interventions targeting the poor are required.

As expected, the direct cost of managing diabetes and its complications is much higher in private than public facilities. The largest costs are medication, clinical tests, inpatient costs and treatment of microvascular complications, which can result in catastrophic expenditure even in the public sector.[7, 55, 64] The indirect cost is similarly high given that a high number of disability-adjusted life years (DALYS) lost are attributable to diabetes-related illnesses (364 per 100,000 person years of

observation).[64, 65] Seeing that diabetes is a costly disease in Kenya,[55] and that the complications are the largest source of the overall costs, there is a need for programs that can control these complications. Possible interventions include removing out-of-pocket payments, which will require more effective engagement of insurers and other funders of health care.

Based on the epidemiological data from the STEPS survey, to reduce the burden of diabetes at the population level, there is need to ensure all people with diabetes get tested, diagnosed and enter the continuum of care and are retained without dropping out. Successes in access to and retention in the diabetes care cascade can lead to better diabetes outcomes, and reduction in the health, social and economic burden of diabetes. This is likely to be achieved through a chronic care model, which is discussed below.

2.2 Chronic care model for diabetes care

The *Chronic Care Model* (CCM), developed by Wagner and colleagues in the 1990s, [66, 67] has been proposed as a suitable model for managing diabetes, Fig 3-3. The CCM envisions linking actively engaged patients with proactive health care providers.[68] Studies have shown that CCM is beneficial to chronic care especially at primary care, even in SSA.[69-71] Some CCM-related interventions in Kenya have been reported, [72, 73] and some aspects are routinely implemented in the country, but not as a systematically defined package.

The CCM model enumerates six essential elements that encourage high-quality chronic disease care. These elements are *self-management support, delivery system design, decision support and clinical information systems, the health system, and community resources.* Cost-effective interventions within each of these components

can be implemented as a package.[68] Complex interventions that incorporate several of these elements have been shown to be more effective than single interventions, but none of them has been found to be the dominant driver of success in diabetes care.[68] The actual interventions within each component also show heterogeneity in most studies. The next section provides a description of how these components might be operationalized.

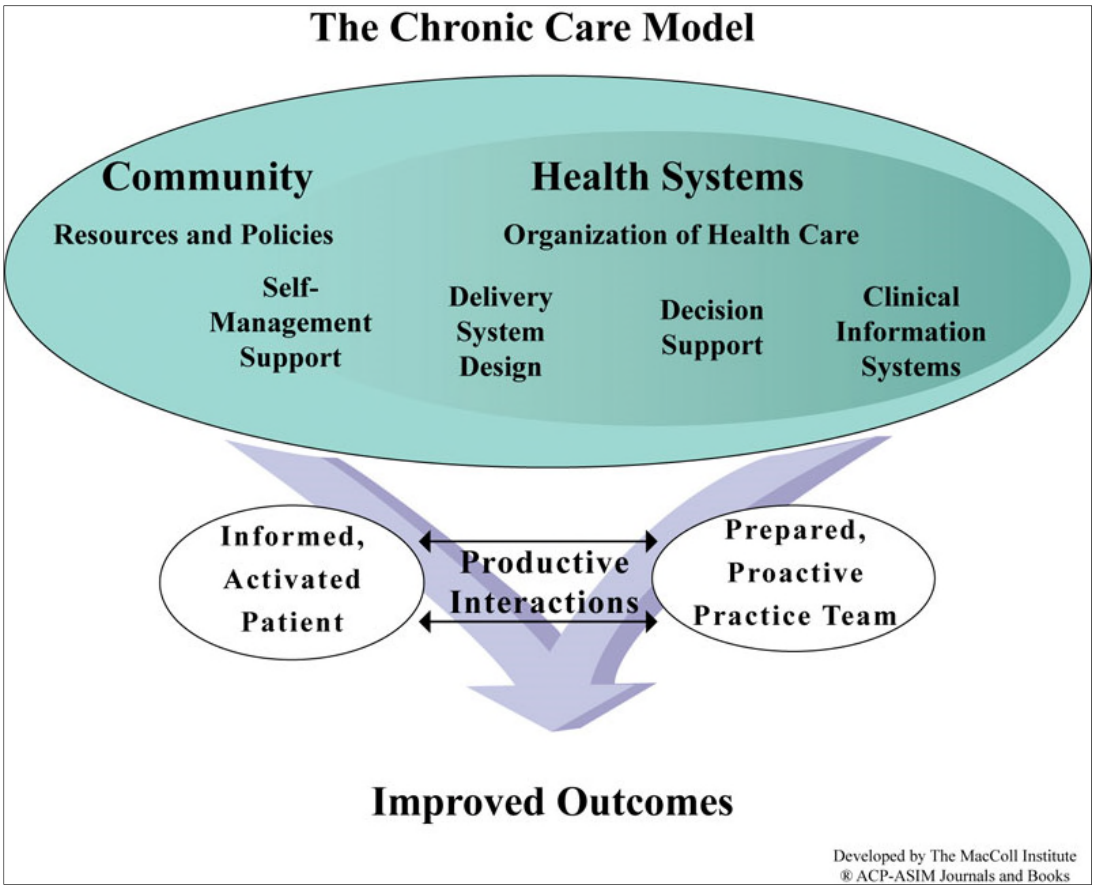


Figure 2-3: Chronic Care Model

Diabetes Self-management support should focus on patient/family empowerment, and development of skills such as self-monitoring/home-based monitoring, administering insulin injections, action-planning and problem-solving.[74, 75] A clinician or trained diabetes educator may provide diabetes education through different

channels such as face-to-face individual education, group education, education materials, online modules or mobile applications for the promotion of healthy lifestyle.[75]

Delivery system support is about strengthening the coordination of patient-centred services for PLWD, both during hospital visits and follow-up. This includes giving standing orders for annual screening tests, automated reminders, and developing a multidisciplinary team (nurses, clinicians, physicians, pharmacists, nutritionists, diabetes educators and other specialists). Team roles are specified (for example who takes care of foot examinations or DR screening), teams are trained, and they meet regularly to review progress.[74, 75]

Decision support helps to ensure that health workers attending to PLWD have the expertise that they need. Typical activities include training of multidisciplinary health care providers on the use of evidence-based guidelines or protocols, and providing these guidelines.[70, 74] This can promote diabetes care by strengthening the workforce to provide quality care, and ensuring timely referral of PLWD who need additional care.

Electronic records, a diabetes registry and reminder or recall systems are important aspects of the *clinical information systems* for diabetes.[74, 75] This can help track referrals, clinical and public health outcomes, and strengthen engagement of PLWD along the care cascade to reduce the potential for dropout. A call and recall mechanism can also ensure that patients are reminded of their screening schedule.

The leadership provided by the *health system* determines how interventions for diabetes are implemented.[70, 76] Providing sufficient resources (space, workforce, standards, information systems, funds); retraining health workers to give them a chronic disease orientation; removing barriers to care; integration of diabetes care

across different health care providers; increasing collaboration between specialists that attend to PLWD; implementing quality assurance measures and removing health system barriers can ensure that PLWD get all the services they require.[70, 74]

Community resources may help patients acquire self-management skills, such as achieving lifestyle modifications that positively influence chronic disease control. For example, community health volunteers (CHVs) and peer supporters are a flexible and cost-effective strategy in the control of diabetes in multiple settings.[77-87] Local gyms, exercise programs and weight loss programs are also useful for lifestyle goals. Diabetes programs and PLWD should be encouraged to engage with these resources to fill gaps in care. As diabetes support groups (DSGs) are an existing community resource external to the formal health system in Kenya, and since the peer supporters are PLWD themselves, the next section explores their unique contribution.

2.3 Peer support interventions

2.3.1 Peer support in health care

Peer support as a health intervention has been defined as 'the provision of emotional, appraisal, and informational assistance by a created social network member who possesses experiential knowledge of a specific behaviour'. [8889, 90] The peer supporter has similar characteristics as the target population and the relationship relies on the following factors: non-hierarchical, flexible and reciprocal relationships,[79, 88, 89] sharing similar life experiences, mastery of self-care behaviours and reduced social distance between peers.[78, 87]

There are diverse modes of peer support interaction (individual or group sessions, face-to-face, telephone or online interaction), which occur in diverse settings such as homes, health facilities, schools, prisons. Support can be structured as an informal or

a formal interaction (for example through training peer supporters). There are varied types of peer supporter training and peer group composition (homogenous or mixed, disease type) [78, 91].

There are multiple applications of peer support in health care. It has been used as a health promotion approach to encourage behaviour change interventions such as for exclusive breastfeeding, prevention of Human Immunodeficiency Virus (HIV) and Sexually Transmitted Infections (STI), smoking cessation, mental health and cancer screening among other areas. In Kenya, peer support has been used to help patients with HIV transition between inpatient and outpatient care, for continuity of follow-up.[92]

A systematic review of peer support for breastfeeding found the role of peer support to be most important during the early postnatal period.[90, 93] Individual peer support for exclusive breastfeeding in Uganda was reported to be acceptable to women.[94] In Bangladesh, women's groups with high population coverage reduced neonatal mortality.[95] In Malawi, women's groups and health education by peer counsellors were similarly found to have positive effects on childhood mortality, maternal mortality and breastfeeding rates.[93] [88, 90, 96] In China, community-based peer support for patients with severe mental illness has been found to be acceptable.[97]

2.3.2 Peer support in diabetes

There is evidence that peer support can promote the implementation of diabetes care.[80, 82, 85, 98] Peer supporters can assist people with their daily diabetes self-management activities, provide emotional and social support, assist and encourage clinical care and be available when needed. [99, 100] A needs assessment in the Kilimanjaro Diabetic Program in Tanzania found that living with diabetes is not associated with stigma, and PLWD have a desire to raise community awareness of

diabetes and support others to live with the disease and secure social support to access hospital services.[101]

Peer approaches in other settings have been found to promote physical activity, healthy eating, glycaemic control and reduce hospitalisation of PLWD.[80, 99, 102-104] A peer intervention led to significant reduction in the combined prevalence of type 2 diabetes and intermediate hyperglycaemia as well as a 2-year incidence of type 2 diabetes among an intermediate hyperglycaemia cohort of adults in Bangladesh.[105]

Several systematic reviews on the effectiveness of peer support have been published. Qi and colleagues in 2015 found that peer support had a significant impact on improving HbA1c levels in patients with poor glycaemic control.[78] Dale et al in 2012 found that peer support improved clinical and behavioural outcomes in some adults with diabetes.[106] Fisher et al in 2017 found that peer support could reduce HbA1c levels. [48] Gatlin et al in 2017 found that peer led self-management education can increase diabetes knowledge and reduce HbA1c.[107]The studies included in these reviews were mostly from high-income settings and the models of peer support were heterogeneous. Having found no literature on the role of peer support specific to the long-term complications of diabetes, research in this area would help to expand knowledge and expand the application of the chronic care model in diabetes care.

Although peer support is a scalable and potentially low cost intervention that would be particularly useful in low resource settings, [79, 100, 108]some literature cautions against over-optimism in its potential to influence health outcomes. [81, 109] Local evidence, especially mixed-methods implementation research would be needed as peer support interventions are developed and evaluated, in order to identify what types of peer support work, where, how and why.

Peer support is not a monolithic 'one-size fits all' concept, and these studies have used different types of peer support. There are community based, home-based and facility-based approaches. Peer support can be peer-led or health worker-led. It can be individual or groups peer support, and can be implemented through face-to-face, telephone, internet or other strategies. Brownson and Heisler summarized six essential contributions of peer supporters to diabetes care in any of these models, which are listed below.[87] These points outline the utility of peer support.

1. Improving access to regular, safe, high-quality clinical care: Peer supporters conduct outreach and case finding; make referrals; help PLWD navigate the healthcare system; serve as liaisons between PLWD and healthcare settings; coordinate care/services (case management); provide language translation; assist with applications and paperwork for insurance or other services/programs.

2. Individualized assessment and tailored management: Assess needs of PLWD; assess readiness to change, level of literacy, and other life influences on their ability to self-manage; individualize education and support; and provide services in non-traditional settings (e.g. home visits).

3. Collaborative behavioural goal setting and problem solving: Help patients set and reach specific behavioural goals; help in problem solving to overcome barriers.

4. Education and skills for managing diabetes: Conduct outreach and recruitment for educational services, lead (or assist with) culturally appropriate and accessible self-management training and education; and teach/reinforce self-management skills.

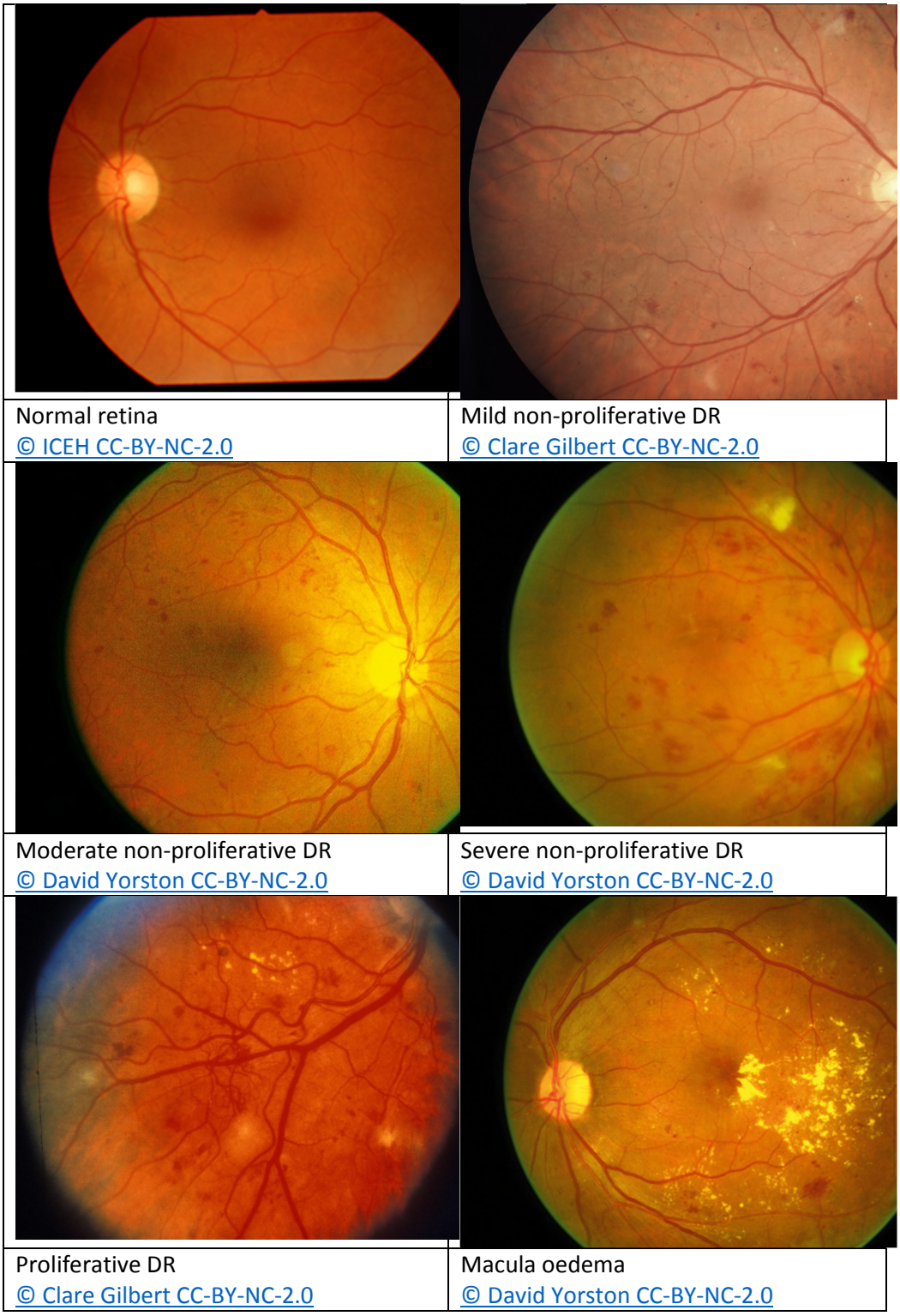
5. Ongoing follow-up and support: Provide non-judgmental follow-up, informal counselling, social support and encouragement; and provide instrumental support.

6. Linkage to community resources: Identify needed resources; develop relationships with community organizations; provide information and support to PLWD regarding available community resources; advocate for needed services; develop capacity within communities to support healthy behaviours

These points provide us with an understanding of the utility of peer support. Looking at these roles, we can construe that the goal of peer support is to empower the individual PLWD and to ensure regular access to diabetes services.

Turning to diabetic retinopathy, can peer support strengthen prevention, screening, diagnosis, treatment or rehabilitation for DR? We did not find any published evidence on peer support for DR. We suggest that this is an important area for investigation.

2.4 Diabetic retinopathy



Normal retina © ICEH CC-BY-NC-2.0	Mild non-proliferative DR © Clare Gilbert CC-BY-NC-2.0
Moderate non-proliferative DR © David Yorston CC-BY-NC-2.0	Severe non-proliferative DR © David Yorston CC-BY-NC-2.0
Proliferative DR © Clare Gilbert CC-BY-NC-2.0	Macula oedema © David Yorston CC-BY-NC-2.0

Figure 2-4: Retinal images showing Classification of Diabetic Retinopathy

Source: Community Eye Health Journal https://creativecommons.org/licenses/by-nc/2.0/legalcode

The long-term sequelae of diabetes, including diabetic eye disease (DED), make diabetes a complex comorbidity. DEDs include cataract, glaucoma, rubeosis iridis, optic neuropathy, ocular muscle dysfunction and retinopathy. The increase in prevalence of type 2 diabetes in LMICs will occasion proportionate increases in the rates of these complications.[110] Cataract and glaucoma may occur in the absence of diabetes, but DR is a specific ocular manifestation of end-organ damage from diabetes (Fig 2-4). These conditions are potentially blinding and PLWD are 25 times more likely to go blind than the general population.[111]

2.4.1 Epidemiology of diabetic retinopathy

Diabetic retinopathy is a progressive disease of retinal microvasculature and the most frequent microvascular complication of diabetes.[112] All PLWD are at risk of developing DR; the risk increases with the duration of diabetes as Fig 2-5 illustrates. After 20 years of living with diabetes, 80% of PLWD will have some form of DR.[113, 114] At any point in time, 35% of PLWD have DR, and about 10% of PLWD (or about a third of those who have DR) have vision threatening DR (VTDR) with a high risk of severe visual impairment from DR.[115] The early stages of DR are asymptomatic, but with progression over time, the main vision-threatening sequelae are diabetic macular oedema (DMO) and proliferative diabetic retinopathy (PDR), both of which are part of VTDR, Figure 4. These complications make DR a leading cause of acquired vision loss particularly in the working age population.[112, 113, 116]

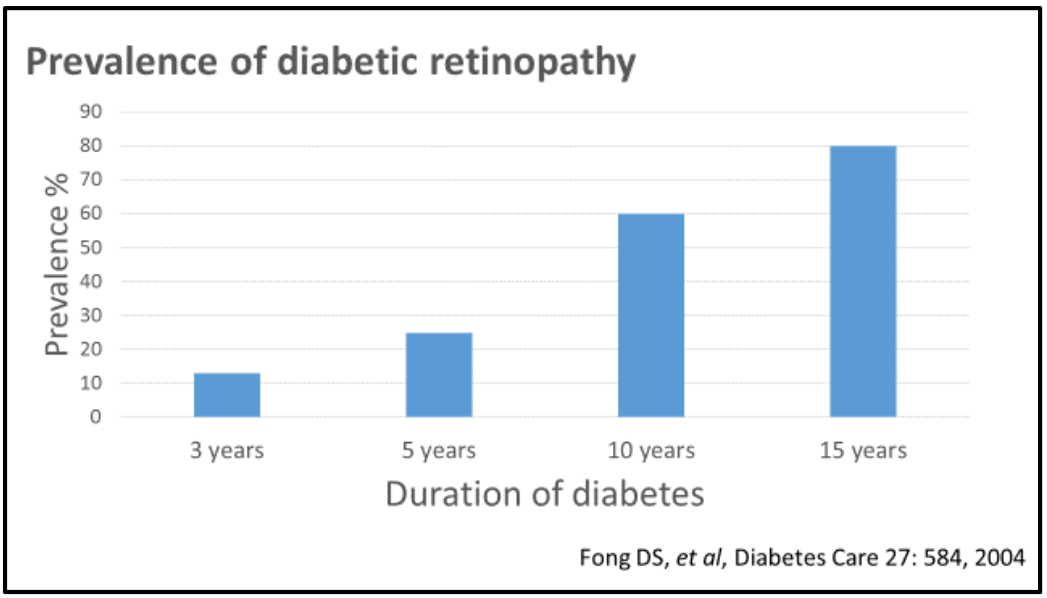


Figure 2-5: Association of prevalence of DR with duration of diabetes

The 2017 report of the Vision Loss Expert Group shows that the crude prevalence of blindness due to all causes except DR reduced between 1990 and 2015 globally.[117] During these 25 years, the number of people with DR-related blindness and visual impairment (VI) increased, and the overall causal contribution of DR to blindness increased by 7.7%.[117] This trend suggests that DR has potential to become one of the leading causes of VI globally in the future. At present, the prevalence of DR-related VI in Asia and SSA is much lower than in high-income countries.[117] This also has potential to reverse, based on the evidence of the escalating prevalence of diabetes and the increasing life expectancy in these regions. An increased focus on the control of DR is thus appropriate. Although large population-based studies on DR in SSA are lacking, posterior-segment eye diseases (PSEDs), grouped together, are the second leading cause of blindness in the region, accounting for 13 to 37% of blindness.[118]

A recent systematic review has shown the annual incidence of DR globally ranges from 2·2% to 12·7% and progression from 3·4% to 12·3% among adult PLWD.[119] In the Malawi Diabetic Retinopathy cohort study, progression from no retinopathy and

background retinopathy to VTDR over five years was approximately 5 and 3 times that reported in the Liverpool Diabetic Eye Study.[120] The 5-year incidence of any DR in Malawi was 48.4%. Poor glycaemic control and HIV infection were predictors of progression.[121, 122] This was the first report of an association between HIV infection and progression of retinopathy. It is a pointer that infectious diseases and other variables in LMICs may affect the epidemiology of DR. The 6-year incidence of DR among PLWD age 50+ in the Nakuru cohort study in Kenya was 225 cases per 1000.[60] The other available incidence data for LMIC is from Bangladesh, where the cumulative incidence of DR over a 15-year period was 50.6%.[123] It is difficult to compare these findings because of different study designs, follow-up rates and insufficient stratification of data by age and other parameters. It is still uncertain whether DR occurs earlier or progresses faster in African populations as compared to PLWD of a similar age in other populations. However, the data is useful for conceptualisation of the need for services such as screening programmes for early detection of these cases.

The prevalence range for any DR among PLWD in SSA, as reported in individual studies (Table 2-1), is 7.0 to 62.4%.[124] This wide variation may result from: the variation in the mean duration of diabetes among the participants in the different studies; differences in study methods and changes in the prevalence of DR over time.

Table 2-1: Prevalence of diabetic retinopathy in sub-Sahara Africa

Country	Author	Year	Study setting	Sample size (n)	Prevalence (%)
Botswana	Mengesha et al[125]	2006	Clinic-based	401	9.2
Cameroon	Jingi et al[126]	2015	Clinic-based	407	17.4
Ethiopia	Seyoum and Mengistu[127]	2001	Clinic-based	302	37.8
Ethiopia	Teshome and Melaku[128]	2004	Clinic-based	1390	28.7
Ethiopia	Gill et al[129]	2008	Clinic-based	105	21
Kenya	Mwendwa *et al*[130]	2005	Clinic-based	100	7.0
Kenya	Mwale *et al*[131]	2007	Clinic-based	96	22.6
Malawi	Glover *et al*[132]	2012	Clinic-based	249	32.5
Nigeria	Omolase *et al*[133]	2010	Clinic-based	100	15
Nigeria	Onakpoya et al[134]	2010	Clinic-based	80	21.6
Southern Africa	Rotchford and Rotchford[135]	2002	Clinic-based	253	40.43
Southern Africa	Carmichael et al[136]	2005	Clinic-based	1517	26.5
Southern Africa	Mash *et al*[137]	2007	Clinic based	400	62.4
Southern Africa	Reed and Cook[138]	2007	Clinic-based	248	32.3
Tanzania	Mumba et al[139]	2007	Clinic-based	86	20.9
Tanzania	Cleland et al[140]	2016	18 diabetes clinics	3187	27.9
Zambia	Lewis et al[141]	2018	Clinic-based	2153	52
Malawi	Burgess et al[142]	2014	Cohort study	357	50.1
Kenya	Mathenge *et al*[143]	2014	Population based survey	4414	35.9
Nigeria	Kyari *et al*[32]	2014	Population-based national survey	1595	20.5

In Kenya, a Nakuru study reported PSED to account for 30.4% of blindness, of which DR accounted for 2%.[144, 145] The Nakuru cohort study found the prevalence of any DR among PLWD to be 35.9%.[143 115] This data can be used for planning services in Kenya, although more studies would help to consolidate the evidence. The Rapid Assessment of Avoidable Blindness (RAAB + DR) is a potential method to collect more local prevalence estimates.[146, 147] Table 2-2 shows how the data on incidence and prevalence can be used for planning DR programs. We propose that interventions to increase access to screening among PLWD are vital in preventing vision loss.

Table 2-2: Planning for DR services in Kenya

NEED FOR DR SERVICES IN KENYA

Population at risk	
Total Population	53million
Population to be covered (consider age- above 20yrs = 45%)	24million
Diabetes Mellitus (PLWD)	
Prevalence of diabetes (number DM / 100 pop)	2%
Number of people with diabetes	480,000
Diabetic Retinopathy	
Proportion (%) of PLWD with DR	35%
Number of people with DR	168,000
Vision threatening diabetic retinopathy (VTDR)	
Proportion of PLWD with VTDR	10%
Number of people with Vision Threatening DR (VTDR) (need treatment)	48,000

2.4.2 Risk factors for onset and progression of DR

The major risk factors leading to development and progression of DR have been elucidated, Table 2-3. Key factors that are consistently associated with DR include longer duration of diabetes, prolonged hyperglycemia, and systemic hypertension.[112, 115] These factors apply to all types and stages of DR.[115] Dyslipidaemia is associated with DMO, but its role in other types and stages of DR is the subject of debate.[115, 148] The duration of diabetes is considered the strongest independent predictor for DR,[114] but in Kenya where >50% of PLWD are undiagnosed, DR may be the first presentation of diabetes.[57] This raises the need to increase early detection of both diabetes and DR.

The Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetic Retinopathy Study (UKPDS) showed the protective effect of good glycaemic control (HbA1c < 7%) in reducing the risk and progression of DR in type 1 and 2 diabetes respectively.[114] This effect has been quantified, such that a 1% decrease in HbA1c corresponds to a reduced risk of retinopathy by 40%, progression of DR to VTDR by 25%, need for laser therapy by 25%, and blindness by 15%.[113] On the other hand, tight glycaemic control carries the risk of hypoglycaemia, and requires a strong compliance from both PLWD and physicians. High levels of undiagnosed diabetes, low treatment coverage for diabetes, and non-adherence to medication, which have been already highlighted in Kenya, are likely to be a challenge for achieving good glycaemic control.[51, 57]

The UKPDS showed the positive influence of tight blood pressure control. Every 10mmHg reduction in systolic blood pressure results in a decreased risk of retinopathy progression by 35%, need for laser therapy by 35%, and visual loss by 50%.[113] Crucial to note, the STEPS survey in Kenya found that 56% of the

population 18-64 years had never checked their blood pressure and 22% of those who were already diagnosed with hypertension were not on treatment.[50, 51] This is another challenge for DR control programs.

Given these risk factors, prevention of DR-related vision loss will require close collaboration between diabetes and eye care services.[149] At present, such collaboration is minimal.[150] The landmark trials mentioned above, along with the Early Treatment Diabetic Retinopathy Study (ETDRS) have shown that blindness from DR is almost entirely preventable with early detection of DR, timely treatment and effective diabetes control.[151] To prevent vision loss, metabolic control and yearly retinal examinations are recommended for PLWD, beginning at the time of diagnosis of type 2 diabetes or 5 years after diagnosis of type 1 diabetes, with increasing frequency once DR is identified.[152, 153] At present, although PLWD in LMICs have some awareness of DR as a possible diabetes complication, specific knowledge about DR is rare, and many PLWD do not have an eye examination before they experience vision loss.[147] One study reported that the mean time between diabetes diagnosis and DR screening for PLWD in different parts of LMICs ranged from 8.0 (±7.0) to 14.4 (±10.8) years.[154] Screening programs must therefore have a strong health education and advocacy component.

As can be seen from Table 2-3, three priority risk factors for NCDs (physical inactivity, tobacco use, unhealthy diet) have been associated with onset and progression of DR. There is therefore optimism that the proposed interventions for NCDs will be useful to prevent and control DR. The association of DR with alcohol intake, another priority risk factor for NCDs, is the subject of debate, and the evidence is inconclusive at present, an area for further research.[155, 156] There is no published evidence on the association of DR with the fifth priority risk factor for NCD, air pollution. Crucially,

there is a need for more evidence on other risk factors that are of special interest to Africa, such as co-pathology with HIV, malaria, tuberculosis, malnutrition, micronutrient deficiencies and anaemia.[33, 142]

Table 2-3: Risk factors for onset and progression of Diabetic Retinopathy

Patient factors *Non-modifiable*: increasing duration of diabetes, [157, 158] increasing age,[159-161] African, South Asian and Latin American ethnicity,[159, 162] male gender[159-161, 163] metabolic hormones (leptin and adiponectin)[164] *Modifiable*: hyperglycaemia [158, 165], high blood pressure [158, 165], dyslipidaemia[158, 166], physical inactivity[157], smoking,[167] obesity,[164] pregnancy,[164] lack of awareness,[168] lack of access to services[169] inflammation and oxidative stress[164]
Health worker factors Lack of knowledge, lack of education in diabetes care, poor communication with patients, failure to individually recommend patients for diabetes screening[168] lack of collaboration between providers of diabetes and eye services[169] ambivalence towards referral of patients, non-adherence to practice guidelines[170]
Health system factors **L**imited and irregular anti-diabetes drug supplies[168], high cost of treatment and tests[168], lack of glucometers, strips and syringes[168], lack of screening programs[168], lack of diabetes registries[168], lack of coordination of care[168], stigma associated with diabetes in the society,[168] lack of clinical guidelines,[170] lack of endocrinologists[168] and ophthalmologists[168]

2.4.3 Impact of DR-related vision loss

The early stages of DR are asymptomatic but the development of severe non-proliferative DR, proliferative DR and diabetic macular oedema causes irreversible vision loss.[113, 171, 172] In the early stages of DR, vision specific functions are maintained at a similar level with those with no DR. However, persons with VTDR are up to 6 times more likely to have a low overall vision-specific functioning (participation in vision-dependent activities such as reading, watching television or driving) compared with those with less severe stages of DR, independent of their presenting visual acuity.[173] Activities requiring fine visual acuity such as reading small print are

particularly affected. Loss of contrast sensitivity also occurs, especially with maculopathy. Laser photocoagulation is destructive to the retina and causes loss of visual field. Further, PLWD who have DR are at an increased risk of falls.[174] As a result of vision loss, physical mobility is reduced, PLWD become socially isolated and often dependent on others.[175] Thus, it is important to bring in interventions that can preserve vision.

PLWD have difficulties in managing diabetes once they are visually impaired. For example, they have difficulty measuring their blood glucose or measuring the dose of insulin. This can lead to poor glycaemic control, deterioration in DR, frequent need for hospitalization and increased mortality. Furthermore, patients with DR are at greater risk of other systemic vascular complications, including stroke, coronary heart disease, and congestive heart failure.[173] Physicians and ophthalmologists should therefore ascertain that patients with DR are receiving appropriate assessment and treatment for these comorbidities.[164] Diabetes, DR and vision loss are independently associated with mental health problems such as emotional distress, depression and reduced psychosocial functioning.[176-178] Fear and anxiety relating to potential visual loss as well as fear of laser photocoagulation treatment for DR has been reported.[175]

There is clear evidence of the heavy economic burden caused by diabetes, DR and vision loss. [4, 64, 179] DR incurs substantial treatment costs, often necessitates increased health care utilization and significantly reduces health-related quality of life, once VI occurs. [55] Further, diabetes and DR are associated with loss of productivity, in terms of loss of employment and lost workdays. In a US population, the presence of diabetes itself reduced employment of PLWD by 3.5%, and the presence of complications reduced employment by 12% as compared to similar population without diabetes.[180] Given the economic impact of diabetes and DR to the PLWD, their

families and society, and given that vision loss worsens this burden and the quality of life, prevention of visual impairment is crucial. Early detection and timely treatment are essential.

2.4.4 The role of health systems in the control of DR

To reduce the incidence of blindness due to DR, a health system should: (1) ensure appropriate metabolic control of diabetes, as previously described; (2) enable early detection of DR through regular retinal screening; and (3) provide appropriate treatment and follow-up for patients with DR.[181] As both diabetes and DR are increasing, and DR awareness remains patchy and low in many populations, there is a need to increase the awareness in PLWD and in health workers regarding these services. [182]

Retinal Screening

The first screening tests for DR were conducted in 1980 in Iceland. [183] Wilson and Jungner (1968) established the criteria for screening in medicine, which was adopted by the WHO (Table 2-4). [184] Subsequent debate on the criteria has led to additional specifications of these criteria (Table 2-5). The St Vincent Declaration of 1989 was the first international commitment to apply screening to DR, targeting the reduction of DR-related blindness by a third over the next 5 years. Three decades since then, the application of these criteria continues. In 2005, the Liverpool Declaration sought to reduce DR-related blindness through systematic screening with a coverage of at least 80 % of PLWD by 2010, using trained personnel and access to the proper therapy. Since then many developed countries have initiated screening programs that use ophthalmoscopy, retinal photography and telemedicine.[185] Understanding how the screening criteria can be translated into practice in LMICs where there is no

established systematic screening programmes is crucial. The implications of these screening criteria in the context of LMICs need to be considered. Although there is an assumption that these criteria apply universally, successful DR screening (DRS) programs should be suited to the context, and context influences the translation of the criteria into practice.[147, 186]

	Table 2-4:Wilson and Jungner classic screening criteria[184]
1.	The condition sought should be an important health problem
2.	The natural history should be adequately understood
3.	There should be a detectable early/latent/asymptomatic stage
4.	There should be a suitable test for the early stage
5.	The test should be acceptable
6.	Treatment at an early stage should be of more benefit that at a later stage
7.	There should be an agreed policy on whom to treat as patients
8.	There should be adequate health service provision for the extra clinical workload resulting from the screen
9.	The costs of diagnosis and treatment should be balanced against benefits
10.	Case finding should be a continuing process and not a “once and for all” project

	Table 2-5: Emerging screening criteria proposed since 1968 [187]
1.	The screening programme should respond to a recognized need
2.	The objectives of screening should be defined at the outset
3.	There should be a defined target population
4.	There should be scientific evidence of screening programme effectiveness
5.	The programme should integrate education, testing, clinical services and programme management
6.	There should be quality assurance, with mechanisms to minimize potential risks of screening
7.	The programme should ensure informed choice, confidentiality and respect for autonomy
8.	The programme should promote equity and access to screening for the entire target population
9.	Programme evaluation should be planned from the outset
10.	The overall benefits of screening should outweigh the harm

In the previous sections the concept of DR as a chronic public health problem with a known natural history has been explored.[152, 188] The previous sections have presented evidence that the increasing prevalence, and the adverse health, social and economic impact are significant factors for PLWD, heath care providers and policy-makers. The goal of DR screening is to identify PLWD with asymptomatic DR and provide timely treatment for those with VTDR.[189] The target population for screening is well defined, since all PLWD are at risk, and will develop some DR if they live long enough. There is consensus that screening is required. However, the evidence base so far is from high income settings. While it is known that DR is generally progressive, the rate of progression in different settings is uncertain. It is also unknown whether the probability of adverse visual outcomes for PLWD in LMIC corresponds to the evidence from developed countries. Yet this is a learning point for LMICs – local evidence collected from screening programs would help identify the optimal screening intervals and methods for LMIC with more certainty.

As DR has a latent asymptomatic stage and effective treatment is available, annual examination of the retina is recommended.[152, 190] However, screening all patients with diabetes for retinopathy has remained an elusive target in most countries.[191] Lack of appropriate screening is a risk factor for VTDR and vision loss. The determinants of uptake of an eye examination are context-specific and can be categorised as personal, provider and health system factors.[171, 192, 193] Evidence on the barriers from different LMIC settings have been collated,[194] but screening programs will need to continually collect and use the evidence from their own settings.

Retinal examination can detect the latent, asymptomatic phase of DR.[189] International classifications of DR gives the specific parameters to be used for classifying DR and the subsequent clinical pathways to pursue.[195] All stages of DR (as specified in these classifications) are detectable with the same screening test. Recognition of early DR is helpful as it provides evidence of early disease, and appropriate metabolic control can prevent or delay further deterioration. There is considerable evidence that prompt treatment of VTDR can prevent vision loss.[113, 196] The challenge in LMICs is to ensure that all PLWD found to have VTDR get appropriate referral for treatment and access the treatment on time. Therefore, it is important that treatment services are available before establishing a systematic screening programme.

Retinal examination is considered safe, non-invasive and relatively quick. One of the requirements that can be challenging is mydriasis (pupil dilatation). Mydriasis is considered safe in SSA, as acute angle closure is not common; in Asia angle-closure is common hence non-mydriatic modes of retinal examination may be preferable.[147] Temporary blurring of near vision after pupil dilatation can discourage PLWD from uptake of retinal examination, especially if adequate explanation is not provided.[186] Further challenges that can discourage uptake of screening include the cost of travel

and time away from work. False positives may raise alarm, while false negatives may raise false security. It is therefore important to consider the diagnostic test accuracy (DTA) of different screening methods in comparison to the gold standard, which for routine practice is clinical examination of the retina by an eye specialist.[197] The recommended threshold for tests used in systematic population-based screening is over 80% sensitivity, over 95% specificity and less than 5% technical failure rate for satisfactory images or examination. [189, 198, 199]

Dilated slit lamp bio-microscopy and ophthalmoscopy (direct or indirect) are the main modes of screening in LMICs.[186] The sensitivity of direct ophthalmoscopy for detection of VTDR is only 65%, which is below the 80% threshold. However it is still useful for opportunistic case-detection.[189] Indirect ophthalmoscopy has the limitation of requiring extensive training, but it's accuracy is high and it is considered an alternative to direct ophthalmoscopy.[200, 201] Slit lamp bio-microscopy through a dilated pupil has a high sensitivity and specificity of 89% and 94% respectively, but is time consuming and requires a slit lamp.[202] The main disadvantages of these clinical examination methods is that the findings cannot be captured and stored for quality assurance. Fundus fluorescein angiography is expensive, time consuming, invasive, requires specific expertise, has a small risk of anaphylaxis and is not readily available in LMICs, hence it is not used as a screening tool. A combined colour camera and Optical Coherence Tomography (OCT) is useful for detection of diabetic maculopathy, however it not widely available or cost-effective for population-based screening. [189]

Screening programs in LMICs are gradually adopting mydriatic or non-mydriatic retinal photography. The limitation is the need for investment, as a single camera may cost $20,000, although low-cost fundus cameras are becoming more available.[201] A recent systematic review reports that single field views of both mydriatic and non-

mydriatic digital imaging methods generate a satisfactory level of sensitivity, i.e. 86% for the detection of any DR, once ungradable images are excluded from analysis.[202] The specificity is 91% (non-mydriatic camera) and 87% (mydriatic camera), which is below the 95% recommended threshold, but this improves to meet the threshold if two or more fields are taken. For the detection of VTDR, the sensitivity and specificity also increases with the number of fields of view, providing evidence that the number of fields taken is an important consideration in photography-based screening. In one study the use of mydriasis reduced the number of ungradable images from 27.1% to 8.3%, using a single-field strategy.[186] This is important because cataract and corneal opacities can be a source of ungradable images.[183] However, non-mydriatic imaging reduces the screening time and inconvenience of pupil dilatation, and may thus be more efficient and acceptable to both PLWD and health care providers.

Bragge and colleagues in their meta-analysis that included 20 studies found that screening involving non-medical photographers yielded lower specificity as compared to screening involving photographers with specialist medical or eye qualification, particularly with non-mydriatic imaging.[203] Low specificity has potential to increase the false positives and unnecessary referrals. It may be attributable to imaging difficulties or poorer image quality in their photographs. However in a more recent analysis that included 26 studies, Piyasena and colleagues found that non-medical retinal image graders could achieve the threshold level of sensitivity and specificity in both mydriatic and non-mydriatic strategies.[186] As screening is not an efficient use of ophthalmologists' time, task-shifting to trained retinal graders is a useful option, as already exemplified by the English DR Screening program.[204] While recommending this option, we emphasise the pre-requisite for training, certification and quality assurance mechanisms for the graders.

Screening at scale is cost-effective but can be expensive and labour intensive particularly for rural communities. One tool to address this is telemedicine. The diagnostic accuracy of telemedicine using digital imaging in DR is overall high (95% sensitivity and 86% specificity for detection of any DR). [116, 205] Considering the high sensitivity in the detection of any clinical level of DR, telemedicine can be used widely for DR screening. It has the potential to deliver cost-effective screening to rural, remote and hard-to-reach PLWD. On the downside, it still requires a fundus camera, which is expensive. Secondly, noncompliance with follow-up appointments has been reported in telemedicine programs, leading to low take-up of the screening results and hospital referrals.[147] One study in Kenya found that only 58% of PLWD return to a tele-ophthalmology site to receive screening results.[206] This illustrates that the telemedicine programs must extend efforts beyond capturing the images, to keep PLWD engaged. Other essential components for the use of telemedicine are robust technology, clear referral pathways and quality assurance. The retinal imaging devices must be validated and meet the specifications for image resolution which some programs have recommended as 20 pixels per degree with a resolution of at least 10–15 mm.[201]

Another tool is automated image analysis. A systematic review found that automated screening has high sensitivity (87-95%) but low specificity (49.6-68.8%). In this review, false negatives were likely to be mild DR with low risk of progression within one year. However, several studies in this review also reported missed cases of DME, which is a concern.[207] The use of cloud-based image analysis software is an additional emerging trend. There is need for more evidence on the diagnostic accuracy of the analytic software especially in the African population. There are only two studies that have tested the use of artificial intelligence (AI) in imaging African eyes, which are usually more pigmented than other ethnic groups, and the results have been positive.[208, 209]

There is also need for research on the ethical considerations, given the data security concerns.

A third tool for which there is growing interest is smart-phone based retinal screening. Validation studies are ongoing for different prototypes that use the principles of direct or indirect ophthalmoscopy. Bilong et al have reported the findings for a study where retinal images were taken through a dilated pupil, using a smartphone attached to an adaptable camera. Indirect ophthalmoscopy was also performed. The retinal images were sent via internet to a retinal specialist for interpretation. Sensitivity and specificity for the detection of any DR, was 73.3% and 90.5%. For DME it was 78% and 95%. However, for severe NPDR and PDR the sensitivity increased above the standard threshold.[210] At present, there is insufficient evidence to make any recommendations regarding this modality in screening.

The cost-effectiveness of DR screening compares well with other screening programs.[199] Data from the Liverpool Diabetic Eye Study showed that photography-based systematic screening is also more cost-effective than opportunistic screening or examination by a human screener, even if the screener has a sensitivity of 95%.[191] Systematic screening is also cost-effective in terms of sight years preserved compared with no screening.[211] Early diagnosis and early treatment of diabetic retinopathy is cost-effective, and even cost-saving[212] if the cost of VTDR is considered and if there is at least 80% compliance to screening.[213] Coverage is an important driver for cost-effectiveness.

Achieving the desired coverage may be challenging especially in rural and remote areas. Outreach DR screening is one way of improving screening coverage and can reduce overall health care costs, although quality assurance should be maintained.[203] The highest DTA (sensitivity 90% and specificity 95%) is observed when screening is

delivered at secondary/tertiary level clinics. [186] However DTA is not the sole factor that needs consideration. Context, resources, costs and coverage vary widely and the success of screening programs depends on understanding the 'best fit' within the existing system.

The appropriate timing and frequency of screening is an important consideration. DR-associated vision loss has been found to increase as the screening interval is extended from one to five years.[214] Annual screening is widely recommended, although some programs are moving to examination every two years if the initial examination is normal.[191, 195, 215] The evidence to-date is that screening every two years is cost-effective, but annual screening is outside the cost-effectiveness range, defined as less than three times the gross domestic product (GDP), or <US$3183 per quality-adjusted life year (QALY) gained.[147, 201, 216] On the other hand, long screening intervals may be a disincentive for PLWD, due to the potential for loss of contact and the interpretation that vision loss is unlikely and therefore not a concern.[217] Therefore yearly intervals for those with no DR are generally preferred, unless individual risk of progression (glycaemic and blood pressure control) can be assessed with certainty.[217] For those with DR, screening intervals depend on the severity of the DR.

There is consensus that VTDR should be treated, and the goal of treatment is to halt progression and prevent vision loss; restoration of lost vision is uncommon.[113] Because treatment is aimed at preventing vision loss and retinopathy can be asymptomatic, it is important to identify and treat patients early in the disease. Early laser treatment for diabetic retinopathy is safe, effective and universally agreed.[190, 218] The DRS and ETDRS studies showed that timely laser decreases the risk of severe vision loss (15 letters) by 52%; early treatment of clinically significant macula oedema

(CSME) reduces the risk of severe vision loss by 50% at five years and reduces the need for treatment to only 8% at two years.[196, 199, 219]

Anti-vascular endothelial growth factor (anti-VEGF) therapy is increasingly being used for DMO and has been shown to maintain visual acuity if used early and frequently in the course of the disease.[196] While both laser and anti VEGF injections are available treatment options for DMO, there is ongoing debate regarding which is the best treatment in LMICs, given the logistical and cost implications for each method.

The realities in LMICs provide important considerations about what policies should be prioritized. Based on the discussion above, it is clear that DR screening as applied to LMICs meets the screening criteria. However, in an environment where there are operational or implementation complexities, screening tends to be neglected. These complexities include infrastructural capacity (equipment, technology), trained human resources, program coordination and evaluation, logistics (reaching hard to reach groups), social considerations (e.g. compliance, informed consent, confidentiality and autonomy) and sparsity of local evidence. Given these uncertainties, innovative and context-specific solutions to improve screening services are required.

Photography-based systematic screening strategies are recommended, as they offer patient convenience, efficient use of skills, quality assurance and ability to detect other eye conditions. Retinal imaging devices must meet the minimum acceptable standard for screen resolution. The standards used in the English program is a vertical resolution of 1080 (1920 9 1080) with an achievable and recommended standard of a minimum of 1200 (1920 9 1200 or higher). It is recommended that a minimum of 60% of the image should be viewable on the grading screen to avoid too much scrolling to see the full image.[204] Opportunistic screening programs can use the tools available.

A potential leverage spot for screening programs is program management. To make the most of resources, and cause ripple effect in the capacity, volume, quality and cost-effectiveness, it is necessary to strengthen capacity to manage screening programs. For example, a program manager may help to bring endocrinologists, physicians, ophthalmologists, epidemiologists, economists, funders and policy-makers together on one page, for a coordinated and concerted response. There is no published literature specifically investigating approaches to sustain and coordinate program management in DR programs. This is an important area for future research.

Table 2-6 summarizes the interventions for control of DR-related vision loss. In LMICs barriers to the access and utilization of these interventions abound, including lack of diagnostic equipment and treatment infrastructure (lasers, laser maintenance, anti-VEGF, vitrectomy machines).[33] International clinical practice guidelines (CPGs) on the use of these interventions have been developed,[190] but locally adapted CPGs are often lacking.[33, 150]In SSA where the mean ophthalmologist density is 3.7 per million population,[220] there is need to invest in developing sufficient workforce as well as task shifting.[221]

Table 2-6: Interventions for control of vision loss from DR
1 Prevention of diabetes Lifestyle measures, especially healthy diet, regular exercise and weight vigilance.[58, 170, 222]
2 Prevention of DR in PLWD Good blood glucose control, BP control, control of hyperlipidaemia; avoid smoking[113, 114, 222, 223]
3 Prevention of visual loss from DR Annual retinal screening examination, timely identification, referral and treatment of VTDR (laser for PDR, and laser or anti-VEGF or intravitreal steroids for DMO), with regular follow-up.[191, 212, 224-227]
Restoration of vision in severe PDR with vision loss from vitreous haemorrhage Good tertiary eye care services, including vitreo-retinal surgery[113, 195, 223, 228]
5 Improving functioning in PLWD with visual loss Visual rehabilitation services[164, 195, 228]

2.5 Control of DR within an NCD, UHC and the health systems agenda

The previous sections have presented evidence from the literature that the health, economic and social burden of both diabetes and DR is likely to increase, and that LMICs carry a disproportionately high burden. It is clear that diabetes is a global health priority along with other NCDs. The NCD agenda recognizes diabetes not as a single disease, but as a complex comorbidity.[5] To this extent, NCD 'best buy' interventions that are relevant to DR have been recommended in the agenda. What is less clear is why relevant targets and indicators for DR, or any other long-term complication of diabetes, are not included in the global NCD targets and indicators.[229]

The NCD targets focus on preventing mortality from diabetes. As we have described, DR causes morbidity and other social and economic effects, but it is not in itself fatal. Including targets relevant to DR, such as the number of people going blind or the loss in productivity from DR, might increase its visibility and attract investment in DR control at country level.

Many PLWD in LMICs who would benefit from the interventions for diabetes and DR do not use them. For example many are undiagnosed and untreated, or fall off the diabetes care cascade.[4, 5] Addressing DR at the individual PLWD level is therefore a priority need for PLWD. However, interventions that only have effect at the individual level are insufficient for control of DR, as there is need for system level impact. This chapter has made a case about the relevance of interventions based on the multifaceted chronic care model.

To reduce the burden with NCD interventions, there is also need to prioritize surveillance and research, strengthening services and equity. These are some of the strategies that have contributed to the success of UHC and DR programs, for example in the United Kingdom.[22, 198] Although LMICs cannot directly copy strategies used in high-income countries, they can learn from them. The Diabetic Retinopathy Network (DR-NET) provides an important learning opportunity in which existing VISION 2020 LINKS between UK and overseas eye departments share learning on DR screening and treatment.[171, 230] At present there are 22 DR LINKS in the network representing 18 countries in Africa, the Caribbean and the Pacific.[230] The DR-NET helps LMICs to develop collaboration between diabetes and eye services, set up diabetes registries, acquire screening and treatment infrastructure, develop clinical guidelines and plan for DR services using the DR-NET toolkit.[228]

Although three in four of PLWD reside in LMICs, there is a dearth of data from these countries, which makes it challenging to define needs and priorities.[231] National governments are making effort to address this; for example, the Ministry of Health Kenya has carried out a STEPS survey on the risk factors of NCDs.[51] The data has helped to understand the epidemiological profile of diabetes, as discussed in this chapter. Local evidence about DR is required for planning DR services. In Kenya, the DR prevalence data so far has come from three observational studies (Table 1) and one longitudinal cohort study that provided the incidence data.[60] While using this data to plan for services, we need solution-based research to identify feasible approaches to engage PLWD and prevent non-adherence along the care cascade. We also need surveillance data for both process and clinical outcomes, such as the number of PLWD screened for DR and the number that progress to vision-threatening DR. This evidence might then serve to attract investment in services.

Like other NCDs, the control of DR has strategic links with health systems and UHC. The services required for control of DR are the interventions for prevention, screening, diagnosis, treatment and rehabilitation. These services have to be provided within a health system that is responsive to the changing epidemiology.[232, 233] There is need to build a health system that will help people live in a way that prevents diabetes, achieve good control of their diabetes, provide regular retinal screening to detect DR in its early stages, and provide accessible and affordable laser or anti-VEGF treatment for those with VTDR to prevent blindness.[171] As countries aspire to attain UHC, these health systems need these services to be comprehensive, have sufficient coverage, high quality and be at an optimal cost.[22] Heath systems therefore play a crucial role in the response to the burden of both diabetes and DR. The WHO's global report on diabetes in 2016 reported variation in the capacity of health systems to deliver diabetes services.[233] For example some LMICs countries did not have national

policies or guidelines, basic technology for diagnosis of diabetes, or sufficient supplies of insulin in primary care. Planning services for DR also requires an assessment of the health system capacity.[149] There is value in periodic health system assessment, specific to diabetes and DR, as it helps to identify the needs, and facilitate subsequent health system strengthening to address priority gaps.

As NCDs become the leading disease category in developing countries, the provision of NCD-related services will increasingly form the backbone of health systems. Given the pluralistic needs of PLWD, there is need for investment in systems that make DR control programmes accessible, affordable, and sustainable. Weak health systems are an obstacle to access services, as well as to equity.[15] At present, in many African health systems, laser photocoagulation and anti-VEGF drugs for DR are either unavailable or unaffordable, while the health workforce is insufficient, especially in rural areas. [149, 234]. Without equitable coverage, for example with the 'best buy' interventions, the poor / rural PLWD will continue to be left behind and jeopardize the attainment of the 2030 SDG agenda. Populations of PLWD that are disadvantaged should be prioritized, not necessarily by interventions that target them exclusively, but those interventions that bring them most benefit. As health systems differ, the interventions to improve equity are likely to be context specific.

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Section B
Health System Assessment

'An epidemic is the wrong time to discover our preparations have not been sufficient, or that we have overlooked crucial components of the response.'

Dr Tedros Adhanom Ghebreyesus, 2018
Director General, World Health Organization

'The pathway to UHC is not something you reach by investing in something called UHC. You make that pathway by building parts of the health systems, addressing the health care needs of a specific population and by addressing specific conditions. It will inevitably involve a mix of focusing on specific segments of populations, specific diseases and functional components of the system.'

Peter Sands, Executive Director, 2019
The Global Fund to Fight AIDS, Tuberculosis and Malaria

Chapter 3: Health system assessment for diabetes and diabetic retinopathy

3.0 Overview

Health systems play an integral role in the response to the diabetes and DR epidemic, as described in chapter two. The concept of health system assessment (HSA) has gained significant emphasis in research and policy, because it can identify important areas of action to influence the achievement of health outcomes.[1] Chapter three reports on the health system assessment for diabetes and diabetic retinopathy in Kenya. This includes a summary of the purpose and research questions (3.1), the conceptual framework (3.2), an overview of theoretical frameworks for HSA (3.3), adaptation of a framework for this study (3.4), and a summary of study methods (3.5). Section 3.6 outlines the results, culminating in the identification of priority interventions. A detailed description of study methods and additional results are provided in *Research Papers 1 and 2* in the next chapter.

3.1 Purpose of the health system assessment

Building on the WHO definition of a health system,[2] the system for diabetes and DR can be defined as 'all resources, institutions and activities whose purpose is to promote, restore or maintain health for PLWD, including eye health'. The assessment of the strengths and weaknesses of the system in its ability to respond to the rising burden of these conditions is a lever that countries can use to strengthen the health system.[1, 3] There is broad commitment at the global level to strengthen health systems as an approach to addressing emerging health needs,[4] but there is no consensus on the optimal combination of strategies to improve the response of health systems to diabetes and DR. Examples of interventions that have been applied to ensure that

effective diabetes and DR services are available include diabetes registers, task shifting, telemedicine, mobile screening clinics, integrated models of care, photographic retinal screening and artificial intelligence.[5-7] However, it is uncertain whether any of those interventions would be feasible and appropriate in the context of Kenya. Therefore, there is a need to identify the local needs and resources, suitable interventions to address the needs, and suitable methods to test these interventions. This HSA is designed to identify the gaps and strengths in the health system, as a first step towards addressing the gaps.

A general HSA,[8] and an Eye Health System Assessment (EHSA) were conducted in 2010 and 2017 respectively.[9] Both HSAs showed that the health system is highly pluralistic, with formal and informal public and private sectors. However, the two HSAs did not provide evidence of an interaction between the two systems, or the specific issues relating to diabetes and DR services. Given that these conditions are a priority, the need for such evidence to inform the next eye health plan for Kenya has been articulated.[10]

This chapter describes a HSA for diabetes and DR, which sought to answer the following research questions:

1. What are the strengths and weaknesses in the health system for diabetes and diabetic retinopathy?
2. What priority intervention(s) can address the key gaps in the services for diabetic retinopathy?

3.2 Conceptual Framework of the health system

The conceptual framework of the health system for diabetes and DR, Figure 3-1, corresponds to the typical care pathway that a PLWD in Kenya would follow. In the *community*, there are health promotion activities and screening camps for diabetes.

Persons who do not access screening in the community are encouraged to visit a health facility for testing. Those diagnosed with diabetes are linked to the nearest *diabetes clinic* for metabolic control, follow-up and screening for complications. Assessment for metabolic control, through HbA1c, is a key service indicator for all PLWD. Diabetes services should also refer all PLWD for screening for DR, which is available at the *eye clinics*. Attendance at DR screening is another key service indicator. The eye clinic also provides treatment for VTDR. Strengths and weaknesses can exist at any or all of the three levels (the community, diabetes clinic or eye clinic), which has impact on the burden of visual impairment from DR.

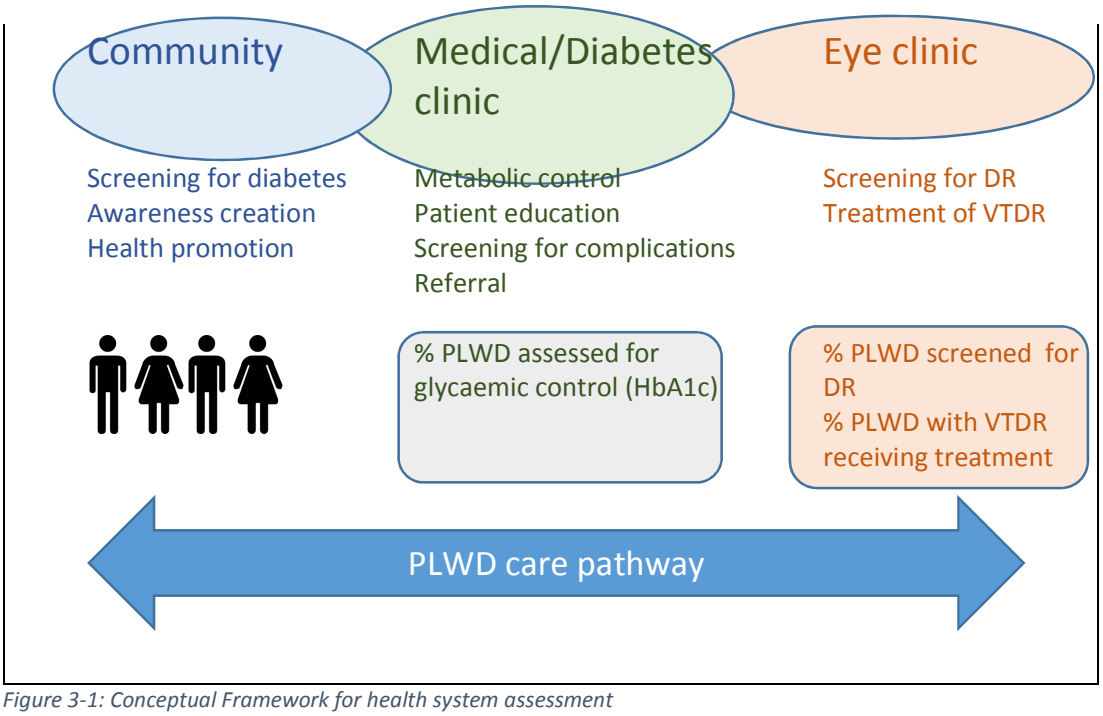

Figure 3-1: Conceptual Framework for health system assessment

3.3 Health system frameworks

The purpose of a HSA is to take stock of a specific health system.[1] There are several frameworks for health system assessment in the literature. Hoffman and colleagues identified 41 different health systems frameworks.[11] The volume and diversity of existing frameworks highlights several things. First, the variation in the way different people or institutions conceptualize health systems. Second, the high interest around the concept of health systems. Third, the difficulty in capturing all the attributes of health systems in one framework, since health systems are complex. Fourth, the evolution of the understanding of health systems over time. Surprisingly, although many frameworks have been described in the literature, examples of how they have been applied in health system assessments are relatively few, with some of the frameworks being dominant.[12]

In 2007 the WHO described the health systems building blocks framework, which is ubiquitous and highly influential in the literature.[13] In this framework, the health system is composed of six interacting building blocks, and each of them is relevant to diabetes and DR: – a) service delivery, b) health workers, c) health information, d) medical products, technology and vaccines, e) health finance, and f) governance and leadership. The framework has been used in studies relating to DR, vaccines, measles, polio, HIV and malaria, although it was originally designed for resource mobilization, not for research.[4, 14]The widespread use of the framework for assessing health systems fosters a shared understanding among researchers and the users of research evidence.[15] Kenya has adopted this framework, and in 2010 used it for a general HSA.[8] Subsequently Kenya added two building blocks to the framework (infrastructure and research), to make eight blocks, Figure 3-2. [16]

The limitations of using the building blocks framework in research have previously been described.[4, 17] In particular, it does not capture the experiences of PLWD along the care pathway, a parameter of interest in this study. Additionally, there is need to capture evidence on the strengths and weaknesses on both the supply-side and the demand-side of the health system. As the framework is predominantly a supply-side model [17] it is necessary to complement it with other approaches that take into account the demand-side.

In 2015 the WHO developed a specific tool for the assessment of diabetic retinopathy and diabetes management systems (TADDS).[18] This tool is based on the WHO building blocks framework. Its stated focus is to assess the collaboration between diabetes and DR services. It has seven elements a) service delivery, b) health workers, c) health information, d) health technology, e) health finance, and f) policies, priorities and programs g) health promotion for diabetes and DR. It has the advantage of focusing the HSA on the condition of interest, but it narrows the scope of the "leadership and governance" building block to 'policies, priorities and program' and the medicines and other products building block to health technology. At the time of this study, this tool was new and had not yet applied in practice. Figure 3-2 compares the building blocks in these frameworks.

WHO health systems building blocks	Health systems building blocks (Kenya's modification)	WHO TADDS tool key sections
Leadership and Governance	Leadership and Governance	Priorities, policies and programs
Service delivery	Service delivery	Service delivery
Health workforce	Health workforce	Health workforce
Medical products and technologies	Medical products and technologies	Health technology
Health information management system	Health information management system	Health information management system
Health financing	Health financing	Health financing
	Infrastructure	Health promotion for diabetes and DR
	Research	

Figure 3-2: Comparison of building block focused frameworks

Another approach to HSA is the use of tracer conditions. Kessner and colleagues in 1973 were the first persons to describe the use of tracer conditions to assess health systems.[19] A tracer condition is a carefully selected health problem that makes it possible to capture differences in the performance of a health system.[20] There are six criteria for a tracer condition.[21, 22] Table 3-1 shows how the criteria apply to diabetes and DR. The combination of the two conditions is suitable as a tracer for the responsiveness of a health system to chronic diseases in general and NCDs in particular, for three reasons. First, they occur in association with other chronic comorbidities, such as hypertension.[23, 24] Second, for people with NCDs and other chronic diseases, preventing complications is an important aim of the health system.[25] As DR is a specific complication of diabetes, the two conditions can mirror the subtleties of the

progression of disease. Thirdly, chronic diseases require an integrated health system,[25] which can be exemplified by the level of integration between services for diabetes and DR. A HSA using this approach therefore provides useful evidence for the health system for chronic diseases, including NCDs. Diabetes has been used as a tracer condition for health systems in several studies.[20, 22, 26-28] This is the first study to consider the combination of diabetes and DR as a tracer condition.

Table 3-1: The suitability of diabetes and DR as tracer conditions

Criteria	How diabetes and DR fit the criteria
Disease has a known epidemiology	The epidemiology of both conditions globally, in SSA and in Kenya has been described in chapter 2
Disease is well defined and easy to diagnose	The definition and criteria for diagnosis are provided in chapter 1 (diabetes) and chapter 2 (DR)
Its prevalence in the population is large enough to enable adequate data to be collected	Both population-based and clinic-based surveys have shown that that the prevalence is sufficient to enable collection of data that can be used for planning (chapter 2)
Its natural history is known, and it varies with the utilization and effectiveness of health care	The predictors of the development of complications in both conditions, which include metabolic control, have been described in chapter 2
It requires specific treatment, in the absence of which functional impairment results	Hypoglycaemic drugs and lifestyle measures are required for glycaemic control, and the treatments for DR have been described in Chapter 2, without which visual impairment results
Available and well-defined techniques of medical management exist for at least one of the following: prevention, diagnosis, treatment or rehabilitation	Prevention, diagnosis and treatment apply to both diabetes and DR. Rehabilitation is provided for those who develop severe visual impairment and blindness

Nolte and colleagues assessed the performance of health systems using diabetes type 1 as a tracer condition in 29 countries.[20] Using routine data, they demonstrated a remarkable variation in case-fatality across these countries, suggesting differences in

the ability of the various health systems to respond to diabetes. In this study, it is envisaged that using diabetes as a tracer will provide a broad understanding of the health system response to the needs identified along the care continuum. We did not use mortality as an indicator due to lack of suitable registers for diabetes and death in Kenya.

Diabetes type 1 has also been used as a tracer condition to investigate the capacity of the health system in Mozambique, Zambia and Mali, using a rapid assessment protocol for insulin access (RAPIA).[20, 29] The RAPIA method is a rapid and low cost method of situation analysis, centred on access to insulin. The RAPIA study was conducted in three areas; the capital city, a large urban centre and a rural area, to provide a picture of the national health system. It involved studying the path of insulin from its arrival in the country to the point of the end-user, including identifying determinants along the pathway. In Kenya a RAPIA study to assess insulin access in two counties of Kenya (Meru and Trans-Nzoia) found that a public-private partnership (the *Base of the pyramid* project) helped to stabilize the cost of insulin but was not sufficient to improve access to diabetes care.[27]

3.4 Adaptation of the WHO health system framework for this study

Each of the frameworks provides conceptual contributions and a general direction for health system assessment. However they do not serve all purposes and require adaptation for use in different settings.[4, 30] This study is anchored on the WHO framework as the main assessment framework, since all the building blocks are relevant to diabetes and DR. Since the study is in Kenya, the eight building blocks model was considered appropriate for facilitating shared understanding with Kenyan policy-makers and for future comparison with other local studies. The tracer approach, used in

combination, helped to illuminate how the various building blocks of the health system are responsible for health system performance along the care pathway. This combination has the benefit of focusing the study on issues pertinent to diabetes and DR whilst retaining the benefits of a common framework. It is important to note, for replication of this approach in other studies, that familiarity with the typical patient pathway is a key prerequisite for adapting the framework for this purpose.

3.5 A summary of study methods

Bennett and Peters have proposed a set of three key principles to guide HSAs: relevance, coherence and trustworthiness.[1] These principles were operationalized by consulting local stakeholders and obtaining consensus on: the purpose of HSA and the choice of the appropriate study counties (relevance), the fitness of the HSA framework for the purpose (coherence), and the choice of study procedures (trustworthiness). The stakeholders included the NCD division and the Ophthalmic Services Unit at the Ministry of Health, the national DR working group and the national eye care coordinating committee.

Three counties were purposively selected for the study, based on geographic context (rural/urban), location within the diabetes belt (Figure 3-3) and other unique characteristics highlighted below. The 'diabetes belt' is an area that stretches from the coast to the Lake Victoria region, corresponding to the area along the railway (marked red). However, there are also additional pockets outside this belt that also have high prevalence (also marked red). It was named the 'diabetes belt' based on a historical perception of high prevalence as reported from some screening camps in this region. Nairobi (population 3.6 million, 100% urban) is a cosmopolitan city with a unique social structure compared to the rest of the country (high population, heterogeneous social

strata including the affluent, the middle class and the urban poor) and a unique health system structure (a large number of both private and public health facilities, including primary, secondary and tertiary centres). Nakuru (population 1.8 million, 46% urban) has been the focus of previous DR prevalence and incidence studies reported in chapter two, and it is of interest to relate these research efforts to the national health system.[31] Kirinyaga (population 0.6 million, 16% urban) is considered to have a relatively high prevalence of diabetes compared to other counties within the 'diabetes belt'.
Through simple random sampling from a sampling frame of clinics, three diabetes clinics were identified in each county (public, private-for-profit and private-not-for-profit facilities), giving nine diabetes clinics. Eye clinics were also identified using the same procedure. Data for this mixed-methods analytical cross-sectional study was collected through:

a) Patient interviews at the diabetes clinic (n=270)

b) Interviews with service providers for diabetes (n=18) and eye care (n=9)

c) Interviews with key informants who were familiar with the organization and delivery of healthcare at the national or at county level, with particular reference to diabetes and eye care (n=18)

d) Review of documents provided by key informants

The data collection tools were designed to collect information on the eight building blocks, with reference to the community, diabetes and eye clinic settings. This data was then triangulated. Research papers 1 and 2 provide additional details on the methods. The London School of Hygiene and Tropical Medicine (LSHTM) and the African Medical Research Foundation (AMREF) granted ethics approval.

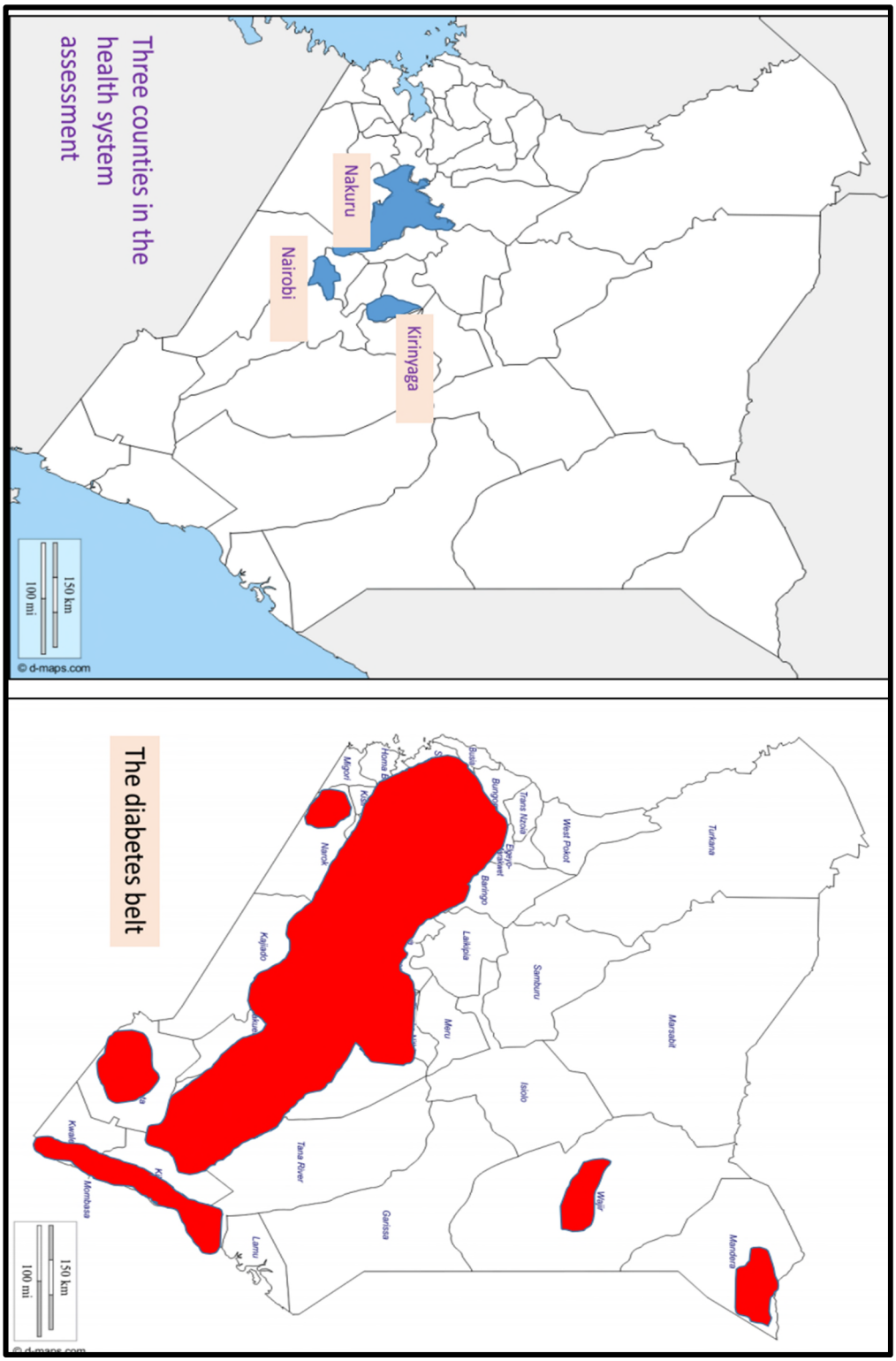

Figure 3-3: Study counties and the diabetes belt

3.6 Results

Based on the data from all the interviews and the document review, the findings for each building block are discussed concisely below**.** Additional results are presented in the research papers in chapter 4.

Service delivery

Community

Strengths: Local radio and television programs have health programs that include diabetes education for the public. This reflects recognition that before people become patients, they need to be empowered to protect their health.[32] Testing for diabetes is available at outreach screening camps. Community health volunteers (CHVs) link those diagnosed with diabetes to primary care clinics and diabetes support groups (DSGs) in the community. These DSGs and CHVs are important examples of linkage between patients and community resources, one of the elements of the chronic care model (CCM).[25, 33] At the DSGs, PLWD receive self-management education, glucose-monitoring services and peer support. DSGs value disclosure and PLWD discuss their illness and treatment freely. There is no stigma associated with diabetes in adults in the community and in the DSGs. This is important because it influences the capacity of PLWD to take on self-care tasks, including attending appointments and adhering to treatment.[34]

Weakness: Public education through mass media is inadequate and mainly concentrated around advocacy events such as the World Diabetes Day, World Health Day and World Sight Day. This portrays a lack of emphasis on prevention of both diabetes and DR. A high proportion of adults have not been tested for diabetes, therefore many PLWD remain undiagnosed. The first point of care for the community is local clinics and pharmacies, many of which do not offer routine blood glucose testing, causing delay in

diagnosis. Children with Type 1 diabetes often avoid disclosure of their condition to the school community for fear of stigmatization. This may reduce their capacity to enact self-care within the school context, and hence undermine health outcomes.[35] Similarly, formal and informal places of employment do not offer any type of diabetes services, and employees may not disclose their illness to the employer since they do not perceive this as beneficial. Work sites and schools therefore require strategic engagement.[36] Although DSGs exist in the three counties, they are not uniformly active. For example, DSGs are very active in Kirinyaga and Nairobi, and less active in Nakuru, which is attributed to variation in DSG leadership capacity at county level.

Diabetes clinic

Strengths: There are dedicated diabetes clinics in all the counties, where PLWD are booked to attend appointments for follow-up. All the clinics in Kirinyaga and Nakuru run twice a week. In Nairobi, some clinics run five days a week but most run two days. On the day of appointment, PLWD are seen on a 'first in first out' basis. PLWD are free to switch clinics or use multiple clinics. This aspect of autonomy is valued by PLWD, but its effect on quality of care in LMICs has not been investigated. Diabetes clinics work closely with DSGs, which ensures that PLWD in the community are linked with diabetes clinics. DSGs also mobilize communities for screening camps organized by diabetic clinics.

Weaknesses: Most of the diabetes clinics run only two days a week, rather than the five working days. This results in a high volume of patients and long waiting queues at the clinics. The result is short consultation interactions that focus on the immediate complaint, and comorbidities such as depression and hypertension may be missed. This differs from the productive patient-provider interactions envisaged in the CCM.[37]

Outpatient and inpatient services are delinked, such that it is not possible to track the frequency of hospitalizations of PLWD attending the clinic. Other supply side barriers to services are: inefficiencies such loss of patient files, lack of facilities for HbA1c testing, stock out of insulin, oral drugs and glucose test strips. PLWD receive care from multiple diabetes clinics which is likely to deter continuity of care.[5, 38]

Demand side barriers include long distances to diabetes clinics, with its associated transport costs and travel inconveniences. Some of the PLWD have to connect two or three routes to reach the health facilities, and they are typically required to arrive by 8am in order to be attended that day. The cost of tests and medication, the opportunity cost of waiting time at the clinic and lack of permission from employers to attend clinic appointments are additional problems, similar to the experience in other settings.[38]

Barriers to accessing HbA1c services

Only 27% of PLWD have had an HbA1c test in the preceding 12 months, and only 40% have ever had the test, with Kirinyaga county having the lowest indices, Figure 3-4. HbA1c testing is often not available in diabetes clinics due to malfunctioning equipment or lack of reagents. Therefore PLWD have to get HbA1c done privately, incurring high costs. In addition, health workers often use fasting blood sugar to monitor glycaemic control, rather than send PLWD for HbA1c test outside the health facility. Considering that HbA1c measures the glycaemic control over three months, is a proxy for the quality of care and a predictor for complications, it is a more suitable test for chronic care.[39-41] This reflects that resource challenges in the health system are hindering adoption of chronic care.[42]

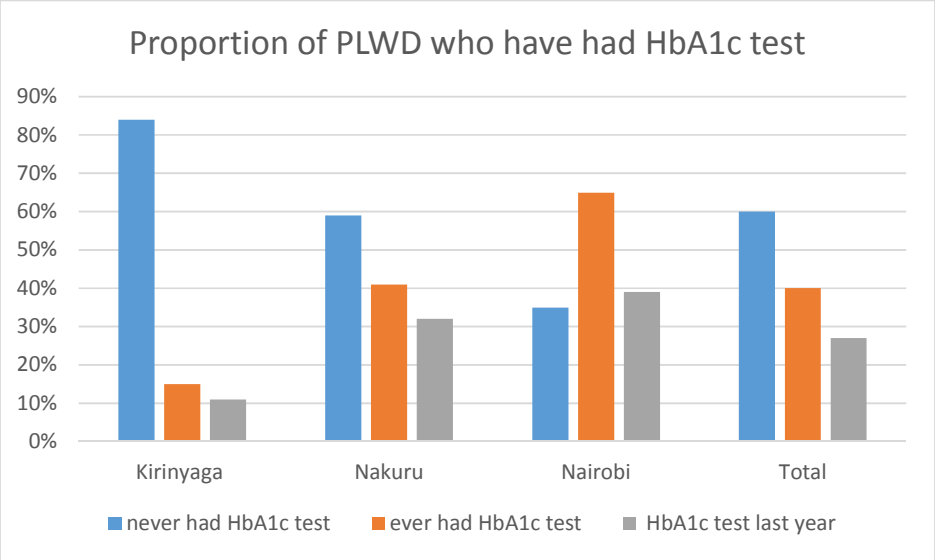

Figure 3-4: Access to HbA1c testing by county in 270 PLWD (90 in each county)

Barriers to accessing DR screening services among PLWD attending diabetes clinics

DR screening rates are low among PLWD attending diabetes clinics in all counties, with the lowest indices being in Kirinyaga, Figure 3-5 and 3-6. The predictors of DR screening are discussed in research paper 1. Supply side barriers include failure to refer PLWD for screening.[43] Service providers attribute this to forgetting, heavy clinic workload, diabetes being a complex disease that requires too many tests, more pressing concerns such as renal failure, lack of guidelines on DR screening and lack of point of use materials such as checklists to ensure screening is not forgotten. Further, they cite the lack of coordinated links with eye care services. The diabetes and eye clinics are located in different buildings in most of the facilities and sometimes PLWD who are referred for DR screening are "lost" along the facility corridors, and do not arrive at the eye clinic. Diabetes clinics do not have a formal way of following up PLWD to monitor uptake of referral or to obtain feedback from eye care services.

Demand side barriers include low levels of awareness of PLWD on the need for DR screening and failing to take up the appointment, especially if they did not have symptoms.[43] This delay or refusal to take up screening services even when they are available has been noted in the literature on diabetes care in LMICs.[38] It points to a level of screening hesitancy (delay in acceptance or refusal of a service despite its availability), mostly associated with lack of awareness, low perceived risk of DR or perceived inconveniences of screening services or undervaluing of the services. This suggests a need for PLWD education about DR and its treatment as well as research on effective strategies for risk communication.

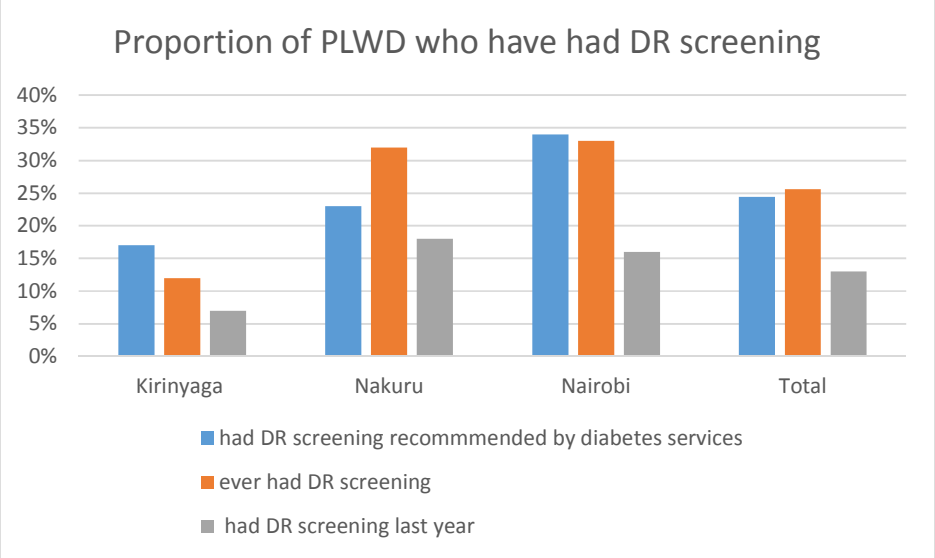

Figure 3-5: Access to DR screening by county among 270 PLWD (90 per county)

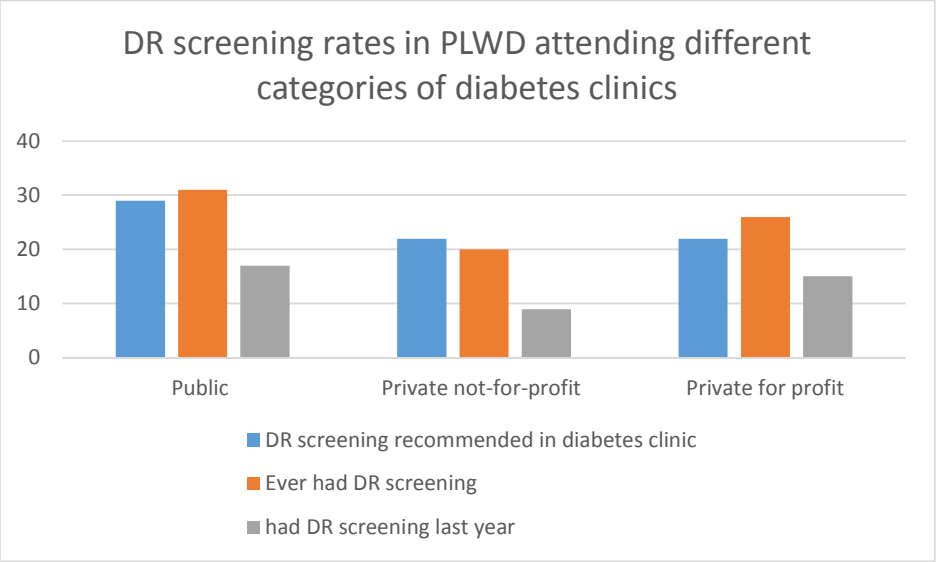

Figure 3-6: DR screening rate in different categories of diabetes clinics

Eye clinic

Strengths: There are written information brochures on DR, which are provided for PLWD and general health care providers. Opportunistic screening services and case finding for symptomatic PLWD are available at the static eye clinics and outreach eye care camps on a walk-in basis. Tertiary eye clinics have a retina clinic at least once a week. There is no waiting list for screening in any of the eye clinics. There are waiting lists for laser photocoagulation in some clinics, but the waiting time is only one week.

Weaknesses: Eye care services are underutilized by asymptomatic PLWD. This is paradoxical, since screening services provide significant benefit for early detection of DR.[44] Most of the PLWD attending diabetes services do not attend the eye clinic for screening, because of the demand side and supply-side barriers highlighted above. There are missed opportunities for screening at the eye clinics as well, mainly attributed to lack of clinical guidelines to standardize care. Common with diabetes in other SSA

countries, patients with DR present late when they have advanced DR and vision loss.[45] The eye clinics do not engage with the DSGs.

Opportunities

Service provider and key informants suggested the need to integrate diabetes and DR services to improve service coordination on the long-term. The rationale for this integration is discussed in research paper 2. Previous studies have identified a positive association between different integrated models of care and diabetes outcomes.[5] Progress with such integration will require time and capacity development across the system.

National DR Guidelines are needed to ensure services are available to PLWD, and that all actors in eye health services for PLWD speak from a common guideline. There are opportunities for peer-led education on diabetes eye health in the community and for engaging DSGs to link PLWD with eye clinics for DR screening. These interventions will be discussed in subsequent chapters of this thesis.

Health workforce

Community

Strength: Community health volunteers (CHVs) link community members with primary care facilities, for instance for testing for diabetes. Peer supporters in DSGs carry out health education and link PLWD with diabetes clinics, which is a form of task shifting. Previous studies have identified task shifting as a successful intervention in some parts of SSA, which has potential to influence diabetes care.[5, 45]

Weakness: The peer supporters and the CHVs are not trained to provide education on the component of diabetes eye health, resulting in low heath literacy on this aspect.

Diabetes clinic

Strengths: All clinics have a multidisciplinary team available, including a physician, diabetes educator, pharmacist, nurses, nutritionists, records clerks, medical officers, clinical officers and social workers. PLWD are referred to additional specialists such as surgeons based on need. Most of the team is trained locally, though some have foreign training. This is important because multidisciplinary care is a facilitator for effective diabetes care within a chronic care model.[5, 46] The extent to which the different cadres provide care as a coordinated team rather than separately is uncertain. This is an important area for research — as diabetes care by uncoordinated specialists may overwhelm both health workers and PLWD, given its effect of increasing workload.[34]

Weaknesses: The number of health workers is inadequate for the population, and the distribution is generally skewed in favour of Nairobi. Table 3-2 provides an example of the distribution of physicians and diabetes educators. Service providers identify limited training as a major hindrance to providing services, coupled with frequent transfers of trained workers. This points to the need for effective and constantly available training opportunities.[38, 45]

Table 3-2: Health workforce for diabetes services - physicians and diabetes educators

	Kirinyaga	Nakuru	Nairobi	National
Total pop (millions)	0.6	1.8	3.6	55
Physicians - N (per 100,000 pop)	3 (0.5)	33 (1.8)	120 (3.3)	501 (9.1)
Diabetes educators - N (Per 100,000 pop)	5 (0.8)	50 (2.8)	2500 (69.4)	3000 (54.5)

Eye clinic

Strengths: The eye care workforce includes ophthalmologists, ophthalmic clinical officers and ophthalmic nurses, mostly trained in two training institutions in the country. These cadres provide service delivery but also have roles as educators, administrators and researchers.

Weaknesses: There are no optometrists, patient counsellors, equipment maintenance technicians or records clerks in most of the public service eye clinics. There is only one equipment technician at the Ophthalmic Services Unit, and another at one tertiary hospital, which leads to delays in equipment repairs. The eye care workforce is insufficient in number and distribution, as in other LMICs.[47, 48] Table 3-3 shows the cadre to population ratio. The training capacity of the training institutions is insufficient to meet the needs. Although the pre-service training is perceived as high quality, the lack of opportunities for continuous professional development especially regarding eye care

for PLWD is a major hindrance to service delivery. Thus the capacity of both individuals and institutions influence the service delivery.[42]

Table 3-3: Distribution of eye care workers

	Kirinyaga	Nakuru	Nairobi	National	VISION 2020 recommendations (ratio by 2020)
Total pop (millions)	0.6	1.8	3.6	55	-
Ophthalmologists (Per 100,000)	1 (0.2)	3 (0.2)	46 (1.3)	130 (2.4)	1:250,000 (0.4:100,000)
Ophthalmic clinical officers (per 100,000)	3 (0.5)	5 (0.3)	20 (0.6)	200 (3.6)	1:100,000
Ophthalmic nurses- N (per 100,000)	0 -	3 (0.2)	21 (0.6)	180 (3.3)	1:100,000

Opportunities

Empowering peer supporters in DSGs to deliver education on eye health to PLWD may be a useful form of task shifting, given the workforce shortage. An integrated open-access training program for diabetes and eye heath workers may address the need for a training program that is flexibly available.

Health Management Information Systems (HMIS)

Community

Strengths: DSGs keep paper-based records of PLWD, recording sociodemographic details, comorbidity with hypertension and the measurements taken at every DSG meeting: blood sugar, blood pressure and weight or body mass index (BMI). PLWD keep a copy of this data (patient-held records).

Weaknesses: The data collected is not shared or used to inform services beyond the DSG. There is no system of risk factor surveillance, which is an important target for countries looking to improve their health system performance for diabetes.[49]

Diabetes clinic

Strengths: There is a gradual shift from paper-based records to electronic records, though currently both forms are used. Aggregate facility data (such as numbers attended) is transmitted to the national HMIS system.

Weaknesses: Individual PLWD do not have access to the comprehensive medical record from the diabetes clinics. There is no diabetes registry with call and recall mechanism and there is no way of tracking the movement of PLWD along the care pathway. The Chronic Care Model recommends that HMIS systems foster the formation and use of diabetes registries, to enhance access to clinical data, patient engagement and generation of evidence.[46, 50, 51] The facility and county data is not used for decision-making at the local level. Without complete electronic medical records (EMR), it is difficult to use the HMIS to track inputs and outputs such as medicines used, to avoid stock-outs.[45, 46] The data transmitted to the national HMIS is mainly workload data, and some facilities do not submit this data, which limits the use of the data.

Eye clinic

Strengths: Sociodemographic and clinical data is collected at the eye unit mainly using paper-based systems.

Weaknesses: Individual PLWD do not have patient-held records. Indicators for DR, such as number screened for DR are not reported. There is no mechanism for tracking PLWD who have been screened, referred or treated, and most clinics do not have infrastructure for capturing and storing retinal images. There is no surveillance system for DR. The data collected also has missing/incomplete information, as most eye clinics do not have a trained and dedicated records officer. Training the people entering data to also analyse it and present it can improve the performance.[52]

Opportunities:

There is a need to develop a diabetes database to provide longitudinal information on individual PLWD. The HMIS system should alert the provider to the needed tests and provide tracking. Given the mobile phone penetration of about 77% in Kenya, mhealth interventions such as patient reminders through short message service (SMS) would be useful for scheduling follow-ups or educating PLWD.[53]

Health Financing

Community:

Strengths: In some counties, public-private partnerships (PPPs), such as the 'base of the pyramid program' by Novo Nordisk have helped to stabilize the cost of insulin at about $5 per vial of Mixtard insulin, compared to $18 in other counties. This is because they supply the insulin at subsidized cost to some facilities, introducing competition among retail suppliers, and hence prices come down. [27]

Weaknesses: Less than 20% of the population has any form of insurance coverage, which implies that a correspondingly small proportion of PLWD have insurance.[54] DSGs have not been adequately sensitized on the need for PLWD to register with the national hospital insurance fund (NHIF), the largest provider of health insurance. Comorbidity with hypertension or depression increases the financial burden on PLWD.[55] In addition, the transport burden is high for patients in rural areas, which may impede access to services.[27, 56] The other weakness is that peer supporters and CHVs work on a volunteer-basis, but the community is responsible for keeping them incentivized. This often involves a form of payment in kind, but this is largely invisible and unaccounted for in the health financing indicators. The sustainability of PPPs, as mentioned above, is in doubt, since they are not integrated within national plans.[27]

Diabetes clinic:

Strengths: NHIF covers some of the costs for laboratory tests and treatments for diabetes, within the chronic disease package of care.[57] Some commodities and services are available at subsidized cost, due to PPPs mentioned earlier.[27] There is a centralized payment system at each health facility for financial accountability.

Weaknesses: Most of the services have to be paid for at the point of care (out of pocket payment) as only a small proportion of PLWD have NHIF, mainly those in formal employment. This means that the unemployed PLWD are more likely to suffer financial barriers to access, leading to inequity. In addition, some of the services are not available at the diabetes clinics, and have to be sourced from external pharmacies and laboratories, at a high cost.[57] Further, only 40% of health facilities in the country are covered by NHIF, hence PLWD attending facilities outside this network have to pay for services out of pocket.[54]

Eye clinic

Strengths: The cost of screening is included in the consultation fee at the eye clinic, hence there is no extra cost to the patient requiring DR screening. NHIF has recently expanded coverage to include treatments for DR: laser, anti-VEGF and vitrectomy. This incremental coverage has resulted from lobbying by interest groups especially the Ophthalmologic Society of Kenya, as has been the experience of other countries.[58] Some of the outreach screening programs provide transport for PLWD so that they can obtain treatment at static eye clinics. This innovation to reduce the transport burden is in keeping with the delivery support element of CCM.[34]

Weaknesses: A consultation fee is paid out-of-pocket for each clinic visit, with PLWD attending both diabetes and eye clinics having to pay a double fee. Most PLWD present to the eye clinic late, when DR is advanced, yet the cost of treatment would be lower if DR is detected and treated early.[7, 59] Without NHIF cover, PLWD have to pay for treatment out of pocket. The financial burden for DR treatments is considerable, reflecting that universal health coverage has not yet been achieved.[57, 60] On the other hand the sustainability of financing UHC through NHIF is doubtful, given that the current premium rates are quite low (averaging 2.4% of gross pay for formal sector workers) and yet the benefit package is very generous.[61] The country is currently facing these sustainability concerns.

Opportunities

CHVs and DSGs can be instrumental in ensuring that their members are registered with NHIF, if they are adequately sensitized.

Medicines and health technologies

Community

Strengths: DSGs have glucometers and blood pressure machines and sometimes they have some drugs at subsidized cost. There are some mobile phone applications for health promotion, such as *Afya Pap*, but their use among PLWD has been limited to a pilot project in Nairobi, perhaps because the highest coverage with mobile phones is in urban areas.[53, 62]

Weaknesses: Technology to aid lifestyle modification such as wearable devices are not commonly available. Most PLWD do not have devices for home glucose monitoring. DSGs have the devices for group use but often run out of strips for testing blood glucose. PLWD have difficulty obtaining insulin syringes, as they sometimes have to buy them in private pharmacies. This is of concern because it limits glycaemic monitoring and increases the risk of complications.

Diabetes clinic

Strengths: Access to diabetes medicines is facilitated by two main factors. Firstly, the Essential Drugs List for county hospitals includes key medications, such as insulin and metformin. Secondly, some clinics have insulin at subsidized cost, through arrangements with stakeholders in the supply chain management, such as Novo Nordisk, the International Diabetes Federation, the Changing Diabetes in Children program, Medicins Sans Frontieres, and distributors of drugs.

Weaknesses: Clinics experience shortages of drugs at different points in the year, mostly due to procurement delays. As the cost of diabetes medicines is unaffordable to many PLWD, non-adherence is likely to result.[45, 57] Clinics sometimes run out of glucose test strips, and most of them do not offer HbA1c testing.

Eye clinic

Strengths: Treatment services (laser photocoagulation) for DR are available in at least one facility in most counties.

Weaknesses: Eye clinics sometimes run out of supply of mydriatic drugs. Anti-VEGF is not routinely available in government clinics, hence PLWD are asked to buy it and bring it for injection. This negatively affects compliance with anti-VEGF treatment. The multi-dose vial of anti-VEGF is expensive, and can lead to drug wastage.

Opportunities: The use of artificial intelligence and telemedicine in DR screening has been tested in research settings, but is not yet applied in routine use.[63] There is potential for automated AI-based grading systems to improve efficiency in DR screening.

Governance

Stewardship for diabetes care is under the auspices of the Division of Non-Communicable Diseases (NCDS) of the Ministry of Health. There is a comprehensive national strategy for the control of NCDs 2015-2020 which is actively used.[64]

Community

Strengths: The Kenya Defeat Diabetes Association, a civil society organization responsible for the DSGs, is strongly engaged in advocacy with the government and other stakeholders at national level, such as the Diabetes Management and Information Centre, Diabetes Kenya Association, World Diabetes Federation, and International Diabetes Federation. These stakeholders, coordinated by the Division of NCDs, mobilize communities and schools for events such as annual diabetes walks, community screening and health promotion activities especially around annual advocacy weeks. At facility level, local health committees provide a forum for community participation in governance.

The national strategy for control of NCDs includes a strategic objective on implementing legislation regarding the content of processed foods and drinks (refined sugar, salt, saturated and trans fats), as well as the labelling and marketing of these products.[64] Another strategic objective in the strategy relates to implementing economic incentives for encouraging consumption of healthy foods, such as taxes and subsidies.[64]

Weaknesses: The component of eye health is often missing in the health promotion program. Action on the social and economic determinants of health, such as engagement with the agriculture, food industry and urban planning sectors has been challenging, as has been enacting legislation on processed food products, because these require lengthy political processes.

Diabetes clinic

Strengths: There is a national diabetes strategy, albeit it requires updating.[36] The Ministry of Health has a focal person for NCDs in each county who provides leadership. The NCD division is in the process of establishing some diabetes clinics as centres of excellence for diabetes care in children. Diabetes services actively engage DSGs, non-governmental organizations (NGOs), and pharmaceuticals as stakeholders.

Weaknesses: The NCD and diabetes strategies do not include eye health. The strategies are not available in some of the diabetes clinics outside Nairobi, which hinders their use, though they have potential to improve diabetes care.[46, 65] The diabetes strategy does not provide guidance on managing prediabetes, and most of the people with prediabetes do not attend diabetes clinics. Although there is a focal NCD lead, coordination between public, private-for-profit and private-not-for-profit actors is challenging as they have different lines of accountability. In addition, the role of the focal NCD lead in fostering implementation of the chronic care model is not explicit.

Eye clinic

Strengths: The national level has strong links with professional associations, academia, NGOs and other sectors besides the Ministry of Health. Decentralisation of governance to county level has increased efficiency, for instance in procurement of supplies. Each county has a focal eye care person who provides leadership. Some non-governmental organizations such as the Fred Hollows Foundation and Operation Eyesight Universal support DR services in some counties.

Weaknesses: There is no long-term strategy for control of DR, and no national guidelines for DR. There have been several attempts to develop the guidelines in the past, but the process was not completed. A recent systematic review identified clinical guidelines as one of the interventions that have improved diabetes care in SSA.[38, 45] This might be because guidelines articulate a consistent set of priorities and attract stakeholder support.[42]

Opportunities

The upcoming updating of the diabetes strategy is an important window of opportunity to include eye health in the strategy and to implement CCM in diabetes care. Leveraging on the stakeholder support can facilitate the development of clinical guidelines for DR.

Infrastructure

Community

Strengths: DSGs can use public facilities, such as bus parks, churches or schools for outreach screening camps.

Weaknesses: There is no infrastructure and equipment for screening for DR at the community level.

Diabetes clinic

Strengths: In a few facilities, diabetes clinics and eye care clinics are located within the same building. This proximity is advantageous for linking PLWD to the two services. One diabetes clinic in Nairobi has a retinal camera for DR screening, facilitating screening at the point of diabetes care.[14]

Weaknesses: Often the clinics are in separate buildings and do not have sufficient space hence they are over-crowded. Equipment inventories are not regularly done. Most clinics reported that the equipment was insufficient, reflecting suboptimal infrastructure for diabetes.[40, 41]

Eye clinic

Strengths: Some of the eye clinics have renovated buildings and vehicles provided by partners, especially NGOs.

Weaknesses: The equipment for screening is insufficient, and most eye clinics do not have retinal cameras. There are not enough treatment facilities including space and equipment for laser, as well as theatre for vitrectomy or administration of anti-VEGF. Some of the equipment such as lasers and vitrectomy machines are broken down and not functional. Spare parts are often unavailable locally.

Research

Community

Strengths: Previous population-based research includes epidemiologic studies such as the STEPS survey[66] and the Nakuru cohort study.[63, 67-70] Some studies have investigated access to medicines.[27, 71] Kenya has adopted risk factor surveillance based on the STEPwise approach.

Weaknesses: Public engagement and dissemination of research to rural communities is insufficient.

Diabetes clinic

Strengths: There are strong national research partnerships, such as the Kenya Diabetes Research Group. The types of research that have been done include operational research and epidemiological studies. A recent study has examined the cost of diabetes care to the patient.[57]

Weaknesses: Most of the research is quantitative, and there is a need for more qualitative research, for example on patient-related outcomes such as quality of life and treatment burden. Appraising the evidence is not systematically performed, and it is unclear how much this research has been used to inform policy and practice.

Eye clinic

Strengths: There is a national DR working group coordinated by the Ministry of Health, which is interested in collating all the research on DR and conducting collaborative research. There is a strong link between the national level and research institutions, both local and international. Some studies have investigated the effectiveness of a DR screening program,[72]the use of telemedicine,[73] and the use of AI in DR screening.[63] The most recent Kenya Demographic and Health Survey (KDHS) has included data on visual impairment.[74]

Weaknesses: The research conducted does not include patient-related outcomes. There is a shortage of skills in implementation research.

Opportunities

The research endeavours should contribute to developing local research capacity as robust research can provide evidence to improve DR services.

There is a need for research that focuses on the experience of patients along the care pathway and patient-related outcomes, such as financial protection.

3.7 Synthesis of gaps and strengths

Although there are some differences between the counties, the findings revealed gaps in health systems in all the counties, suggesting the need for health system strengthening (HSS) in the country. Both supply-side and demand-side barriers lead to gaps in access and continuity of care. There is low access to both HbA1c and DR screening. As DR is asymptomatic, without screening there are long delays before detection and treatment, with worse health and cost outcomes.

Three key strengths of the health system should be harnessed. First, there are community resources such as DSGs whose task profile can be expanded to include educating PLWD on eye health and linking them to screening services. Second, there is high stakeholder support for strengthening services. Third, key informants and service providers recognize the need to foster collaboration between diabetes and DR services, and they could provide support for collaboration and integration.

3.8 Priority-setting – health system strengthening

The results of the health system assessment were shared with the national DR working group. Taking consideration of the main gaps, and the strengths, as well as the resources available, the DR working group prioritized two HSS actions:

(a) the development of national clinical guidelines for diabetic retinopathy

(b) the development of a flexible training program on eye health for DR

Guidelines were considered a priority because they would influence multiple interacting factors to improve services, such as mobilise resources for DR, strengthen a referral system and provide a quality assurance mechanism for DR services. Guidelines would

also have long-term effects. Training was considered important because health workers identified it as a need. These HSS activities are discussed in chapter 5 and 6 of this thesis.

3.9 Priority-setting- Intervention to improve access to DR screening

DR screening is the entry point to DR services, and since attendance at screening is low, increasing the attendance at screening is a priority. The HSS action points above target the supply-side barriers to screening. It is unclear whether a peer supporter-led intervention within DSGs can help to address the demand side barriers and increase demand for screening. A clinical trial to test the effectiveness of this intervention was designed with input from stakeholders in diabetes and DR care. As Kirinyaga county has the lowest uptake of DR screening, and the most active DSGs among the three counties, it was selected for this intervention. Additional information on DSGs is provided below, while Chapter 7, 8 and 9 of this thesis describe this clinical trial.

Diabetes Support Groups

The Kenya Defeat Diabetes Association (KDDA) is a not-for-profit civil society organization that brings together the DSGs in the country. It has a national and county level governance structure and works in partnership with the Ministry of Health, particularly the Division of Non-Communicable Diseases. KDDA trains peer educators, mobilizes resources for DSGs (glucometers, glucose test strips, blood pressure machines, weighing scales, stationery), and organizes community diabetes screening camps. These activities are funded by partners such as Non-Governmental Organizations that work with the county health services. KDDA also engages in advocacy for improved access and quality of services at the facility, county and national level.

PLWD become aware of DSGs through community events such as health talks and announcements provided at various meetings – at village *barazas* (public meetings), places of worship, women's groups, door to door visits by community health volunteers and community diabetes screening camps. Peer educators also give health talks at the diabetes and nutrition clinics in health facilities, and recruit PLWD to join DSGs.

A DSG is established when at least 15-20 PLWD in a particular location have been recruited and two DSG leaders (1 male, 1 female) have been selected from among them. The target size of DSGs is 50-100 PLWD. Formal membership status is obtained by payment of a one-off requisite fee (Ksh 1500, $15), upon which one receives a KDDA membership card. However attendance and participation in DSG activities is open even to those who do not have formal membership status. DSGs meet once a month at a designated venue agreed on by the group e.g. at a church, school, market or health facility. The activities at the meeting include health talks by peer educators, measurement of weight, blood pressure and blood glucose. PLWD pay Ksh 100 ($1) at each meeting to support the purchase of resources such as glucose test strips.

The role of the DSG leader is administrative – organizing the DSG meetings, stewardship of DSG resources and linking the DSG with county and national leadership of KDDA. The DSG leaders are volunteers and do not receive formal training for that role. Peer educators on the other hand are trained by KDDA to deliver health talks on self-management, and to provide group/ individualized peer support; they also are volunteers. In some DSGs, one individual has the dual role of leader and peer educator. Being volunteers, they do not receive formal remuneration for their work, and the DSG activities are not expected to interfere with their usual economic activities.

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Chapter Four: Additional findings from health system assessment

4.0 Overview

This chapter includes two results papers. Research paper 1 is on the predictors of uptake of DR screening (DRS). This paper has been included since it describes the barriers and enablers for screening in the specific context of PLWD in Kenya. These results provide the basis of thinking for developing the interventions described throughout the rest of the thesis.

Research paper 2 is on the rationale for integration of diabetes and DR services, as proposed by key informants and service providers who participated in the health system assessment. The health system context influences the nature, extent and success of integration. This paper has been included because it provides evidence on how integration might be implemented and includes a contextual framework that may be generalizable to similar settings.

4.1 Research paper 1

Preamble

The barriers and enablers that influence the access and uptake of screening for DR among people living with diabetes (PLWD) are poorly understood, and there is little evidence on how these factors vary by context. Understanding the predictors for attendance to DRS is essential to refine strategies to improve access to DRS. There are no known studies which have looked at the specific predictors to attendance at DRS in Kenya, and this study addresses this gap. The evidence from this study has been used to inform the development of interventions to increase attendance at DRS, which are discussed in subsequent chapters. This paper was published in the journal BMC Tropical Medicine and Health in December 2017 after peer review.

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4.2 Research paper 2

Preamble

The lack of linkage between diabetes services and eye care services for PLWD is a challenge for the health system in Kenya. PLWD in diabetes clinics receive diabetes care, largely without an eye heath component e.g. eye health education, screening or referral for treatment. PLWD attending eye clinics for DR care may receive services to address this ocular complication but without adequate attention to other aspects of diabetes management. This limits the continuity of care for PLWD, who also have difficulty navigating the health system.

To strengthen health systems and to achieve continuity of high quality care, some integration between diabetes and DR services is important. Experts recommend tailoring integrated care

interventions to the local context, which highlights the potential value of this paper's focus on understanding integration of care within Kenya's health system.

The evidence presented in this paper is part of the results of the health system assessment for diabetes and diabetic retinopathy. Integration of DR into diabetes services emerged as a key theme during interviews with key informants and service providers, as they described the factors related to lack of integration, ways to remedy the lack of integration, and the priorities for integration.

The paper has been submitted to BMC Health Services Research.

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Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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Student Signature: Nyawira [redacted] **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] **Date:** SEPT 17, 2019

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Tropical Medicine and Health

RESEARCH Open Access

Predictors of uptake of eye examination in people living with diabetes mellitus in three counties of Kenya

Nyawira Mwangi[1,2*], David Macleod[1], Stephen Gichuhi[3], Lawrence Muthami[4], Consuela Moorman[5], Covadonga Bascaran[1] and Allen Foster[1]

Abstract

Background: Diabetic retinopathy (DR) is a significant public health concern that is potentially blinding. Clinical practice guidelines recommend annual eye examination of patients with diabetes for early detection of DR. Our aim was to identify the demand-side factors that influence uptake of eye examination among patients already utilizing diabetes services in three counties of Kenya.

Methods: We designed a clinic based cross-sectional study and used three-stage sampling to select three counties, nine diabetes clinics in these counties and 270 patients with diabetes attending these clinics. We interviewed the participants using a structured questionnaire. The two outcomes of interest were 'eye examination in the last 12 months' and 'eye examination ever'. The exposure variables were the characteristics of participants living with diabetes.

Results: The participants had a mean age of 53.3 years (SD 14.1) and an average interval of 4 months between visits to the diabetes clinic. Only 25.6% of participants had ever had an eye examination in their lifetime, while 13.3% had it in the preceding year. The independent predictors of uptake were referral by diabetes services, patient knowledge of diabetes eye complications, comorbid hypertension and urban or semi-urban residence.

Conclusions: We conclude that access to retinal examination for DR is low in all three counties. An intervention that increases the knowledge of patients with diabetes about eye complications and promotes referral of patients with diabetes for eye examination may improve access to annual eye examination for DR.

Keywords: Diabetes, Diabetic retinopathy, Eye examination, Access, Screening, Kenya, Sub-Saharan Africa

Background

Diabetes mellitus (DM) causes visual impairment and blindness through diabetic eye disease, which includes cataract and diabetic retinopathy. Diabetic retinopathy (DR) is a progressive microvascular complication of diabetes. Approximately one third (34.6%) of people living with diabetes (PLWD) have DR and 10% have sight-threatening DR (STDR) [1]. The increasing magnitude of DM and DR is a significant public health challenge [2, 3]. There is strong evidence for the cost-effectiveness of screening for DR in prevention of blindness [4, 5].

There are several reasons why access to eye examination for PLWD in Kenya is important. First, the prevalence and magnitude of DM and DR is increasing. An estimated 14.2 million people in the African region had diabetes in 2015 [6]. This number is expected to increase by 140% between 2015 and 2040 [6]. The greatest increase is predicted to be in countries transitioning from low to middle income, like Kenya. The prevalence of diabetes in the Kenyan population aged 20–79 years was 2.2% in 2015 [7]. This translates into 484,000 adults with diabetes, of whom approximately one third have DR (150,000–170,000) and 10% (40,000–50,000) have STDR. Second, both DR and STDR are asymptomatic and STDR can progress to blindness if not treated early [8–10]. An eye examination of the retina through a dilated pupil, usually annual, can identify those with DR who

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are at risk of developing STDR and needing treatment [10, 11]. Third, treatment of patients who have STDR reduces the risk of vision loss [12–14].

The determinants of access to retinal examination are complex and include both supply and demand factors [9, 15]. Understanding the demand-side factors facilitates the development of targeted demand-side interventions that reduce the barriers and support the enablers to increase the uptake of eye examination. Several studies have examined the use of eye care among patients with diabetes in America, Asia, Europe, and Oceania [16–21]. Many studies in Africa have focused on access to eye care for cataract but not DR [22–30]. In this paper, we report on factors influencing the uptake of eye examination for DR in PLWD. We define this test as a retinal examination through a dilated pupil conducted by an eye care worker using either an ophthalmoscope or retinal camera.

Research in context panel

Evidence before this study

We searched Ovid MEDLINE, Cochrane Library, and EMBASE (2000–2016) using the terms 'diabetes' and 'diabetic retinopathy' in combination with the following terms: 'access', 'screening' and 'eye examination'. We also searched cited references in articles identified by this search strategy. The evidence is that uptake of annual retinal examination is low in resource-poor settings (Table 1). However, the predictors of uptake of retinal examination have not been documented.

Added value of this study

We found the uptake of retinal examination among patients utilising diabetes services in three counties of Kenya to be even lower than documented in other studies. Predictors of uptake of retinal examination were (a) referral from diabetes services, (b) knowledge of diabetes eye complications and (c) comorbid hypertension. About half of the patients had the perception that a retinal examination was not necessary in the absence of ocular symptoms. Using this evidence, we present a conceptual model on how to improve uptake of retinal examination.

Implications of all the available evidence

An intervention to reverse low uptake of retinal examination should include both health education and referral pathway interventions. From our findings, the education component should prioritize two aspects of knowledge: (1) information on diabetes eye complications and (2) information on eye examinations (importance and frequency). The referral intervention should address barriers to uptake of examination. These interventions are potentially cost-effective and may also strengthen integration of diabetic retinopathy screening into diabetes services.

This study was conducted when Kenya has just completed a STEPwise survey on risk factors for noncommunicable diseases and determined the prevalence of DM. It could form the baseline from which trends in uptake of retinal examination can be compared as prevalence of DM increases in the next decade.

Methods

Study setting

This study was part of a cross-sectional health system assessment for diabetes and diabetic retinopathy. A three-stage sampling process was used. Three counties were purposively selected to represent different environments and populations within the diabetes belt in Kenya: Kirinyaga (predominantly rural), Nakuru (semi-urban) and Nairobi (urban). Three diabetes outpatient clinics were selected in each county. A list of public, private and faith-based clinics in each country was obtained, and 1 clinic was selected in each category through random sampling. In each of these nine diabetes clinics, 30 patients were selected by random sampling from the PLWD attending the clinic on the day of interview. The list of male and female patients was used as the

Table 1 Summary of other studies in developing countries

Study	Current study	Mumba et al. [32]	Onakpoya et al. [36]	Njambi, L [33]	Adriono et al. [19]	Wang et al. [20]	Shivashankar et al. [34]	GV Murthy et al. [35]
Country	Kenya	Tanzania	Nigeria	Kenya	Indoneshia	China	Delhi, India	11 cities, India
Year	2016	2009	2009	2012	2011	2010	2016	20
Target PLWD population	Adults in nine diabetes clinics	Adults in one diabetes clinic in a tertiary hospital	Adults in one diabetes clinic	Adults attending a diabetes clinic in one hospital	Adults in three clinics	Adults attending health facilities	Adults attending 23 primary care clinic	Adults attending diabetes hospitals/clinics
Sample size	270	316	84	253	196	824	406	285
Screening rate (last 12 months)	13.3%	28%	Not reported	Not reported	15.3%	33.3%	7.4%	Not reported
Screening rate (ever)	25.6%	59.1%	28.9%	29%	Not reported	56.8%	Not reported	67.7%

sampling frame, with a random starting point and a regular sampling interval of between three and five depending on the volume of the patients attending each clinic. This procedure made it possible to recruit an equal number of men and women. A minimum sample size of 73 per county (thereafter increased to 90) was determined based on the estimate that 5% of the population of PLWD attending diabetes clinics have an annual dilated eye examination, with the desirable degree of accuracy set at 0.05.

The study followed the tenets of the World Medical Association's Declaration of Helsinki. The London School of Hygiene and Tropical Medicine and African Medical Research Foundation granted ethical approval. All participants gave written informed consent.

Participants

Eligible persons included those 18 years of age or older, known to have diabetes, resident in the county, receiving services at participating outpatient diabetes clinics, and willing to participate in the study. Non-residents in the county and acutely ill patients were excluded.

The primary investigator and research assistants interviewed the participants in English or Kiswahili using a pretested structured questionnaire. Prior to data collection, the questionnaire was reviewed by local diabetologists, ophthalmologists and statisticians. A pilot test with diabetes patients was conducted in two different diabetes clinics within the study area (which were not part of the study sample).

Participation was voluntary and participants did not receive any financial incentives. The questionnaire had four broad categories of questions for PLWD: (a) sociodemographic characteristics, (b) experience with diabetes services, (c) knowledge of complications of diabetes and (d) experience with examination for complications of diabetes (including DR). All subjects reporting previous eye examinations were questioned as to whether the eye care worker instilled eye drops to dilate the pupils before the eye examination. This differentiated a regular eye examination and a dilated eye examination.

Statistical analysis

STATA version 14 was used for data analysis [31]. The study had two outcomes of interest: 'eye examination in the last 12 months' and 'eye examination ever'. Both were dichotomous 'yes' and 'no' variables. The exposure variables were characteristics of participants in relation to living with diabetes.

Descriptive statistics were shown as counts and percentages for categorical variables, and means and standard deviations for continuous variables. For each of the two outcomes of interest, tests of crude association were performed using chi-square tests for categorical exposure variables and t tests for continuous variables. Univariate logistic regression was used to identify exposure variables that were predictors of uptake of examination in the last year, and in analysing the ever had an eye exam outcome, all logistic regressions were adjusted for age. Multivariable analysis was performed using forward stepwise selection where exposure variables with the lowest p value were sequentially added to the regression model, using a cutoff for inclusion in the model of $p < 0.05$.

Role of funding source

The funders did not participate in study design, data collection, analysis, writing of the paper or submission for publication.

Results

Outcome variables: uptake of dilated eye examination

Ninety participants were interviewed in each county ($n = 270$). None of the participants declined to participate, and data for all variables was collected for all participants. Only 25.6% ($n = 69$) had ever had fundoscopy, while only 13.3% ($n = 36$) had been examined in the preceding year. The uptake of eye examination in other resource-poor settings is shown in Table 1.

Exposure variables: participant characteristics

The mean age of participants was 52.3 years (SD 14.1, range 25–88 years). Approximately 47% were male, 23.7% had a family history of diabetes and 37.4% had comorbid hypertension. The mean duration of diabetes was 7.3 years (SD 5.5), and participants attend the diabetes clinic every 4 months (SD 1.5) on average. The main reason for that frequency is the physician's recommendation. The other variables are shown on the first column of Table 2.

Determinants of eye examination

Table 2 also shows the patient-level determinants for fundoscopy. Only 24.4% had been referred from the diabetes clinic for a retinal examination, and 13.3% had taken this examination (fundoscopy) *in the last 12 months*. Variables that had the strongest evidence of an association with having had the exam in the last 12 months were (a) referral for an eye examination ($p < 0.001$), (b) knowledge of diabetes eye complications ($p = 0.002$), (c) comorbid hypertension ($p = 0.02$) and (d) county of residence ($p = 0.07$) (Table 3). Participants referred for an eye exam had almost eight times the odds of having attended an eye exam in the last 12 months compared to those who had not been referred (OR 7.9, 95% CI 3.7–16.4, $p < 0.001$). Participants who had a knowledge of diabetes eye complications had four times the odds (OR 3.9, CI 1.6–9.1) of attending as those who had no knowledge of eye complications. Hypertensive

Table 2 Patient characteristics and association with eye examination

Variable	Summary of participants characteristics	Retinal exam last 12 months			Retinal exam ever		
	N (%) Mean (SD)	Had eye exam	No eye exam	*p* value	Had eye exam	No eye exam	*p* value
Number (%) in each category	270	36 (13.3%)	234 (86.3%)		69 (25.6)	201 (74.4)	
Number (%) by county				0.07			0.002
Kirinyaga	90	6 (6.7%)	84 (93.3%)		11 (12.2)	79 (87.8)	
Nairobi	89	14 (15.7%)	75 (84.3%)		29 (32.6)	60 (67.4)	
Nakuru	91	16(17.6%)	75 (82.4%)		29 (31.9)	62 (68.1)	
Age (mean years, SD)	53.3 (14.1)	57.1 (11.7)	52.7 (14.4)	0.08	60.5 (13.8)	50.8 (13.4)	< 0.0001
Sex (no. %)				0.7			0.5
Men	127 (47%)	18 (14.2)	109 (85.8)		35 (27.6)	92 (72.4)	
Women	144 (53%)	18 (12.5)	126 (87.5)				
Literacy				0.3			0.05
Primary or below	88 (32.8%)	13 (14.8)	75 (85.2)		30 (34.1)	58 (65.9)	
Secondary	111 (41.4%)	11 (9.9)	100 (90.1)		21 (18.9)	90 (81.1)	
Post-secondary	69 (25.8%)	12 (17.4	57 (82.6)		18 (26.1)	51 (73.9)	
Occupation				0.4			0.014
Unemployed	70 (25.9%)	6 (3.6)	64 (91.4)		19 (27.1)	51 (72.9)	
Low skilled	70 (25.9%)	9 (12.9)	61 (87.1)		14 (20)	56 (80)	
Professional	90 (33.3%)	13 (14.4)	77 (85.6)		18 (20)	72 (80)	
Retired	40 (33.3%)	8 (20)	32 (80)		18 (45)	22 (55)	
Duration of diabetes (mean years, SD)	7.3 (5.5)	8.9 (4.5)	7.1 (5.6)	0.06	9.4 (5.5)	6.6 (5.3)	0.0002
Interval of diabetes clinic visits (months)	4.0 (1.5)	4.3 (1.3)	4.0 (1.5)	0.4	4.3 (1.4)	3.9 (1.5)	0.08
Referred for eye examination				< 0.001			< 0.001
Yes	66 (24.4%)	23 (34.9)	43 (65)		47 (68.1)	19 (28.8)	
No	204 (75.6%)	13 (6.4)	191 (93.6)		22 (10.7))	182 (89.2)	
Perceived level of glucose control				0.02			0.4
Very good	10 (3.7%)	0	10 (100)		2 (20)	8 (80)	
Well	73 (27%)	17 (23.3)	56 (76.7)		23 (31.5)	50 (68.5)	
Adequate	107 (39.6%)	9 (8.4)	98 (91.6)		24 (22.4)	83 (77.6)	
Poor	68 (25.2%)	10 (14.7)	58 (85.3)		19 (27.9)	49 (72.1)	
Very poor	12 (4.4%)	0	12 (100)		1 (8.3)	11 (91.7)	
Diabetes in family member				0.8			0.6
Yes	64 (23.7%)	8 (12.5)	56 (87.5)		18 (28.1)	46 (71.9)	
No	206 (76.3%)	28 (13.6)	178 (86.4)				
Information on diabetes given at health facility				0.3			0.8
Yes	205 (75.9%)	30 (14.6)	175 (85.4)		53 (25.9)	152 (74.2)	
No	65 (24.1%)	6 (9.2)	59 (90.8)		16 (24.6)	49 (75.4)	
Knowledge of diabetes complications				0.4			0.9
Yes	103 (38.1%)	16 (15.5)	87 (84.5)		26 (25.2)	77 (74.8)	
No	167 (61.9%)	20 (12)	146 (88)		43 (25.8)	124 (74.3)	
Knowledge of diabetes eye complications				0.001			0.001
Yes	150 (55.6%)	29 (19.3)	121 (80.7)		50 (33.3)	100 (66.7)	
No	120 (44.4%)	7 (5.8)	113 (94.2)		19 (15.8)	101 (84.2)	

Table 2 Patient characteristics and association with eye examination *(Continued)*

Variable	Summary of participants characteristics	Retinal exam last 12 months			Retinal exam ever		
	N (%) Mean (SD)	Had eye exam	No eye exam	*p* value	Had eye exam	No eye exam	*p* value
Comorbid hypertension				0.02			0.04
Yes	101 (37.4%)	20 (19.8)	81 (80.2)		33 (32.7)	68 (67.3)	
No	169 (62.6%)	16 (9.5)	153 (90.5)		36 (21.3)	133 (78.7)	
Opinion on need for an eye examination				$P < 0.001$			$P < 0.001$
No need	51 (18.9%)	1 (2.0)	50 (98)		6 (11.8)	45 (88.2)	
Only for ocular symptoms	115 (42.6%)	15 (13)	100 (87)		27 (23.5)	88 (76.5)	
Acceptable	80 (29.6%)	13 (16.3)	67 (83.8)		25 (28.8)	57 (71.3)	
Already doing it	9 (3.3%)	5 (55.6)	4 (44.4)		9 (100)	0	
Other opinion	15 (5.6%)	13 (13.3)	2 (86.7)		4 (26.7)	11 (73.3)	

individuals had twice the odds of attendance, compared to those with normal blood pressure (OR 2.3, CI 1.1–4.7). The PLWD in Kirinyaga (rural) were the least likely to have had an eye examination in the last 12 months, with PLWD in Nairobi (urban) having 2.6 times the odds (CI 1.1–7.1) and PLWD in Nakuru (semi-urban) having three times the odds (CI 1.1–8.0).

The main predictors for having *ever* had fundoscopy included (a) referral for eye examination (OR 20.5, CI 10.2–40.9, $p < 0.001$), (b) knowledge of diabetes eye complications (OR 2.7, CI 1.5–4.8, $p < 0.001$), (c) county ($p = 0.02$) and (d) comorbid hypertension (OR 1.8 CI 1.0–3.1 $p = 0.02$). The PLWD in Nakuru or Nairobi had three times the odds of attendance as compared in Kirinyaga (OR 3.4, CI 1.6–7.5 and OR 3.5, CI 1.6–7.5) (Table 3).

There was strong evidence of association of having a dilated eye examination (ever) with both increasing age and duration of diabetes ($p < 0.0001$), but the effect size was quite small, with the odds increasing by 1.1 times each year (thus, 2.6 times every decade), Table 3. In multivariable analysis, (a) referral, (b) knowledge of diabetes eye complications and (c) county of residence remained independent predictors for fundoscopy. Referral and knowledge of diabetes eye complications had the strongest relationship with uptake of eye examination and thus were included in the final multivariable analysis model. Interaction between referral and knowledge of

Table 3 Predictors of eye examination last 12 months

Variable	Eye exam last 12 months		Eye exam ever	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Demographic factors				
Increasing age (every year)	1.2 (1.1–1.6)	0.08	1.1 (1.0–1.1)	< 0.001
Male gender	1.1 (0.6–2.3)	0.7	1.2 (0.7–2.1)	0.5
County of residence (compared to Kirinyaga)				
Nakuru	3.0 (1.1–8.0)	0.03	3.4 (1.6–7.5)	0.02
Nairobi	2.6 (1.1–7.1)	0.06	3.5 (1.6–7.5)	0.02
Education				
Post-secondary education	1.1 (0.5–2.8)	0.8	0.7 (0.3–1.4)	0.3
Occupation (as compared to the unemployed)				
Professional	1.8 (0.6–5.0)	0.3	0.7(0.3–1.5)	0.3
Retired	2.7 (0.9–8.3)	0.09	2.2 (1.0–5.0)	0.06
Duration of diabetes	1.1 (1.0–1.1)	0.06	1.0 (1.0–1.1)	< 0.001
Referral for eye examination	7.9 (3.7–16.4)	< 0.001	20.5 (10.2–40.9)	< 0.001
Knowledge of diabetes complications	3.9 (1.6–9.2)	0.002	2.7 (1.5–4.8)	0.001
Comorbid hypertension	2.3 (1.1–4.7)	0.02	1.8 (1.0–3.1)	0.04

diabetes eye complications was tested, and these remained significant independent predictors ($p < 0.0001$).

As referral for examination (ever) was the strongest predictor of uptake of examination, the variables associated with referral were analysed. The main exposure variables positively associated with referral (Table 4) were (a) increasing age ($p < 0.0001$), (b) longer duration of diabetes ($p = 0.0005$), (c) knowledge of diabetes eye complications ($p = 0.003$), (d) positive opinion on need for an eye examination ($p < 0.001$), (e) retirement ($p = 0.01$) and (f) residence in Nairobi or Nakuru ($p = 0.03$).

For the 109 (40.4%) who had knowledge that diabetes causes complications, the complications that were of concern were losing a leg 34%, kidney failure 31.2%, stroke 22% and blindness 9%. Although 150 (55. 6%) knew that diabetes can affect the eye, 18.9% of the participants felt that there was no need for an eye examination and 42.6% would only go for an examination if they developed ocular symptoms.

Discussion

The results indicated that both initiation and maintenance of annual fundoscopy is low. This may be due to the lack of systematic DR screening programmes in the country. Similar findings have been documented in other resource-poor settings (Table 1) [19, 20, 32–36]. The findings can be generalised to examination for DR in adult PLWD populations in Kenya since the study included any PLWD above 18 years in three geographical locations representing the rural-urban continuum within the diabetes belt. The lowest uptake was in Kirinyaga, suggesting that the macro environment in which PLWD live is a determinant of uptake [15]. Referral by the diabetic clinic for an eye examination, positive opinion on need for an eye examination and knowledge of diabetes

Table 4 Variables associated with referral for eye examination

Variable	Referred	Not referred	*p* value
Number (%) in each category	66 (24.4)	204 (75.6)	
Number (%) by county			0.03
Kirinyaga	15 (16.7)	75 (83.3)	
Nairobi	30 (33.8)	59 (66.3)	
Nakuru	21 (23.1)	70 (76.9)	
Age mean years, SD	59.8 (13.3)	51.2 (13.8)	< 0.0001
Sex *N* (%)			0.09
Male	37 (29.1)	90 (70.9)	
Female	29 (20.3)	114 (79.7)	
Occupation *N* (%)			0.01
Unemployed	17 (24.3)	53 (75.7)	
Low skilled	13 (18.6)	57 (81.4)	
Professional	18 (20)	72 (80)	
Retired	18 (45)	22 (55)	
Literacy *N* (%)			0.6
Primary or below	24 (27.3)	64 (72.7)	
Secondary education	24 (21.6)	87 (78.4)	
Post-secondary education	18 (26.1)	51 (73.9)	
Duration of diabetes years: mean, SD	9.3 (5.4)	6.6 (5.4)	0.0005
Diabetes in family member *N* (%)			
Yes	16 (25)	48 (75)	0.9
No	50 (24.3)	156 (75.7)	
Comorbid high BP *N* (%)			
Yes	31 (30.7)	70 (69.3)	0.07
No	35 (20.7)	134 (79.3)	
Knowledge of diabetes eye complications *N* (%)			0.003
Yes	47 (31.3)	133 (68.7)	
No	19 (28.8)	101 (84.2)	

eye complications are the modifiable factors that were positively associated with uptake of examination.

Sociodemographic attributes of patients were found to affect uptake of examination. The heterogeneity by county reflects geographic, social, cultural and/or economic influences. Rural populations are known to have low access to screening services [20]. This could be related (in part) to a rural-urban gap in awareness, resources or empowerment [37]. Paksin-Hall et al. [38] found income level, education level and health insurance status to be important determinants of annual dilated eye examinations, but these were not significant independent predictors in this study.

In previous studies, increasing age was a predictor for having an eye examination [39, 40]. In our study, the evidence for this association with strong for eye examination ever ($p < 0.0001$) and weak for an examination in the last year ($p = 0.08$). Although the effect size was small, the findings of an association are consistent with an increased likelihood of examination with age. Given that the risk of developing DR increases with age, older adults, more than any other age group, need to have regular eye examination, and as the population is aging, an expanding need for retinal examination in the country is predictable. Duration of diabetes is an important predictor for incidence and prevalence of DR, [40–42] so as more people live longer with diabetes, the need for an annual eye examination will increase.

Gender was not a predictor of uptake of examination, although there was very weak evidence that male gender was a predictor for referral ($p = 0.09$). A positive family history of diabetes was similarly not a predictor of uptake of examination, which suggests that barriers to access are not just at the individual level but also within households [15].

Hypertension in PLWD was a positive predictor of uptake of eye examination in this study, as also reported in another study [19]. Comorbidity is known to increase health care utilization in diabetes, [43] and hypertension is a common vascular comorbidity [11, 33, 35, 37, 40]. Uncontrolled hypertension is a risk factor for development of DR. There was weak evidence that PLWD with hypertension were more likely to be referred ($p = 0.07$) than normotensive PLWD, perhaps because the diabetes is considered more severe. This association strengthens the case for integration of eye care into non-communicable disease care.

There was very strong evidence that knowledge of any diabetes eye complication increases the uptake of examination (Table 3). Other studies have also found that knowledge is a predictor for uptake of screening [19, 20, 42]. However, in this study, only 9% listed blindness as a complication that they were concerned about. Another finding in this study is that PLWD need knowledge about the necessity and the frequency of eye examinations. Nearly half (42.6%) of the participants thought that DR screening should be symptom-led, which is a misconception that can lead to delay in getting an examination and treatment resulting in visual loss. Educational messages need to be tailored to an awareness of eye complications from diabetes and the need for diabetics to have the eyes examined once a year. This tallies with the finding that the most frequently reported suggestion for improvement given by PLWD was the need for more information/education. Thus, there exists a real opportunity for demand-driven health education.

Although there was strong evidence that knowledge of diabetes eye complications is a predictor of examination, there exists a gap between possessing this knowledge and the uptake of examination. About 56% of PLWD knew that diabetes causes eye complications, but only 25% of all PLWD had ever received an eye examination. Similarly, although approximately 25% were given a referral, only 13% had actually gone for the examination in the last year. This suggests that there are additional factors besides knowledge and referral that influence uptake.

The health belief model (HBM) is a widely used theoretical framework for understanding health behaviours within public health. Weiss et al. have previously shown that behavioural interventions can improve uptake of eye examination [44]. Taking the predictors found in this study into consideration, and using HBM as a theoretical framework, we conceptualise that self-efficacy is on the pathway between knowledge, referral and uptake of examination (Fig. 1). Research has shown that health behaviours such as taking an eye examination are associated with self-efficacy. In turn, self-efficacy can be increased in four ways: performance accomplishment, vicarious experience, verbal persuasion and psychological cues [45]. We postulate that interventions that increase knowledge, referral and self-efficacy can increase uptake of eye examination. Our conceptual model captures these different aspects (Fig. 1).

Only a quarter of PLWD had received a referral for DR screening. Similarly, in other studies in China and India, less than a half had been referred [19, 20], although in one study in India, over 60% had a referral [35]. We found that the strongest predictor for having an eye examination was referral from diabetes services. Participants already attend the diabetes clinic every 4 months because of the recommendation of the diabetes services. As there is no systematic DR screening programme, a referral to the eye clinic is a crucial bridge. These three visits a year are missed opportunities for referral for eye examination. Lack of a diabetes provider's recommendation has been documented as a barrier in Germany [9] and Paraguay [42], diabetes services being gate keepers to other services required by PLWD.

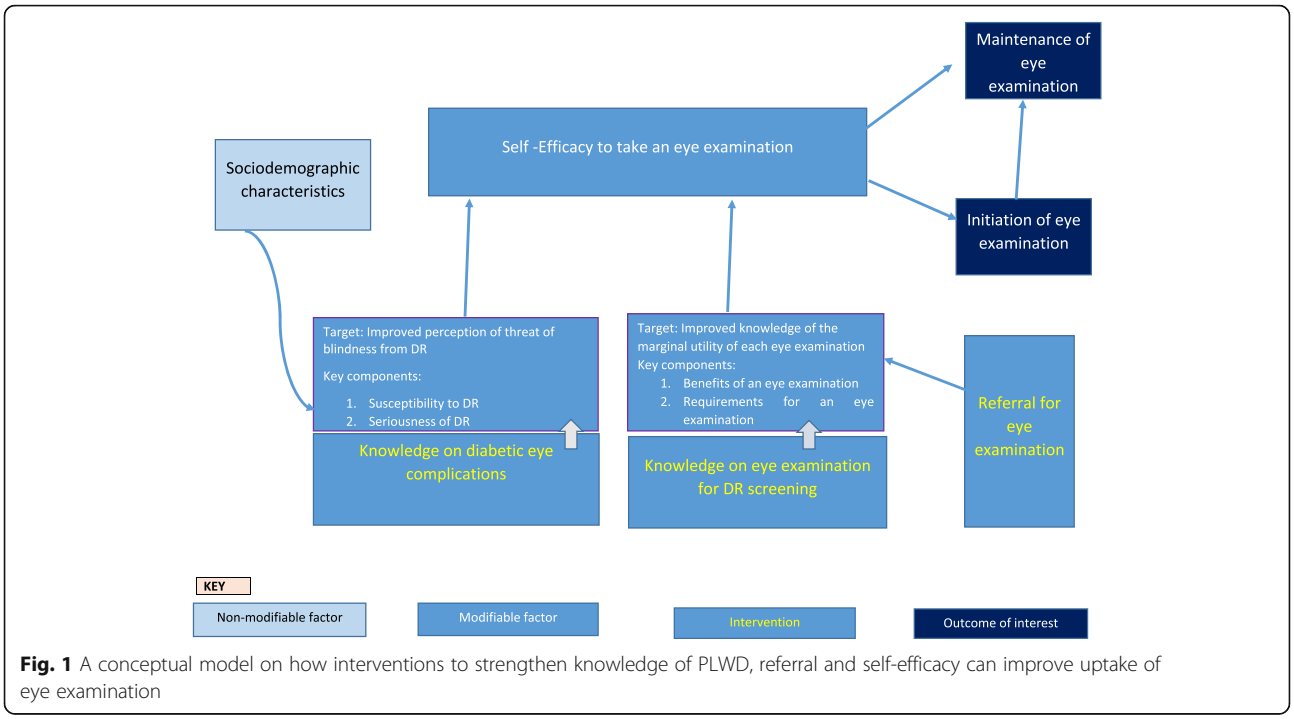

Fig. 1 A conceptual model on how interventions to strengthen knowledge of PLWD, referral and self-efficacy can improve uptake of eye examination

Written communication from the patient's ophthalmologist to the primary care provider has also been found to increase adherence to future dilated eye examination [46]. Conversely, as entry to the eye clinic in Kenya does not actually require a formal referral note from diabetes services, an intervention that empowers patients for 'self-referral' might increase uptake of the examination.

There was strong evidence that older people with diabetes, those with longer duration of diabetes and those with a knowledge of diabetes eye complications were more likely to be referred. There was evidence that PLWD in Kirinyaga were less likely to be referred than those in Nakuru or Nairobi. Interventions to strengthen the use of clinical guidelines can ensure that all PLWD get a referral for an annual eye check.

Limitations

This study has several limitations. First, as this is a cross-sectional study, a temporal relationship cannot be established between the predictor factors and the uptake of screening. In addition, the association between the variables is still subject to residual confounding by unmeasured variables such as distance from home to the eye clinic, medical conditions such as depression, disability and membership of diabetes support groups. Self-reported data was used and is prone to recall bias and social desirability bias. Under reporting of health behaviours, such as the duration since the participant had the last eye examination, may introduce information bias. This is a clinic-based study and did not include PLWD not attending diabetes services; however, we presume that they would have an even lower uptake of screening for DR.

Conclusions

There is poor compliance with recommendations for annual eye examination among PLWD who have access to diabetes services. An intervention targeted at motivating adherence is essential. Such an intervention should empower PLWD to request/demand an eye examination and strengthen knowledge, referral and self-efficacy.

The opportunity to increase uptake of eye examination is also a valuable avenue for integrating diabetes care and eye care. Programmes to increase awareness regarding the importance of eye examinations can be combined with interventions to improve blood pressure monitoring and other aspects of diabetes management.

Implications

Our study has demonstrated the low uptake of screening for DR by PLWD and described the attributes associated with uptake of eye examination. Low uptake has adverse effects at individual level and at the health system level because of the associated increased risk of blindness from DR. The low uptake highlights barriers in the link between diabetes services and eye care services. There is need to integrate screening for DR within the routine diabetes services and to implement interventions to increase uptake of screening.

Future work

As the burden of diabetes grows over the next decade, there is a need to investigate the trend in uptake of annual eye examination and to examine sustainable interventions that can maximise increase uptake for eye examination. There is also need to investigate why there is a lack of attention to DR screening among diabetes clinicians and to evaluate the effect of providing them with clinical decision-making tools such DR guidelines.

Abbreviations

CI: Confidence interval; DM: Diabetes mellitus; DR: Diabetic retinopathy; HBM: Health Belief Model; PLWD: Persons living with diabetes; SD: Standard deviation; STDR: Sight-threatening diabetic retinopathy

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Availability of data and materials

The data that support the findings of this study are available from the authors, but restrictions apply to the availability of these data, which were used under license for the current study, and so, are not publicly available. Data are however available from the authors upon reasonable request.

Authors' contributions

NM, CB and AF designed the study, which was then reviewed critically by SG, DM, CM and LM. NM and LM obtained the data and analysed it with DM. All authors were involved in the data interpretation. NM had full access to the data. NM drafted the manuscript. All authors reviewed it and approved the final version.

Ethics approval and consent to participate

The ethics review committees of the London School of Hygiene and Tropical Medicine and the African Medical Research Foundation granted ethics approval for the study. All participants gave informed consent for participation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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Additional notes on methods reported in Paper 1

The study was conducted in three counties that vary in size and demographic characteristics. Disproportionate equal allocation was used in sampling, with an equal number of facilities and participants being recruited for the study in each of the counties. Proportionate sampling was not feasible as we do not have the county-level data on prevalence of diabetes and distribution of PLWD which would be required to calculate the sample size in each county.

Additional information on Table 2* in Paper 1

Mwangi, N., Macleod, D., Gichuhi, S.* et al. *Predictors of uptake of eye examination in people living with diabetes mellitus in three counties of Kenya.* Trop Med Health ***45,* *41 (2017). https://doi.org/10.1186/s41182-017-0080-7*

Table 2: Participant characteristics and association with eye examination*

Variable	**Sample statistics**	**Retinal exam (last 12 months)**			**Retinal examination (ever)**		
		Had eye exam	No eye exam	P value	Had eye exam	No eye exam	P value
Number (%) in each category	270 (100%)	36(13.3%)	234 (86.3)		69(25.6)	201(74.4)	
Number (%) by county				0.07			0.002
Kirinyaga	90	6 (6.7)	84 (93.3)		11(12.2)	79(87.8)	
Nairobi	89	14 (15.7)	75 (84.3)		29(32.6)	60(67.4)	
Nakuru	91	16(17.6)	75 (82.4)		29(31.9)	62(68.1)	
Age (mean years, SD)	53.3 (14.1)	57.1(11.7)	52.7(14.4)	0.08	60.5(13.8)	50.8(13.4)	<0.0001
Age (median, IQR)	52(43-65)	56.5(49-65.5)	50.5(41-65)		61(51-71)	48(41-62)	
Sex (no, %)				0.7			0.5
Men	127(47%)	18(14.2)	109 (85.8)		35(27.6)	92(72.4)	

Women	144(53%)	18 (12.5)	126(87.5)		34(23.8)	109 (76.2)	
Literacy				0.3			0.05
Primary or below	88(32.85)	13(14.8)	75(85.2)		30(34.1)	58(65.9)	
Secondary	111(41.4%)	11(9.9)	100(90.1)		21(18.9)	90(81.1)	
Post-secondary	69(25.8%)	12(17.4	57(82.6)		18(26.1)	51(73.9)	
Occupation				0.4			0.014
unemployed	70(25.9%)	6(3.6)	64(91.4)		19(27.1)	51(72.9)	
Low-skilled	70(25.9%)	9(12.9)	61(87.1)		14(20)	56(80)	
Professional	90(33.3%)	13(14.4)	77(85.6)		18(20)	72(80)	
Retired	40(14.8%)	8(20)	32(80)		18(45)	22(55)	
Duration of diabetes (mean years, SD)	7.3 (5.5)	8.9 (4.5)	7.1(5.6)	0.06	9.4(5.5)	6.6(5.3)	0.0002
Duration of diabetes (median, IQR)	6(3-7)	8(5-12)	6(3-10)		9 (5-13)	5(3-9)	
Interval of diabetes clinic visits (months) – mean (SD)	4.0 (1.5)	4.3(1.3)	4.0(1.5)	0.4	4.3(1.4)	3.9(1.5)	0.08
Interval of diabetes clinic visits (months) -median and IQR	4 (3-5)	4(3.5-5)	4 (3-5)		4 (3-5)	4 (3-5)	
Referred for eye examination				<0.001			<0.001
yes	66(24.4%)	23(34.9)	43(65)		47(68.1)	19(28.8)	
no	204(75.6%)	13(6.4)	191(93.6)		22 (10.7))	182 (89.2)	
Perceived level of glucose control				0.02			0.4
Very good	10(3.7%)	0	10(100)		2(20)	8(80)	
well	73(27%)	17(23.3)	56(76.7)		23(31.5)	50(68.5)	
adequate	107(39.6%)	9 (8.4)	98(91.6)		24(22.4)	83(77.6)	
Poor	68(25.2%)	10(14.7)	58(85.3)		19(27.9)	49(72.1)	
Very poor	12(4.4%)	0	12(100)		1(8.3)	11(91.7)	

Diabetes in family member				0.8		0.6
yes	64(23.7%)	8(12.5)	56(87.5)		18(28.1)	46(71.9)
no	206(76.3%)	28(13.6)	178(86.4)		51(24.8)	155(75.2)
Information on diabetes given at health facility				0.3		0.8
Yes	205(75.9%)	30(14.6)	175(85.4)		53 (25.9)	152 (74.2)
No	65(24.1%)	6(9.2)	59(90.8)		16(24.6)	49(75.4)
Knowledge of diabetes complications				0.4		0.9
Yes	103(38.1%)	16(15.5)	87(84.5)		26(25.2)	77(74.8)
No	167(61.9%)	20(12)	146(88)		43(25.8)	124(74.3)
Knowledge of diabetes eye complications				0.001		0.001
yes	150(55.6%)	29(19.3)	121(80.7)		50(33.3)	100(66.7)
no	120(44.4%)	7(5.8)	113(94.2)		19(15.8)	101 (84.2)
Comorbid hypertension				O.02		0.04
yes	101(37.4%)	20(19.8)	81(80.2)		33(32.7)	68(67.3)
no	169(62.6%)	16(9.5)	153(90.5)		36 (21.3)	133 (78.7)
Opinion on need for an eye examination				P<0.001		P<0.001
No need	51(18.9%)	1 (2.0)	50 (98)		6(11.8)	45(88.2)
Only for ocular symptoms	115 (42.6%)	15(13)	100 (87)		27(23.5)	88(76.5)
Acceptable	89(29.6%)	13(16.3)	67(83.8)		25(28.8)	57(71.3)
Already doing it	9(3.3%)	2 (13.3)	13 (86.7)		9(100)	0
Other opinion	15(5.6%)	36(13.3)	234 (86.7)		4(26.7)	11(73.3)

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RESEARCH PAPER COVER SHEET

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	BMC Health Services Research
Please list the paper's authors in the intended authorship order:	Nyawira Mwangi, Covadonga Bascaran, Jacqueline Ramke, Lawrence Muthami, Stephen Gichuhi, David Macleoed, Consuela Moormon, Mathew Kipturgo, Allen Foster
Stage of publication	**Undergoing revision**

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. (Attach a further sheet if necessary)	I designed the study, conducted the research, analysed and interpreted the data, drafted the manuscript and have prepared revisions in consideration of the comments from the co-athors and peer reviewers

Student Signature: Nyawira **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] **Date:** Sept 17 2019.

Paper 2

Rationale for integration of services for diabetes mellitus and diabetic retinopathy in Kenya

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Abstract

Background: Good diabetes mellitus (diabetes) and diabetic retinopathy (DR) management depends on the strength of the health system, prompting us to conduct a health system assessment for diabetes and DR in Kenya. We used diabetes and DR as tracer conditions to assess the strengths and weaknesses in the health system, and potential interventions to strengthen the health system. In this paper, we report on the need and relevance of integration to strengthen diabetes and DR care.

Methods: Using a mixed methods study design, we collected data from service providers in diabetes clinics and eye clinics in three counties, from key informants and we reviewed documents.

Results: There is interest in integration of diabetes and DR services to address discontinuity of care. We report the findings describing the context of integration, why integration is a goal and how these services can be integrated. We use the results to develop a conceptual framework for implementation.

Conclusions: The principal rationale for integrated service provision is to address service gaps and to prevent complications of diabetes and DR. The stakeholder interest and the existing infrastructure can be leveraged to improve these health outcomes.

Key Words: diabetes mellitus, diabetic retinopathy, non-communicable diseases, screening, integration, health systems, service delivery, Kenya, Africa

Abbreviations

DR	Diabetic Retinopathy
DR NET	Diabetic Retinopathy Network
KI	Key Informant
NCD	Non-Communicable Disease
NGO	Non-Governmental Organization
PLWD	People Living With Diabetes
SARAM	Service Availability and Readiness Assessment Mapping
WHO	World Health Organization

Introduction

Integration of services is a strategy for improving the performance of health systems and achieving clinical outcomes. The World Health Organization's (WHO) working definition of "integrated service delivery" is: "the management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system."[1] This definition posits integration as a composite construct with continuity and quality of care being essential components. The aim is to provide services that meet the needs of the user: services that are not disjointed, that are easy to navigate and that provide a smooth link to specialist services, if required.[1, 2] Although there is consensus on the desirable outcomes of integration, and its importance for universal health coverage in every country, the rationale and the operational models remain contextual.[3, 4]

Diabetes Mellitus (hereafter referred to as 'diabetes') is associated with the development of organ damage, leading to multiple morbidity. Providing care for people living with diabetes (PLWD) thus requires balancing diabetes management with management of its chronic complications. Diabetic retinopathy (DR) is the major ocular morbidity in diabetes, and there is strong epidemiologic evidence that its prevalence is increasing.[5, 6] In common with other chronic diseases, the management of both conditions requires: promotion of healthy lifestyle, early detection, compliance to treatment, regular monitoring of treatment outcomes, and active involvement of the patient and family in the care. An integrated approach is an efficient and effective method of addressing inter-related chronic diseases.[4, 7, 8] At present, diabetes and DR care are provided in diabetes and eye clinics respectively, with minimal collaboration between them. Given that the patient with DR also requires diabetes services, and the similarities in the approach to management, it is appropriate to explore the extent to which

diabetes and DR services provided in a comprehensive or integrated manner.[9] This provides an opportunity to consider how integration would intersect with the need for specialist services.

The literature on integration of diabetes services has largely focused on integration with HIV, tuberculosis and hypertension.[8, 10-12] The paucity of literature on integration with services for diabetic retinopathy services might be based on the assumption that these services are automatically integrated, since they are intricately linked. However, the point of entry into integration is often unspecified. Further, the interventions that should be integrated, and in which ways and by whom, is not explicit even in clinical guidelines. The evidence on what diabetes practitioners and eye care practitioners think of the integration, or of their professional relationship is also sparse.[13]

Proactive prevention and early detection of DR is an important best practice that is often missing in the services for PLWD. As this population has regular contact with diabetes services, this platform is a good entry point to bring DR services to where the patient is, or to link the patient to the eye service, where the DR services are. Innovative approaches such as integration can augment access, quality and continuity of care for PLWD. In this paper, we explore the interface between diabetes services and eye care services in Kenya, as an unexploited area for integrated care for DR. We use our results to develop an operational framework for integration.

Methods

Study design and theoretical approach

A mixed methods cross-sectional health system assessment for diabetes and diabetic retinopathy was conducted in three counties of Kenya, guided by the WHO's health system building blocks framework and the tracer condition approach.[14],[15] The aim of focusing the assessment on diabetes and DR was to provide evidence relevant to services for the two conditions that may be missed in a general health system assessment. Both conditions meet the criteria for a tracer condition, Table 4-1. In line with the WHO framework, we defined a good service as one which delivers effective, safe, quality, personal and non-personal health interventions to PLWD, when and where needed, with minimum waste of resources.[16] In this paper we report on integration as a theme that emerged from interviews with key informants and service providers.

Table 4-1: Diabetes and diabetic retinopathy as tracer conditions

Criteria	**How diabetes and DR fit the criteria**
Disease has a known epidemiology	The epidemiology of both conditions globally, in SSA and in Kenya has been described
Disease is well defined and easy to diagnose	The definition and criteria for diagnosis of each condition is well-established
Its prevalence in the population is large enough to enable adequate data to be collected	Both population-based and clinic-based surveys have shown that the prevalence is sufficient to enable collection of data that can be used for planning services
Its natural history is known, and it varies with the utilization and effectiveness of health care	The natural history of diabetes and DR including the predictors of the development of complications is known
It requires specific treatment, in the absence of which functional impairment results	Hypoglycaemic drugs and lifestyle measures are required for glycaemic control, and the treatments for DR have been described, without which visual impairment results
Available and well-defined techniques of medical management exist for at least one of the	Prevention, diagnosis and treatment apply to both diabetes and DR. Rehabilitation is provided for those who develop severe visual impairment and blindness

following: prevention, diagnosis, treatment or rehabilitation	

Sampling and data collection

Kirinyaga (predominantly rural), Nakuru (semi-urban) and Nairobi (urban) counties were selected through stratified purposive sampling to represent these different regions within the diabetes belt in Kenya. Three health facilities providing outpatient diabetes services in each county were identified by simple random sampling from a sampling frame of the clinics. Two clinicians who provide diabetes services were interviewed (n= 3 counties*2 clinicians*3 facilities=18). Three eye care workers providing services in the county were also interviewed (n=3 workers*3 facilities=9). The primary investigator and research assistants interviewed the 27 service providers at the clinics using a structured questionnaire with both closed-ended and open-ended questions.

The key informants were representatives of stakeholders in these services, who were familiar with the organization and delivery of healthcare at the national or at county level, with particular reference to diabetes and eye care, but whose principal role in the health system is non-clinical. The key informants (n=18) were identified using an initial sampling frame and subsequently through snowballing from those interviewed. These included eight health service managers, four NGO program leaders, four policy makers and two members of the umbrella PLWD body that represents patients. The primary investigator interviewed the key informants at their work sites or preferred locations. Interviews lasted 45-60 min, were audio-recorded and extensive field notes were taken. We also conducted document review of health system documents provided by the key informants and service providers.

We collected data at national level (key informant interviews) and county level (interviews with service providers, key informant interviews). The structured questionnaire and the topic guide had questions on the strengths and weaknesses of the health system for diabetes and DR, and potential interventions to strengthen the health system.

Ethics

The study was conducted according to the tenets of the World Medical Association's Declaration of Helsinki. The London School of Hygiene and Tropical Medicine and African Medical Research Foundation (AMREF) granted ethical approval. All participants gave written informed consent. Participation was voluntary and participants did not receive any financial incentives.

Data analysis

Audio records were transcribed verbatim. All qualitative data (from interviews and documents) were analysed using thematic content analysis, guided by the theoretical frameworks.[17] The primary investigator and a second independent coder read and coded the transcripts independently section by section, after agreeing on a coding structure. Where clarifications with participants were required, they were contacted by telephone. The codes were then grouped together into subthemes. These were later collapsed into themes within the six building blocks of the health system, as well as within the areas of prevention, diagnosis, treatment, and rehabilitation. We reviewed themes repeatedly across all transcripts. Quantitative data and data from document review was summarized using descriptive statistics and summary tables respectively. Triangulation of different types and sources of data was useful for elaboration and providing complementary insights.

Results

Characteristics of participants

We interviewed 18 key informants and 27 service providers from diabetes services (n=18) and eye care (n=9). None of the participants invited declined to participate. Of the 45 participants, 25 (56%) were male, the median age and duration of employment being 41 years and 15 years respectively. We examined 22 documents, which were strategies and strategic plans, reports, policies, published literature and meeting presentations related to diabetes and DR in Kenya.

Integration as an emerging theme in participant interviews

When the participants were prompted to discuss potential interventions to strengthen the health system for diabetes and DR, integration emerged as a dominant theme. Table 4-2 shows sample quotes within the integration theme.

Table 4-2: Integration as a theme in the different building blocks

Leadership and Governance

> *We have been working very closely (with ophthalmic services) at national level…the next step is integration of diabetes eye care services into comprehensive diabetes services (Key informant, diabetes care)*
>
> *Our policies, which include DR care, fit into the NCD policies…but in practice they do not seem to work in an integrated way (Key informant, eye care)*

Service delivery

> *We offer a wide range of services in the diabetes outpatient clinics…but there is a missing link with the eye services…you know, for the annual eye examination (Key informant, diabetes care)*

Eye care services for DR are part of the wider community of diabetes services, and also part of the wider community of eye care services (Key informant, eye care)

Human resources for health

We need integration of the training on comprehensive diabetes management…we have to integrate the eye component into it, and we have to integrate this training in the preservice curriculum of colleges and universities…this is actually a low-hanging fruit (Key informant, diabetes care)

Nurses in the diabetes clinic and in the eye clinic should also be trained as trainers of trainers in diabetes eye care…they need to be part of the team (Service provider, eye care)

Medicines and health technologies

NHIF [National Hospital Insurance Fund] caters for the costs of inpatient care for both diabetes and diabetic retinopathy, now we need to include all tests and medicines for both conditions in this cover (Key informant, eye care)

We value integration of services,…it may help to ensure we don't lose PLWD to informal services… we would not integrate herbal medicine into our services, but this is a cultural and social issue that cannot be addressed by us alone (Key informant, diabetes services)

Health Management Information System

Surveillance of chronic illnesses like diabetes and diabetic retinopathy is difficult. The solution is an integrated electronic medical records system (Key informant, diabetes care)

Even though we do not use the same reporting system or software, it should still be possible for us to have access to relevant data from the diabetes system, and vice versa….we are not talking of a merger (Key informant, eye care)

Health financing

I would suggest that an integrated implementation framework be developed at the county level, and it should have a dedicated budget (Service provider, diabetes care)

DR being principally a diabetes issue, we need to present the case for financing for DR by NHIF as part of diabetes services (Key informant, eye care)

Integration as envisaged in government policies and plans

Integration is a key policy objective as reflected in a sample of the documents, Table 4-3. Possible integration with HIV, Tuberculosis and Malaria programs is envisaged, though how it should be done is not explicit. Integration of diabetes and DR is not mentioned.

Table 4-3: Examples of concepts of integration in a sample of health system plans and strategies

Kenya Health Sector Strategic and Investment Plan 2013-2017

> *The health sector will focus on:*
> *• Integrating health service provision tools, mechanisms and processes for responding to NCDs*
> *• Establishing screening programs at community level and in health facilities for major NCDs (Page 25)*

Kenya Essential Package for Health

> *Institutional screening for NCDs is one of the KEPH interventions for reversing the rising burden of NCDs. The services targeted are routine BP, routine BMI and blood sugar testing.*

Kenya National Strategy for the Prevention and Control of Non-Communicable Diseases 2015-2020

> *Several bottlenecks of NCD prevention and control have been identified and addressed in this strategy, including: "Silo" nature of the health system with minimal opportunities of integrating NCDs in well-established public health care platforms like HIV, TB, family planning, maternal and child health. (Page 31 and 32)*
>
> *Strategic Objective 1 of the strategy: To establish mechanisms to raise the priority accorded to NCDs at national and county level…The interventions for this objective include integrating NCD prevention and control into policies across all government sectors.*

Kenya National Diabetes Strategy (2010-2015)

The objectives of the Kenya diabetes strategy include:

- *To improve early detection for diabetes and its complications through screening*
- *To network and integrate diabetes care with other national programs e.g. HIV/AIDS, TB and malaria (Page 9)*

One of the activities in the resource mobilization strategy is:

- *Integrate diabetes prevention and control into the national and district health plans (Page 11)*

Kenya Service Availability and Readiness Assessment Mapping (SARAM) Report 2013

- *General service readiness for provision of NCD services is 34% (for the KEPH defined NCD services)*
- *There is an overall limitation on the availability of KEPH services contributing to reversing the burden of non-communicable diseases (Page 112-126)*

Norms and Standards for Health Service Delivery 2006

> *Integration of care: Every contact with individuals, households and communities is used to ensure that a comprehensive set of defined services is made available. This is different from using "every opportunity to do everything". (Page 4)*

How integration of diabetes and eye care services can be implemented

Participants described a positive existing relationship between diabetes and eye care services in the context of DR, and envisioned a closer and newer way of 'mutual accommodation':

> *In the DR NET [Diabetic Retinopathy network] program, we have worked very well as physicians and ophthalmologists (Key informant, diabetes service)*
>
> *Diabetes services need to accommodate us more, it seems that DR gets forgotten (Service provider, DR)*

We identified three points of emphasis regarding how the integration of the two services should be implemented. Firstly, is that DR should be integrated into diabetes services. This is because of the pre-requisite for a functional service, such as the diabetes services, to which the DR service can be integrated. Policy documents recognize that services should be integrated into existing well-established health services or programs, Table 4-3.

> *Sometimes we forget the eye, because there are too many different things that have to be done for the patient… but we need to make sure it is not" (Service provider, diabetes)*

We would like DR to be seen as a diabetes issue, not an eye care issue (Key informant, eye care)

When we review the diabetes guidelines, DR will take centre stage (Key informant, diabetes service)

Of the 18 key informants, 17 (94.4%) believed that DR services should be integrated with diabetes care. 61.1% of key informants (n=11) reported that diabetes services should lead in the integrated service because they have a stronger infrastructure and accessibility to PLWD. However, 33% of key informants (n=6) indicated that eye care infrastructure in some hospitals is stronger than the diabetes infrastructure, but diabetes services should lead the integration because they have a stronger reach to the PLWD. One key informant (5.5%) felt that the discourse on the relative merit of integration should not focus on the infrastructure but should strengthen links between the services.

The second point of emphasis is that eye care workers have a role in enhancing care for diabetes care, as well as care for other non-communicable diseases:

Using the eye examination, eye clinicians can monitor diabetes, and hypertension…because the finding of diabetic or hypertensive retinopathy is useful information (Key informant, diabetes service)

Eye care workers should also ask patients about diabetes control (Service provider, diabetes)

Thirdly, both diabetes and eye care services need to work together:

I see that sometimes they {eye care services} will just examine the eye and not be interested in the medical management of the diabetes…we should all be seen to be involved with this (Service provider, diabetes)

Those of us on the ground…we know that DR is being missed in diabetes services…I think we need to go to the diabetes clinic…get involved with diabetes and get to look into the eye (Service provider, DR)

Key informants identified that referral and screening for DR might be strengthened through integration:

Although we have links with diabetes services, there are unexploited opportunities to integrate DR, particularly screening, with routine diabetes services (Key informant, eye care)

There is no follow up system so that even if a diabetes patient is referred to eye clinic and disappears, there is no system of follow up or feedback, as currently we work as separate services (Service provider, diabetes)

Of the 18 diabetes clinicians, only one had received a patient referred from eye services in the preceding month, while four of the nine eye care clinicians had received a referral from diabetes services in the same period. This implies that cross-referral is ineffective; there are missed opportunities for referral or patients are lost in transit. Furthermore, none of the diabetes clinics had visual acuity charts or ophthalmoscopes, and none of the eye clinics had a functional glucometer, which shows there is a big role for referral. The lack of readiness of health facilities for provision of NCD services is also noted in the Service Availability and Readiness Mapping (SARAM) report, Table 4-3.

Benefits of integration

We identified three main benefits of integration. First, integration can help to address service fragmentation, Table 4-3, as well as other gaps identified by participants, Table 4-4. Participants suggested that integration may provide opportunities for joint on-the-job training for staff, which is a priority because 12/18 diabetes clinicians and 4/9 eye care clinicians had not had a recent training update on DR and diabetes respectively. Secondly, participants suggested that integration might enhance continuity of care and increase awareness of DR among diabetes care providers. Thirdly, participants also identified that integration can attenuate potential problems, such as conflicting clinical recommendations that confuse PLWD and staff. However, none of the participants suggested that integration would have an economic benefit.

Table 4-4: Benefits of integration

Purpose of integration	**Why integration is required**
1. To solve current gaps in care	
	Services are fragmented
	Services are duplicated
	Patients are lost between the diabetes clinic and eye clinic
	Patients do not get referred appropriately
	No screening program for DR
	Glycaemic control is not monitored
	DR is not detected early enough
	Staff in each service work in isolation
	There are missed opportunities for adequate assessment
	Patients are not empowered for self-management

2. To obtain benefits of integration

To increase first contact of PLWD with eye examination

To facilitate continuity of care

To increase staff awareness of DR

To provide follow up system for patients who are referred

To increase the chances of timely detection rates of DR

To increase coverage of DR screening

Eye care workers can monitor and report diabetes and comorbidities through an eye exam

To emphasise health promotion

To improve equity by increasing access to services by the poor

To avoid burdening the patient with multiple visits

To have a platform for monitoring health outcomes

To use the available resources for maximum benefit

To have the two services 'speak the same language'

To develop joint clinical guidelines and tools

To make the service user-friendly

3. To avoid potential problems

To avoid conflicting recommendations for patient care

To avoid overloading the clinicians with different information

Even patients who have a retinal image taken in the diabetes clinic will still need a comprehensive eye examination, this will be missed if there is no integration

To reduce the number of PLWD going blind from diabetes

Steps towards implementing integration

We found that the policy documents do not elaborate how integration should occur. However, the norms and standards document states that integration "*does not mean 'doing everything'…"*. This implies the need to establish the priorities. The participants identified four main priorities: referral (n=34), retinal screening for DR (n=23), patient monitoring (n=19) and patient education for self-management (n=16). Seven participants remarked that the interaction between diabetes and eye clinics must be continuous, particularly through bidirectional referral; otherwise, "*integration will be ineffective*". Five participants indicated that the integration should be gradual, and preceded by a pilot.

The inputs that will be needed to achieve integration were listed: joint planning, joint training of health workers on diabetes and DR, equipment for monitoring diabetes (glucometer, test strips), DR screening equipment, a database that includes both diabetes and DR, clinical checklists and guidelines. Key informants suggested that financing for the additional inputs and processes would be sourced from the government and partners. All diabetes clinicians indicated that they would be happy to have a retinal camera situated in their clinic, though they had space constraints. Six of the nine eye care service-providers were willing to hold regular outreach clinics to screen PLWD for DR.

All participants concurred that they would have roles in the integration, which include; getting buy-in from all staff and administrators, facilitating or participating in joint planning, obtaining the resources and supporting implementation. Participants identified that integration should be led by the team leads in diabetes and eye clinics, and should prioritize strengthening

referral, metabolic control, self-management and screening for DR. Based on the findings in this study, we present a conceptual framework for integration, Figure 4-1, showing the inputs required to make integration feasible and the outcomes envisaged in successful integration.

Discussion

Integrated health systems have been promoted as a means to build a more effective, efficient and patient-focused health system that better meets the needs of the populations served.[4] Integrated DR services can blur the boundary between diabetes services and eye care services, to create a shared repertoire and synergy for the investments made in these services. Such synergy is vital for strengthening the health system responsiveness to the rising burden of diabetes and DR.[7, 13] It can ensure equity by reducing the exclusion and difficulty in navigating the services by PLWD, since comprehensive diabetes care would include DR services. Further, it provides a unique opportunity to integrate primary, secondary (early detection) and tertiary prevention (treatment to prevent complications), Figure 1. This can lead to improved health outcomes and therefore more cost-effective use of health system resources by PLWD. For example, screening and detection of DR might improve adherence to self-management and optimal metabolic control, which would prevent additional complications of diabetes that require expensive treatment.

The endorsement of integration in the health policies is relevant to its sustainability, because it implies long-term government commitment.[7] Integration of comprehensive diabetes care with HIV, tuberculosis and malaria services would entail investment at all levels of health care, as services for these communicable diseases are offered across the continuum of primary, secondary and tertiary care. To ensure that comprehensive diabetes care includes DR, we

propose a service-level model of integration at the diabetes clinics and eye clinics, which are usually located at secondary and tertiary hospitals. This is expedient for three reasons. One, the resources for integration are already available at this level of the health system, where the two clinics are already functioning. This would avoid aggravating existing resource challenges, such as health workforce shortages.[18] Two, the integrated service removes the complexity that patients face while navigating the care pathway, and which often presents a barrier to access to DR services.[1, 19] Three, the integrated services includes specialist diabetes and eye care services, which shows that integration does not imply compromising specialist functions.[1, 2] Such a fear can cause resistance by specialists, although this was not evident in our study.[1, 19]

Furthermore, there was high level of interest on integration among all participants, which is likely to facilitate successful implementation of integration. This is important because reluctance, opposition or lack of ownership by the service providers would lead to poor integration results.[20] In other studies, service providers have been concerned about the likely increase in workload.[11, 20] In this study, staff shortages, inadequacy of space for additional services, lack of equipment and weak referral linkages were identified as potential challenges but not as deterrent to the integration. Although we did not investigate the reasons for this enthusiasm, it might be because diabetes and eye care services target the same population (PLWD) and have a converging goal in relation to diabetic retinopathy (prevention of blindness). It might also have resulted from several system antecedents: (1) An ongoing pilot program of the DR NET hospital-twinning initiative, which is a link program involving both diabetes and eye care stakeholders, with the aim of strengthening DR services. (2) A recent national STEPwise survey for risk factors of non-communicable diseases, and (3) Sensitization of participants on DR as a potentially blinding condition.

The reasons for integration nominated by participants reflect the perceived differences between integrated and non-integrated care. The main impetus is local service gaps, such as fragmentation, and missed opportunities for early detection of DR or inefficiency and discontinuity of care, which concurs with the drivers cited in other literature.[2, 7, 10, 13, 20] These are typical barriers to access to care that will be addressed through integration.[2] The necessity for integration has also been recognised in a previous study in Kenya.[13] Cost-control was not identified as the major driving force for integration in this study, unlike in other contexts.[19] However, integration is likely to reduce costs by reducing duplication of services and multiple client visits.[1, 12, 20] In addition, early detection or DR is a sound economic investment because timely treatment is cost-effective.[21, 22]This shows that the interest in integration among these participants was predicated on improved services outcomes and not as an end in itself.

The conceptualisation of integration around screening is significant because Kenya does not have a systematic screening program for diabetes or DR.[13] It reveals an excellent opportunity to develop an effective screening program inclusive for all PLWD attending diabetes services. The bidirectional referral strategy shows the pertinence of organising integration as a process of mutual but not symmetric accommodation. It is not symmetric because the entry point is the diabetes services, which PLWD are already accessing even without integration; hence, it is the primary service. An excellent example of how synergy might be realised is that eye care workers can identify and monitor comorbidities. Ocular findings in hypertension, hyperlipidaemia, and other medical conditions may be the first sign of these diseases, and these can be identified during the screening examination. Medications used to treat these comorbidities might also have ocular adverse effects that can be identified upon ocular

examination. A comprehensive dilated eye examination can be a radar for detection or monitoring several comorbidities and medications.

The integration could be operationalized through co-implementation of the key interventions, which are self-management, glycaemic control, DR screening and referral. This scope focuses on prevention of complications, rather than treatment.[23] Some integration models, such as sexual and reproductive health programs integrated into HIV programs, have focused on clinical services, such as testing or prescription of treatment, rather than lifestyle modification.[11, 24] Conversely, other integration models for diabetes, HIV and hypertension have emphasised adherence counselling for medication and lifestyle modification.[25] Still other models have included a mix of patient education and prescription of medications for PLWD.[10, 26, 27]No method is inherently good or bad, the scope largely depends on the objectives of the two services.[1, 7, 8] Given the priority for diabetes and DR is to prevent progression or complications, bidirectional referral and health promotion approaches would be useful.[13, 21] In the event of future integration with HIV, Tuberculosis and Malaria programs, a treatment component may be added, since the main priority for these conditions is universal coverage to treatment for those eligible.[7, 27]

Several inputs are required: inter-professional collaboration, joint planning, clinical governance, training, clinical tools, database and equipment. This means that supply-side resources are required, and need to be allocated differently.[7, 13] Integration is not monolithic but encompasses all building blocks of the health system and hence requires resource mobilization. Given that integration cannot mitigate against lack of necessary resources or infrastructure, failure to invest in it would hamper the desired benefits .[1, 23] For example, the lack of a monitoring and evaluation component has been identified as a weakness in previous integration initiatives.[28] This being one of the first studies to discuss this context of

integration, we have proposed a conceptual framework for integration, which can be used by policy-makers for planning, Fig 4-1.

What are the expected effects of integration? Investing in this integrated service delivery system creates distinct deliverables, such as increased demand for the specified services and reducing the unmet need for DR screening.[7], [12, 21]Integration should translate to prevention of complications of diabetes and DR, which is a widely agreed priority of health systems.[21] To monitor whether integration confers these benefits, an appropriate metric will need to be jointly determined.

Our study has several strengths. Geographical variability (three counties) accentuated the external validity of the study. The inclusion of clinicians from both diabetes and eye care services, as well as patient representatives, enabled us to obtain unique perspectives of service providers. The data is subject to social desirability bias as the participants are directly involved in the services, however we used triangulation to mitigate this. This is the first study to document the interventions and the platforms for integration of these services in the region. The main limitation is the novelty of the concept of integration with respect to diabetes and DR but this shows that this health system is dynamic, and it may jumpstart the process of broader integration of diabetes services.

Conclusion

Integration, as envisaged in this paper, is relevant to the goals of the health system and congruent to the existing health system for diabetes and DR and to the broader health strategies in Kenya. The purpose of integration is to address service gaps, ensure universal access to a range of services and prevent complications of diabetes and DR. This is evidence

that the health system is not static in its response to NCDs, and integration may be applicable to other countries with similar health systems.

Future research

Further research is required to test and refine this empirical conceptual framework. The impact of integration on the following parameters will also need to be evaluated: performance of health workers, service utilization, patient satisfaction and cost of the services. The effect of integration on equity may be determined by disaggregating the health outcomes of PLWD by gender, social strata and other indices of vulnerability.

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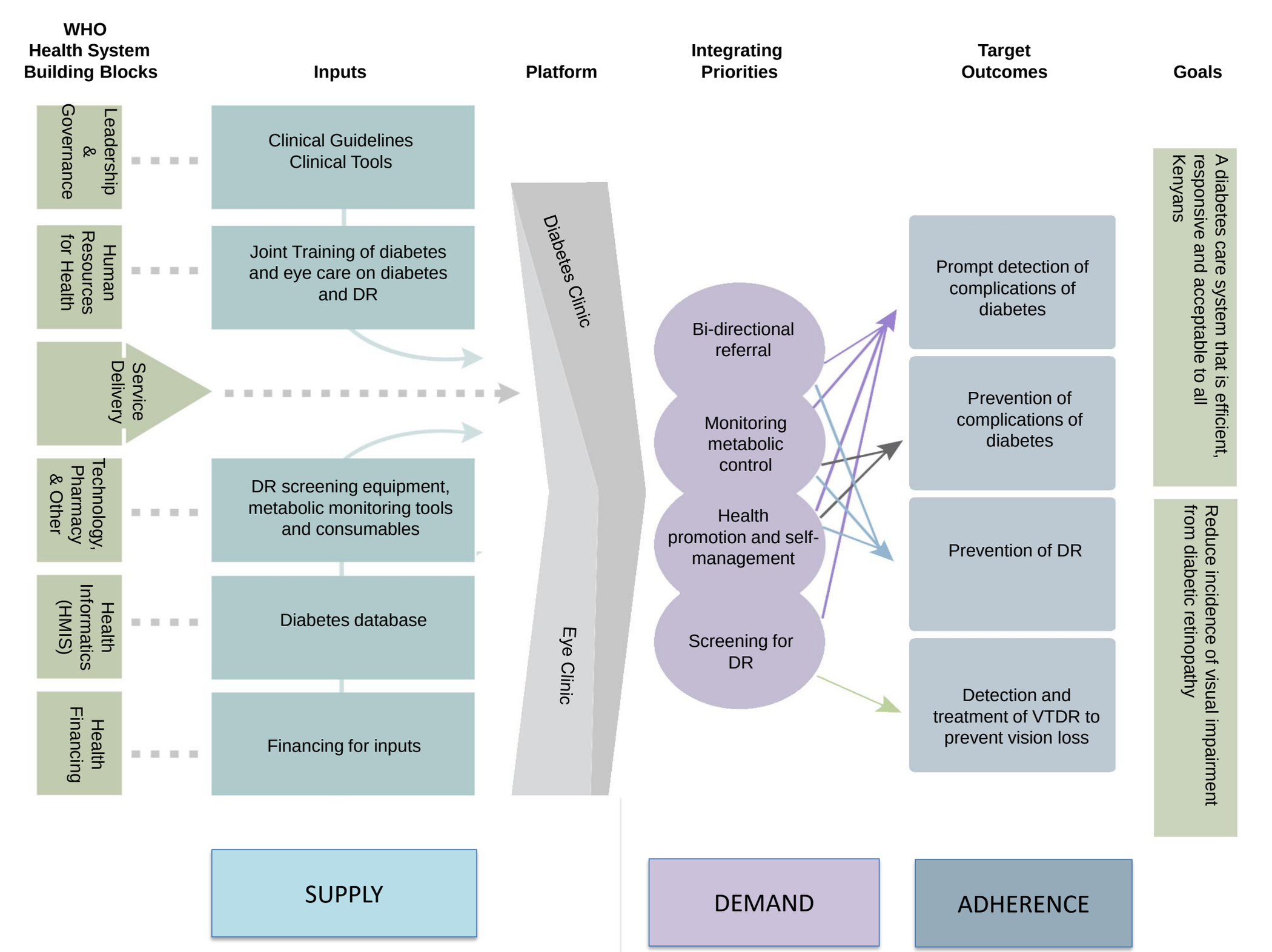

Figure 4-1: Conceptual Framework for integrated diabetes and diabetic retinopathy (DR) services

KEY
DR: diabetic retinopathy
VTDR: vision-threatening diabetic retinopathy

Section C

Health System Strengthening

“Mosquito [...] had asked Ear to marry him, whereupon Ear fell on the floor in uncontrollable laughter. "How much longer do you think you will live?" she asked. "You are already a skeleton." Mosquito went away humiliated, and any time he passed her way he told Ear that he was still alive.”

“You do not know me,’ said Tortoise. ‘I am a changed man. I have learned that a man who makes trouble for others makes trouble for himself.”

“Eneke the bird says that since men have learned to shoot without missing, he has learned to fly without perching.”

Prof Chinua Achebe 1930-2013

Nigerian novelist, poet, professor of literature, and critic

In his book ‘Things Fall Apart’

Chapter Five

Health system strengthening: Development of clinical guidelines for diabetic retinopathy in Kenya

5.0 Overview

Multiple supply and demand factors interact to influence health systems. These factors are responsible for low access to diabetic retinopathy (DR) services in Kenya (chapter 3). *Health system strengthening* involves broad interventions designed to permanently make the health system function better in relation to the long-term goals for population health, including prevention of vision loss and blindness from DR.

Chapter 5 and 6 address Objective 3 of the thesis: To use the evidence from the literature and evidence from the health system assessment as a platform for health system strengthening. This chapter focuses on this health system strengthening initiative and includes two papers.

Evidence-based clinical guidelines for diabetic retinopathy define what services people living with diabetes (PLWD) should receive for prevention, screening, diagnosis and treatment of DR. The health system assessment identified that lack of national clinical guidelines for DR in Kenya leads to lack of standardization of services. Addressing this supply-side barrier can ensure that the required resources, tools and services for DR control are available and aligned to the local needs. This aspect of health system strengthening was considered critical at national level. (Chapter 3). National clinical guidelines were therefore developed through a process of adaptation from generic guidelines.

The adaptation process followed internationally defined good practice, which include defining the PICO framework (population, intervention, comparator and outcome), determining the

clinical questions, using a systematic approach for literature search, appraising the quality of generic guidelines using validated instruments, identifying contextual considerations and following established guideline adaptation frameworks.

The adaptation process requires high-level skills in finding, appraising and interpreting evidence, in stakeholder engagement for a participatory process as well as in writing the guideline documents. The PhD provided opportunity to develop these skills, while guideline development provided opportunity to apply the skills in a real-life situation, and to participate in knowledge translation to close the gap between evidence and practice.

5.1 Research Paper 3

Research paper 3 is on the process and outputs of guideline development. This paper has been included since it describes the opportunities, challenges and lessons learnt that might need to be considered in future guideline development. Given that Information on guideline development in LMICs is sparse, the paper facilitates understanding of the feasibility and implications of this initiative in similar contexts. This paper was published in the journal BMC Implementation Science in December 2018 after peer review.

articles available to the widest audience, and contributes to the furthering of research in ways that would have seemed impossible two decades ago. All articles published by *BMC Implementation Science* are made freely and permanently accessible online immediately upon publication, without subscription charges or registration barriers. "

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5.2 Research Paper 4

Research paper 4 provides a summary of the content of the guidelines. This paper has been included because it provides an understanding of the recommendations for DR care in Kenya, and because the guideline document is too large to include in this chapter. This paper was published in the Journal of Ophthalmology of Eastern, Central and Southern Africa in December 2017 after peer review.

The following terms apply:

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PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	BMC Implementation Research		
When was the work published?	2018		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	Not applicable		
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

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. (Attach a further sheet if necessary)	I led the work described in the paper, drafted the manuscript and prepared subsequent revisions in consideration of the comments from the co-athors and peer reviewers

Student Signature: Nyawira _____ **Date:** 17 SEPT 2019 _____

Supervisor Signature: [redacted] Date: SEPT 17, 2019.

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Implementation Science

RESEARCH Open Access

Adapting clinical practice guidelines for diabetic retinopathy in Kenya: process and outputs

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Abstract

Background: The use of clinical practice guidelines envisages augmenting quality and best practice in clinical outcomes. Generic guidelines that are not adapted for local use often fail to produce these outcomes. Adaptation is a systematic and rigorous process that should maintain the quality and validity of the guideline, while making it more usable by the targeted users. Diverse skills are required for the task of adaptation. Although adapting a guideline is not a guarantee that it will be implemented, adaptation may improve acceptance and adherence to its recommendations.

Methods: We describe the process used to adapt clinical guidelines for diabetic retinopathy in Kenya, using validated tools and manuals. A technical working group consisting of volunteers provided leadership.

Results: The process was intensive and required more time than anticipated. Flexibility in the process and concurrent health system activities contributed to the success of the adaptation. The outputs from the adaptation include the guidelines in different formats, point of care instruments, as well as tools for training, monitoring, quality assurance and patient education.

Conclusion: Guideline adaptation is applicable and feasible at the national level in Kenya. However, it is labor- and time -intensive. It presents a valuable opportunity to develop several additional outputs that are useful at the point of care.

Keywords: Clinical practice guidelines, Diabetes mellitus, Diabetic retinopathy, Guideline development, Guideline adaptation, Kenya

Background

The first definition of clinical practice guidelines (CPG), hereafter referred to as "guidelines," was provided by the Institute of Medicine (IOM) in the USA in 1990: "systematically developed statements to assist practitioners and patient decisions about appropriate healthcare for specific circumstances" [1]. Guidelines-related initiatives have subsequently increased globally since the 1990s. This definition was revised in 2011 to: "statements that include recommendations to optimize patient care that are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative care options" [2]. Guidelines constitute one tool for good decision-making in clinical practice, which has potential to reduce variations in health care and its cost. Although a plethora of barriers may compromise their effectiveness, guidelines are instruments to improve the quality of care.

Guideline adaptation is potentially an efficient alternative to de novo guideline development, particularly in resource-constrained contexts [3]. Adapting guidelines to suit a local context may also improve local uptake of the guidelines [4, 5]. Adaptation requires an active, systematic, and participatory process [4] that preserves the integrity of the transferable evidence-based recommendations. Although this adaptation process is context-specific and may not be transferable or generalizable, it needs to be systematic, explicit, transparent, rigorous, and reproducible. The ADAPTE and Practice Guideline Evaluation

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and Adaptation Cycle (PGEAC) framework of adaptation are validated approaches to conduct and document this process [4].

The Institute of Medicine [2] has described eight attributes of good guideline development. These are (a) validity, (b) reliability and reproducibility, (c) clinical applicability, (d) clinical flexibility, (e) clarity, (f) documentation, (g) development by a multidisciplinary process, and (h) plans for review. Guidelines are likely to reflect these attributes when they are developed via a transparent process by a multidisciplinary team without potential bias and conflicts of interest, and supported by a systematic review of the evidence [2].

This paper describes the process involved in adapting the diabetic retinopathy (DR) guidelines for Kenya, in order to assist others undertaking a similar endeavor.

The STEPwise survey [6] for risk factors of non-communicable diseases in 2015 reported that diabetes mellitus (DM) affects an estimated 2% of the Kenyan population aged 18–69 years, with the highest proportion (5%) being in the 45–59 years age group. Every person living with diabetes (PLWD) is at risk of potentially blinding diabetic retinopathy (DR). In turn, visual loss from DR is associated with additional morbidity, such as falls, fractures, and difficulties with taking medications. Both DM and DR are associated with significant morbidity, mortality, and excess health care costs. The prevalence of DM is predicted to rise steeply over the next decade [7], and consequently DM and DR are important public health concerns.

Effective and quality service delivery in relation to DR in Kenya is required within the existing health system [8–10]. Currently, there are notable gaps in DR screening, diagnosis, referral, treatment, and follow-up. Although screening and laser treatment are cost-effective interventions for prevention of blindness from DR [11], there are inequities in access to them. Some of the services are underutilized for a variety of reasons, while some of the services delivered are of insufficient quality. This disparity is linked to multiple supply and demand factors, such as variation in referral practices of diabetes care providers, screening practices of eye care providers, integration of services, and level of awareness of patients [9, 12, 13].

Clinical guidelines offer recommendations to improve service delivery, advocate for resources, leverage existing resources, and improve outcomes. Implementing evidence-based practice guidelines for DR is thus vital to address the gaps and prevent blindness from DR. International guidelines for this purpose exist, but there are no published local guidelines. This guideline adaptation aimed to address this lack of national guidelines. We envisaged providing a user-friendly guideline that describes appropriate care based on the best available scientific evidence.

Methods

We relied on adaptation instead of de novo development of the guideline in order to avoid duplication of effort, to use the available resources cost-effectively, and to facilitate customization of the guidelines prepared for other income and health system settings to reflect local context.

The process of standardizing clinical practice recommendations for DR in Kenya began over a decade ago. Several guideline documents have been produced although none has been formally published as a national guideline. Our reflection was that opportunity costs, turnover of experts involved in the process, and other contextual factors might have slowed down further development of the guidelines. The methodology discussed here is that followed over the last 2 years leading to the production of the published guideline. However, we expect that a similar process was undertaken in the previous period.

The adaptation process has been systematic, consultative, and guided by a technical working group (TWG). Several widely used toolkits and guidelines provided a point of entry [14–20]. We followed the tasks of adaptation, as applied within the ADAPTE framework, although some of the tasks were synchronized and we often had to return to previously completed steps. The ADAPTE process is a well-known framework for guideline adaptation, which consists of 3 phases and 24 steps. Seven core principles underpin this framework, and the TWG adopted them for this adaptation [14]. Figure 1 provides a simplified schema of our methods.

The identification of the need for the DR guidelines by stakeholders prompted the Ophthalmic Services Unit to constitute a steering team of five members. This team prepared terms of reference and a list of potential members for the TWG. At the first few meetings of the TWG, we discussed the following: the need for the guidelines, the feasibility of guideline development, the required expertise, funding, work plan, outputs, and role definition of the members. In subsequent meetings, the topic and clinical questions were defined.

We identified the methodological resources, the clinical guidelines, and the evidence for effectiveness of various DR interventions through a literature search on various databases including Cochrane Library, ELDIS, Embase, Global Health, and PubMed. We also searched the websites of agencies that develop these resources. The search strategy (Additional file 1) was limited to reports published in English from 2000 up to date.

Two TWG members conducted the literature search and recorded the characteristics and content of retrieved guidelines. Guidelines that did not meet the predefined inclusion and exclusion criteria were eliminated. Two reviewers assessed the quality of the retrieved guidelines using the AGREE II instrument and presented the findings in a TWG meeting. All TWG members participated

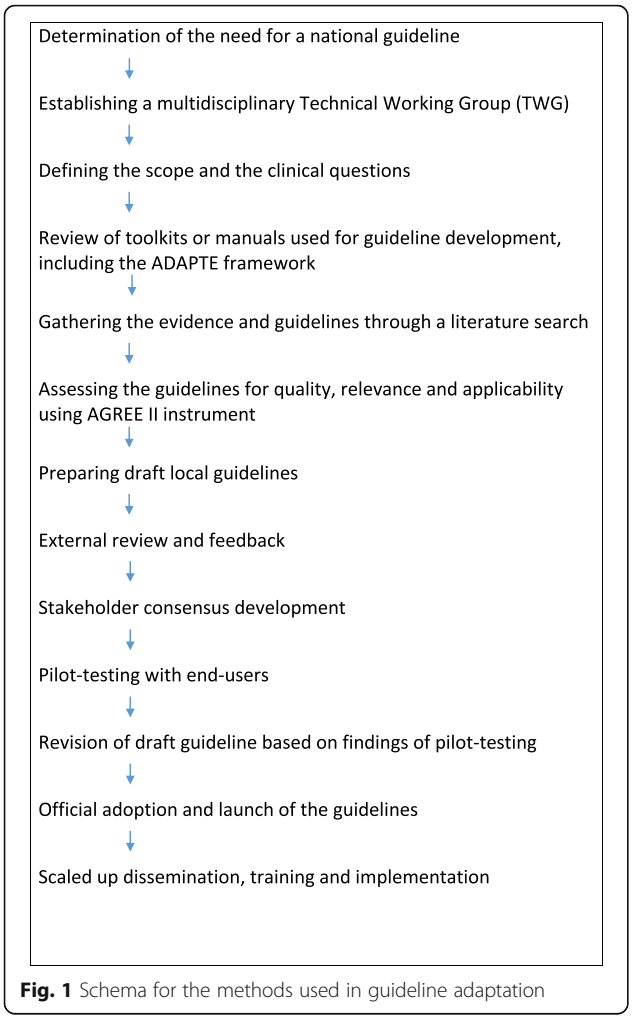

Fig. 1 Schema for the methods used in guideline adaptation

in the assessment for currency, content, consistency, acceptability, and applicability of the recommendations. Following consensus on the results of the assessment, guidelines suitable for adaptation were selected.

The clinical guidelines that were selected for reference were the American Diabetes Association (ADA) Standards for Medical Care in Diabetes [21], International Council of Ophthalmology (ICO) guidelines for diabetic eye care [22], the Royal College of Ophthalmologists' diabetic retinopathy guidelines [23], and the Canadian Diabetes Association's retinopathy guidelines [24]. We chose the ADA and ICO guidelines as the prototypes for DM and DR guidelines respectively and collated evidence from Cochrane systematic reviews relevant to diabetic retinopathy. None of the guidelines contained an adaptation template for different contexts.

We utilized the AGREE II (Appraisal of Guidelines Research and Evaluation II) instrument to assess the quality of the clinical guidelines. This instrument consists of 23 items grouped into six domains: (a) scope and purpose, (b) stakeholder involvement, (c) rigor of development, (d) clarity and presentation, (e) applicability, and (f) editorial independence.

The following additional guidelines were also reviewed, so as to identify any potential conflict in recommendations for care of diabetes and other comorbidities: Kenya national guidelines for management of diabetes [25], Kenya national strategy for the prevention and control of non-communicable diseases [26], and International Diabetes Federation's diabetes eye health guide for health professionals [27]. Similarly, we reviewed previous drafts of local DR guidelines.

Draft guidelines were prepared by the TWG and circulated via email to all members for review. Three drafts were circulated, with the final draft also being circulated to external reviewers to assess content validity, clarity, and applicability. The TWG evaluated the final draft guidelines for the quality requirements of the AGREE II instrument prior to release. A consensus stakeholders meeting approved the final draft.

Pilot testing was conducted in different health care settings in purposively selected counties that differed in characteristics that may influence applicability. We collected feedback on the usability through interviews, reports, and observation. Dissemination of guidelines was done through county coordinators, conferences, training institutions, professional associations, social media, and distribution of print material.

Results

Table 1 shows the results of the adaptation process in each of the steps of the ADAPTE framework. We applied the guiding principles as exhibited in Table 2. We further applied the AGREE II instrument to ensure quality of our draft guideline as reported below.

Scope and purpose

The TWG's first task was to define the scope. The main options were to include only DR or diabetic eye disease as a whole. The consensus was to limit the scope to DR because of its unique natural history and public health implications. The overall objective of the guideline is to reduce the proportion of PLWD who go blind due to diabetic retinopathy in Kenya through interventions for prevention, early detection, and effective treatment of DR. The adaptation process aimed to reduce inappropriate variation in screening and treatment, to provide a rational guide for referral, and to use the diabetes care and eye care resources efficiently to meet these goals. The recommendations needed to be germane to the social context, the patient pathway, and the referral systems in addition to being capable of integration into the routine workflow. The Population, Intervention, Professions, Outcomes and Health care system (PIPOH) summary (Table 3) defined the clinical questions addressed in the guidelines.

Table 1 Adapting the guidelines using the ADAPTE process

Step	Activity	Result
Phase I Set up		
1.	Establish a resource team	The Ophthalmic Services Unit constituted a steering team of five members which developed the terms of reference and prepared a list of 25 potential members for the technical working group (TWG), who were subsequently invited to the group
2.	Determine criteria for selection and select a topic using criteria	DR was selected because it is a public health concern and there is variation in standards of care
3.	Check if adaptation is feasible	Evidence-based guidelines were already in use internationally, and there was high interest from the Ministry of Health, clinicians, and other users to develop guidelines
4.	Identify necessary resources and skills	There was high level of commitment by members of the TWG. The Fred Hollows Foundation committed to provide funds, and the required expertise was available: retinal specialists, public eye health specialists, endocrinologists, diabetes educators, epidemiologists, search and retrieval of information, critical appraisal, research, policy, guideline development, and eye health systems. A need for input from other professions in the multidisciplinary care team for type 1, type 2, and gestational diabetes was identified
5.	Complete tasks of the set-up phase	Members of the group decided to function as a working group coordinated by the Ophthalmic Services Unit. A set of guiding principles to foster development of the guidelines was adopted (Table 2). Potential conflicts of interest were explored, and there were none to declare
6.	Write the plan for adaptation	A timeline for completion, list of additional resource persons to be included, list of outputs to be developed in conjunction with the guidelines and task allocation among the TWG members were agreed upon
Phase II Adaptation		
7.	Determine and clarify the question	A PIPOH summary was prepared (Table 3). The areas of interest for standards of care were determined as screening, diagnosis and management of DR, and the management of DM in relation to DR, within the existing care pathway for PLWD in the Kenyan health system
8.	Search for guidelines and other relevant documentation	The TWG searched for relevant DR guidelines and evidence on DR interventions in systematic reviews
9.	Screen the retrieved guidelines and record their characteristics and content	The recommendations of the guidelines for screening, diagnosis and management of DR, and the management of DM in relation to DR was reviewed, extracted, and compiled in summary tables. Evidence from Cochrane systematic reviews was also reviewed
10.	Eliminate a large number of the retrieved guidelines using the AGREE instrument	The rigor dimension of the AGREE II tool was utilized to eliminate guidelines that did not meet the stipulated criteria
11.	Assess the quality of the guideline	The AGREE II instrument was used to scrutinize the quality of the guidelines
12.	Assess the currency of the guideline	The guidelines retrieved were sufficiently current, and we did not identify any new evidence
13.	Assess the content of the guideline	Recommendations for screening, diagnosis, grading, referral and treatment were examined and did not differ significantly between guidelines
14.	Assess the consistency of the guideline	There was clear consistency between the evidence from systematic reviews, the interpretation of the evidence, and the recommendations in the guidelines in all the areas of interest
15.	Assess the acceptability and applicability of the recommendations	Care was taken to ensure the recommendations are not in conflict with other local guidelines and to appraise the implications of the guidelines on health service delivery
16.	Review assessments	The results of the assessment of the guidelines were discussed in meetings of the TWG
17.	Select among guidelines and recommendations to create an adapted guideline	The ICO guideline for DR was the main guideline used because the recommendations compared well with the other high-quality DR guidelines and the practice-based recommendations were well-stated
18.	Prepare a draft of the adapted guideline	The facilitators of the working group compiled the results of the deliberations and wrote the draft guideline document
Phase III Finalization		
19.	Seek feedback on the draft guideline from those who would be using it	Three revisions of the draft were circulated for comment to TWG members as well as surgeons, pediatricians, ophthalmologists, Kenya Defeat Diabetes Association, vitreoretinal surgeons, physicians, diabetes educators for agreement and identification of gaps
20.	Consult with endorsement bodies	The Ministry of Health adopted the guidelines
21.	Consult with developers of guidelines used as sources	No substantive changes were made to recommendations so this step was not undertaken

Table 1 Adapting the guidelines using the ADAPTE process *(Continued)*

Step	Activity	Result
22.	Acknowledge source documents	The key guideline documents and other resources used have been acknowledged through attribution
23.	Plan for aftercare of the adapted guideline	A review date was planned for 5 years. Monitoring indicators were also identified. Pilot-testing has been used to check for usability. Distribution will be through electronic and print copies
24.	Produce a final document of the guideline and other outputs	The following additional outputs were produced (along with the guideline): posters and brochures for patient information, posters, brochures and checklist to be used by clinicians, workshop slides for training health workers, quality assurance guidelines

Stakeholder involvement

The Ophthalmic Services Unit at the Ministry of Health convened a steering group of five members. They drafted the terms of reference for a task-oriented TWG, which were to (1) determine the scope and focus of the required guidelines, (2) appraise the evidence and recommendations in existing DR guidelines, (3) develop the national guideline, and (4) craft messages to be used at the point of care, to influence practice.

The steering group identified 25 potential members of the TWG, based on the criteria of diverse expertise, experience, representation of multiple stakeholder groups, and commitment to the process, all aimed at increasing both internal and external validity of the guidelines. These members received personal invitations to participate. An average of 15 were active members of the TWG at any given time, but the others remained involved on the periphery and received frequent reminders to participate remotely. Participation was through attending meetings, email and telephone correspondence, face-to-face consultations, availing resource documents, reviewing drafts, providing evidence, and informal consultations. This proactive integrative and flexible approach was designed to ensure ownership, external validity, and the involvement of end users of the guideline.

The TWG members were all volunteers with other clinical, educational, administrative, and policy roles related to DM and DR in public, private, or faith-based health facilities, academia, ministry of health, and professional organizations. Participation on a volunteer basis inferred limitation of availability, though additionally, it implied indirect institutional participation of the employer. They had diverse expertise including clinical, public health, research, epidemiology, literature search, systematic reviews, and health systems. Differences in opinion were encountered in the deliberation of some recommendations, particularly regarding the role of different cadres in making DR treatment decisions and delivering treatment. This was resolved through varied strategies: expressing judgements about values and risks, making reference to regulation, reviewing the evidence for role specification, and adapting the role definition prescribed by the source guidelines and informal consensus techniques.

We did not employ a research assistant, because the team had skills in literature review, recent systematic reviews on interventions for DR were available and the

Table 2 Guiding principles for guideline adaptation

	Guiding principle	Indicator
1.	Respect for evidence-based principles in the development of guidelines	The evidence on which the recommendations are based is included in the guidelines
2.	Ensuring that the quality of guidelines is high	Well-known frameworks for guideline development were used to guide and assess the quality of the adaptation process
3.	Participation of key stakeholders to foster acceptance and ownership of the adapted guideline and ultimately promote its use	The involvement of stakeholders was acknowledged in reports of the adaptation process
4.	Consideration of context during adaptation to ensure relevance for local practice and policy	The context of application of the guidelines has been explicitly stated and the content adapted for the Kenyan health system
5.	Transparency to promote confidence in the guideline development process	The methodology in the adaptation process has been documented so that it is accessible and reproducible
6.	Flexibility to accommodate specific needs and circumstances in the health system	The guideline presents recommendations for diverse categories of PLWD (such as those with different stages of DR or comorbidities) who receive service in different clinical settings
7.	Respect for and acknowledgement of guideline materials used as sources	Citation and referencing have been used to acknowledge all source documents

Table 3 PIPOH summary of the clinical questions

	Parameter	Specification
P	Population	All patients with diabetes mellitus who are aged ≥ 12 years
I	Intervention	Screening, diagnosis, referral, and management of diabetic retinopathy
P	Professions (target users)	Primary care workers, diabetes care providers, eye care workers, administrators, policy-makers
O	Outcomes	All persons living with diabetes are screened for DR at least annually and blindness from DR is prevented
H	Health care setting	Community, Primary, Secondary, and Tertiary level health care settings

existing guidelines were current. The team did not have a health economist and did not conduct an economic appraisal. As the guidelines were in English, we did not require expertise in foreign languages.

The TWG considered it is important to include patients' values and perspectives in the guidelines. A patient group was invited and PLWD who are clinicians were included, but despite our efforts, we did not succeed in having patients directly participate in the adaptation. We also aspired to have the participation of large groups of PLWD in a way that adequately represents the diversity of perspectives of PLWD from different geographical locations, social strata, and stages of disease. Since we do not have a comprehensive database of PLWD in the country, this was not feasible.

Rigor of development

We obtained high quality and current international guidelines. We examined the methods and the quality of the evidence used to formulate the recommendations for interventions for DR. We also considered the implications for resources and health service delivery in Kenya. Further, we searched for any recent evidence from systematic reviews and for relevant domestic research. In the absence of this, and judging the recommendations current and evidence-based, we incorporated them in our guidelines. The draft guidelines were subsequently reviewed by external multidisciplinary reviewers and pilot-tested in various health facilities. The guideline will be updated in 5 years to incorporate any new evidence that will have emerged.

Clarity and presentation of the guideline

We used the Conference for Guideline Standardization (COGS) checklist [20] as a guide to the content that needed documentation, although we excluded those items on the list that we did not consider necessary. The adapted guideline also includes additional information that was not in the international guidelines, such as the pattern of diabetes in Kenya, integrating DM and DR services, dissemination, and review plans.

In writing the guidelines, we avoided vague, nonspecific, or ambiguous terms and phrases. We aimed to produce a user-friendly guideline in which the precise recommendations are easily identifiable and clear, and the formatting is appropriate.

Applicability

We recognized the facilitators and barriers to the application of this guideline in the Kenyan health system. To overcome the barriers, the guideline provides tools to facilitate its implementation at the point of use. These include workshop slides for training guideline implementers. Flexible 1- day training programs have been executed at implementing health facilities, conferences and training institutions, in conjunction with guidelines dissemination. The potential resource implications (equipment, staff, and training) and resultant work burden of applying the recommendations were considered. A monitoring and evaluation plan has also been included to assess adherence to recommendations and the outcomes of the implementation.

We required data on the costs of DR services in Kenya, but we did not undertake this as the Division of Non-Communicable Diseases had recently undertaken costing for diabetes services, including DR services. We lacked a costing model for guideline adaptation at the start of the exercise, but in our experience, the largest cost of the adaptation process was the production, pilot-testing, dissemination, and implementation of the print outputs. This may be reduced with progressive enhancement of digital literacy of the users and increased utilization of the electronic resources.

Editorial independence

The basic logistic needs of the adaptation process (administrative and meeting costs), as well as the implementation costs, were funded by The Fred Hollows Foundation. The funders did not influence the content of the guideline. There was a 100% consensus on the desired outcome of the guidelines, which is prevention of blindness from DR. Members and funders did not have any conflict of interest with respect to this outcome.

Context-specific modifications

Unlike the reference guidelines, the Kenyan guideline is designed for use by both diabetes and eye care clinicians, as well as other stakeholders in eye care. The population of interest is all PLWD aged 12 years and over, without any exceptions. The guideline attempts to take care of various complexities of service delivery. The role of different cadres in the screening, diagnosis, and treatment

of DR is highlighted. Noting the variability in access to required equipment and skills, a referral mechanism has been determined through mapping of the services available in different facilities in the country. We found it practical to constantly relate the guideline to the patient pathway. Additional specifications have been made on linking diabetes care and eye care services, clinical governance for the services, and using the health information management systems (HIMS) to monitor the effect of implementation of the guidelines.

Outputs

This process has led to several outputs: (i) the national guidelines in various formats—print copies, electronic version, and an executive summary of the recommendations. The guideline has a national coverage and applies to persons with any type of diabetes.' (ii) quality assurance guidelines; (iii) mapping of DR services in the country; (iv) posters and leaflets for patients; (v) posters and checklists for clinicians; (vi) workshop slides for training health workers; and (vii) monitoring and evaluation tool. These outputs are to be used at the point of care by diabetes and eye care clinicians, as well as by administrators and policy makers. They were chosen because they were perceived to increase convenience of users and to intensify user adoption of the guidelines. They are in English, but they can be translated. An executive summary of the guidelines is published in a separate paper [12].

Feedback from pilot-testing indicated that the guideline is useful in various clinical and geographic settings in the country. It served an educational role for clinicians and reduced missed opportunities for screening and referral. The demand for the print outputs continued after pilot-testing. The point-of-use outputs were reported to boost user satisfaction because they contained simplified key messages for different users. During prospective collection of feedback, the lack of a tool to guide integration of diabetes and eye care services has been identified as a gap, and its development is being considered.

Discussion

The process of DR guideline development in Kenya has taken several iterative episodes. This trajectory may reflect the intensive work that guideline adaptation entails, as well as the capacity building that has resulted over that process. This experience is not unique to this initiative; long timelines have been reported in other guideline initiatives in the same context [28]. Contextual factors such as transitions in the guideline development team or critical leadership may result in delays, repetition of effort, and modification of approach.

We did not experience a shorter time scale for adaptation compared to the 2–3 year period suggested for de novo development or shorter timelines for adaptation [29]. This could be because we did not conduct this guideline development process continuously and the team of experts had other primary engagements. However, it is evident that the adaptation approach also requires a heavy time commitment. From our experience, which concurs with the literature, it is an essential prerequisite to realistically determine the workload, resources, access to expertise, and the need for dedicated leadership [29].

The diverse expert skills and commitment of our multidisciplinary TWG are a recognizable success factor for our initiative. This is pertinent for both the internal and external validity (generalizability) of the guidelines [4, 17]. As adaptation requires significant investment from this team, the selection of potential TWG members is a pivotal priority step. Kenya being one of the countries with facing health workforce crisis [30], the major drawback we faced was availability of the TWG members to attend face to face meetings, as they had competing clinical and managerial responsibilities. This was predictable and inexorable, necessitating strategies to ensure group functioning was not interrupted.

The integrative participation method, which allowed both in-person participation and remote participation of the working group, helped to mitigate this constraint. This may have provided impetus to the process and achievement of the outcome. The enabling factor was that both electronic communication and face-to-face meetings were feasible, allowing for flexible engagement.

Involving patients in the process of guideline development is recommended [1, 29], because their opinions about the process of investigation and treatment and their outcomes are often quite contrary to the views of professionals. The lack of practical methods for engagement of PLWD precluded it. Although there are resources to guide this, such as the toolkit from Guideline International Network [16], local literature or precedence to guide such a process is lacking. Despite invitation of patient representatives to attend meetings and to review the drafts, we did not get this direct input. This may be because this type of involvement is not instinctively consistent with patient expectations or felt needs in our setup. Recruiting diverse groups of PLWD in a representative manner in a setting without comprehensive databases also requires contextual strategies. These limitations call for further local research.

We found that the guideline adaptation had the pattern of back and forth interlinked steps. We did not follow the ADAPTE steps sequentially as a stringently linear progressive and prescriptive tool. Further, even with the use of methodological tools, we found that there is need to maintain focus so that the process is not staggered. Clarity of the scope and significance to the patient pathway helped to maintain focus and continuity. Focus

helped to avoid attrition, considering that universal completion of guideline development is not the norm [1].

Similar to de novo development, adaptation requires a review of the evidence and explicit use of valid evidence [15]. It would have enriched the process if we had additional domestic evidence. There is need for local research to fill gaps in scientific knowledge regarding interventions for DR in this population and health system. Local evidence on economic analysis such as cost-minimization and cost-utility evidence of the interventions is also necessary.

Adaptation itself has cost implications, and although we did not have a large dedicated budget for the process, we found it important to have a budget for the variable costs. In the absence of funding for fixed costs, we cannot provide an estimate of the funding required. Such estimates would help to calculate the cost-effectiveness of the process, considering the opportunity costs, and comparison with the cost of de novo development. The interventions described in the guidelines are clinically effective, but we need to investigate whether these interventions and the process of guideline development are also cost-effective in our setting. At present, we assume that guidelines augment the efficiency of DR services and optimize value for every shilling invested in the health system. In order to balance cost and accessibility of services, the guidelines promote the use of existing resources while aspiring to progressively mobilize the range of resources that are recommended.

National guidelines for various conditions may contain conflicting recommendations, which can be confusing for clinicians. This is especially the case for PLWD, as they often have comorbidities. We avoided such discrepancies by reviewing the other diabetes-related guidelines, and we recommend this as an important step in adaptation.

The output from the adaptation process is a guideline that is different from the generic guidelines (or source guidelines) and contains additional information that will be useful for the target user. An additional benefit is the production of additional tools for use at the point of care. This shows that the role of guideline adaptation is not limited to endorsing generic recommendations.

This initiative has coincided with other DR activities, such as the initial steps towards implementing regular retinal screening for PLWD attending diabetes services. This may have contributed to its success, and we can further leverage on this to market the guidelines. Given that countries in the African region, particularly the Eastern, Central, and Sothern African region may face similar needs to develop guidelines, a network or collaboration of sharing and learning may be an efficient approach to develop them.

Conclusions

Guideline adaptation is a structured investment -intensive process that is feasible at the country level. Rigor and focus are important in this process. The ADAPTE process and AGREE II instrument are valuable tools for this process, though it would be helpful for the generic guidelines to have an adaptation template for other contexts.

Multiple informational, technological, economic, social, and professional variables influence the effectiveness of guideline adaptation. Beyond the utility of this process in producing the outputs we required, it could also be useful to inform the development of other guidelines in similar contexts. Our experience has helped to provide insights on the use of the adaptation methodology in the African context. We have also identified guideline development as a potential area for collaboration.

Involvement of the end user of the guidelines (diabetes and eye health clinicians) in this adaptation process aims to increase adherence to the guidelines. We expect that DR services that were not routinely available to PLWD in Kenya will now become accessible as a response to the guidelines.

Implications for practice

Availability of a national guideline is a necessary but not sufficient impetus to standardize patient care. The extent to which the prevention of blindness from DR is realized will depend on the effectiveness of guideline dissemination and implementation, in tandem with other interventions.

Future research

An economic analysis is required to determine whether guideline adaptation is cost-effective. Research evidence is also required to determine the effective methods of involving patients, such as DR patients, in the adaptation process. In addition, the effectiveness of the guidelines in reducing DR blindness will need evaluation.

Additional file

Additional file 1: Search strategy for "Adapting Clinical Practice Guidelines for Diabetic Retinopathy in Kenya" (PDF 568 kb)

Abbreviations

ADA: American Diabetes Association; AGREE: Appraisal of Guidelines for Research and Evaluation; COGS: Conference for Guideline Standardization; CPG: Clinical practice guideline; DM: Diabetes mellitus; DR: Diabetic retinopathy; ICO: International Council of Ophthalmology; IOM: Institute of Medicine; PGEAC: Practice Guidelines Evaluation and Adaptation Cycle; PIPOH: Population, Intervention, Profession, Outcomes, Health care system; PLWD: People living with diabetes; TWG: Technical Working Group

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Availability of data and materials
The data that support the findings of this study is available from the Ophthalmic Services Unit, Ministry of Health, Kenya. The data is available from the authors upon reasonable request to the corresponding author and with permission of the Ophthalmic Services Unit, Ministry of Health, Kenya.

Authors' contributions
NM drafted the manuscript, and had the responsibility for the decision to submit it for publishing. NM, SG, MGi, LM, CB and AF conceptualized the design. All authors except CB and AF were members of the Technical Working Group that collected data. All authors participated in interpretation of the data and critically reviewed the manuscript. NM revised the paper in consideration of feedback from co-authors. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Journal of Ophthalmology of Eastern Central and Southern Africa		
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Student Signature: Nyawira **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] Date: SEPT 17, 2019

Clinical guidelines for diabetic retinopathy in Kenya: an executive summary of the recommendations

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ABSTRACT

All persons living with Diabetes Mellitus (DM) have a lifetime risk of developing Diabetic Retinopathy (DR), a potentially blinding microvascular complication of DM. The risk increases with the duration of diabetes. The onset and progression of DR can be delayed through optimization of control of blood glucose, blood pressure and lipids. The risk of blindness from DR can be reduced through cost-effective interventions such as screening for DR and treatment of sight-threatening DR with laser photocoagulation and anti-VEGF medications.

Several factors make it important to provide guidance to clinicians who provide services for diabetes and diabetic retinopathy in Kenya. First, the magnitude of both DM and DR is expected to increase over the next decade. Secondly, as the retina is easily accessible for examination, the early signs of retinopathy may provide clinicians with the first evidence of microvascular damage from diabetes. This information can be used to guide subsequent management of both DM and DR. Thirdly, there are notable gaps in service delivery for the detection, treatment and follow-up of patients with DR, and the services are inequitable. Strengthening of service delivery will require close collaboration between diabetes services and eye care services.

Following a systematic and collaborative process of guideline development, the first published national guidelines for the management of diabetic retinopathy have been developed. The purpose of this paper is to highlight the recommendations in the guidelines, and to facilitate their adoption and implementation.

Key words: Clinical practice guidelines, Diabetic retinopathy, Kenya

INTRODUCTION

Diabetes Mellitus (DM) is a priority non-communicable disease that requires multidisciplinary care and continuity of care. Its prevalence and incidence is increasing in every country. According to the STEPwise survey[1] for risk factors of non-communicable diseases in 2015, DM affects an estimated 2% of the Kenyan population aged 18-69 years with the highest proportion (5%) being in the 45-59 years age group. Every patient with diabetes is at risk of potentially blinding ocular complications, particularly Diabetic Retinopathy (DR). In turn, visual loss from diabetic retinopathy is associated with additional morbidity, such as falls, fractures and difficulties with seeing and taking medications. Both DM and DR are silent diseases that patients may be unaware of until they cause complications. Clinicians attending to patients with these conditions have a role to reduce the associated morbidity, disability and mortality.

Diabetic Retinopathy (DR) is the leading cause of blindness in diabetes, and for this reason it warrants specific attention. It is estimated that a third of the people with diabetes have diabetic retinopathy, and one third of the latter (or 10% of those with diabetes) have vision threatening DR[2]. Early signs of retinopathy or maculopathy in a patient with diabetes, identified on retinal examination, may be the first evidence of generalised microvascular damage from poor control of diabetes. This information would be very useful in planning subsequent holistic management of the patient. There is therefore need to strengthen links between eye care services and diabetes services.

The risk factors for DR include both modifiable and non-modifiable factors. Epidemiologic studies have identified the non-modifiable risk factors to include increasing duration of diabetes and genetic factors[2,3]. The leading modifiable risk factors include poor control of blood sugar, poor control of blood pressure and dyslipidaemia[2,4-6]. Service providers need to pay attention to these factors, as well as to other lifestyle factors associated with diabetes in order to delay onset or progression of DR. These are interventions for primary prevention of blindness from DR.

Stronger service delivery for DR is required within the existing health system[7-9]. Currently there are notable gaps in the screening, diagnosis, referral, treatment and follow-up. Although screening for DR and laser treatment are cost-effective interventions for prevention of blindness from DR[10], there are inequities in access to them. Some of the services are underutilised and of insufficient quality. DR guidelines and use of clinical guidelines is an important step towards ensuring that all people with diabetes have access to quality DR services.

The purpose of these clinical practice guidelines is to give guidance regarding screening and diagnosis of DR, management of diabetes as it pertains specifically to DR, and treatment of DR. These guidelines apply to all patients with type 1 or type 2 diabetes who are at least 12 years old, who receive care at the primary, secondary or tertiary level of the health system. They should be used by health workers providing diabetes services and eye care services, as well as by administrators and policy-makers who plan for the resources for these services.

METHODOLOGY FOR GUIDELINES DEVELOPMENT

The development of these guidelines was a systematic, widely consultative process guided by an expert technical group over a lengthy period and involving many stakeholders. The process was guided by the use of several toolkits and guidelines which include: ADAPTE toolkit[11], PGEAC framework[12], AGREE 11 instrument[13] and WHO handbook for guidelines development[14].

The guidelines were adapted from existing relevant standards and guidelines, particularly the American Diabetes Association standards for medical care in diabetes[15] International Council of Ophthalmology guidelines for diabetic eye care[16] Canadian Diabetes Association's retinopathy guidelines[17] and the Royal College of Ophthalmologists' diabetic retinopathy guidelines[18]. The following guidelines were also reviewed, and the recommendations are in line with their provisions: Kenya national guidelines for management of diabetes[19], Kenya national strategy for the prevention and control of non-communicable diseases[20], and International Diabetes Federation's diabetes eye health guide for health professionals[21]. The adaptation strategy was chosen instead of de novo development in order to avoid duplication of effort, to use the available resources cost-effectively and to facilitate customization of the guidelines to reflect local context. These guidelines were identified through a literature search followed by application of the AGREE 11 instrument to evaluate the quality of the guidelines. Previous drafts of local DR guidelines were also reviewed. Care was taken to ensure that the guidelines are evidence-based, locally applicable, of high quality, and that the process of adaptation was consultative. The guidelines were subjected to external review by a multidisciplinary team as well as pilot-testing in various health facilities.

The process of guideline development is discussed in detail in a separate paper.

Key messages

1. Stronger service delivery is needed for People Living with Diabetes (PLWD) in Kenya in relation to DR. There is need to develop strong links between diabetes services and eye care services within the existing health system.
2. Blindness from DR is avoidable, but only if diabetes care givers and eye health professionals perform their roles in ensuring early detection and treatment of DR.
3. Screening is important for early detection of treatable diabetic retinopathy. It is also a cost-effective intervention for reducing blindness from DR. All patients with diabetes aged 12 years and above should have a retinal examination (usually a dilated eye examination or a retinal photograph) once a year or more frequently if recommended by the eye specialist.
4. Consistent and appropriate metabolic control reduces the onset and progression of sight-threatening diabetic retinopathy.
5. Laser photocoagulation therapy, local intraocular pharmacological therapy and surgery reduce the risk of significant visual loss.

Recommendations

Domain: Strengthening links between diabetes services and eye care services at primary, secondary and tertiary level of care

1. All health workers providing diabetes services should raise awareness of PLWD on diabetic retinopathy and support them to access eye examination (Panel 1).
2. The health worker attending to a PLWD at any health care level should use a checklist (Panel 2) to identify whether the patient has had a retinal examination in the preceding 12 months. Any patient who has not should be referred to the nearest facility for screening for DR.

3. The screening examination for DR should be performed by trained personnel (health care worker, eye care workers or technicians) and should consist of a minimum of:
   a. A retinal examination appropriate for DR, which would include dilated direct or indirect ophthalmoscopy, slit lamp bio-microscopic examination of the retina or retinal photography.
   b. Visual acuity test using distant and near charts. If the visual acuity is reduced, then pin hole test is also performed."
4. All PLWD require follow up, therefore service providers in both eye clinics and diabetes clinics should encourage compliance with follow-up.
5. A service charter for diabetes services and eye care services should be available in all clinics offering these services to inform PLWD of the minimum care they should expect and to highlight the importance of yearly comprehensive risk assessment including dilated eye examination.
6. The ophthalmologist and the physician/diabetologist/endocrinologist will provide clinical governance as the team leads for diabetes services and eye care services. The clinical governance team would also include: (a) liaison diabetes nurse (from the diabetes clinic), (b) liaison ophthalmic nurse (from the eye clinic), (c) designated medical records officer and (d) a biomedical / equipment maintenance technician.
7. The physician/diabetologist/endocrinologist and the ophthalmologist would be responsible for oversight on the screening for DR, training of health workers and data management.
8. The Ophthalmic Services Unit would be responsible for clinical governance for DR services at national level.
9. Data would be systematically collected in both diabetes clinics and eye clinics. The liaison nurse in the diabetic clinic and eye clinic would forward the captured data to the designated records officer for reporting.
10. The Ophthalmic Services Unit would coordinate the use of this data to inform decisions on service improvement strategies.

Panel 1: Key messages for health workers attending to PLWD

1 in 3 of patients with diabetes has diabetic retinopathy. Act to save their vision today!

1	Send all newly diagnosed patients with diabetes for a baseline retinal examination.
2	Ensure all patients with diabetes have an annual retinal examination.
3	Refer any patient with diabetes who has poor vision to an eye specialist urgently.
4	Do not wait for visual loss to refer patients with diabetes to an eye specialist- 'prevention is better than cure.'
5	Glycated hemoglobin (HbA1c) is a good indicator for long-term sugar control and should be done at least annually for all patients. Good glycemic control prevents or delays diabetic retinopathy.
6	Assess for other end organ damage- oral examination, diabetic foot review, renal and cardiac function, tests for neuropathy at least annually
7	Assess for hypertension, hyperlipidemia and other co-morbidities as these may impact negatively on diabetes and diabetic retinopathy.
8	Send all pregnant patients with diabetes for a retinal examination at least each trimester and post-delivery, or more frequently if recommended by the eye specialist.

Panel 2: Checklist for screening for DR

Patients name: ……

Date of birth: ……

Date of screening: ……

Duration of diabetes: ……

Have you ever had an examination of the back of the eye (either a photograph was taken or drops were instilled into the eye before examination)?
a. YES b. NO

How long ago was the last examination of the back of the eye?
a. < 12 months b. ≥ 12 months

Where was the eye examination done? ..... facility

Recommendation: ……
Have an eye check: as soon as possible / in the next ……. months at……. health facility

Domain: Eye examination for DR

Annual dilated and comprehensive eye examination is recommended for all patients with diabetes, aged 12 years and above, starting at the time of diagnosis of diabetes mellitus, unless the eye specialist recommends a different frequency. For type 1 diabetes, an eye exam should be done at diagnosis, at 5 years of diagnosis and annually thereafter.

Domain: Patient-centred care

1. Health workers should provide verbal and written information on diabetes, diabetic retinopathy, and on the health care that is needed, including self-management.
2. All PLWD should receive regular and individualised self-management support on healthy diet, appropriate physical activity and weight reduction if they are overweight. All smokers should be encouraged to quit smoking.
3. Patient education materials such as posters, leaflets, booklets and flyers on DR should be available (Panel 3) to patients and to peer support groups.
4. Diabetes support and structured self-management education should also be provided to family members of PLWD.
5. PLWD should be treated with dignity and involved in decision-making for their care. The results of their examination and the implications should be explained to them, and they should be encouraged to ask questions. The presence of co-morbidities should be taken into consideration in the care of each patient.

Panel 3: Key messages for patients

DID YOU KNOW THAT DIABETES AFFECTS THE EYES?
What can you do to prevent blindness?

1	Diabetes mellitus is marked by high sugar levels in blood. High blood sugar destroys small blood vessels in the body including those at the back of the eyes, leading to a condition called diabetic retinopathy.
2	Damage to the eyes is slow, painless, gets worse with time and finally leads to blindness if not treated in good time.
3	The damage to the eyes needs to be detected early, before permanent damage occurs.
4	An eye check by an eye specialist can detect damage to the eyes before symptoms develop. During the examination, the eye specialist will check vision, and instil an eye drop to assess the damage in the eye. Both eyes need to be examined.
5	For prevention and treatment of diabetic retinopathy, the eye specialist may advise on sugar, blood pressure, and lipid control.
6	For treatment of diabetic retinopathy, the eye specialist may perform laser or administer injections in the eye or perform eye surgery.
7	All persons with diabetes should have their eyes checked once every year by an eye specialist, even before any symptoms or poor vision develop or as frequently as recommended by the eye specialist.
8	A child with diabetes should have the eyes checked annually from the age of 12 years, or more frequently if recommended by the specialist.
9	A pregnant mother with diabetes should undergo an eye check by an eye specialist at least once every trimester, and soon after delivery, or as frequently as recommended by the eye specialist.
10	If the eyes are found to be normal at your eye check by an eye specialist, please continue with an eye check annually. If you notice any abnormality with your eyes, visit the eye specialist as soon as possible.

Domain: Metabolic control

1. All PLWD should be asked about the level of control of glucose, blood pressure and lipids.
2. To prevent the onset and delay the progression of diabetic retinopathy, people with diabetes should be treated to achieve optimal control of blood glucose.
3. Regular monitoring of blood sugar at home should be encouraged.
4. Regular monitoring of blood pressure in a health care setting or at home should be encouraged. Target blood pressure is 140/90 mmHg. Drugs blocking the Renin-Angiotensin System (RAS) may have benefits, particularly for mild retinopathy, but should be discontinued during pregnancy.
5. A comprehensive biochemical profile (risk assessment) should be done at least annually, and include fasting lipid profile, HbA_{1c}, urine microalbumin among other tests.
6. Aim for a target glycosylated haemoglobin (HbA_{1c}) of <7%.
7. Serum fasting lipid profile should be assessed at diagnosis and annually. Consider statins in primary and secondary prevention of DR but discontinue statins in pregnancy.

Domain: Pregnancy

1. All female PLWD of reproductive age should be asked if they are pregnant.
2. Patients should be assessed for diabetic retinopathy before pregnancy, at least once every trimester of pregnancy, as well as within 6 months after delivery or more frequently if recommended by the eye specialist.
3. Statins and angiotensin inhibitors should be discontinued in patients who are planning for pregnancy.
4. All women of child-bearing age who have diabetes should be educated that pregnancies should be planned.

Domain: Screening programs for DR

1. All PLWD should be screened for DR at least once a year, irrespective of whether they have ocular symptoms or not.
2. Screening programs can utilise whatever screening method is available (ophthalmoscopy, slit-lamp bio-microscopy and retinal photography), and should be conducted by a suitably trained person. Pupil dilation is recommended. Visual acuity should be assessed before pupil dilation.
3. Photography based screening
   a. Where a fundus camera is available, ideally the fundus camera should be located in the diabetes clinic.
   b. Fundus photographers should be trained to identify cataract, other causes of media haziness and glaucoma on the images. Patients who have these pathologies should be referred to an ophthalmologist. Ultrasonography may be useful in assessing the posterior segment in the presence of cataract or vitreous haemorrhage.
   c. Regular retraining in form of short courses (either online courses or standard contact courses) should be provided for screeners.
4. The following patients should be referred to an ophthalmologist:
   a. Where the screening examination is unsuccessful, or the results of the visual acuity test or retinal examination are unclear
   b. Where the retinal examination is unsuccessful, for example due to additional pathologies
   c. Any grade of retinopathy, except mild non-proliferative retinopathy
   d. Visual acuity worse than 6/12 and all patients with ocular symptoms
5. Screening should identify true positives (patients with DR). For this to be achieved, it is important to use the correct equipment, adhere to the standards of practice, make correct diagnosis and have a quality assurance mechanism. The guidelines for quality assurance are provided as an addendum to the guidelines.
6. All health workers have a role in ensuring patients undergo screening. All health workers should also document and collect data on screening activities, as the data is useful for planning and monitoring services. Health workers at each health facility will collect this data using standard monthly data collection forms. The Ophthalmic Services Unit in the Ministry of Health will coordinate the collection of data.

Domain: Diagnostic evaluation of patients at the eye clinic

Once the person with diabetes has been referred to an eye specialist, he or she should undergo a complete ophthalmic assessment. Ophthalmic evaluation by an eye care worker is available at the secondary level of the health system. This should include taking medical history, assessing visual acuity, and identifying and grading DR or Diabetic Macula Oedema (DME), using standard procedures described in the guidelines.

Domain: Referral pathway

Once a decision for referral for evaluation or treatment has been made, it should be carried out as soon as possible. The nearest health facility offering DR services will be identified (mapping of services has been conducted, and this information is provided as an addendum to the guidelines), and patients will be referred to reach the facility on the designated days that the services can be provided.

Domain: Treatment interventions

The ophthalmologist will make the final diagnosis and the decision on the treatment that the patient should receive. There is evidence from Cochrane systematic reviews included in Panel 4 to support the use of laser photocoagulation in proliferative diabetic retinopathy[22] anti-VEGF injections in diabetic macula oedema[23] and intravitreal steroids in refractory diabetic macula oedema[24]. Laser or intravitreal injections can be administered by the ophthalmologist at secondary level. Surgical interventions for DR will be provided by the vitreo-retinal surgeon at tertiary level. Practical information on these procedures is provided in the guidelines.

Panel 4. Evidence from Cochrane systematic reviews for Interventions used to treat diabetic retinopathy.

Laser photocoagulation is beneficial in reducing the risk of severe visual loss and the risk of progression 12 months after treatment in patients with proliferative diabetic retinopathy compared to no treatment or deferred treatment. However most trials here are old and the quality of evidence is judged as low[22].

There is very low or low quality evidence from randomized controlled trials that anti-VEGF injections are effective in patients with proliferative diabetic retinopathy but they prevent intraocular bleeding[25].

There is high quality evidence that anti-VEGF injections are effective in preserving and improving vision in patients with diabetic macula oedema compared to grid laser[23].

Intravitreal steroids delivered either by injection or implants may improve visual outcomes in patients with persistent or refractory diabetic macula oedema but it is unclear whether they are beneficial in other earlier stages[24].

Domain: Follow up

All PLWD screened for DR will require follow up. The frequency of follow-up depends on the clinical findings, and the grading/severity of DR, as described in the guidelines.

Domain: Patients with low vision

Refer the patient with low vision (best corrected visual acuity of <6/18) for rehabilitation. PLWD who would benefit from counselling and social services should be referred as appropriate.

Domain: Monitoring DR services

Specific process and outcome indicators will be used to monitor services on a quarterly basis at each level of service delivery, using the hospital health management and information system. Health workers at each health facility will therefore collect this data using standard monthly data collection forms. The Ophthalmic Services Unit will coordinate the collection of data. The indicators of interest are listed in the guidelines.

CONCLUSIONS

Patients with diabetes require specific care relevant to diabetic retinopathy, which includes patient education, screening, referral, treatment and follow-up. These are the first published national clinical practice guidelines for the screening and management of diabetic retinopathy. Their goal is to ensure best practice throughout the whole pathway from primary care to tertiary care. Implementation of the guidelines has potential to reduce blindness from DR.

The Working Group welcomes feedback from all users of these guidelines. In particular, data on the enablers and challenges experienced in the use of the guidelines would be very useful in informing revisions on the guidelines. Please email feedback to the Ophthalmic Services Unit, Ministry of Health, through ophthalmicserviceske@gmail.com.

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Chapter Six

Health system strengthening: The development of an open online training course on control of DR

6.0 Overview

The unavailability of educational opportunities for health workers providing care to people living with diabetes (PLWD) hampers the capacity of the workforce for control of DR (chapter three). Health systems strengthening through health workforce capacity building is therefore a critical factor for expanding availability of comprehensive DR services. Online courses provide a useful model allowing flexible access to training for health workers providing services in different institutions while minimizing work-place disruption. Although much attention has been given to the number and distribution of health workers, little focus has been directed at developing models of training that address these real-life workplace needs.

This chapter describes the experience and lessons learnt from developing an online course to strengthen capacity of health workers in Kenya to deliver services for DR. Section 6.1 highlights how online learning may address the needs for continuing education for health workers. Section 6.2 describes the role of mentorship in the development of the course. Section 6.3 and 6.4 describe the systematic process of course development following the theories of instructional design and adult learning. The course will be launched in late 2019 and the implications are discussed.

6.1 Online learning for continuous professional development of health workers

Continuous professional development (CPD) is required because preservice training alone is not sufficient to keep health workers equipped to respond to the rapidly evolving changes in health care.[1-3] Importantly, CPD has been linked to professional competence, health worker motivation and job satisfaction.[4, 5]Traditional forms of CPD include educational meetings with face-to-face contact, such as conferences, symposia and workshops, but the literature points out numerous challenges. These include difficulties juggling clinical workload and time-off for CPD, especially with inflexible CPD sessions that do not consider work commitments.[1, 6, 7] In low-resource settings, where the need for training and CPD may be highest, the limited CPD sessions available often occur off-site, in urban areas, at tertiary training institutions or central teaching hospitals. For those living remotely, the expenses in terms of registration fees, accommodation and transport are often prohibitive.

Online learning can enhance education experience, support professional development, ease time constraints, overcome geographic limitations and offer greater flexibility in CPD.[8] Online platforms for CPD may enable care providers to remain at their place of employment while continuing their education.[7] Richmond et al in their systematic review found that online methods may be as effective as alternative methods for training health workers.[9] Such platforms are gaining in popularity because of their relatively low costs, high flexibility, and reduced dependence on geographical or site boundaries.[10] Studies have shown that online CPD opportunities are acceptable across a diverse group of health care workers in sub-Saharan Africa.[6, 11]

Despite these benefits, there are also barriers to the use of online CPD such as cost of developing programmes, possible technology problems, lack of computers, lack of continuous

internet and data costs. Sub-Saharan Africa has a lower level of internet use than other regions, but this is rapidly changing in East Africa.[12] Kenya is one of the countries with the highest smart phone penetration and mobile adoption.[13, 14] This presents an opportunity for online CPD learning to take place. However investment in developing CPD courses is a complex undertaking, this is likely to remain a significant barrier.[15] Documenting experiences related to course development would therefore be of interest to policy makers, medical educators, regulators and front line workers involved in designing or supporting implementation of CPD interventions.

Developing CPD courses is particularly pertinent in the subject of diabetes eye health because of the dynamic epidemiology of diabetes-related vision loss, and the technology and competencies required for addressing it. [16-18] Studies from Africa have reported insufficient training about diabetes, on specific procedures such as examination of the retina (fundoscopy) and on the management of DR.[17] In addition, the recent advances in knowledge and technology in the field of diabetes eye health will only offer benefits to PLWD if health workers remain up to date in the field. At present, there is a paucity of local online CPD courses on this subject. However, there is evidence from a free online course '*Global Blindness: Planning and managing eye care services*' that appropriately designed online courses can deliver training at scale, support educational capacity building and impact health practice in LMICs.[19] Another major weakness is the insufficient information on how the few courses available were developed, the contextual factors considered and the instructional design methodology used.[9, 15, 20]For that reason, the existing literature does not adequately advance an understanding of how courses can be developed, hence failing to promote interpretation and replicability. To address this gap, the process of developing this open online course on control of DR, and the lessons learnt from this process are described in this chapter.

6.2 Adult learning theory

In order for knowledge transfer to translate into effective CPD for health workers, there is a need to leverage adult learning theories, because they provide the conceptual frameworks for the acquisition of knowledge, skills, and attitudes to achieve behaviour change.[21] Adult learning theories hold a set of assumptions about how adults learn and emphasize the value of the process of learning. They postulate that adults are independent and self-directing, have prior knowledge and experience, apply learning to real life, are interested in problem solving and have internal motivation for learning.[15, 22, 23] Although the theories were developed for traditional classroom education, the basic principles effectively transfer to the online learning environment. Online CPD programmes take into account these principles through integrating the following factors: - voluntary participation, autonomy of learning, self-pacing, mutual respect, reflection, collaboration and responding to emergent learning.[7, 24] Examples of how these approaches were applied in the development of the course are provided in the sections below.

6.3 The ADDIE instructional design framework

The use of an instructional design framework in course design helps to ensure that the process is credible and transparent, and that the course is likely to be relevant and effective in professional improvement.[25, 26] A literature search for evidence on effective models of online course development identified at least 30 models, but the ADDIE (acronym for Analysis, Design, Development, Implementation, and Evaluation) model is the most ubiquitous, with good evidence of its effectiveness.[27, 28] The framework was first used during the World War II when the United States military developed strategies for rapidly training people to perform complex technical tasks.[29] It has remained the most influential instructional design framework in the

literature.[30, 31] It involves analysis of learning needs, the design and development of a curriculum, and the implementation and initial evaluation of the training programme.

The ADDIE framework has previously been used to design high quality educational programmes, both print-based and online.[32] It is particularly useful where the focus of the programme is targeted toward changing participant behaviour.[33] It takes into account learning theories, the learner's needs and context, and can be applied to teach knowledge, skills, or attitudes.[28, 30] In health and medicine, it has been used to design training interventions to change practice behaviours in the management of various medical conditions.[26, 28, 33-35]

6.4 Mentorship for course development

Improving clinical care rapidly, comprehensively, at large scale, and sustainably is a fundamental challenge for health systems.[36] Mentorship is an effective approach for developing knowledge and skills, and it could potentially be used to enhance knowledge transfer between researchers, educators and clinicians.[37] For example, mentoring can build the expertise and self-efficacy of mentees from LMICs to develop online courses.[38] However, little empirical research in healthcare settings has specifically described the application of mentorship for this purpose.[36, 37]

Insights from mentoring initiatives can inform the conduct of future mentoring initiatives to optimize chances of success. An overview of mentorship to develop this course within the UNESCO *Open Education for a Better World* (OE4BW) is documented and discussed below, so that future efforts towards developing similar mentoring programmes could draw from this learning and experience.[39] This is an international online mentoring programme run by the United Nations Educational, Scientific and Cultural Organization (UNESCO) to unlock the

potential of open education in achieving the United Nations' 2030 Sustainable Development Goals (SDGs).[40] Mentees develop course materials that address one or more SDGs, finding a solution with impact on society and ensuring quality of the course materials. The mentor's role is to advise on the design of the course, and to ensure that the course is supportively but critically reviewed. At the end of the six-month mentoring period, the mentees and mentors attend a face-to-face workshop organized by UNESCO to present the outputs and lessons learnt. The formal mentoring structure provided by UNESCO ends at six months, but mentoring may extend post-programme, given that courses often take a long time to develop. Some mentoring programmes have reported difficulty maintaining the mentoring relationship during this transition period, but I did not experience this.[41] UNESCO provides a website to host information on the course and mentorship.[40] This is particularly helpful because it helps to form a community of practice for professional networking.

6.5 Developing the online course on control of DR using the ADDIE framework

Figure 6-1 depicts the conceptual model of the five phases of the ADDIE framework as operationalized in the development of this course. The analysis, design, development and implementation phases are cyclical and iterative. Each phase depends upon the successful completion of the preceding phase.[26] Formative evaluation provides feedback specific for each phase, facilitating refinement of the outputs.[25] Table 6-1 shows the tasks and outputs in each phase. Experts on diabetes, ophthalmology and medical education reviewed the outputs from each of the phases for quality assurance.

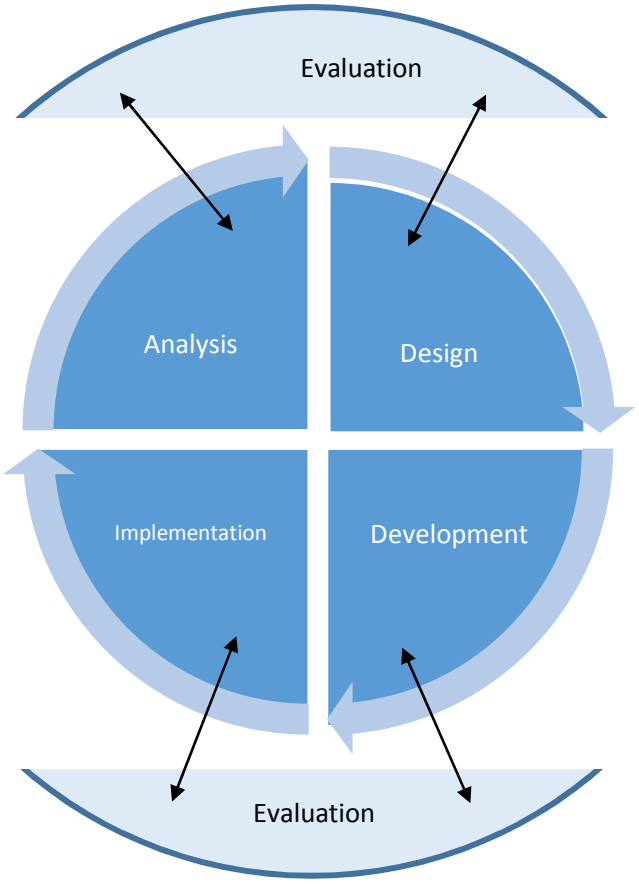

Figure 6-1: Conceptual model of the ADDIE framework as applied in the development if this course

Table 6-1: Tasks and outputs within the ADDIE framework in this course

Phase	Sample tasks	Sample outputs
Analysis Defining what is to be learnt	• Identification of target learners • Identification of needs and problems of target learners • Analyse subject field • Work with content experts to determine the content • Search for evidence • Search for materials	• Target learners identified • Description of current constraints • Current environment described • Course goal and objectives

	• Identify optimal methods of content delivery	
Design Determine the learning objectives and strategies	• Identify the learning theory • Identify the media for course delivery • Consult with subject experts • Identify the creative commons licence • Write objectives • Plan instruction • Identify resources • Identify course site • Vetting of design document by key stakeholders	• Measurable objectives • Instructional strategy • Product prototype specifications • Storyboard
Development Prepare course materials	• Work with multimedia team, content experts and instructional designers • Develop learning materials • Peer review • Work with institutional accreditation team	• Slides • Scripts • Videos • Graphics • Exercises
Implementation Course delivery	• Upload content on the course site • Testing the prototype • Official launch • Course advertisement • Support learners	• Course link • User feedback
Evaluation Formative and summative evaluation of the course	• Pre-course user survey • Post-course user survey • Monitoring course analytics	• Course analytics • Course evaluation reports • Revised prototype based on the evaluation

6.5.1 Analysis

The first step in course development is to analyse the need and context of the learners. The health system assessment (chapter three) provided the evidence on the need for the course. The literature provides evidence of other courses developed as a result of needs identified from health system assessment.[33] The health system assessment also identified the population (P) of interest for the training, the intervention (I), which is the development of the course, the comparator (C), which is the current situation with few educational opportunities. The expected outcome (O) of the course development endeavour is the availability of the online course and the achievement of the learning outcomes. This analysis phase also involved searching for the relevant published evidence (E) and setting a timeframe (T). The EPICOT format[42] provided the context for the course development, Table 6-2.

Table 6-2: EPICOT description for the Control of Diabetic Retinopathy course

Evidence	Online courses are acceptable and feasible in this setting, as described within this chapter
Population	Heath workers providing care for PLWD
Intervention	Development of a flexible course on eye health for PLWD, which will enable learners to understand eye health complications in diabetes, especially DR, holistic care for PLWD, the role of the health care provider in the care pathway and how to strengthen health systems
Comparator	The current situation, where training opportunities are few, for both service providers and trainers
Outcome	Availability of a free online course that can be used on mobile devices or computers
Timeliness	Course should be ready for launching by World Diabetes Day, 2019

The target population is the heterogeneous and multidisciplinary group of health care providers who provide services along the care pathway described in chapter three. The topic of focus was chosen to address the training needs identified in the health system assessment. The needs of the target learners, including the working environment, technological and economic needs were identified. Analysing these factors helps to ensure the relevance of the course within the realities of the health system.[12, 43] Over the long term, the course is expected to improve provision of DR services. Accreditation is an anticipated need, and this is expected to be provided through local training institutions in the future.[43] This is not easy to achieve, but experts from the two institutions that currently offer ophthalmology-related training in the country have reviewed the course materials, as a starting point for further engagement. In this way, health system strengthening (HSS) through development of an online course has potential to influence education services and health services, and support local institutions.[44, 45] It also shows the need for sustainability and evolution of HSS interventions over time, in response to local needs.[44, 46] However, this long-term impact of the course will need to be evaluated.

Although the course was developed for the local context, it was also intended to have an appeal to an international audience. As other researchers have documented, developing an online course from a LMIC is challenging because the audience might undervalue the quality of the course content, since the MOOC originated from an LMIC.[47, 48] To address this potential challenge, quality assurance through peer review from experts from a mix of income settings was planned. It is significant that institutions in LMICs offer only 3% of the health and medicine-related online courses, and this is partially attributable to this barrier to entry into knowledge production and curation.[49, 50] Another factor might be challenges related to weak health systems, where health workers are few and there is lack of time and incentives to

engage in knowledge production.[45] What is critical is that the unequal production and accumulation of knowledge is as worrying as the inequitable distribution of wealth and health.[48, 51] Academic and professional communities in LMICs may be missing opportunities to address this gap.

Subject matter analysis is essential to defining the content of a course. Experts (ophthalmologists and physicians) who are active in both clinical and training services were consulted and clinical guidelines on diabetes eye care were reviewed.[52-55] Based on this consultation, the literature review on the subject (chapter two), the gaps identified in the health system assessment as well as the standards set in clinical guidelines, there was consensus that the course should be organized in four units (Box 1). In consideration of the principles of adult learning, the course will be available throughout the year, to provide flexible access to learners.

A search for existing online resources identified a few courses relevant to diabetes eye heath, such as from the International Centre for Eye Health[56] and the International Diabetes Federation.[57] However these courses are only available during two or three runs in a year to participants who register, which is a limitation to access for the target population.[58] Using best practices to design, develop, implement, and evaluate courses designed locally can provide creative solutions to this accessibility gap.[43] At the same time, the local courses can include links to the external online courses, thus maximising access to all the available learning opportunities. The strategic linking of the course to other online courses offers an opportunity to expand the educational scope of this HSS initiative. This might also trigger the development of partnerships to offer additional courses.

Table 6-3 Course Units

Unit 1	Understanding the disease
Unit 2	Understanding the patient
Unit 3	Understanding the health care provider
Unit 4	Understanding the health system

6.5.2 Course Design

The contextual realities of the target learners were considered as design decisions were made. English was chosen as the preferred language because it is the language used in educational programmes in Kenya. Language appropriateness and tailoring materials to reflect country-specific health care realities in LMICs are crucial to successful CPD.[12] In addition, the use of English will reduce barriers to access by an international audience.[49, 58] The technological requirements for this course are access to a computer or a smart phone and internet connection. The course is designed to be compatible with all internet browsers at no cost to the learner, in order to promote access. In line with the principle of autonomy, participation is voluntary, self-paced, and without rigid deadlines, which allows learners to revisit the materials whenever they need to. Learners from LMICs are known to favour these attributes. [6, 47]

The instructional materials include different media elements such as text, graphics, images, research papers, and short .mp4 videos that are downloadable for offline use. Simplicity in course design and low technological demand are imperative given the uneven technological resources of learners.[15, 58] All videos are captioned and text description is provided for non-text visuals, to create engaging learning experiences for adult learners with different skill-sets,

interests or disabilities. Adult learners also learn better where they can see the immediate value and application of content, hence real world case scenarios are included. Useful hyperlinks to relevant external resources are also provided to facilitate autonomous exploration and curation, without overwhelming the learner with too many of them.[15] To allow the learners to reuse the materials, all the course materials are published under a creative commons licence.[59]

Social media use is integrated in the course design, since learners are likely to have used this strategy to accumulate experience in digital literacy, and this can stimulate active engagement of adult learners.[24] The course uses Google Drive and Dropbox to manage documents, Flickr for photographs, and Youtube for videos. Twitter and LinkedIn are used to connect with the course instructor. Pre- and post-course surveys will further enhance learner-instructor communication.

Open-source online platforms for hosting the course were investigated, and the free version of WordPress was chosen for the course website. WordPress has also been used before for educational purposes.[60] Some of the attributes of the platform are popularity with users, free access to learners, user-friendly content editing options, ease of administration, large variety of plugins, allowance to export content to other online platforms and opportunity for use on computers, tablets or smartphones. The setup of the website requires technical expertise, therefore it is recommended that a website designer be included in the course development team.[24]

Storyboarding is the systematic and iterative process where all the elements to be included in each unit are mapped.[30] Storyboarding is helpful for pointing out steps that might be overlooked in instructional sequence, and allows for modification of the course structure.[30, 32]

Storyboards shared with collaborators, such as mentors and web designers, enhance shared understanding. The storyboard was prepared on a Microsoft Word template, since it is predominantly text-based. Each of the four units is designed to take a maximum of 1 week if learners allocate 3-4 hours per week, which can be spread within the week. The course duration is four weeks. This is important because the most prevalent point of dropout from online learning occurs after week 4, which suggests that a four-week duration is more convenient for learners than longer courses.[58] Each unit is composed of several topics, which are chunked into short sections. This signposting makes it easier to navigate the course.[31] The stakeholders reviewed the outputs from the design phase (Table 1) for quality assurance.

6.5.3 Developing course content

The storyboards created in the design phase were used to develop learning materials. This process required thinking through each step of the storyboard, with an unexpectedly high investment in time and labour. Preparing content for each week took several weeks, and as other researchers have found, the time required and the opportunity cost are often underestimated.[50, 61] This challenge was overcome by dedicating blocks of time to content development, and working with mentors, in addition to utilizing the evidence synthesis and writing skills developed over the PhD. It is advisable not to underestimate the amount of workload involved, especially for course developers with other responsibilities.[47] Collaborative creation of course materials by a team of experts may alleviate this challenge, as the heavy workload can be shared.[12] However feasibility may be constrained by existing health workforce challenges in LMICs and course development may divert time from other activities such as service delivery, research, teaching or administration.[50] On the other hand, online courses may

enhance the effectiveness of the limited faculty.[12] This raises the question as to how best to calibrate participation such that LMICs contribute and gain from online learning.

Preparing instructional audio-visual content was challenging because it required access to studios, compressing the content into short lectures, recording in front of cameras and editing the multimedia materials. Like in other LMICs, access to resources and expertise for digital capture was limited at local level.[47] Once the slides and scripts were ready, the multimedia team at LSHTM filmed the narration and provided video editing services. Access to these institutional resources was an opportunity provided by being a student at the school and by linkage from the mentors. Building on such educational presence and networks is therefore pivotal to successful completion. Recording was challenging because speaking in front of a camera with no audience did not feel natural. In addition, listening to playback of my own voice was quite disconcerting, as the voice did not sound authentic. The literature reports similar experiences with digital production and these can potentially slow progress.[61] However mentorship helped to manage expectations and acclimatize to the experience, hence increasing efficiency.[37]

Developing course materials requires balancing the use of multiple formats to enhance usability and ensuring scientific accuracy and clarity.[15] Metadata such as an overview of the course and strategic instructions that have been provided at the start of the course help to enhance navigation. To facilitate comprehensibility, precise language has been used. Sentences have been formulated in a way that is not too abstract or scientific. The webpages are not text-heavy, as this often has an adverse effect on readability. Medical educators and subject experts have reviewed the materials and their suggestions for improvement, such as including definitions of important concepts, have been incorporated.

Adult learners are self-directed, so although the four course units are arranged in sequence, learners can complete the units in any order. Further, adult learners are goal and relevancy-oriented, so the practical application to the care of PLWD is emphasised. In order to provide for personalized learning, which is important for adult learners, 'to do' prompts, questions for reflection and links to optional resources are provided for those interested in deeper study of particular concepts. This enables learners to apply autonomy and personally select from a diverse array of actions. Other online courses have attempted to personalize learning through weekly course announcements and emails that may make learners feel more personally connected.[15, 60, 61] However, such a high level of personalization was beyond the scope and feasibility of this course, since it would require extensive instructor support all year round.

6.5.4 Implementation

The course content was uploaded to the WordPress course site: https://oerdiabeticretinopathy.wordpress.com/. The course instructor, the mentors, and a learning designer have done usability testing of the site on a variety of browsers and devices. Feedback from this usability testing helped to fix errors (duplicate pages and inactive hyperlinks) in navigation and improve user experience.

For the course to have acceptability among learners, it should be user-friendly and meet the expectations of the users. Pilot testing with users can be helpful to establish the content validity (the utility of the course for training on the different components of control of DR) and face validity (the appropriateness and relevance to real life needs of the users of the course).[62] For that reason, after testing usability the course was piloted by ten potential learners and ten potential instructors. They were asked to run through the course slowly, identifying unforeseen practical difficulties and providing feedback. Most of the feedback related to the format of the

website, and not to the content. In addition, users recommended accreditation and certification by an academic institution, which is not currently available but is planned for the future, as already discussed. Instructors recommended that such certification should be based on a pre-test and post- test scores so that educational effectiveness can be measured.

6.5.5 Evaluation

In each stage of the ADDIE framework, formative evaluation was constantly applied to identify limitations in course outputs (Table 6-1), and to modify them appropriately. Once the course is launched, learning analytics from the course site will be used to track learner engagement. In addition, Kirkpatrick's framework for evaluating training will be used to evaluate the effectiveness of learning on the course. This framework focuses on evaluation at four levels: immediate reaction to the training, learning obtained from the training, behaviour change and results (effect on the initial training gap).[63] The first two levels (reaction and learning) will be assessed using the post-course survey as well as pre-test and post-test scores. To evaluate the extent to which the course supports behaviour change in clinical practice, a questionnaire will be emailed to learners three months after the course. The effect on training needs and performance will be assessed in a subsequent needs assessment.

6.6 Potential challenges in running the online course

The literature reports a variety of barriers to implementation of online courses.[45, 47, 49, 50] These include existing norms and behaviours, the lack of appreciation of investment in online learning by the academic and health community, and lack of corresponding alignment of resources. The official launch of the course as part of the activities organized by the Ministry of Health for the World Diabetes Day 2019, and course advertisement through the mailing lists of

professional groups will promote engagement with learners and educators. This integration into local structures and processes is expected to facilitate local ownership and implementation of the course at scale in Kenya.[45]

An educational website needs to be maintained over time and content updated, if it is to be a sustainable solution.[15] The instructor will update content annually, and collaboration with institutions and the Ministry of Health will help to overcome the funding and opportunity costs. Other researchers have found that support for the long-term implication of maintaining, updating and upgrading the site is often overlooked, yet it is vital to the quality of the online courses.[12, 15, 50] Institutional and country-level support will be critical for sustainability.[36]

Adapting to the online environment can be a challenge for both learners and facilitators.[45] The WordPress interface used in this course is simple to use, therefore users are unlikely to experience technical problems with the site, however this will be monitored and technical support provided.[60] The popularity of WordPress increases the risk of academic fraud, viruses or breaches of data protection, but this is not considered a major concern as all the materials are open access.[60, 64]

Other researchers have reported the inherent challenges in the evaluation of online courses. For example, high dropout rates and the need to adjust for contextual factors affect the validity and complexity of assessment of online learners.[61, 65] These are challenges that the online course community must learn to overcome. Although there are no easy solutions, the use of diverse methods of evaluation in this course will provide evidence on the effectiveness of learning.[65] The long-term impact of these evaluation strategies will need to be evaluated.

As mentioned earlier, certification is an important motivator for learners in online courses in health and medicine in LMICs.[6, 49, 61] Assessments for accreditation will not be provided on the

platform, but through institutional websites once the course is accredited. Educational institutions accredit courses through a rigorous quality assurance, which will provide further quality assurance, in addition to the peer review already mentioned. The accreditation process is likely to be a time-consuming and complex process, which is a major challenge. However, the engagement of stakeholder institutions may provide an enabling environment.

6.7 Lessons learnt during course development

The learning gained from the PhD research was a significant starting point in terms of subject domain knowledge. Reflecting on the principles of control of DR gained from the PhD was a useful prompt for knowledge transfer within the health system. The potential impact of public health training on health system strengthening in LMICs has previously been examined.[66, 67] Given that health workers in Kenya also often work as educators in training institutions (chapter three), health service delivery and education are closely connected. Considering the unique demands of this dual role, it is important to understand how learning from a PhD might interact with the health system and the education context, thereby enhancing capacity for health system strengthening. This is of interest because success of training researchers for Africa should not only be measured by research outputs, but also by the ability to execute other programmes that will advance population health in Africa.[67]

Being a mentee from Kenya (LMIC) and my mentors being from other income settings provided rich diversity within the mentorship process. The diversity fostered access to learning from contrasting perspectives and led to a concrete conception of the detailed task of course development in the early stages of course development. This was useful because at the beginning I was unfamiliar with the online course design process, leading to underestimating the complexity of the design task. Mentorship illuminated the strategic opportunities, for

example, the digital technologies for online courses. It also allowed the recognition of contextual complexities that needed to be overcome, such as how to make a business case for free online courses, which is a nascent concept in LMIC training institutions.[47] In addition, mentoring helped to contextually apply theories of learning and theories of course design, either explicitly or implicitly, to the designing of the course.[68] The literature reports that interactions between foreign mentors and local researchers may create tension or conflicts due to variations in mentoring culture, but this was not experienced.[41, 69]

6.8 Conclusion

Reflecting on the synergy between the academic skills important in both PhD and course development can provide an understanding of the value that can be leveraged from a doctoral programme. The academic discourse around the potential contribution of PhD studies in African health systems is ongoing.[67] There is growing recognition that such training should provide the skills to apply theories to inter-relationships between health and other factors, such as education.[51, 70] In particular, doctoral researchers need to be agents of change and seek solutions to the challenges in education, research and health caused by scarce resources and other contextual factors. This is because they have the advantage of familiarity with local challenges, context-specific determinants, and the expertise to apply relevant global concepts to local problems. As an example, effective course development requires a facilitator who is familiar with the subject field and possesses the requisite expertise, which a PhD provides.[12, 62] There is potential for doctoral programmes to contribute to capacity building for the health workforce. This model can be replicated in other settings in sub-Saharan Africa with similar health workforce challenges.

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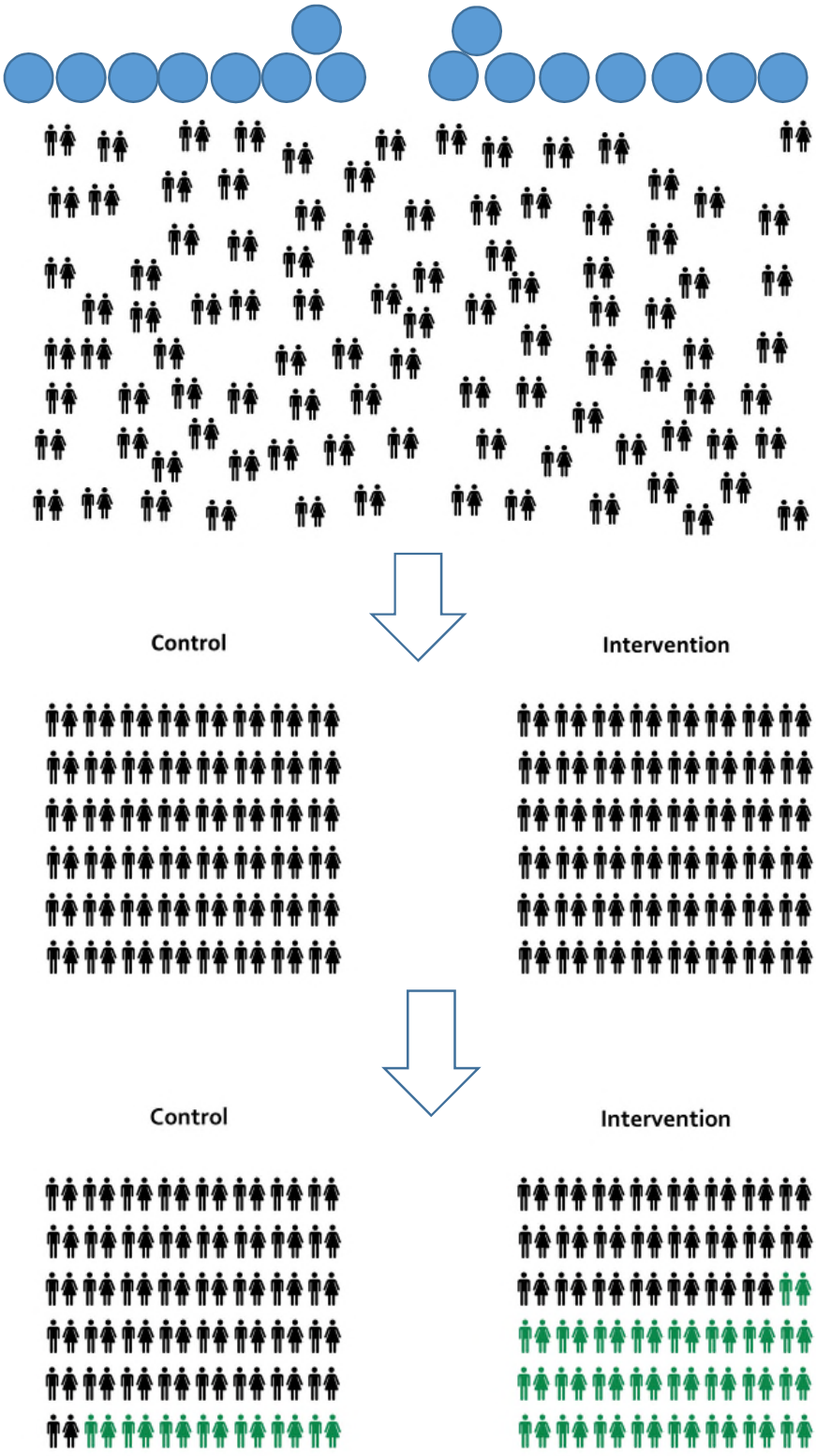
Section D

DURE Cluster randomized controlled trial

"I stand before you and the world humbled by this recognition and uplifted by the honor of being the 2004 Nobel Peace Laureate. As the first African woman to receive this prize, I accept it on behalf of the people of Kenya and Africa, and indeed the world. I am especially mindful of women and the girl child. I hope it will encourage them to raise their voices and take more space for leadership."

Prof Wangari Muta Maathai (1940-2011)

Environmentalist, professor of veterinary anatomy and political activist



16 clusters

104 PLWD (pilot trial)

734 PLWD (main trial)

Two arms (1:1)

Screening attendance

The DURE trial

Chapter Seven

Effectiveness of peer support to increase attendance at DR screening - a pragmatic cluster randomized clinical trial

Study protocol

7.0 Overview

A prospective cluster randomised clinical trial (RCT) was conducted to investigate whether a peer support can increase attendance to diabetic retinopathy screening (DRS). Members of diabetes support groups who have never had DRS were recruited into the study. Diabetes support groups were randomised on a 1:1 basis to one of the following arms: 1) Intervention arm, to receive a peer led health education intervention, in addition to usual care provided in support groups 2) Control arm, to receive usual care alone. The proportion of participants attending DRS was evaluated over a six months period.

7.1 Intervention development

The intervention was developed following the guidance provided by the United Kingdom Medical Research Council's (MRC) guidelines on developing and evaluation complex interventions.[1]

1. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655. https://doi.org/10.1136/bmj.a1655.

The MRC recommends that interventions are developed systematically, using the best available evidence and appropriate theory to understand the likely process of change. Interventions

should then be tested in a pilot phase targeted at feasibility objectives before full-scale implementation. A clear description of the intervention and a detailed report of both process and outcome evaluations of the trial are important to enable replication and synthesis of evidence. Figure 1 outlines the focus of each of the four phases of the trial, based on the MRC guidance.

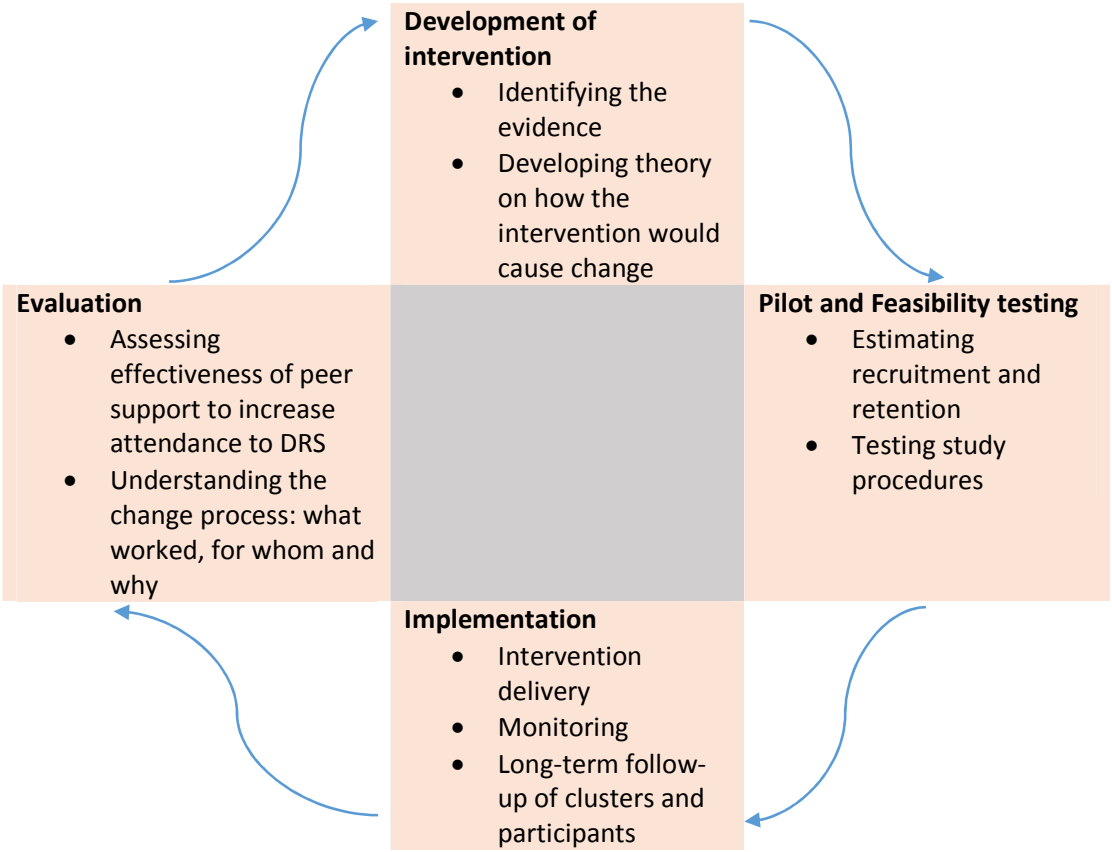


Figure 7-1: Development, piloting, implementation and evaluation of the clinical trial

Research paper 5 gives a detailed description of the methods for this clinical trial in Kirinyaga, Kenya. This paper was published in the journal BMC Implementation Science in December 2018 after peer review.

Subsequent chapters provide the results for the pilot trial (chapter 8), process evaluation (chapter 9) and outcome evaluation (chapter 10).

7.2 Research Paper 5

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Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

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Student Signature: Nyawira **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] Date: SEPT 17, 2019.

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BMC Public Health

STUDY PROTOCOL Open Access

Effectiveness of peer support to increase uptake of retinal examination for diabetic retinopathy: study protocol for the DURE pragmatic cluster randomized clinical trial in Kirinyaga, Kenya

Nyawira Mwangi[1,2*], Mark Ng'ang'a[3], Esbon Gakuo[4], Stephen Gichuhi[5], David Macleod[2], Consuela Moorman[6], Lawrence Muthami[7], Peter Tum[1], Atieno Jalango[8], Kibata Githeko[9], Michael Gichangi[10], Joseph Kibachio[11], Covadonga Bascaran[2] and Allen Foster[2]

Abstract

Background: All patients with diabetes are at risk of developing diabetic retinopathy (DR), a progressive and potentially blinding condition. Early treatment of DR prevents visual impairment and blindness. The natural history of DR is that it is asymptomatic until the advanced stages, thus annual retinal examination is recommended for early detection. Previous studies show that the uptake of regular retinal examination among people living with diabetes (PLWD) is low. In the Uptake of Retinal Examination in Diabetes (DURE) study, we will investigate the effectiveness of a complex intervention delivered within diabetes support groups to increase uptake of retinal examination.

Methods: The DURE study will be a two-arm pragmatic cluster randomized clinical trial in Kirinyaga County, Kenya. Diabetes support groups will be randomly assigned to either the intervention or usual care conditions in a 1:1 ratio. The participants will be 700 PLWD who are members of support groups in Kirinyaga. To reduce contamination, the unit of randomization will be the support group. Peer supporters in the intervention arm will receive training to deliver the intervention. The intervention will include monthly group education on DR and individual member reminders to take the eye examination. The effectiveness of this intervention plus usual care will be compared to usual care practices alone. Participant data will be collected at baseline. The primary outcome is the proportion of PLWD who take up the eye examination at six months. Secondary outcomes include the characteristics of participants and peer supporters associated with uptake of eye examination for DR. Intention-to-treat analysis will be used to evaluate the primary and secondary outcomes.

Discussion: Eye care programs need evidence of the effectiveness of peer supporter-led health education to improve attendance to retinal screening for the early detection of DR in an African setting. Given that the intervention combines standardization and flexibility, it has the potential to be adopted in other settings and to inform policies to promote DR screening.

Trial registration: Pan African Clinical Trial Registry PACTR201707002430195, registered 25 July 2017, www.pactr.org

Keywords: Diabetes mellitus, Diabetic retinopathy, Diabetes support groups, Retinal screening, Blindness, Health education, Self-efficacy theory, Peer-support, Kenya, Africa

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Background

The global prevalence of diabetes has escalated in recent decades, with important implications on the health system. In 2015 the International Diabetes Federation estimated that there were 415 million people with diabetes aged 20–79 years (global prevalence of 8.8%), and this is predicted to increase to 642 million by 2040 (global prevalence of 10.4%). [1] The incidence and prevalence of diabetes is increasing disproportionately faster in resource-poor regions and 75% of people living with diabetes currently reside in low- and middle-income countries. [1–3] This dramatic increase in incidence is occurring in both rural and urban areas. [4] The regional prevalence for Africa was 3.8% in 2015, and the number of people with diabetes in this continent is expected to increase by 140% between 2015 and 2040. [1] In Kenya, the STEPwise survey for risk factors of non-communicable diseases in 2015 found a diabetes prevalence of 2% in the population 18–69 years, and 5.4% in the population 45–59 years. [5]

All patients with diabetes are at risk of developing diabetic retinopathy (DR), the most severe and progressive ocular complication of diabetes. One third of patients with Type 2 diabetes have DR while 10% of them have sight-threatening DR, which represents a significant public health concern. [6, 7]. A population-based study in Nakuru county, Kenya found that 35.9% of people living with diabetes (PLWD) have DR [8]. Visual impairment and blindness from DR is preventable mainly through early detection and timely treatment. Since DR is asymptomatic until the advanced stages, regular retinal screening is of paramount importance. DR meets the Wilson and Jungner (1968) criteria for screening, and current clinical guidelines support annual screening [9–12]. Participation of PLWD in regular retinal screening, has been shown to be clinically effective in preventing blindness and is also cost-effective. [13, 14]

In developed countries, health systems have formal surveillance programmes for detection of DR. Kenya does not have a national population-based DR screening service where PLWD are systematically invited for screening, but opportunistic screening is available in various hospitals. Importantly, participation and re-participation rates in screening for DR are sub-optimal in Kenya and other resource poor settings. [15–22]. The determinants of the attendance to retinal examination are complex and include both supply and demand factors. [23, 24] For instance, a Tanzanian study found that PLWD also have limited awareness on diabetic retinopathy, particularly on the need for annual eye examination [25]. This is a barrier that appropriate demand side interventions could address. A health system assessment conducted before this study has shown that 87% of PLWD in Kenya have an unmet need for *annual* retinal screening. [22] One of the gaps associated with this is the lack of strong links between diabetes services and eye care services. There is need for context-specific pragmatic solutions to address this gap.

A systematic review of interventions to increase diabetic retinopathy screening attendance reported that several strategies are effective, including those targeting the patient (e.g. increasing patient awareness), the health care practitioner (e.g. improving adherence to recommendations) or the organization (e.g. improving patient records) [26]. Members of diabetes support groups (DSGs) are a population subgroup that might benefit from additional support to initiate screening, and adhere to re-screening. Targeting screening interventions towards PLWD in DSGs provides a timely opportunity for three reasons. Firstly this is a community resource that is already available in the community setting. Secondly this population is likely to consider health as an important rationale for behaviour change and the health seeking behaviour of members is potentially malleable to change through peer support. Peer support refers to the provision of emotional and informational support from a created social network member who is considered an equal and who has characteristics similar to the target population. [27] Thirdly it is an economical, culturally-sensitive and flexible intervention for improving diabetes care and outcomes. [28, 29]

Self-efficacy is a direct predictor of health behaviour, according to the social cognitive theory and the self-efficacy theory [30] [31]. Self-efficacy is a predictor of uptake of screening for DR among PLWD. [32] Interventions that improve patients' self-efficacy decrease perceived barriers and improve the likelihood of initiating the desired health behaviour. There are four main sources of self-efficacy [31]: (i) Successful performance accomplishments (e.g. having attended a previous eye examination) (ii) vicarious experience (e.g. learning that peers have successfully attended an eye examination) (iii) verbal persuasion (e.g. encouragement and recommendation to go for an eye examination by a trusted person, such as a peer or a health care worker) and (iv) psychological cues (decreased sense of isolation of PLWD interacting with a peer, or increased awareness of the risk of DR after receiving educational messages on DR). Fig. 1 shows how self-efficacy for taking a retinal examination might improve through peer support in the Uptake of Retinal Examination in Diabetes (DURE) study.

Rationale

Although there is evidence that peer support improves glycaemic control and quality of life among adult PLWD, and that peer support is both cost-effective and flexible [33], evidence on whether or not it would increase uptake of eye examination in an agrarian African population is lacking. DURE study aims to provide this evidence.

The development of the intervention has been informed by the following:

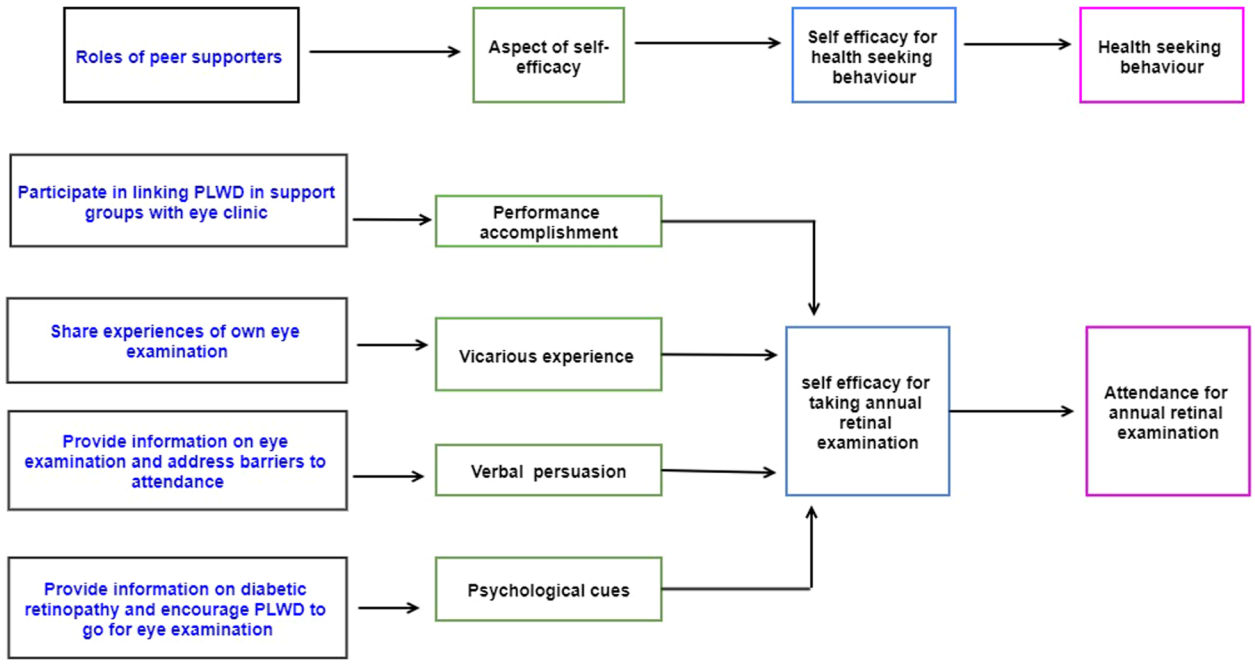

Fig. 1 Peer support and self-efficacy for retinal examination

i. A review of the literature on peer support in diabetes [34–42] and other chronic conditions in resource poor settings. [43–51] There is evidence that peer approach is widely used in the management of diabetes, to promote physical activity, healthy eating and improvemt in glycaemic control.
ii. The results of a recent published meta-analysis of randomized clinical trials on effectiveness of peer-support for glycaemic control in Type 2 diabetes [52] which concluded that peer support had a significant impact on improving HbA_{1c} levels in patients with poor glycaemic control.
iii. A health system assessment in three counties of Kenya conducted before this study showed that services for DR are underutilised: 74% of PLWD have *never* had a retinal examination in their lifetime, and 76% have *never* had a recommendation for an eye examination by their diabetes care provider [22].
iv. Evidence that improving health literacy, provider patient interaction and linking patients to health care improves patients' self-efficacy and glycaemic control. [42, 53, 54]

Aim

To evaluate, by means of a pragmatic cluster randomized controlled trial, the effectiveness of a peer supporter- led community education programme in Kirinyaga county, Kenya.

Research questions

1. To what extent can health education delivered by peer supporters increase the demand for annual retinal examination among PLWD?
2. What are the contextual factors that determine the effectiveness of the intervention?

Hypothesis

The hypothesis is that the proportion of PLWD having a retinal examination for DR is higher in diabetes support groups (DSGs) allocated to the peer supporter-led educational package than in DSGs randomized to the usual standard of care.

Methods

Design

This is a two-arm pragmatic cluster randomized controlled trial with additional process evaluation. It is a complex intervention to empower patients to undergo an annual eye examination. It is complex because those delivering and receiving the intervention require to demonstrate different behaviours and to engage in multiple interactions. [55] Its design is guided by the Medical Research Council framework for complex interventions,

available at https://mrc.ukri.org/documents/pdf/complex-interventions-guidance/ [55].

The study will be conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement and its extension to cluster randomized clinical trials (cRCTs). [56, 57] The cRCT design is adopted for the following reasons: (i) to reduce the effect of intervention contamination, as compared to an individually randomised trial, as patients in the same DSG often interact with one another (ii)to make it feasible to study the effect of the intervention at the individual level and the cluster level.

Definition of eye examination for DR

We define this test as: measurement of visual acuity and a retinal examination through a dilated pupil conducted by an eye care worker (using either an ophthalmoscope, a slit lamp or a retinal camera). Retinal examination for DR and DR screening in this protocol are used interchangeably.

Study setting

This trial will be conducted among the DSGs in Kirinyaga county, Kenya. The target population is members of the 16 support groups and volunteer peer supporters within these groups. Eye examination will be conducted at Kerugoya County Referral Hospital.

Sample size calculation

We aim to randomize seven diabetes patient support groups (clusters) with an average membership of 50 each to each arm. The study thus has two arms of equal size (350 participants in each arm).This sample size has been calculated using standard formula for sample size for cRCTs and taking into consideration the primary outcome of interest [58, 59]. A 15% loss to follow-up contingency has been built into the sample size calculation. This sample size would have 80% power to detect a two-fold difference in the proportion of PLWD who take up eye exam, with a 5% level of significance. Member registers of the DSGs will be obtained from the team lead. These registers will be the frame for identification of participants for the study.

Pilot study

A pilot study will be conducted in two clusters with 50 PLWD in each arm (intervention arm and control arm), selected through convenience sampling. The pilot will be conducted for 3 months and will involve: Testing study operational procedures; Implementation of the intervention in the intervention clusters; Testing study instruments for quantitative and qualitative data collection (questionnaires, observation sheets and topic guides); Outcomes evaluation. The primary outcome will be the proportion of participants in each arm that take up eye examination.

Inclusion and exclusion criteria

Participants will be included if they are PLWD aged 18+ years, will reside in Kirinyaga for the next 12 months, are members of DSGs in Kirinyaga, have a mobile phone and are willing to participate in the study. In addition to these criteria, peer supporters will be selected from those willing to participate as peer supporters, willing to commit two days for training and many hours of peer support, fluent in Kikuyu or Kiswahili, and have had a retinal examination for DR before the start of the study. PLWD who will be excluded are those already attending annual retinal screening, have a severe debilitating medical condition, are already on treatment for DR or do not meet the inclusion criteria.

Recruitment

Eligible participants will be recruited into the study by the research nurse, who will also obtain informed consent at the cluster level using the consent form approved for the study. Participants will be asked for consent to receive the intervent ion and for follow up. If the patient does not consent, reasons will be sought and recorded. After recruitment, a unique identifier number will be issued. All those recruited will be given an identification card which contains the name and a unique study number. They will be required to present this card at the eye clinic when they go for retinal examination. The flow diagram for the study is presented in Fig. 2.

Randomization

Randomization will be done after recruitment. The randomization will be through computer generated random numbers prepared by a statistician (DM) using STATA version 15 (StataCorp 2017), away from the project site. The allocation sequence will be concealed from the other trial personnel. Block randomization with block sizes of two or four will be used to ensure that the two arms are balanced over time, and to maintain unpredictability of allocation. Masking will not be possible but only the research team will have formal knowledge of the allocation.

Intervention

Two peer supporters will be recruited from each cluster in the intervention arm (one male and one female). These peer supporters will be selected from volunteers who meet the specified criteria. They will receive structured training in a two-day workshop. The content of the training sessions includes: an introduction to the project, the role of the peer supporter, diabetic eye disease and DR, retinal examination for DR, communication skills, managing groups, confidentiality and behaviour change. The training team will include a certified diabetes educator.

They will receive support to retain them in the study (airtime vouchers for delivering the telephone reminders).

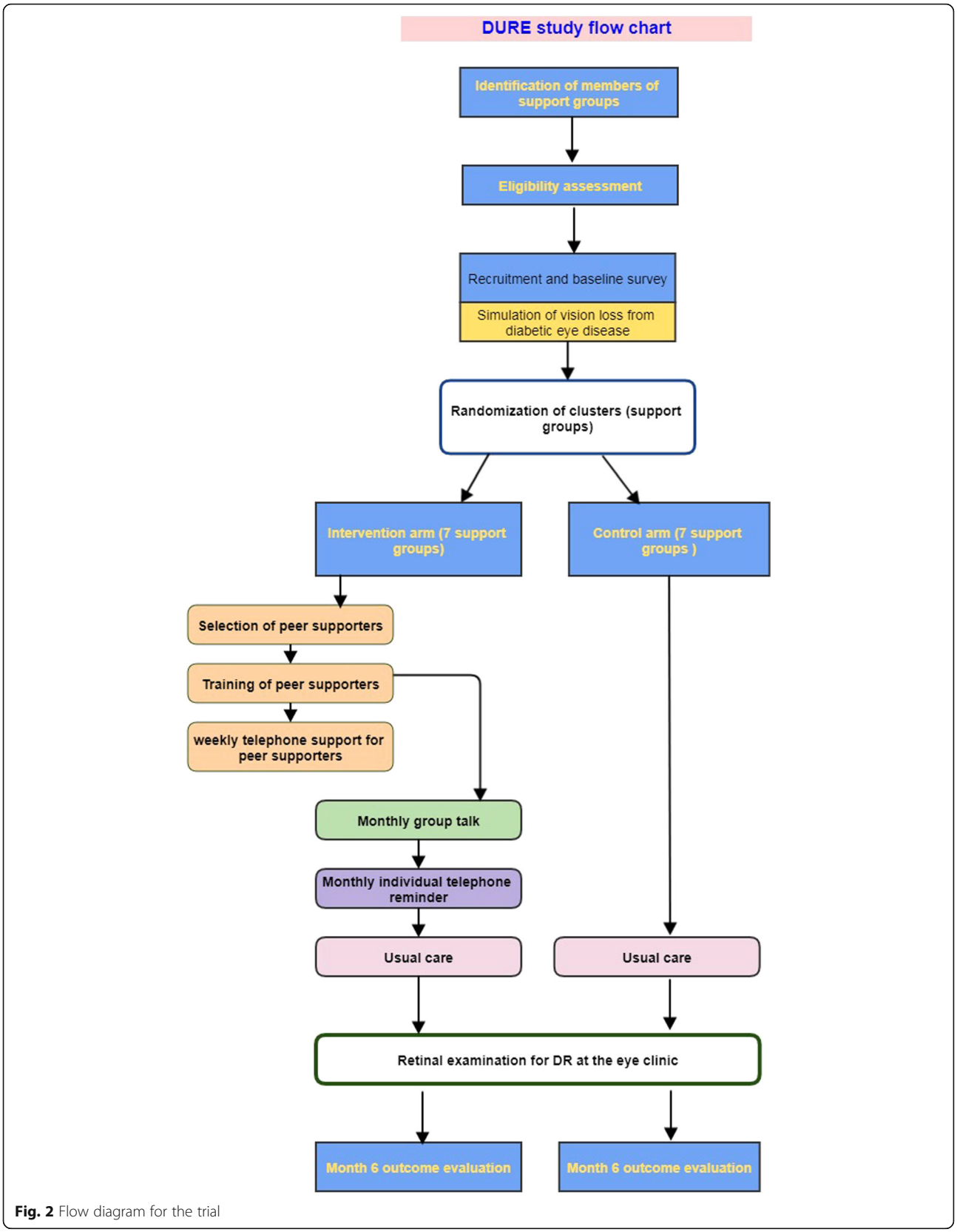

Fig. 2 Flow diagram for the trial

Table 1 Key messages to be delivered to participants

Messages on diabetic eye disease	
1	Diabetes causes several complications in the eye, including DR
2	DR is a progressive condition that leads to blindness if treatment is not provided in good time
3	DR has no symptoms until the advance stages
4	An eye check by an eye specialist can detect damage to the eyes before symptoms develop
5	All persons with diabetes should have their eyes checked once every year by an eye specialist, even before any symptom or poor vision develops
6	Do not wait for your vision to get worse or for any other symptom to occur before you see an eye specialist
7	If eyes are found to be normal at your eye check by an eye specialist, please continue with an eye check annually
8	If you notice any abnormality with your eyes between your clinic appointments, visit the eye specialist as soon as possible. It may not mean that you have diabetic eye disease, it may be a simple problem that requires treatment.
9	The eye check may help to determine if your sugar, blood pressure, and lipid control needs to be re-assessed. Good control of your blood sugar levels, blood pressure and cholesterol reduces the risk of diabetes-related sight loss.
10	If you are found to have DR the eye specialist will inform you about the diagnosis, and how it will be treated.
Messages on retinal examination for DR	
1.	Ensure you have a dilated eye examination at the eye clinic at least once a year.
2.	You do not need to have a referral note to go to the clinic. However we will give you a card to present at the clinic.
3.	At the eye clinic, your vision will be checked first.
4.	A examination for DR is different from any other type of eye examination. It is called a dilated eye examination.
5.	In this examination, the doctor puts eye drops into your eyes to dilate (widen) your pupils. This allows the doctor to have a good view of the back of the eye. Both eyes need to be examined.
6.	The examination is not painful. When the eye drops are first instilled, there may be a slight stinging sensation but this only lasts about a minute. You may feel uncomfortable because of light sensitivity and blurred vision once the pupils are dilated.
7.	Do not be afraid to ask the doctor questions about the examination or about diabetic eye disease.

They will also receive a weekly telephone call from the principal investigator for support. The intervention group will receive the usual care, a monthly group talk and a monthly individual telephone reminder to attend retinal examination. The key messages to be delivered in the group talk are shown in Table 1. The control group will receive the usual standard of care, which consists of ad hoc diabetes educational talks, blood sugar and blood pressure measurements during support group meetings.

Data collection

Standardized operating procedures will be used to collect data at baseline, using approved tools in the study proposal. Demographic and anthropometric (height, weight, waist circumference) as well as blood pressure, blood sugar and visual acuity will be recorded at baseline. Study participants will be given their body mass index and blood pressure measurements in the field, at the point of data collection; where these results are abnormal, participants will be referred to a health worker. Completed questionnaires will be monitored and data entry staff will be trained to minimize errors in data entry into computerized databases. Identifiers will be removed from participant data, and all paper data will be stored in locked cabinets. Electronic data will be password protected for confidentiality. A detailed data management plan is included in the study proposal.

Follow up

Participants in both arms will be followed up for six months to assess attendance to retinal examination. Participants who are lost to follow up will be identified at the monthly contact points with peer supporters. Three home visits will be made to trace participants who are lost to follow up. Characteristics of those lost to follow-up and reasons for loss will be evaluated.

At the end of six months two separate focus group discussions will be held with two participants from each intervention cluster in each arm ($n = 14$ for each focus group discussion) to explore the experience of the support groups with the intervention. A focus group discussion will also be held with peer supporters to explore the impact of 'peer supporting' on the management of their own diabetes, and their role in the health care team.

Process evaluation

A process evaluation will be conducted using qualitative interviews and non-participant observation (Table 2). The findings of the process evaluation will be evidence

Table 2 Domains and methods for process evaluation

Source	Domain	Data collection method	Stage of the trial
Trial registers	Recruitment Retention	Registers in the trial office	Throughout the trial (*n* = 700)
Participants	Fidelity Reach Dose received Effectiveness	Participant Questionnaire 2 Focus group discussions at 6 months	At recruitment (n = 700) Three months: n = 10% pf participants in each intervention cluster(35) Six months: *n* = 10-% of participants in each cluster (35) *N* = 28
Non-participant observations by PI	Recruitment Fidelity Dose delivered Context	PI Field notes	N = 2 group meetings per intervention cluster during the trial (14)
Peer supporters (PS)	Effectiveness Reach Fidelity Dose delivered Context	PS Questionnaires PS Diary for telephone calls PS Group session report form Focus group discussion at 6 months	After training (n = 14) Through the trial (n = 14) Throughout the study (1 report form per group meeting per PS) N = 7
Eye care workers Key informants	Context	In-depth interviews	At 6 months *N* = 3 *N* = 7
Research project manager	Reach Fidelity Dose delivered	Reports	At recruitment of PS At training the PS At 3 and 6 months
Research nurse	Outcome evaluation procedures	Report	At 3 months and 6 months
Study steering committee	Context	Spreadsheet of external events that may have affected study outcomes	At 6 months

PI Principal Investigator, *PS* Peer supporter

on why and how the intervention worked. The following domains of the intervention will be evaluated:

1) Whether the intervention activities are implemented as planned (fidelity).
2) The extent to which the intervention reaches the PLWD (reach).
3) The degree to which PLWD are exposed to the intervention package (dose).
4) The extent to which the intervention is acceptable to PLWD and to eye care workers (acceptability).

5) The contextual factors that may have an influence on the theory of change (context).

Assessment of outcome

Primary outcome

Rates of eye examination in each arm will be assessed in each arm at the end of six months. This outcome will be assessed by an independent and masked research nurse who will review the eye clinic records of all participants. The outcome will be recorded on the outcome evaluation form for each participant. The form contains identification details of each participant recruited into the study (name, residence, telephone number) and will thus differentiate them from other patients who are examined in the eye clinic. The form does not contain information on the intervention arm to which the patient is allocated. The project manager will receive the completed outcome evaluation forms and link the data to the participant database for each arm.

Secondary outcomes

These outcomes will be assessed at six months:

1. Contextual factors that affect the effectiveness of the intervention
2. Characteristics of peer supporters associated with uptake of eye examination
3. Barriers to uptake of eye examination among PLWD.

These outcomes will be evaluated using the database for participants and peer supporters, as well as data from focus group discussions with peer supporters and in-depth interviews with eye care workers at six months.

Statistical analysis

Baseline comparability of the two groups will be assessed to check that the important confounders and baseline characteristics that would affect uptake of eye examination are balanced between the two arms through randomisation. If the arms are found to be substantially

imbalanced an appropriately adjusted logistic regression model will be used.

Study-wide pooled analysis will be conducted for the primary outcome. Missing data will be reported using standard flow charts. Repeated measures mixed models regression with adjustment for age, sex, and baseline anthropometric measures will be used to compare the two groups for the primary outcome.

Analysis will be conducted on intention-to-treat basis. Regression analysis will be used to determine the extent to which individual and support group characteristics are associated with the primary outcome. Models for comparing continuous outcomes will use linear regression while models for categorical outcomes will use logistic regression. Kaplan-Meier analysis will be used to plot the survival curves for both treatment arms. Cox regression will be used to assess the impact of the intervention on time to first eye examination. The hazard ratio will be estimated with Cox regression, adjusting for substantial baseline imbalances if appropriate. Interim analysis is not planned.

Data monitoring

The principal investigator will coordinate and monitor all recruitment, intervention and follow up procedures. A data monitoring committee will not be required. There is no reason to expect significant adverse effects and there are no stopping rules. The principal investigator will have access to all the trial data sets.

Harms

Neither arm of the trial has serious anticipated harms. The retinal examination involves the use of mydriatic eye drops. This may cause temporary blurring of vision, but this is only expected to last for a few minutes or hours. In this trial the drugs will be instilled by highly experienced clinicians, and patients will be made aware of this effect beforehand. Any unexpected effects of the trial will be documented and reported to the sponsor and ethics committees.

Dissemination

The dissemination strategy will include a summary of the findings for support groups, a report to Kerugoya County government and the Ministry of Health Kenya, publications in peer-reviewed journals and presentations at national and international conferences.

Post-trial care

It is recommended that all PLWD have an annual retinal examination for DR, and more frequent examinations are required for those found to have any stage of DR. This is best practice that is recommended by the national guidelines for screening and management of DR in Kenya. [12] The service will continue to be available as routine care to PLWD at the Kerugoya County Referral Hospital beyond the study.

Discussion

This study is pragmatic in that it tests the effectiveness of this intervention in the real-world situation of the community and the health system in Kirinyaga. There is a strong need to develop interventions that can reach PLWD populations in real world settings to ensure that any effect found is generalizable.

Public health strategies to manage the diabetes and DR in sub-Saharan Africa (SSA) are known to be inadequate or non-existent. [60, 61] Given that we are at the emergence of the epidemic, this is an appropriate time to develop contextual interventions that will enable our health system to cope with this challenge. To our knowledge, this is the first study that has targeted the DSG population in DR research. The use of peer support in DR is a relatively new field and little has yet been published on the topic.

The trial is important for a number of reasons. For the *individuals with diabetes*, this trial is in line with the growing global focus on patient empowerment. The PLWD will be empowered to demand for retinal examination, thus reducing demand side barriers to uptake of the examination. These actively engaged PLWD will be linked to eye care providers by the peer supporters. The *Chronic Care Model*, which has been proposed as a suitable model for managing diabetes, emphasises on the need to implement such links between patients and the health system using community resources. [62] [47] As all PLWD are at risk of DR, empowerment to initiate and maintain screening will be beneficial to all.

For the *support groups*, if this intervention positively influences uptake of retinal examination, this could in turn influence how the DSGs define their role. It has potential to instigate a new agenda, making the groups key sites for preventive public health initiatives that are adaptable, feasible and embedded within support group culture. The peer supporters will remain a valuable resource in the DSG, which enhances sustainability of effect.

For *Kirinyaga county*, our study findings might help the county (formerly district) health services to develop initiatives to promote early detection of DR, by involving DSGs, empowering patients and developing effective referral systems for DR services. The role the support groups can play in strengthening the health system for diabetic retinopathy in the county will become explicit.

The intervention will be provided by trained peer supporters, which is a form of task-shifting. Task shifting is commonly applied in both diabetes and eye care services in our setting. It helps to address the severe shortage of human resources for health. The peer supporters will refer patients to the eye clinic, thus linking diabetes patients with eye clinics and strengthening the referral system in the county.

In *national context*, Kenya aims to achieve universal eye health, which includes care for DR. This study provides a framework for the promotion of retinal screening in the population with the risk of developing DR. If effective, the intervention would be a sustainable and scalable to other countries.

In the *international contexts*, the DURE study has the potential to extend current evidence and inform the scientific debate as to whether embedding retinal screening into DSGs is an effective next step toward meeting health goals.

The explicit use of a theoretical construct (self-efficacy theory) to conceptualise the potential determinants that would influence attendance to DR screening is a key strength of the study. It enhances the understanding of the plausibility of the intervention. The intervention package combines both standardization and flexibility, which allows for scalability in diverse settings. A further strength of this study is the inclusion of process evaluation, which will assist in the interpretation of how and why the intervention did, or did not, bring about the predicted effects.

The study has potential limitations. There are only 16 support groups in the county, which limits the possibility of increasing the number of clusters to further enhance statistical power. Delayed recruitment of the required sample size and loss to follow-up during the trial may be a challenge. In mitigation, a 15% loss to follow-up contingency has been built into the sample size calculation. Sample attrition can result from any inaccuracies in the data collection, such as incorrect address and telephone number information. Other diabetes studies have documented that patients were unable or unwilling to participate due to transportation issues and lack of time or interest [63]. However this is not anticipated because: alternative contact information of participants will be documented, only one visit to the eye clinic is required of participants, and the intervention is expected to build participants' self-efficacy. Attrition bias may occur if whole clusters drop out, however this is not anticipated as the study period is short.

Despite these limitations, DURE study illustrates the tremendous potential of implementing pragmatic cluster RCTs in the diabetes support group setting. Implementing the trial in this at-risk population will be an invaluable learning opportunity. Many of the lessons learned from this experience could be useful to other research projects.

Trial status

At the time of submission, the trial is at the stage of enrolment.

Abbreviations

CONSORT : Consolidated Standards of Reporting Trials; cRCT: Cluster Randomized Clinical Trial; DR: Diabetic Retinopathy; DSG: Diabetes support group; DURE: Uptake of Retinal Examination in Diabetes; PACTR: Pan African Clinical Trials Registry; PLWD: People living with diabetes; SE: Self-Efficacy; STDR : Sight-threatening diabetic retinopathy

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Authors' contributions

NM, CB and AF conceptualised the study. SG, DM, CM and LM reviewed and revised the study design that was written by NM with the help of CB and AF. Thereafter MN, EG, PT, AJ, KG, MG and JK participated in the development of the study interventions as well as recruitment of the study centres to participate in the study. All authors critically reviewed of the protocol prepared by NM. Thereafter, NM obtained the ethics approvals and drafted the manuscript. All authors read and approved the final version, and agreed to participate in the study.

Ethics approval and consent to participate

Ethical approval has been granted by the Ethics Review Committees of London School of Hygiene and Tropical Medicine and the African Medical Research Foundation. Any protocol amendments will also be approved by these committees. Procedures and methods used in this study conform to the ethical guidelines defined by the World Medical Association's Declaration of Helsinki and are described in detail in the study protocol (version May 2017). Written informed consent will be sought at the cluster level (before randomization) from the leaders of the DSGs. Participants will be asked for verbal consent to receive the intervention (before randomization), and for verbal consent to follow-up.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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Sample size calculation for DURE study

The formula for calculation of sample size for cluster-randomized trials whose primary outcome is a proportion is

$$c = 1 + (z_{\alpha/2} + z_{\beta})^2[\pi_0(1-\pi_0)/n + \pi_1(1-\pi_1)/n + k^2(\pi_0{}^2 + \pi_1{}^2)]/(\pi_0 - \pi_1)^2$$

(Hayes and Bennett, 1999)

Based on this formula:

Parameter	**Value**	**Notes**
Zα/2=the normal distribution value corresponding to risk for Type 1 error (at 95% confidence level)	1.96	
Zβ = the normal distribution value corresponding to β for statistical power at 80%	0.84	
pi0 = true population proportion in control group	0.12	(using data from the health system assessment – 12.2% of PLWD in Kirinyaga had ever had a screening eye examination
pi1 = true population proportion in the intervention group	0.24	Reflecting an expected two-fold increase in the proportion that has ever had a screening eye examination
n = number of individuals in each cluster	45	Increased to 50 to account for potential loss to follow-up
k = coefficient of variation of the true proportions between clusters within each arm	0.25	Estimate gained from assessment of pattern of uptake of DR screening in LMICs
(Zα/2+Zβ)^2	7.84	
pi0(1-pi0)/n	0.1056	
pi1(1-pi1)	0.1824	
k^2(pi0^2+pi1^2)	0.0045	
(pi0-pi1)^2	0.0144	
c = number of clusters	6.9344	=7 clusters in each arm

Chapter Eight

Effectiveness of peer support to increase attendance at DR screening - a pragmatic cluster randomized clinical trial

Pilot of the DURE trial

8.0 Overview

The previous chapter of this thesis (chapter 7) described the trial methods to addresses objective 4 in chapter 1 of the thesis: To develop and test an intervention through a randomized clinical trial (RCT) to improve eye care services for PLWD in Kenya.

This chapter consists of a research paper that describes the randomised pilot and feasibility study conducted in advance of the definitive RCT (Uptake of Retinal Examination in Diabetes, DURE trial), with the primary aim of assessing feasibility. The RCT is reported in adherence to the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement and its extension to randomised pilot and feasibility trials (www.consort-statement.org).

*Research paper 6 (*submitted to BMC Pilot and Feasibility Studies) includes data on baseline characteristics of participants, feasibility outcomes as well as an interim measure of the effectiveness of the intervention. Publishing these results contributes to maximising the benefits of this research to other organisations or researchers seeking to understand the value of pilot and feasibility studies to the progression to full RCTs.

8.1 Research Paper 6

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SECTION A – Student Details

Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?			
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Where is the work intended to be published?	BMC Pilot and Feasibility Studies
Please list the paper's authors in the intended authorship order:	Nyawira Mwangi, Covadonga Bascaran, David Muraguri, Mark Ng'ang'a, Jacqueline Ramke, Mathew Kipturgo, Stephen Gichuhi, Min Kim, David Macloed, Consuela Moorman, Esbon Gakuo, Lawrence Muthami, Allen Foster
Stage of publication	**Submitted**

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. (Attach a further sheet if necessary)	I designed the study, conducted the research, analysed and interpreted the data, drafted the manuscript and prepared subsequent revisions in consideration of the comments from the co-athors and peer reviewers

Student Signature: Nyawira [redacted] **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] **Date:** SEPT 17, 2019

Chapter 8

Research paper 6

Feasibility of a cluster randomized controlled trial on effectiveness of peer –led health education interventions to increase uptake of retinal examination for diabetic retinopathy in Kirinyaga, Kenya: a pilot trial

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Abstract

Background

People living with diabetes can reduce their risk of vision loss from diabetic retinopathy by attending screening, which enables early detection and timely treatment. The aim of this pilot trial was to assess the feasibility of a full-scale cluster randomized controlled trial of an intervention to increase uptake of retinal examination in this population, as delivered within existing community-based diabetes support groups (DSGs).

Methods

All 16 DSGs in Kirinyaga county were invited to participate in the study. The first two groups recruited took part in the pilot trial. DSG members who met the eligibility criteria were recruited before the groups were randomized to the two arms. In the intervention group, two peer-supporters were trained to deliver monthly DSG-based eye health education and individual telephone reminders to attend screening. The control group continued with usual DSG practice, which is monthly meetings without eye health education. The recruitment team and outcome assessors were masked to the allocation. We documented the study processes to ascertain the feasibility, acceptability and potential effectiveness of the intervention. Feasibility was assessed in terms of clarity of study procedures, recruitment and retention rates, level of acceptability and rates of uptake of eye examination. We set the target feasibility criteria for continuation to the main study to be recruitment of 50 participants in the trial, 80% monthly follow-up rates for individuals and no attrition of clusters.

Results

Of the 122 DSG members who were assessed for eligibility, 104 were recruited and followed up; 51 (intervention) and 53 (control) arm. The study procedures were well understood and easy to apply. We learnt the DSG meeting days were the best opportunities for recruitment. The study

had a high acceptance rate (100% for clusters, 95% for participants) and high follow up and retention rate (100 % of those recruited). All clusters and participants were analysed. We observed that the rate of incidence of eye exam was about 6 times higher in the intervention arm as compared to the control arm. No adverse unexpected events were reported in either arm.

Conclusions

The study is feasible and acceptable in the study population. The results support the development of a full-scale cluster RCT, as the success criteria for the pilot were met.

Trial registration

Pan African Clinical Trials Registry PACTR201707002430195 Registered 25 July 2017

Keywords

Diabetes, Diabetic retinopathy, peer-support, Kenya, pilot, cluster randomised controlled trial

Background

The long-term complications of diabetes, such as diabetic retinopathy (DR), are a threat to health among people living with diabetes (PLWD). DR is a growing concern in global epidemiology due to the high proportion of DR that remains undetected. Vision loss from DR can be prevented through regular retinal screening (hereafter referred to as 'screening') and timely treatment.[1-3] There is notable geographic variation in the incidence and visual impairment burden of DR, both within and between countries, reflecting variation in access to health care.[4-8] Services for DR prioritize early detection, metabolic control, regular monitoring and timely treatment. Access to these services is a significant challenge due to demand side barriers (such as low awareness of the need for services among PLWD) and supply side barriers (such as availability of clinical guidelines or screening services).[9] There is a need for better evidence and patient empowerment to address

the demand side barriers, as well as health system strengthening to address supply-side barriers.[9-11]

In the *Global action plan for the prevention and control of non-communicable diseases(NCDs) 2013-2020,* the World Health Organization (WHO) highlighted the need to empower people with NCDs to seek early detection, and to provide them with appropriate education, incentives and tools for self-management.[12] The peer-support model has been used in diabetes and other chronic conditions to improve social support and self-management, with positive outcomes in other countries.[13-17] In contrast, peer-support has not been used in diabetes eye health services, and subsequently there is a knowledge gap regarding its effectiveness to reduce vision loss from diabetic retinopathy. Leveraging on peer-support in a clinical or community setting might be a potential enabler for the adoption of healthy behaviours, such as screening.

Clinical guidelines target to have a 100% attendance to regular screening.[18] Our health system assessment reported that PLWD in three counties of Kenya have low attendance to annual screening, which is the frequency recommended in this setting.[19] This is consistent with findings that uptake of DR screening is low in many parts of the world, but more so where access to health care is generally limited.[9] To address this deficit, the Uptake of Retinal Examination in Diabetes (DURE) trial[20] aims to test the effectiveness of peer-support in increasing the uptake of retinal examination among members of diabetes support groups (DSGs). Diabetes support groups are volunteer social groups of PLWD in which peers provide mutual support for improving diabetes care. The support may include information and skills for self-management, as well as emotional support. Given this objective, DSG members are likely to be health conscious and interested in adopting healthy behaviours. The intervention in this study is based on the self-efficacy theory[21]and is targeted to PLWD who are already members of support groups and have not had screening in the previous 12 months or longer. Screening in this setting involves a visual acuity test and a retinal examination through a dilated pupil.[18, 22]

The study setting is a rural county whose inhabitants are mainly small-scale farmers. The DSGs are spread over the 1200km^2 area of the county. Undertaking the DURE study raises important practical concerns. In this pilot study, our aim was to gain experience in delivering the intervention, and to assess if the DURE cluster randomized clinical trial (cRCT) is feasible by: (1) Testing clarity and ease of study procedures for enrolment and data collection. (2) Determining the potential for participant recruitment and retention. (3) Assessing the acceptability of the intervention, by considering the level of adoption of the study interventions by different actors. (4) Documenting an interim measure of the effectiveness of the intervention on the primary outcome. Our hypothesis was that it is feasible to conduct the DURE study. We set the target feasibility criteria for continuation to the main study to be recruitment of 50 participants in each cluster, at least 80% follow-up rate of participants in each month of the trial and no attrition of clusters. The 90 - day duration of the pilot trial was considered sufficient for these feasibility objectives, while the main trial will take six months.

Methods

Study setting

The demographic and health statistics of Kirinyaga county are highlighted in Table 8-1. The study intervention was developed following a health system assessment for diabetes and DR in three counties of Kenya, which identified gaps in access to services for DR, as well as the need for health system strengthening. We found that only 7% of PLWD in this county had a DR screening exam in the preceding 12 months. The main barriers to access are lack of referral from diabetes services, lack of knowledge of diabetes eye complications among PLWD and the belief that a screening exam is only necessary once ocular symptoms develop.

An estimated 25-30% of the PLWD in the county are regular members of DSGs (with a registration number) while another 20% of PLWD attend some DSG meetings even though they are not members. Peer group leaders and community health volunteers recruit members as they give

group health talks at community meetings, churches, outreach camps, and diabetes clinics in health facilities. As membership is voluntary, the distribution of members by demographic parameters in different groups varies. All groups are under the Kenya Defeat Diabetes Association, which provides them with equipment for use within the group (such as a glucometer and a blood pressure machines). The association also trains peer-supporters and DSG leaders.

Table 8-1: Demographic and health statistics- Kirinyaga county

Parameter	**Kirinyaga county**	**Kenya**
Total population (estimates based on 2009 census)	595,379	48.5million
Females	50%	50%
Age > 18 years	409,995	22,005,235
Urban population	16%	29.9%
No of people with diabetes (2%)[23]	8,185	440,104
No of people needing an annual eye exam	8,185	440,104
No of eye care facilities	1	112
No of ophthalmologists	1	115
No of ophthalmic clinical officers	3	300
No of ophthalmic nurses	0	200

DSGs hold routine monthly meetings at a dedicated time and location in the community. An estimated 80% of the members attend at least two thirds of the meetings annually. The meetings are held in the morning, starting between 8 and 9am and last 2-3 hours. Each member's fasting blood sugar, blood pressure and weight are recorded. The group then shares a light meal. The cost of the blood sugar test strips and meal are met by a contribution of Kenya shillings 100 (the equivalent of 1$ dollar) per PLWD attending the meeting. The other activities in the meeting include: group health talks delivered by peer-supporters; informal discussions among PLWD; planning for advocacy and awareness-raising activities. A record of these activities are captured in attendance registers and minutes of the meeting.

Sampling

All 16 DSGs in Kirinyaga were eligible for inclusion. We invited the DSG leaders to a meeting where we explained the objectives of the DURE study and invited all the groups to participate. The leaders then took time to discuss the study with their members before giving approval through signing consent forms. The first two DSGs to confirm willingness to participate were included in the pilot study, for simplicity, transparency and visibility to the DSG leaders. All sixteen DSGs consented to participate hence the remaining 14 will participate in the main study.

We aimed to recruit at least 50 members who met the eligibility criteria (Table 8-2) in each DSG (size of DSGs is 80-100 members). This is the same cluster size calculated for the main study, using the formula for sample size calculation provided by Hayes and Bennett.[24] A statistician not involved with the fieldwork conducted the sample size calculation. We also recruited two peer-supporters (1 male and 1 female) who met the eligibility criteria to deliver the intervention in the intervention cluster.

Design

The pilot study design mimics the design of the main study, being a two-arm cRCT with a 1:1 ratio. A research nurse who is a local health worker recruited participants who met the eligibility criteria during a DSG meeting. The list of existing DSG members was provided by the DSG lead. Participants were recruited through random selection. The research nurse assessed each potential participant for eligibility using the criteria in Table 8-2. Verbal consent for recruitment and follow-up was obtained at the time of recruitment, from individual participants who met the eligibility criteria (DSG leaders provided cluster-level consent). For those who did not consent, the reasons for non-consent were recorded. Baseline demographic, anthropometric and metabolic data was collected at the time of recruitment using standard operating procedures (appendix 3). All participants were given a study identifier card to present at the eye clinic at the time of eye exam.

Two members of the research team observed the recruitment process to identify any difficulties with participant recruitment, eligibility criteria or completing the data collection tool. The recruitment nurse provided additional feedback on these critical components in a debriefing session after each recruitment session.

Table 8-2: Eligibility criteria for participants and peer-supporters

Criterion	**Participants**	**Peer-supporters**
Age > 18 years		
Member of a diabetes support group		
Will reside in the county for the next 12 months		
Has a mobile phone		
Willing to participate in the study		
Had not had a screening exam in the last 12 months		
Has had a screening exam in the preceding 12 months		
Willing to be a peer-supporter		
Willing to commit two days for training		
Willing to commit many hours to peer-support work		
Fluent in Kikuyu or Kiswahili		
Already attending DR screening		
Already receiving treatment for DR		
Has a debilitating illness		

KEY	Include	Exclude	Not applicable

Following participant recruitment within each of the DSGs, random allocation of the intervention was through drawing of lots. A lay person not participating in the study picked one of four sealed and opaque envelopes from a container, in the presence of two members of the research team. Each envelope contained a card bearing the name of one DSG and either 'intervention' or 'control'. Opening the envelope revealed the arm allocation for one group, and by inference the allocation of the other group. This allocation was copied on the envelope and stored to provide a reference trail. The remaining envelopes were destroyed. A research assistant (not involved in

recruitment or outcome assessment) followed up the participants in each group at monthly intervals for 90 days from the first group education session, to check retention rates.

The primary outcome was the feasibility of recruiting 50 participants in each cluster, and achieving at least 80% follow-up rate of participants in each month of the trial. The records at Kerugoya County Hospital eye clinic were monitored daily and the identifier cards of participants that attended screening were deposited in a specific container by the eye care team. These cards were then collected and given to the outcome assessment nurse (not involved in recruitment or follow-up). During the study, we also found that some eye care teams external to the county health services held outreach camps in the county and provided screening for some of the participants. As our team was alerted ahead of the outreach camps, we liaised with these teams and monitored the attendance of any study participants. As they used the same screening guidelines, any participant screened at the outreach site was taken to have the outcome of interest.

The recruitment nurse, research assistants and the outcome assessors had no training in eye care, and were masked to the cluster and participant allocation, to avoid contamination and bias. The eye care providers were also masked to the intervention allocation. It was not possible to mask the study participants or peer-supporters in the intervention arm, because the peer-supporters' activities within the DSG were overt. As the primary outcome was assessed from hospital records, we concluded that the lack of masking could not incentivise over-reporting or under-reporting in either arm.

Intervention

The DSGs in the intervention arm received the study intervention combined with usual care for 90 days, while the control group received the usual standard of care alone (Table 8-3). The intervention was a monthly group health talk and individual monthly telephone reminders to attend eye exam, delivered by two peer-supporters (1 male, 1 female) collaboratively. The

intended mechanism of the intervention and the key messages to be delivered in the health talk are described in the trial protocol.[20] Fidelity to the intervention and the influence of peer-supporter characteristics will be assessed in the process evaluation of the main trial.

We trained the peer-supporters for two days to deliver the intervention. They had already received previous training as peer-educators (training provided by the Kenya Defeat Diabetes Association), and had about four years' experience with providing peer education. We also supported them during the implementation phase in the following ways. (1) Telephone calls were made by the team before and after each group session to discuss the sessions and any challenges faced by the peer leaders. (2) Practical support was provided to help organize the logistics for local program delivery, such as provision of telephone airtime and reimbursement for transport costs for peer-supporters. (3) The research team attended two of the three DSG meetings. Peer-supporters kept logs of the DSG attendance during group sessions and the individual reminders.

Table 8-3: Trial Interventions

Domain	**Intervention group**	**Control group**
Usual care	Monthly group meetings with general diabetes education talks, blood sugar and blood pressure measurements	Monthly group meetings with general diabetes education talks, blood sugar and blood pressure measurements
Intervention		
Peer-supporters training	Two days training following a structured curriculum regarding diabetes eye disease, retinal screening, role of peer-supporters, communication and other aspects specified in the protocol[20]	
Group education	Monthly group education provided by trained peer-supporters, with structured content on diabetic eye disease and retinal screening as specified in the protocol[20]	
Individual participant reminders	Monthly individual telephone reminder by peer-supporters	

to participants to take a screening exam as specified in the protocol[20]

Reporting and analysis

This study is reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines for pilot studies.[25] The CONSORT flow chart and the checklist are included as appendices. We documented recruitment procedures and rates, reasons for ineligibility and non-participation, and follow-up rates. We calculated descriptive statistics for each study arm at baseline. We also summarized survival outcomes at arm level as per intention-to-treat analysis and estimated hazard ratio for any differences. All data analysis was carried out using Stata version 15 (StataCorp, Texas, USA).

Results

The results are reported under four headings corresponding to the specific objectives of the pilot trial:

Study procedures for enrolment and data collection

We found that the enrolment rate was high during the DSG meetings. The peer group leaders could predict which meetings would be well attended, considering other concurrent community activities, and they mobilised members to attend. We found it helpful to liaise with these leaders in planning for the recruitment.

The study materials were easy to carry around and work with. We did not identify any practical, ethical or interpretation difficulties in the use of the eligibility criteria and the completion of the data collection tools. The eligibility criteria were therefore found to be appropriate and the data collection tools were well understood. We collected baseline data for all participants, before randomization.

The time taken to complete the data collection processes per participant exceeded the planned time. Some of the participants had difficulty finding some of the data that we needed for the purpose of follow-up, such as the telephone numbers of the next of kin, but with assistance they were able to retrieve this from their phones or to contact other people who had the data. However, this added about 10 minutes per participant over the initial estimates for the recruitment process. This resulted in increased waiting time for the other persons awaiting recruitment. Learning from this, we trained three additional research nurses for the recruitment team, so that at least two of them could attend each recruitment meeting.

A research assistant checked the data collection tools for completeness at the recruitment site. All the data forms were also checked by the team lead for quality assurance after each recruitment meeting. Thereafter the forms were sent to the data entry assistant where further quality checks were carried out as data was entered into a database.

We used standardised protocols for all measurements, and the descriptive data is provided in Table 8-4. The two arms were balanced for most characteristics except age and gender. Females and older people were over-represented in the intervention arm. This difference reflects the variation in the existing composition of the DSGs.

Potential for recruitment and retention

The response rate of clusters was good (both accepted to participate). All 122 participants assessed for eligibility were willing to participate, but 6 (4.9%) withdrew during the recruitment process because of long waiting time. Of the 122 assessed for eligibility, 12 (9.8%) were ineligible as they were temporary visitors (non-resident) or were going to be absent from support groups during the study period (school and employment commitments).

By conducting recruitment at well-attended routine DSG meetings, all or most of the regular DSG members had an equal chance to be recruited in the study. We were able to recruit within the

anticipated time such that all the participants entered the study at time 0, and we had similar recruitment levels in both clusters. Follow-up rates were high in both arms. Both DSGs remained in the study and received the intended intervention (Fig 1). One peer-supporter fell sick over part of the period, but by this time most of participants in intervention arm already had the outcome of interest, and the other peer-supporter was able to carry on with the intervention. All participants were followed up for 90 days, and there was zero loss to follow up.

Table 8-4: Baseline characteristics

	Intervention (N=51)	**Control (N=54)**	**Total (N=104)**	
Age (years)				
Median (IQR)	69 (60-72)	57 (57-62)	63 (54.5-70)	P=0.002
Sex				
Female (%)	41 (80.4)	30 (56.6)	71 (68.3)	P=0.009
Duration of diabetes (years)				
Median(IQR)	5.0 (2-10)	5.0 (2-8)	5.0 (2-10)	
Duration of support group membership (years)				
Median(IQR)	3.0 (1-3.5)	2.0 (1-4)	2.0 (1-4)	
Anthropometric measures				
Body Mass Index (kg/m^2)				
Male	25.0 (2)	25.3 (4.4)	25.2 (3.8)	
Female	25.4 (3.9)	26.4 (3.4)	25.8 (3.7)	
Waist circumference (cm)				
Male	96.5 (7.3)	96.0 (11.1)	96.1 (10)	
Female	97.0 (8.9)	100.0 (8.4)	98.3 (8.8)	
Metabolic measures				
Fasting blood sugar (g/dl)	7.4 (2.7)	9.1 (4.5)	8.3 (3.8)	
Systolic blood pressure (mmHg)	139.0 (20)	142.0 (26)	141.0 (23)	
Diastolic blood pressure (mmHg)	81.0 (7.6)	78.0 (13)	80.0 (11)	

Acceptability of the intervention

Before the start of the study, we had initial meetings with the Ophthalmic Services Unit at the national level, the Kirinyaga county director of health, eye care providers in the county, and the national officials of Kenya Defeat Diabetes Association (KDDA) that is the umbrella body for DSGs. We obtained their buy-in for the study, and they linked us with the DSGs.

Given the recruitment rates, the follow up rates and the attrition rates (Figure 8-1, Flow chart at the end of the paper), the study and the intervention were acceptable to participants and clusters. The peer-supporters attended all the sessions of the two-day training and gave the group talks as planned. For the individual telephone reminders, we found that peer-supporters supplemented this with face-to-face discussions with the individuals who were yet to take a retinal exam (in addition to the telephone reminders). This flexibility reflects a sense of ownership of the intervention by the peer-supporters.

We did not record any adverse event related to the intervention. Temporary blurring of vision after dilatation of the pupils during retinal examination (the outcome of interest) is a common undesirable effect but this was explained to the participants before examination and none of them declined to have the examination.

The 'drop-in' referral mode of patients from the DSGs for screening for DR was acceptable to both patients (who adopted it) and eye care providers (as they screened all who dropped in). The attendance to the eye clinic showed some peaks, and during these peaks the workload in the eye clinic was significantly increased, however all who turned up were screened. None of the participants who presented at the eye clinic had lost or forgotten the identifier card, which would suggest that the card was highly valued. Such participants would still have received screening and this would be captured in the eye clinic records.

Estimating the effectiveness of intervention

We estimated the tentative effectiveness of the intervention in both arms, although the study was not powered for hypothesis testing. Participation rates are presented without adjustment for clustering.

The intervention arm had a substantially higher uptake of eye exam during the trial (Fig. 8-1). Of the 104 participants, 31(29.8%) attended screening during the trial: 25/51 (49%) in the intervention arm, as compared to 6/53 (11.3%) in the control arm.

In the intervention arm, the rate at which participants attended an eye exam was high immediately after the start of the intervention and then it decreased (Figure 8-1). The highest rates were observed between day 10 and 20 following the first group education session, even though the education sessions continued on a monthly basis. The pattern suggests that most of the benefit of the intervention occurs early in the intervention. In the control arm, the rate of eye exam was nearly constant. Although it increased around day 50 (without any intervention) it didn't reach the rate in the intervention group.

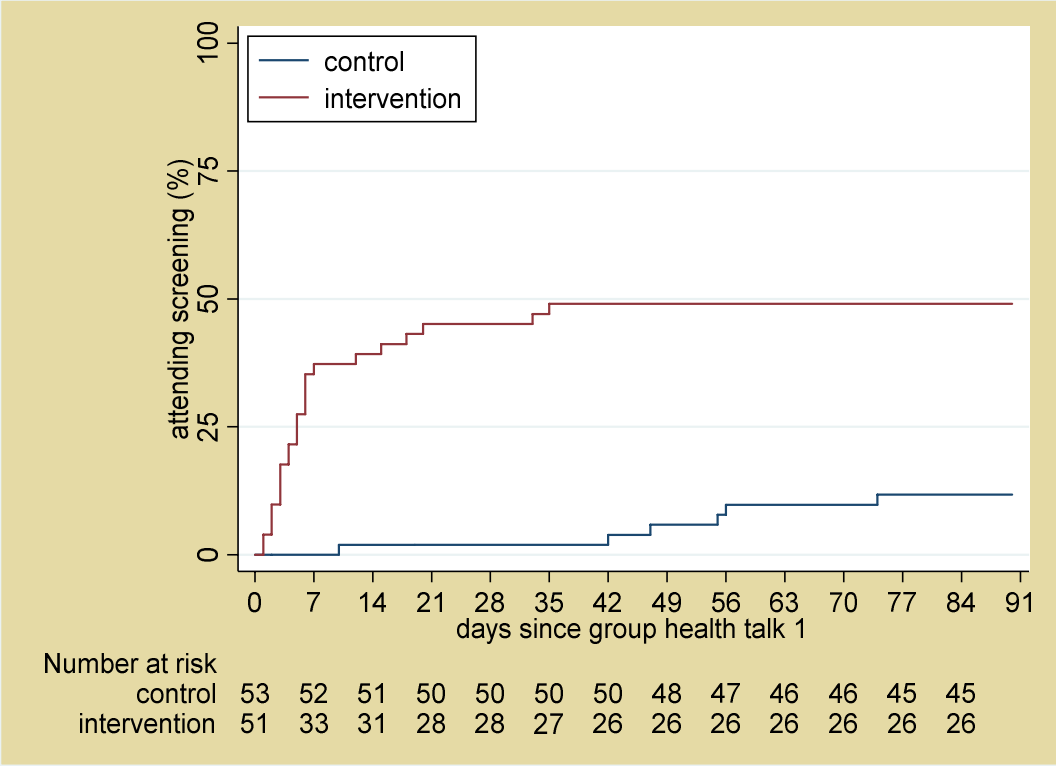

Figure 8-2: Time to screening among PLWD in intervention and control arms

Discussion

We are the first to report a pilot cluster RCT on the feasibility of a full-scale RCT to assess the effectiveness of a community-based DSG intervention to increase uptake of DR screening among PLWD. Other studies have examined the effectiveness of such community-based groups on health outcomes such as maternal, neonatal and childhood survival.[26-29]

The study has several strengths. Firstly, a mixed methods health system assessment[30] preceded the trial. This helped to identify DSGs as a community resource that was a potential channel for increasing uptake of screening. Secondly, this study targets PLWD in a rural setting who have not had screening in the last 12 months. However, we found that our participants had never had screening, meaning the people who are the most vulnerable to DR-related blindness and who need the intervention most were included. It is known that screening programs are more cost-effective in people who derive more benefit from screening.[2, 7]

Thirdly, it is known that demand-side behaviour changes alone may be insufficient to change the health outcomes being addressed, therefore health system strengthening is important before or within a trial.[26, 27, 31]. Before this study, we developed and implemented national clinical guidelines for DR, and our training program for peer-supporters is currently being embedded in the Kenya Defeat Diabetes Association peer-support manual. Therefore, a further strength of the study is that we tested the intervention within a bigger health system strengthening context.[32, 33] Fourth, the study setting, eligibility criteria, study design and amount of data collected in the pilot is by design, similar to what will be collected in the main study. This makes it easy to transfer the learning from the pilot to the main study.

Our findings show that the potential for recruitment and the feasibility of data collection, study implementation and follow-up is high. There was high acceptability of the study in general and the intervention by participants. This might be because the DSG members are already health conscious, or because of the community entry process that we followed. The top leadership of KDDA and the county director of health introduced us to the county support group leader, who in turn introduced us to the DSGs. We had strong liaison with these stakeholders and with local health care workers, which helped successful study implementation. We considered this to be important because the feasibility of the implementation and future scalability of the intervention depends on acceptability not only among the participants but also among these stakeholders in health care.[34] Further, the intervention itself requires constant engagement with the DSGs and the participants, which may have aided the acceptability and retention of participants in the study. Of note, we did not pay the participants— they participated voluntarily.

The recruitment process was embedded in DSG meetings, which was a critical factor for efficiency in recruitment. We learnt that recruitment required more time and more research nurses than initially planned, and this will be taken into account in the main study. The pilot findings suggest that the trial should achieve high recruitment and retention. We excluded PLWD who were

temporary visitors to the DSGs, as they were not likely to stay long enough to receive the intervention. Other studies have used a similar approach to avoid contamination between clusters.[33] We monitored support groups attendance and did not have evidence of inter-cluster migration in our study. We also learnt the necessity of liaison with mobile eye care providers from other counties who visit Kirinyaga county on eye camps, as they provided screening to this population (besides the static eye clinic at Kerugoya county referral hospital).

When interventions are implemented in real-world settings, some degree of flexible adaptation of program components occurs.[34-36] Although mobile phone interventions are useful due to their ubiquity even in this population[37], we found that face-to-face contact is valued and that peer-supporters still supplemented individual telephone reminders (prescribed in the protocol) with additional face-to-face reminders to persons who had not yet taken a retinal examination. This is perhaps because of the close residential proximity of the members and the existing personal relationships between them. It also reflects that in the 'real world' setting peer-support is not provided in tightly sequential or discrete categories. These flexible interactions may have contributed to the success of the intervention. The peer-supporters in this study were highly experienced with peer-support, having been peer-supporters for a long time and having had other trainings. This may have contributed to the success of the study, and it is not known whether if we have less experienced peer-supporters in the main study we will have different findings.

In the pilot study, we observed a much greater proportion of individuals attending retinal screenings in the intervention arm than in the control arm. Given only one cluster was randomised to each arm we cannot draw inferences from this, but it does suggest that the intervention has potential and is worth bringing forward to the full trial. Among those in the intervention arm who had an eye exam, there was a striking uptake of the exam in the first two weeks of the intervention. This means the benefit of the intervention was visible within a short period. Conversely, it also means that there is risk of eye care provider fatigue if the same pattern

of uptake is seen in the larger full trial. Kwaku et al[31] have noted that such negative effects can be experienced in a clinical trial. We did not experience this in the pilot. In the full trial, we will stagger the intervention over time hence this challenge is unlikely to occur. As most of the PLWD only need one screening examination annually, we do not expect this to be a significant problem beyond the study.

Although the participants were aware of the risk of temporary blurring of vision during dilated eye exam, this was not a barrier to uptake of eye exam. However, since this is the first screening examination for the participants, we do not know whether it would be a barrier to future screening.

It is good practice to consider the attributes that contribute to the scalability of interventions, even at the stage of pilot trials.[38]This pilot trial represents a step towards developing a scalable intervention because of its acceptability to participants. Acceptance by PLWD is necessary but not sufficient for scalability, since it also needs the support of service providers, administrators and policy-makers. Based on the evidence from the pilot trial, scalability might also be feasible because of (1) the acceptability and involvement of state and non-state stakeholders who run the support groups and health services (2) the trial is implemented within routine (pragmatic) conditions (3) we documented the processes involved in the trial.

The pilot study had some limitations. We only involved two DSGS in the study (out of the 16 DSGs in the county) but we considered this to be sufficient to address the issues of uncertainty in the feasibility of the study. For the main trial, we have recruited the other fourteen support groups (seven in each arm).

The first two DSGs that accepted to participate in the study were recruited in the pilot study. This convenience sample might mean that these initial findings are not generalizable to all DSGs. However, we considered that this method was helpful to demonstrate transparency to the DSG leaders and to meet the feasibility objectives. As women and older people were over-represented

in the intervention arm, the extent to which the interim results of the primary outcome can be extended to men is not clear. This over-representation is a reflection of the composition of the two DSGs - it is a reflection of the participants that would receive this intervention if it became the usual standard of care. This composition was previously undocumented, therefore it is an important contribution of this pragmatic trial. With the larger sample size of the main trial (700 participants), we expect more balance, but if this is not the case we will conduct subgroup analysis.

Given that this is pragmatic trial[20], we anticipate that co-interventions may occur in the 'real-world' setting of the study. We found that there were external outreach eye camps in the county during the trial period. These camps have potential to introduce co-intervention bias, particularly if they include eye health promotion activities. However, the exposure to this co-intervention was likely balanced between the two arms, since the camps were widely publicised through community meetings and held at diverse locations across the county. In the main trial, we will identify any pre-specified or unplanned co-interventions, assess the risk of co-intervention bias and estimate its effect on the trial outcomes.

We did not perform a process evaluation at this stage, however this is planned as part of the main study,[20] when we will have data on the primary and secondary outcomes. The process evaluation will help us understand the way the intervention worked to lead to these outcomes.

Conclusion

The pilot study met our success criteria for the feasibility objectives. We conclude that a full trial of the intervention is feasible, and the results of this pilot will inform this full trial. The findings of this study may be relevant to other countries with a similar model of DSGs. Given the paucity of literature on implementing community-based interventions, the results of this pilot may be of interest to other researchers interested in addressing feasibility challenges in cRCT interventions targeting community groups.

Abbreviations

CONSORT	Consolidated Standards of Reporting Trials
cRCT	Cluster randomized controlled trial
DSG	Diabetes support groups
DR	Diabetic retinopathy
DURE	Uptake of retinal examination in diabetes trial
KDDA	Kenya Defeat Diabetes Association
NCDs	Non-Communicable Diseases
PLWD	People living with diabetes
RCT	Randomized controlled trial

Declarations

Ethics approval and consent to participate

The ethics review committees of the London School of Hygiene & Tropical Medicine (LSHTM) and the African Medical Research Foundation (AMREF) approved the DURE study, and this pilot falls within the scope of that trial. Informed written consent was obtained at the cluster level, while informed verbal consent was obtained at the individual level. The study adhered to the tenets of the Declaration of Helsinki and the principles of Good Clinical Practice.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from Ministry of Health, Kenya but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Ministry of Health.

Competing interests

The authors declare that they have no competing interests.

Funding

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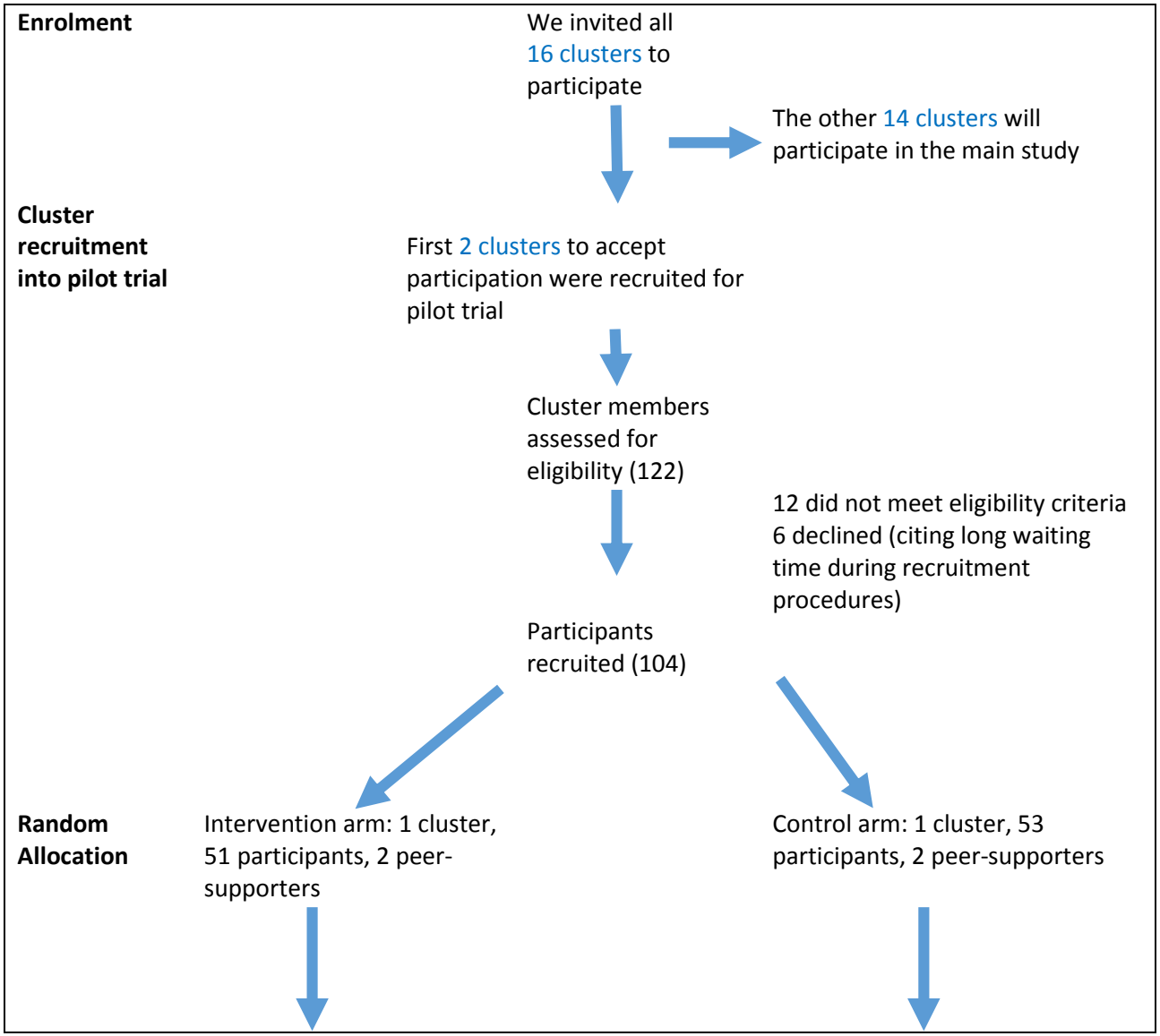
Enrolment
We invited all 16 clusters to participate
The other 14 clusters will participate in the main study
Cluster recruitment into pilot trial
First 2 clusters to accept participation were recruited for pilot trial
Cluster members assessed for eligibility (122)
12 did not meet eligibility criteria
6 declined (citing long waiting time during recruitment procedures)
Participants recruited (104)
Random Allocation
Intervention arm: 1 cluster, 51 participants, 2 peer-supporters
Control arm: 1 cluster, 53 participants, 2 peer-supporters

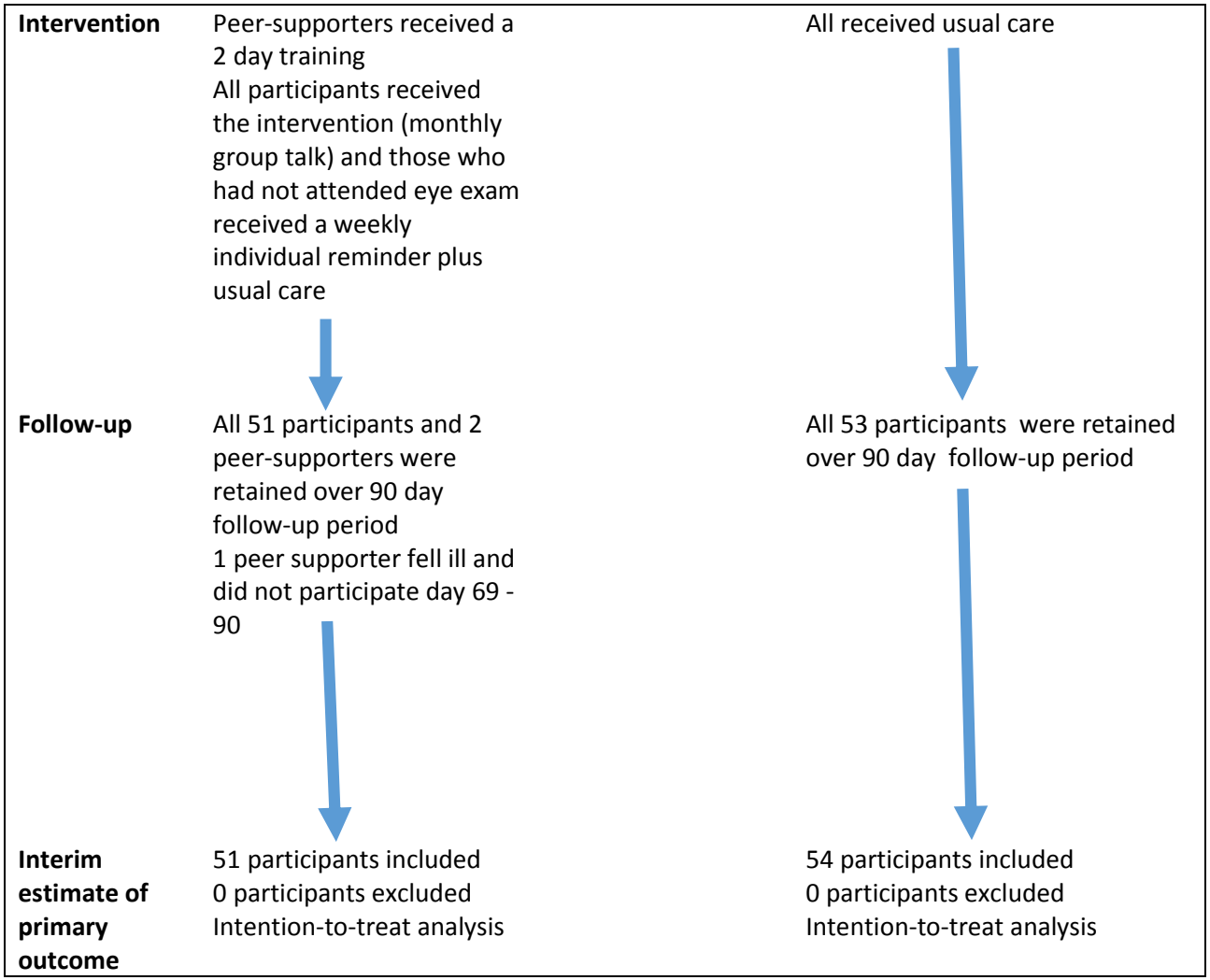

Figure 8-1: Flow diagram for pilot study

Chapter Nine

Effectiveness of peer support to increase attendance at DR screening - a pragmatic cluster randomized clinical trial

Process Evaluation of the DURE trial

9.0 Overview

The effectiveness of complex interventions is estimated through outcome evaluation of randomized clinical trials (RCTs). Chapter 10 will provide information on the effectiveness of the DURE trial in increasing attendance to DRS. There is also a need to understand the factors shaping implementation and outcomes of the trial in order to provide possible explanations for the effect of the intervention. Process evaluation of clinical trials provides evidence about what and how interventions are implemented, how interventions generate change in outcomes (mechanism of impact) and how the context affects the outcomes.[1]

This chapter consists of a research paper that describes a mixed method process evaluation of the DURE full trial, guided by the Consolidated Framework for Implementation Research (CFIR).[2] This framework is an implementation science tool that is used to investigate the influence of the characteristics of the intervention, the individuals involved, the inner and outer setting of the intervention, and the implementation processes.

1. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015;350:h1258.doi:10.1136/bmj.h1258

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Research paper 7 (submitted to BMC Tropical Medicine and Health) includes our analysis of the quantity and quality of what was delivered, the role of context, why the intervention did or did not work, what elements appear to be the 'most essential components' of the intervention, barriers and facilitators, and implications for scale-up of the intervention. These findings can inform stakeholders on how to change or improve implementation of this intervention in the current settings or replication of the intervention in different settings.

9.1 Research Paper 7

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Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

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Stage of publication	**Submitted**

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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. (Attach a further sheet if necessary)	I designed the study, conducted the research, analysed and interpreted the data, drafted the manuscript and prepared subsequent revisions in consideration of the comments from the co-athors and peer reviewers

Student Signature: Nyawira [redacted] **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] **Date:** SEPT 17, 2019

Tropical Medicine and Health

RESEARCH Open Access

Peer-support to increase uptake of screening for diabetic retinopathy: process evaluation of the DURE cluster randomized trial

Nyawira Mwangi[1,2*], Covadonga Bascaran[1], Jacqueline Ramke[1,3], Mathew Kipturgo[2], Min Kim[1], Mark Ng'ang'a[4], Stephen Gichuhi[5], Dorothy Mutie[2], Consuela Moorman[6], Lawrence Muthami[7] and Allen Foster[1]

Abstract

Background: There is limited evidence on how implementation of peer support interventions influences effectiveness, particularly for individuals with diabetes. We conducted a cluster randomized controlled trial to compare the effectiveness of a peer-led health education package versus usual care to increase uptake of screening for diabetic retinopathy (DR).

Methods: Our process evaluation used a mixed-method design to investigate the recruitment and retention, reach, dose, fidelity, acceptability, and context of implementation, and was guided by the Consolidated Framework for Implementation Research (CFIR). We reviewed trial documents, conducted semi-structured interviews with key informants (n = 10) and conducted four focus group discussions with participants in both arms of the trial. Three analysts undertook CFIR theory-driven content analysis of the qualitative data. Quantitative data was analyzed to provide descriptive statistics relevant to the objectives of the process evaluation.

Results: The trial had positive implementation outcomes, 100% retention of clusters and 96% retention for participants, 83% adherence to delivery of content of group talks (fidelity), and 78% attendance (reach) to at least 50% (3/6) of the group talks (dose). The data revealed that intervention characteristics, outer setting, inner setting, individual characteristics, and process (all the constructs of CFIR) influenced the implementation. There were more facilitators than barriers to the implementation. Facilitators included the relative advantage of the intervention compared with current practice (intervention characteristics); awareness of the growing prioritization of diabetes in the national health policy framework (outer setting); tension for change due to the realization of the vulnerability to vision loss from DR (inner setting); a strong collective sense of accountability of peer supporters to implement the intervention (individual characteristics); and regular feedback on the progress with implementation (process). Potential barriers included the need to queue at the eye clinic (intervention characteristic), travel inconveniences (inner setting), and socio-political disruption (outer setting).

Conclusions: The intervention was implemented with high retention, reach, fidelity, and dose. The CFIR provided a valuable framework for evaluating contextual factors that influenced implementation and helped to understand what adaptations may be needed during scale up.

Trial registration: Pan African Clinical Trials Registry: PACTR201707002430195 registered 15 July 2017

Keywords: Diabetes, Diabetic retinopathy, Peer support, Cluster-randomized clinical trial, Consolidated Framework of Implementation Research (CFIR), Process evaluation

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Background

Early detection of diabetic retinopathy (DR) poses a significant medical and public health challenge, particularly because DR is asymptomatic until the advanced stages. The benefits of regular screening have been documented [1], but uptake remains low for people living with diabetes (PLWD) in settings without systematic DR screening programs [2]. Diabetes Support Groups (DSGs) provide an opportunity for demand-side interventions to increase attendance at screening and confront this inequity [3]. However, there is need for evidence on the factors that influence implementation and outcomes of DR interventions involving DSGs.

The DURE (Uptake of Retinal Examination in Diabetes mellitus) trial was a 6-month pragmatic cluster randomized controlled trial (cRCT) to evaluate the effectiveness of a complex intervention to promote screening for diabetic retinopathy among members of DSGs in Kirinyaga County, Kenya. The DURE trial interventions have been described in detail [3]. Briefly, the trial compared the proportion of PLWD who attended screening in seven DSGs that received the intervention with seven "usual care" DSGs that did not receive the intervention. The intervention consisted of (i) training of peer supporters; (ii) monthly group talks at the DSGs by peer supporters and referral of PLWD to the eye clinic; (iii) monthly individual reminders to PLWD (by peer supporters) to attend screening the eye clinic; and (iv) weekly telephone support to peer supporters from the research team.

The intervention was developed in accordance with the guidelines of the Medical Research Council (MRC) framework for complex interventions [4]. These guidelines recommend using appropriate theory to develop interventions that address the barriers to behavior change. Our formative research identified several barriers to uptake of DR screening [2]. Self efficacy is a strong precursor to behavior change [5, 6] including attendance to screening [7]. Based on the self-efficacy theory, we hypothesized that an intervention that increases self-efficacy can decrease the perceived barriers to attendance to screening. The theory proposes four methods of changing self-efficacy in order to change behavior: providing mastery experiences (e.g., recalling previous screening for other diabetes complications); vicarious learning (e.g., from hearing experiences of peers who have had DR screening); verbal persuasion (of the need for screening); and addressing psychological and affective states (such as anxiety about taking a screening exam) [6]. The theory-driven conceptual framework of intervention effect is illustrated in the protocol [3].

The MRC framework [4] emphasizes four key phases of interventions: intervention development; feasibility and piloting; implementation; and the evaluation of both outcomes and process. In this paper, we describe the results of the process evaluation. Process evaluation is a study which aims to understand the functioning of an intervention, by examining implementation, mechanisms of impact, and contextual factors [8]. The conduct of process evaluations alongside RCTs has been recommended, because they give insight into the "black box" of health care interventions; facilitate the interpretation of the findings; explain why, for whom and how a complex intervention had a particular impact; and determine whether a complex intervention should be scaled up or modified for other contexts [9, 10]. Process evaluations are particularly important in cRCTs, because of the potential for between-cluster differences that need to be understood [10, 11].

Theory-driven process evaluation necessitates that the designers make the theory explicit and then use it to identify how the intervention leads to the outcomes [12]. The Consolidated Framework for Implementation Research (CFIR) is a is a meta-theoretical framework that synthesizes constructs from multiple theories on implementation of interventions, in order to explain what works and why across multiple contexts [13]. The CFIR outlines five major factors that influence implementation of interventions: the characteristics of the intervention, the inner setting, the outer setting, the individuals involved, and the process of implementation (Table 1). By applying this framework to the process evaluation for this cRCT (Fig. 1), we aimed to (1) understand the determinants for the outcomes of the DURE intervention in Kirinyaga and (2) examine the context of implementation in terms of the intervention's recruitment and retention, reach, fidelity, dose, and acceptability (Table 2).

Methods

Ethics

The DURE trial and its process evaluation has ethics approval from the research ethics committees of the London School of Hygiene and Tropical Medicine in London and the African Medical Research Foundation in Nairobi. Trial registration: Pan African Clinical Trials Registry: PACTR201707002430195.

Setting

The setting of the study is described elsewhere [3]. Briefly, Kirinyaga county is a rural agrarian county in Central Kenya. The prevalence of diabetes in Kenya is estimated to be 2% in the population 18–64 years [14]. An estimated 40% of the PLWD in Kirinyaga are members of DSGs, and a health system assessment by our research group found that only 7% of them have had an annual DR screening exam as recommended. DSGs have monthly meetings in the community led by peer supporters, where they measure the weight, blood sugar, and blood pressure of attenders. They also engage in other activities relevant to health promotion and advocacy. At

Table 1 Constructs of the Consolidated Framework for Implementation Research

Construct	How the construct relates to the DURE trial
Characteristics of the intervention—core components and adaptable components	Intervention characteristics (adaptability complexity, relative advantage) can influence whether the intervention is adopted
Inner setting—structural, political, and cultural context that directly affects the implementation	The context of the DSGs and the eye health system in Kirinyaga can influence how participants experience the intervention
Outer setting—broader economic, political and social context	Broader political, economic, health policies, priorities, resources, incentives, and governance may impact trial activities
Characteristics of individuals—people responsible for delivering the intervention (peer supporters)	Training, knowledge, perceptions, motivation, and leadership of peer supporters can influence extent of implementation of the intervention
Implementation process—the activities involved in planning, engaging, execution, and evaluation of implementation process	The involvement of stakeholders in the planning, execution, and evaluation of progress of the trial may influence the acceptability of delivery and reception of the intervention

DSG Diabetes Support Group, *DURE* Uptake of Retinal Examination in Diabetes study

the time of the DURE study, there were 16 DSGs active in Kirinyaga. Two of them participated in the pilot trial, while the other 14 were recruited into the main trial.

Two peer supporters were recruited in each DSG (1 male, 1 female), as per the eligibility criteria in Table 3, and none of them had previously delivered an eye health intervention. They received two days of training using a curriculum developed through the process described in Additional file 1. The content of the training and the key messages that the peer supporters delivered to participants are described in the protocol [3]. An allowance was provided to peer supporters for telephone communication with participants, but no other financial incentives were given. Weekly telephone calls between the principal investigator and peer supporters were carried out to share progress, build a sense of belonging, and address any challenges emerging during the program.

The county has a well-equipped eye clinic at the Kerugoya county referral hospital. Patients at the clinic are attended on a walk-in basis. There were four eye health workers (one ophthalmologist, three ophthalmic clinical officers) in the county during the study period. Guidelines for screening and management of diabetic retinopathy were launched at the national level 3 months before the start of the main trial, and were also being implemented in Kirinyaga county [15].

Design

This is a mixed-methods process evaluation of a cRCT. We used the CFIR to guide the process because it is comprehensive and can be used to develop the evaluation tools, guide the content analysis, and aid interpretation of findings [16].

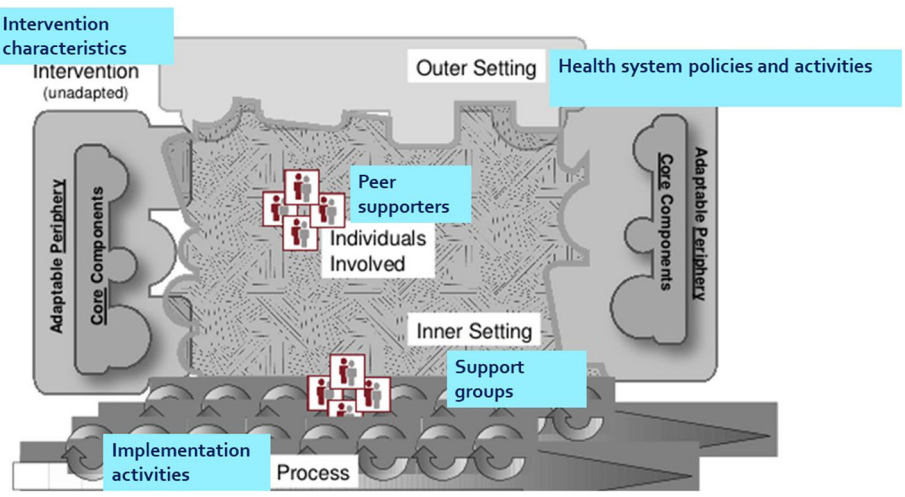

Fig. 1 Consolidated Framework for Implementation Research as it relates to this trial (adapted from Dramschroder et al, 2009 [13])

Table 2 Measures for the level of implementation

Implementation measure	Questions related to DURE study	Quantitative indicator(s)—compared with target
Recruitment and retention	How successful were the recruitment and retention procedures?	-Proportion of DSGs that agreed to participate (%) -Proportion of participants invited who agreed to participate (%) -Peer educators recruited, trained and retained (*n*) -Retention rate of clusters and participants in the study (%)
Reach	What proportion of the intended audience was exposed to the intervention?	-People who were referred (*n*) -People who received individual reminders (*n*) -People who attended group meetings (*n*)
Dosage delivered	What percentage of interventions was delivered most/least successfully by implementers?	-Group talks delivered (*n*) -Referrals made (*n*) -Individual reminders given(*n*)
Dose received	What percentage of the intervention was received most/least successfully by the target audience?	-Proportion of group sessions attended by each participant (%) -Referrals given (*n*)
Fidelity	How much of the intervention was delivered as intended (adherence)? What parts were not delivered?	-Adherence to content of group talks -Adherence to frequency of group talks
Acceptability	How acceptable is the intervention for current and future implementation?	Acceptance of the intervention by peer supporters and participants Willingness of stakeholders to scale up the intervention in future

DSG Diabetes Support Group, *DURE* Uptake of Retinal Examination in Diabetes study

Table 3 Eligibility criteria for participants and peer-supporters

Criterion	Participants	Peer-supporters
Age > 18 years	√	√
Member of a diabetes support group	√	√
Will reside in the county for the next 12 months	√	√
Has a mobile phone	√	√
Willing to participate in the study	√	√
Had not had a screening exam in the last 12 months	√	×
Has had a screening exam in the preceding 12 months	×	√
Willing to be a peer-supporter	N/A	√
Willing to commit 2 days for training	N/A	√
Willing to commit many hours to peer-support work	N/A	√
Fluent in Kikuyu or Kiswahili	N/A	√
Already attending DR screening	×	√
Already receiving treatment for DR	×	×
Has a debilitating illness	×	×

"√" indicates participants or peer-supporters included in the study
"×"indicates participants or peer-supporters excluded in the study
N/A Not applicable

Data collection

Data on recruitment and retention, fidelity, reach, and dose were collected routinely during the trial activities and collated through document review. Peer supporter training records provided information on attendance and content of training. Trial registers provided data on recruitment, while DSG meeting attendance registers captured participants attendance and retention, as they provided the date of the meeting and the list of attendees. DSG meeting minutes, peer supporter diaries, and the research team's activity logs, and field notes contained detailed information on the intervention activities, personnel involved, duration, frequency, and resources used.

We studied the sample interview questions available on http://cfirguide.org/ and tailored our data collection tools to gather information relevant to the DURE study. These questions related to the stakeholders' perception of the intervention and how it worked/did not work.

Ten interviews were conducted with purposively selected key informants to represent recipients, implementers, administrators, and policy-makers. Key informants were recruited until data saturation was reached. Face to face interviews were conducted by the first author in English at locations convenient to the key informant, using a semi-structured interview schedule. Interviews lasted 30–60 min and were captured through field notes.

We conducted four focus group discussions in community settings with 7 participants in the intervention arm who did not take up screening; 7 participants in the intervention arm who took up screening; 8 participants from the control arm; and 7 peer supporters. Focus group discussions were conducted in the Kikuyu language by the first author and two research assistants who were considered culturally appropriate but not involved in the trial implementation. Discussions were audio-recorded, transcribed, and translated into English.

Data analysis

Quantitative data on recruitment and retention, reach, fidelity, and dose were analysed for descriptive summary statistics.

A thematic content analysis of qualitative data was undertaken based on the different constructs and subconstructs of the CFIR: (1) Intervention characteristics (e.g., acceptability of the intervention, compatibility with existing DSG programs, relative advantages, or disadvantages of the intervention, and suggested adaptations); (2) Outer setting (e.g., perceived role of the Ministry of Health (MoH) policies and guidelines in driving which services were implemented); (3) Inner setting (e.g., perceptions about organizational factors within DSGs and the eye clinic, that might have affected the implementation); (4) Individual characteristics of peer supporters who delivered the intervention (e.g., knowledge, attitudes, self-efficacy about their role); and (5) Implementation processes (e.g., planning, engagement, and execution factors that may have affected the delivery and reception of the DURE intervention). Using the CFIR as a template framework, the principal investigator and two other analysts (1 male, 1 female) read the transcripts, coded the data independently, and grouped the codes into themes. Analysis began as soon as the first interview was completed, and then proceeded concurrently with data collection until data saturation was reached. The analysts reviewed the codes iteratively to check for potential biases, and to verify the emerging themes. Discrepancies between coders were resolved through discussion and review of the original transcripts.

Data (qualitative and quantitative) from all sources were organized under the respective constructs and subconstructs to facilitate triangulation and to identify which factors affected the acceptability, recruitment, retention, reach, fidelity, and dose of implementation.

The first author had undertaken training on implementation research and clinical trials, and had expertise on the technical content of the intervention. All the analysts had skills in quantitative and qualitative research methods.

Results

How was the intervention implemented?

Recruitment and retention

All the 16 DSGs in the county accepted to participate in the trial (2 in the pilot trial and 14 in the main trial). All clusters were retained throughout the study. Of 837 members of DSGs approached to participate the main trial, 86 did not meet eligibility criteria (Fig. 2), and 17 did not consent, thus 734 participants were recruited and participated in the trial. Of these, 31 (4.2%) were lost to follow-up during the trial (95.8% follow-up rate rate). The 14 peer supporters (age range was 29–58 years) received the training program. All had at least secondary education, with three having achieved a tertiary level qualification, although this was not a requirement. One peer supporter was absent from day 72 as another DSG project that was being implemented a different county contracted him for their team. The remaining 13 actively participated in the DURE trial until the end of the trial. The research team maintained weekly contact with peer supporters and attended some of the DSG meetings, which minimized the likelihood of loss to follow-up or missing data. Recruitment procedures had already been tested in the pilot trial [17].

Reach

Out of 369 PLWD recruited into the intervention arm, 92% attended the first group talk, while 72% attended all six talks. Seventy-eight percent attended

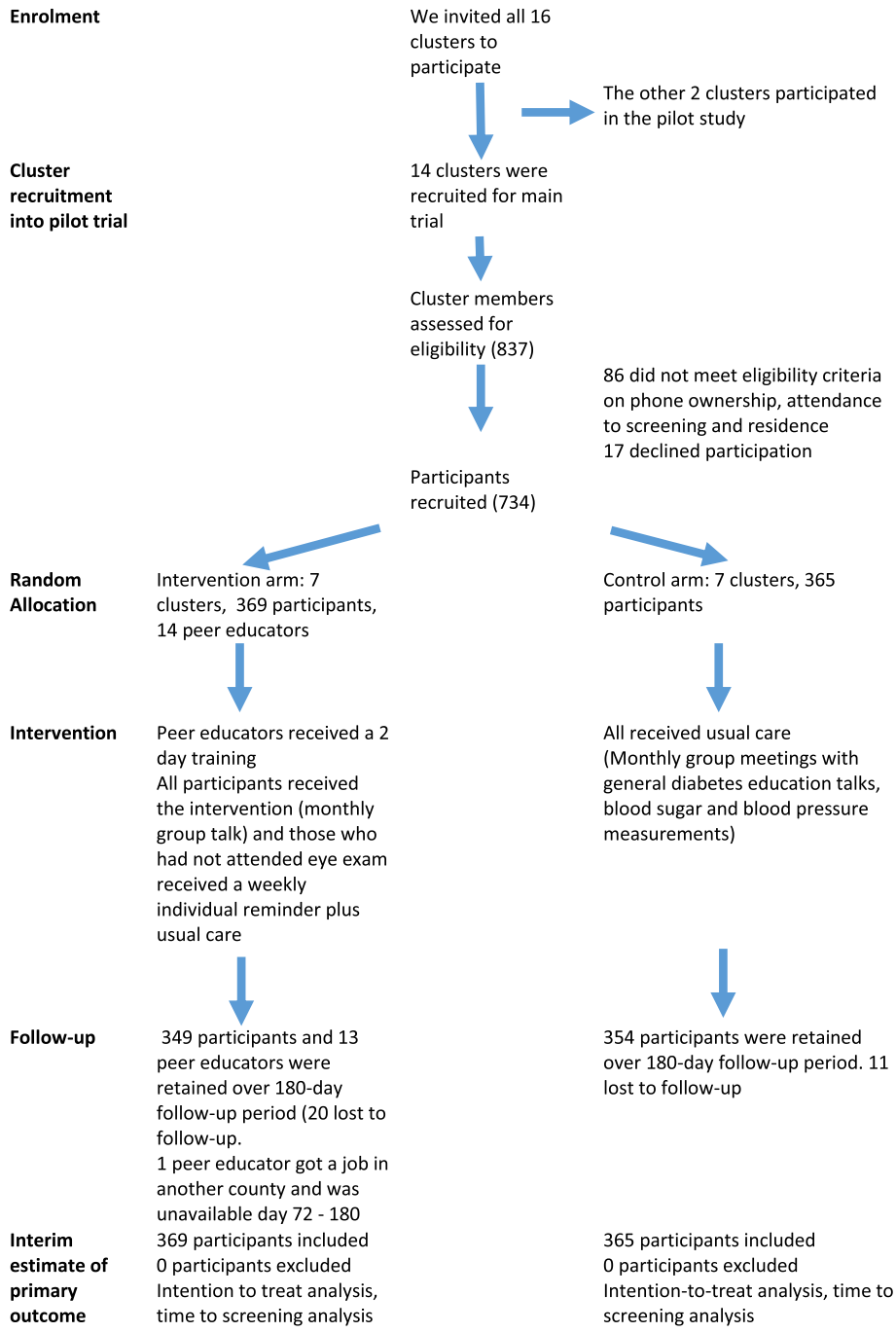

Fig. 2 Flow diagram for the trial

three or more talks (50%), and this ranged from 68% in the most rural DSG to 88% in urban DSGs. One hundred percent of the participants were referred for the screening examination and were issued with a referral card. Peer supporters also gave monthly telephone reminders to those who had not yet taken the screening exam. Seventy-four percent of participants received at least one telephone reminder to attend screening.

Dose delivered and dose received

The 14 peer supporters attended the training. During the 6 months of the study, peer supporters in the seven DSGs in the intervention arm delivered a group talk

each month (total 42 talks, 100% of planned talks were delivered). We found that 34/42 (81%) meetings had an attendance of ≥ 80% of the trial participants.

Of the targeted 369 telephone reminders in the first month, 273 (74%) telephone reminders were made as some of the participants took the screening exam immediately after the first group talk and before the telephone reminders. Forty-eight percent of participants received a reminder each month (six reminders in total) over the 6 months trial period. There were frequent reports of participants being unreachable on phone, as the phones were switched off, or they had changed the number. In such cases, the peer supporter arranged a personal visit to the participant to give a face-to-face reminder (this was a local adaptation of the intervention). During the first two months of implementation, peer supporters from two different DSGs made weekly calls to the principal investigator to seek feedback (in addition to the weekly calls that all peer supporters received from the principal investigator). This was a further form of intervention adaptation; these two DSGs had the highest rates of implementation fidelity.

Fidelity

There was 100% adherence to the frequency of the group talks (one group talk every month). However there were occasional changes on the actual date of the group talk each month (due to other communal activities), such that the intervals between the group talks were not constant. Adherence to content of group talks met the required threshold in 83% of the group talks. Some 43 participants could not be reached on telephone at least once during the trial, and the peer supporters gave them a reminder through a face-to-face communication as mentioned above. We monitored adaptations, which we interpreted as evidence of ownership and adaptation to meet contextual needs.

Acceptability

The acceptance of the intervention in the study population was high, given the high retention in the study. The intervention was perceived as beneficial and acceptable to participants because it was bridging information gaps.

> *I am happy you people are coming here to us, because we are benefiting. Although I have not yet gone [for screening], I now know that I should not wait to have problems with my vision and I know where I should go [for screening]* (*FGD participant*)

There was satisfaction with the study procedures among the participants. This was not surprising as we had tested these with a pilot study [17]. We had anticipated participants to be uncomfortable with temporary blurring of vision due to dilating drops, but it was not perceived to be a significant problem because they were forewarned about it.

> *The difficult seeing after the medicine in the eye…it was not as serious as I expected,… it was not like you could not see at all…, and by the time I was going home I could see very well* (*FDG participant*)

All 10 key informants were willing to scale up the intervention to other counties in future, using the DURE tools such as the PS training curriculum and the community entry mechanism.

> *The DURE curriculum for the peer supporter training is very comprehensive and easy to follow, and we want to formally adopt it in our peer supporter manual, so that we can use it in our routine training of peer supporters* (*KDDA national representative*)

Eye care workers accepted to conduct the screening for DR, even though at first they were concerned about a sudden increase in the screening workload.

> *Initially we had concern that this might increase the workload, but we found that this was only a temporary effect as many participants came at the same time for the screening, which is unlikely to happen in the repeat screening visits. It is good to see the participants asking for the screening… they already have the information about it* (*eye health worker*)

How was the intervention experienced?

Table 4 shows the five CFIR constructs, the sub-constructs identified within them and examples of the related quotes.

DURE intervention characteristics

Stakeholders considered the peer-supporter-led intervention to have relative advantage, as it was not feasible to have health workers go to the community to give the same intervention. All PLWD also perceived the DURE intervention as a relative advantage compared with the usual practice where they were not offered screening. In particular, participants found the referral card highly valuable as it represented personalized care and was perceived to make it easier to navigate interaction with eye care providers. Peer supporters valued the training and task shifting which gave them confidence and recognition that they did not have before.

The intervention components were easy to implement along with the usual duties of peer supporters, and were adaptable to suit local needs (such as additional face-to-face reminders for participants who could not be reached by phone). Although research assistants

Table 4 Quotes on CFIR constructs

CFIR construct/sub-construct	Sample quotes
Intervention characteristics	
Relative advantage	This is more effective than leaving it to health workers from the hospital to go to the community to educate the PLWD, for that is not always feasible (MoH national representative) The training we received was very good. People appreciate my work when I give them talks… (Peer supporter) The referral card…have a look (showing the card)…it has my name, and the date of my next clinic … at the clinic I just showed it (to the staff) and I was attended (FGD participant who attended clinic) I still have my referral card … I never leave it behind…so I know that the day I go to the eye clinic I will show it and get checked (FGD participant who did not attend clinic)
Complexity	Training the peer supporters was not difficult, the training slides are easy to use (trainer) We are not doing things that are very different from what is usually done …[in DSGs]…we were already familiar with group talks, what we have not been doing was the telephone reminders...and giving referrals, but that is not burdensome (peer supporter) When I learnt the reason for the test, and was given the referral card…all I needed was to present myself at the clinic. You could go even the following day, anytime…and you only needed to go once. We went together several of us. Can anyone say that it is difficult? (FGD participant who had screening)
Adaptability and flexibility	I wanted the PLWD to go to the eye clinic as soon as possible…so if I could not reach them on phone because they had put off the phone, I took it upon myself to go to their homes (peer supporter) We carry out the DURE activities because they fit well with our other activities…I go on with my usual work on the farm except for the DSG meetings (peer supporters) During recruitment, we realized that we needed additional personnel in the recruitment team, so we expanded the team (member of research team)
Cost	The intervention uses existing resources in the community and in the hospital…this is the biggest advantage because it can scaled up without cost limitations…(MoH county representative) People's pockets are different…when I went there I had only 100 shillings … I paid 50 for registration. They asked me to pay another 50 for eye examination. I paid it because I had to get the screening. But someone else will just say they will come next week. (FGD participant who attended screening)
Relative disadvantage	The only problem is that at both the diabetes clinic and the eye clinic they make you wait… queuing two times…then in the eye clinic they put some medicine in your eyes and ask you to wait again …you can end of wasting a lot of time waiting. Why should I que twice? (FGD participant who attended screening) But why don't you focus on preventing the complications, rather than just screening? For me

Table 4 Quotes on CFIR constructs *(Continued)*

CFIR construct/sub-construct	Sample quotes
	I have begun with doing exercises, but later I will go for the screening. [names peer supporter] will take me there… (FGD participant who did not attend screening)
Outer setting	
Diabetes as a health priority	We are keen on sustainable interventions for NCDs and we have to go to where the patients are found…We should not wait for patients to come but go to them. This is sustainable because the trained peer educators will remain in the DSG to educate more people. We will work with them more. (MoH representative at national level)
Clinical guidelines for DR are used as a national governance tool that is also useful for resource mobilization	The clinical guidelines have been very helpful. Earlier on I did not routinely screen those who have good vision. Now I dilate and screen all those that come here. We also order more dilating drops (eye health worker)
Peer supporters mitigated potential implementation challenges such as political events	The presidential elections were nullified, everyone left the (DSG) meeting to go and watch the news… and had I not been passionate to mobilise members there would have been very poor attendance at the next meeting… (peer supporter)
Intervention fits within the norms of the health care system	The county health services, including eye care and diabetes care services supported this innovative involvement of peer supporters because we all want to improve quality of life for PLWD (MoH representative at county level)
External outreach camps	There were two external mobile outreach camps organized at a church by a private care provider …some of the people preferred to go for the screening here because it was nearer (DSG county lead) With the mobile outreach clinic, you know it is only for one day, so you don't want to miss the opportunity. For the hospital, some of the people, even if they live near, do not attend… They keep on postponing because the eye clinic will always be here… (Peer supporter)
Inner setting	
Tension for change	I know someone who doesn't go out of his home now, because he can't see…that is why we have been told not to wait till we have eye problems (FGD participant who took screening) I have never had my eyes checked…. Can you check me today? Or give us the referral cards so we can go [to the eye clinic] tomorrow (FGD participant from control arm) We have to find a way of easily identifying those any diabetes patient who has not been screened. May be label their files so that they can easily identified (eye health worker) We have seen people going blind…nobody will come from outside to stop it… we have to do something ourselves (KDDA county representative)
Compatibility	We give the group talks as part of the monthly DSG meetings (peer supporter) We want to have all PLWD screened for DR, thus this intervention is contributing to that mandate (eye care worker)
DSG Organisational Culture	For us we are always open to new things that can help us who live with diabetes, so we are

Table 4 Quotes on CFIR constructs *(Continued)*

CFIR construct/sub-construct	Sample quotes
	happy to work with you on this…it empowers us to not just to go for screening, but to engage in advocacy for diabetes eye health (KDDA local representative) In DSGs, we know about volunteering … and for the good of our people, we all have to work together to ensure everyone goes for the eye check… I do not mind giving my time to do this, though of course it requires extra time … I am happy people got tested (peer supporter) At the DSG I tell them my experience with screening…we don't hide things from one another…(PLWD who has taken screening) In some of the DSGs, participants came together…we would have a large group turn up at one go…they would tell me they all agreed to come together (eye health worker) Here we like to share about ourselves openly, we don't hide things, we are not afraid to open up or keep reminding one another about attending screening (FGD participant who attended screening)
Incentives and rewards	We do not get paid for this work, it is about volunteer work, people who do not want to volunteer their time cannot do this work (peer supporter) But since we are doing good work, and we spend a lot of time on it, if we were paid we could do even more (peer supporter)
Readiness for implementation	We are planning a peer supporter training in [names county]…we want you to come and train them so that they start doing the same in [names county]… (KDDA national representative) Now that you have done this with some groups, you also have to come to our groups and give us the intervention, … you should not leave us out (PLWD from control group)
Adjustments in the eye health system	Sometimes, people did not screen for diabetic retinopathy if the patient's vision was good. But now we have been reminded to screen all PLWD annually and we have started doing that (eye health worker) The eye clinic has recently been renovated, we saw the governor launch it and we heard that it has all the equipment, so we are now happy to go there. (FGD participant who attended screening)
Community volunteers (CVs) reinforced key messages	Community volunteers really support us… because they reinforce what we say. In our DSG, we have a member who is a community volunteer… I usually call her to speak after I given the group talk...it is better when the message comes from two people. (peer supporter)
Geographical barriers hinder uptake of screening	Getting to the eye clinic is a problem because the easiest way is to take a *boda boda* (motorbike taxi) to the main road and then wait for a *matatu* (public van). I avoid *boda boda* because I have a back problem, so I just wait for the outreach camp. (FGD participant who has not attended screening) From this experience, the cost of mobility must be borne by the provider, not the PLWD. We

Table 4 Quotes on CFIR constructs *(Continued)*

CFIR construct/sub-construct	Sample quotes
	must find a way of going to the DSG for screening, rather than asking them to come. (member of the steering team) For me, I haven't gone to the eye clinic. I am looking for the fare. Why can't you come to do the test here? (FGD participant who has not attended screening)
Peer supporter characteristics	
Knowledge and beliefs about the intervention	The peer supporter at [DSG] informed me that they have started a WhatsApp group for peer supporters…to discuss how they can do more to prevent diabetes complications in general…they feel the work they are doing with DURE can be expanded (PI field notes) I observed that the peer supporters enjoyed giving the group talks, and the key messages were easy to explain and it was a social activity, unlike the paper work which was more of an individual task. They still did the documentation since they were trained to do it. (research assistant)
Individual identification with the role of PS	In our support group, most people have gone to the eye clinic, because [names peer supporter] is very active, and he makes us laugh when he is giving the talk…you cannot get tired…and every time he meets you he will remind you, even at church… (FGD participant who attended clinic) I always see [name] here in the diabetes clinic, bringing his DSG members. Then he also takes them to the eye clinic. Sometimes they tell him they do not have the money for the hospital fee but he insists and they pay (diabetes care worker)
Individual stage of change	All the peer supporters had already taken screening so they must have been good role models (KDDA national representative) None of the peer supporters had any previous training on delivering a diabetes eye health intervention, you could tell that they liked it…the novelty of the information seems to have been a motivator… (Trainer)
Personal attributes	"I did not do as much work as [name], though he and I are the supporters in our group. But he did very well…you know he is younger, '*sharp sharp*' (slang for exuberance) and men can do this work more easily… " (Female peer supporter) [Name] is ever punctual so we know (DSG) meetings will run on time. She is a teacher so she explains very well. That is why many people don't miss the meetings, and most of us got tested the very first month (FGD participant who attended screening) What I have seen, is that he [peer supporter] is self-sacrificing…from the heart … he closes his business of selling clothes to bring PLWD to both the diabetes clinic and the eye clinic (diabetes clinician) We did not know whether keeping the peer supporters engaged over six months would be challenging…I would say selection of peer supporters is important as they have to be highly motivated and committed (member of steering team)

Table 4 Quotes on CFIR constructs *(Continued)*

CFIR construct/sub-construct	Sample quotes
Self-efficacy of peer supporters	He took me to the eye clinic, together with others… he did not feel bothered about waiting in the queue with us… (FGD participant who attended screening) When I saw that the first five members had gone for screening right after I gave the first talk, I knew I was doing it right, I felt motivated me to continue with the work (peer supporter) When I observed [names peer supporters giving the talk], they performed so well, they answered all the questions. I think it is because they were trained well… (research assistant)
Process of implementation	
Planning	We were very happy to be involved from the beginning…we have always insisted on being involved as equal partners in things that concern us, so we participated (KDDA national representative) I remember the meeting we had at the beginning…when our chairman of KDDA came and introduced the project…we agreed to support… (peer supporter)
Engaging	The research team was really committed …they were always available and we worked so well together, it made us not to leave the work half- way (peer supporter) …we even took lots of photos The community volunteers, they really embrace us…we support one another in the work (peer supporter) I looked forward to the call from the PI every week – it gave me motivation (peer supporter) Regular briefing helped us to keep involved (steering committee member)
Executing	We were of course concerned about the feasibility of the intervention since we have not used the DSG platform before. But we had success with the pilot trial, so this proved not to be a major issue (member of project steering group) The DSGs in the control arm are left out, but we have understood that they can get the intervention thereafter (peer supporter)
Evaluating	I am looking forward to the findings of the study (research nurse) You need to give us a copy of the results …(MoH county representative) We will organize a forum to share the results with the stakeholders (MoH national representative)

DSG Diabetes Support Group, *DURE* Uptake of Retinal Examination in Diabetes study, *FGD* Focus Group Discussion, *KDDA* Kenya Defeat Diabetes Association, *MoH* Ministry of Health, *PI* Principal Investigator

observed that documentation tasks were time-consuming for peer supporters, these peer supporters did not perceive it as difficult. Given that the pilot trial had provided an opportunity to test-drive the intervention, all stakeholders recognized the intervention as "fit for trial".

Stakeholders noted that the intervention utilized existing resources, rather than requiring additional resources, which pointed to the advantage of cost-efficiency and possibility for scaling up. At the individual level, some PLWD indicated an inability or unwillingness to pay the hospital consultation fee at the eye clinic might be a financial

barrier to screening. Another relative disadvantage was the need for queuing at the eye clinic, especially because those who attended the diabetes clinic on the same day had to queue twice. One participant expressed skepticism about prioritizing screening rather than lifestyle interventions (such as physical exercise).

Outer setting

Stakeholders highlighted the growing health priority given to diabetes and other non-communicable diseases within national health policy framework as an important outer setting construct that increased stakeholder interest in the implementation of the DURE intervention. The intervention was also perceived to be responding to patients' need for a patient-centered approach to care, in addition to being aligned with the norms of the health system such as increasing efficiency and access to services.

The recent implementation of the clinical guidelines for DR had sensitized the diabetes and eye health workers that all PLWD need annual screening for DR. Eye care providers also found the guidelines useful for mobilizing required resources such as mydriatic eye drops. The guidelines were considered an aid to implementing the intervention.

Disruptions in the sociopolitical environment presented a potential outer setting constraint. During the study period, there was a disputed election that was subsequently nullified and had to be repeated. It can be challenging to maintain participant attendance to DSG meetings or to screening during periods of political turmoil. The peer supporters mitigated this potential disruption through persuasive communication with participants. The research team similarly maintained communication with all the stakeholders to ensure continued engagement, fidelity, and availability of screening at the eye clinic.

There were two external outreach eye camps in the county during the study period. Some participants attended screening at these camps instead of the eye clinic. This is because they offered the advantage of proximity, convenience, and the perception of being a scarce but valuable opportunity for screening, which constituted an external incentive. As they used the same screening guidelines, any participants screened at the outreach site was taken to have the outcome of interest.

Inner setting

The implementation climate is a key sub-construct within the inner setting construct that was found to be associated with the DURE implementation. Among the peer supporters, there was tension for change that resulted from the training, since they perceived that PLWD are vulnerable to vision loss from DR. Similarly, eye care workers expressed the need to detect and treat DR in a timely manner, as most patients presented with advanced DR. The PLWD reported having taken up screening early in the intervention because the group talks raised awareness about their vulnerability to DR, thus raising the relative priority of taking up screening.

Peer supporters found the intervention to have high compatibility as it was seen to respond to the tension for change, and it was designed to fit within the usual support group activities. To this extent, the compatibility was a facilitator for implementation. Participants tended to turn up at the eye clinic in groups especially early in the trial, and since screening procedures take time, there was a risk of overloading the health system. However, we recognized that this potential implementation barrier was foreseeably transient, since the participants would get individualized appointments for subsequent screening. Based on this premise, the eye care workers supported the implementation, and thus the potential challenge transitioned to become an enabler. This theme also emerged in relation to acceptability (above).

The organizational culture of DSGs is another subconstruct that influenced the implementation. One of the participants referenced that DSGs are usually receptive for "new things" especially those that empower the PLWD. Participants pointed to the culture of self-disclosure, which was associated with the willingness of participants to update the peer supporter and DSG members on whether they had taken up screening. Further, the culture of collective action led participants in a DSG to team up and go together for screening. Due to the culture of volunteerism, peer supporters were willing to commit time to deliver the intervention and sometimes to accompany the participants to the eye clinic. However, a potential threat to volunteerism was also voiced by peer supporters who expressed that they could be doing other things (opportunity cost) and that since their work was effective they should receive some incentives from the government.

Readiness for implementation was epitomized by the interest of DSG leadership at national level to begin scale up of peer-supporter training and to incorporate the DURE training curriculum in the peer-supporter training manual. Participants referenced national-level stakeholder interest to scale up the intervention to other counties. On the other hand, eye care workers articulated the need to equip the eye clinic with more staff and technology for screening.

Participants in the control arm requested for the intervention to be implemented in their own DSGs as they felt left out. This was already planned to meet the ethical obligation to ensure that control groups also benefit from the intervention [18]. This implementation in control arm DSGs was implemented subsequent to the trial.

A potential barrier in the structural characteristics construct of the inner setting is the geographical terrain and distance to the eye clinic for geographically remote participants—distance, unsuitable transport options,

cost, and time for travel were noted to be challenges for participants of some DSGs.

Characteristics of peer supporters

On the sub-construct of knowledge and beliefs about the intervention, all peer supporters attended the training and rated it as a very useful learning experience because they had no previous exposure to eye health. The training was articulated as a facilitator of implementation since it created self-efficacy to deliver the intervention and to answer any questions from participants. Both the training and the task-shifting inherent to the intervention were valued as sources of personal fulfilment and increased role-recognition by peers and health workers. However, supporters identified that their contribution in the intervention risked being overlooked or under-recognized as they had not received formal recognition such as certificates. Providing certificates was a challenge at this stage because we needed to have the training curriculum formally adopted before certification. Providing certificates may facilitate implementation in scale up of the intervention, by stemming potential burnout or turnover of peer supporters.

Regarding individual stage of change, peer supporters expressed a collective (rather than individual) sense of accountability to implement the intervention: "we are the people to make a contribution to reducing the number of people going blind". This may relate to the culture of collective action, a theme already highlighted under inner setting constructs. Being volunteers, their motivation came from a sense of altruism, but they were also motivated by the training and subsequent initial success of seeing participants attend the screening. The 13/14 peer supporters remained engaged with the trial until the end, and they reported that the weekly telephone contact with the principal investigator kept them engaged. Community volunteers were a further source of motivation, even though they do not have diabetes. This is because they are also volunteers in the community, are well versed with the health system and they reinforced the key messages.

Cultural adaptation was further highlighted at the peer supporter level, especially relating to gender and age norms in the performance of peer support roles. For example, a female peer supporter noted that she took on a smaller proportion of the tasks and left the rest to her younger male counterpart. However, age and gender were not sufficient to account for the effectiveness of peer supporters. Participants identified some personal attributes of peer supporters that influenced them to take up screening. These included interpersonal skills demonstrated while delivering the group talk (e.g., using humour, keeping time), persistence with follow-up, individual reminders and accompanying participants to the eye clinic.

Process

Collaborating with stakeholders emerged as an important attribute. DSG leadership at national and county level were satisfied that they had been involved in the planning of the implementation, through attending pre-implementation meetings. They also noted that the community entry process (through the national, county, and support group leadership) positively influenced acceptability of the intervention.

Continuous engagement was considered critical, in the form of frequent telephone contact or face-to-face contact with all the stakeholders. Peer supporters found the training and weekly telephone calls to give them a sense of identity with the trial. Research assistants valued role modelling for their tasks, while all stakeholders valued regular feedback. In the executing sub-construct, the trial was executed as per the trial protocol. It was not feasible to mask the intervention arm to the intervention, since the intervention activities within a DSG were overt. However, we did not find any evidence of contamination between clusters, perhaps because participants were not privy to the intervention allocation of other DSGs. Regarding reflecting and evaluating, we regularly reviewed the progress and quality of implementation with peer supporter and eye care workers. Peer supporters constantly reflected on their own performance and gave updates particularly on the reach and fidelity. All key informants and participants looked forward to receiving the results of the trial.

Over-arching analysis of the factors influencing implementation

We found that the intervention was in alignment with health system priorities and stakeholder interest. All five constructs of the CFIR impacted the extent to which the intervention was implemented, and the sub-constructs within different constructs were inter-related. For example, among the participants, tension for change developed when the intervention raised awareness of the vulnerability to vision loss from DR. Training of peer supporters enabled them to deliver the intervention, as well as to develop self-efficacy to increase uptake of screening among participants. Getting feedback on the number of people who had attended screening further increased self-efficacy among peer supporters. Prioritization of diabetes and implementation of clinical guidelines for DR also created tension for change among health workers who conducted the screening. Figure 3 illustrates this example of inter-relatedness. Most of the factors identified in each of the constructs were facilitators of implementation, and were modifiable, which means interventions targeting these factors can improve implementation during scaling up.

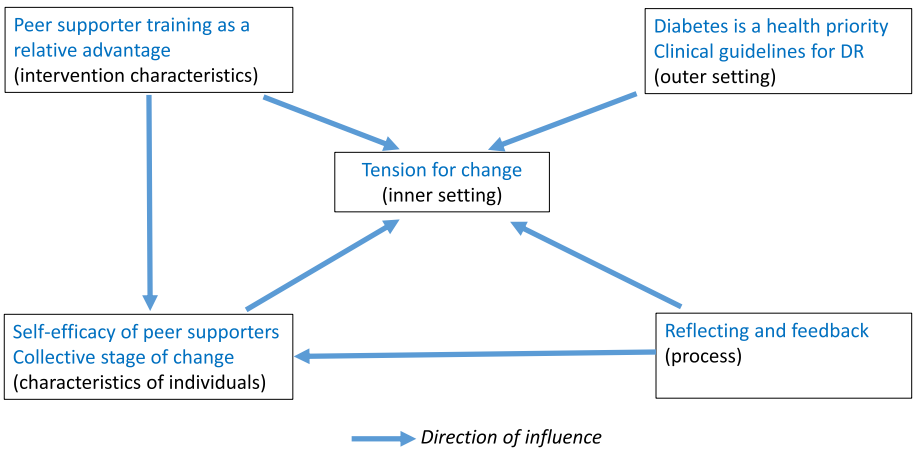

Fig. 3 Inter-relatedness of the CFIR constructs

Discussion

The DURE study process evaluation provides detailed information on the implementation outcomes and the context of implementation to better understand how the intervention and context interacted. This is the first trial to increase access to DR screening through peer support interventions that has also documented the implementation process. The strengths of this study include the use of a validated theory (CFIR). This theory focuses on broad constructs that are representative of the potential influences on the implementation process, which enhances the generalizability and replicability of our methods [12]. We collected data from different stakeholders, which provided an understanding of how different stakeholders experienced the intervention and its implementation strategies. We engaged PLWD who had gone for screening as well as those who had not to identify different perspectives on facilitators and enablers for the intervention. We collected extensive data using mixed-methods, and we triangulated findings from different sources for validity and to reduce the potential risk of bias. The qualitative data were in broad agreement and provided rich context for the quantitative findings, which enhances confidence in the findings.

The trial had success with implementation outcomes, i.e., acceptability, recruitment and retention, reach, fidelity, and dose. This success resulted from the perception of stakeholders and that the intervention was beneficial. The stakeholder interest, the tension for change and the increasing priority given to diabetes in the national health policy suggest that this was an opportune time for the intervention.

Stakeholders identified that the national clinical guidelines for DR positively influence the practice and readiness of eye clinics to provide screening. By sensitizing health workers to the need to screen all PLWD, the guidelines created tension for change. This in turn ensured that all who turned up for screening received the service, as it addressed potential supply-side barriers to screening. We therefore conclude that health system strengthening such as the development and implementation of clinical guidelines was a facilitator for the implementation of the intervention as well as adoption of screening behaviour by the participants. Several studies have found that health system strengthening gives traction to heath care interventions [18–21].

We observed an early response to the intervention activities. The highest attendance at group talks was at the first group talk. In addition, all participants were referred to the eye clinic for DR screening at the start of the trial. Participants who took up screening reported doing so as soon as they received the group talk and referral, and other DSG members accompanied them. This may be related to the influence of the culture of collective action as well as the effect of the group talk and referral card. We therefore hypothesise that the first group talk and the referral are the most essential components of the intervention. We also hypothesise that these components are well aligned to the causes of non-attendance to screening in this population, which we had found to be inadequate knowledge of diabetes eye complications and lack of referral of referral for screening [2].

Among those in the intervention arm who did not take up screening in the intervention arm, lack of knowledge was not identified as a barrier, suggesting that the intervention had good reach and had increased awareness even among those who did not take up screening. At the same time, participants who did not attend screening still indicated intention to take up screening. These points to the need to identify the post-awareness/intention barriers among PLWD. Grimshaw et al. (2014) had a similar finding among physicians who received an educational intervention to increase referrals of PLWD for DR screening [12]. There were some potential relative disadvantages of

the intervention, such as having to queue and pay consultation fee twice if a PLWD was attending both diabetes and eye clinics. This was foreseeable, given the structure of the hospital. These individual, social, and organizational level barriers are consistent with those in the literature [12, 21–23]. Some hospitals are testing the effectiveness of conducting DR screening at the diabetes clinic to overcome this challenge [24]. There is also need to support geographically remote individuals with logistical and financial challenges, such as through multiple access points for DR screening, closer to home [25].

The role of peer supporters in delivering the intervention was a prominent facilitator. Peer supporters delivered the health education talks and telephone reminders, but in addition, they visited participants who were not reachable on phone, accompanied participants to the eye clinics, and waited with them. These are roles of peer supporters that we had envisaged would contribute to increasing the self-efficacy of participants who took up screening [3]. This is evidence that the intervention worked through the anticipated mechanism of the intervention, which strengthens the plausibility of the results [26]. The peer supporters also identified the training and task shifting as very valuable, and these were important enablers for the role of peer supporters. We also found that community volunteers to be an important enabler to peer supporter roles, which we had not anticipated. This is evidence that complex interventions interact with the context in multiple ways to influence the outcomes.

The intervention was compatible with processes and activities of both the DSGs and the eye clinics. We noted adaptation to the delivery of the intervention (but not to the content of the intervention), driven by contextual experience. Like other investigators of pragmatic public health interventions, we recognized the need for fidelity-adaptation balance, since they coexist and are both valuable [10, 27]. To mitigate the risk of intervention drift that may occur with adaptation, we monitored the level of fidelity, which was maintained. Rather than threatening fidelity, we found that this adaptation actually maintained fidelity, because it ensured that those who could not be reached by phone still got the scheduled reminders to attend screening.

Our findings highlight that all the constructs of the CFIR were relevant to the trial, and there were multiple determinants to implementation. We cannot attribute the success of implementation exclusively to the characteristics of the intervention, the peer supporters, the DSGs, eye clinics, the outer setting, or implementation processes. More likely, it is the combination and interconnectivity of these constructs working together. This highlights the importance of alignment of interventions to context.

The process evaluation has potential limitations. We did not conduct evaluation at multiple points in the trial; hence, we could not capture changes over time. As the study was conducted in multiple DSGs with different peer supporters, we cannot account for differences in peer support styles. The social and health system context of the trial may also affect the generalizability of its results. The potential for researcher bias by the project investigator undertaking the qualitative interviews is acknowledged; however, it was agreed among the project team that she was the most culturally appropriate person to probe about how the context affected implementation and the mechanisms of impact. We cannot rule out response bias by social desirability, but the risk was low, given that this was not a sensitive topic, and we relied on diverse sources of data.

Conclusion

The intervention was largely implemented as designed, and achieved high implementation outcomes for acceptability, recruitment, retention, reach, fidelity, and dose. There is high stakeholder interest to support scale up. The intervention worked through the expected mechanisms, but was also aided by unanticipated mechanisms. Health system strengthening was a necessary pre-requisite for implementation. We recommend that future process evaluations are carried out at multiple points and include a cost analysis.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s41182-019-0188-z.

Additional file 1. Methodology for development of training for peer supporters

Abbreviations

CFIR: Consolidated Framework for Implementation Research; cRCT: Cluster Randomized Controlled Trial; DR: Diabetic Retinopathy; DSG: Diabetes Support Group; DURE: Uptake of Retinal Examination in Diabetes study; FGD: Focus Group Discussion; KDDA: Kenya Defeat Diabetes Association; PLWD: People living with diabetes

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Authors' contributions

NM, CB, AF, SG, CM, and LM were responsible for conception and designing the study. NM, MN, LM, and MaK were responsible for fieldwork and acquisition of data. NM, MiK, DM, LM, MaK, MN, CB, and AF were responsible for data analysis. All authors participated in interpretation of the data. NM drafted the paper. JR, AF, MaK, SG, CB, MiK, and DM were responsible for the critical review of the paper. NM was responsible for revision of the paper in view of feedback from the co-authors. All authors read and approved the final manuscript.

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data collection and analysis, interpretation of data, and writing the manuscript.

Availability of data and materials

The data that support the findings of this study are available from Ministry of Health, Kenya but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Ministry of Health.

Ethics approval and consent to participate

The ethics review committees of the London School of Hygiene & Tropical Medicine (LSHTM) and the African Medical Research Foundation (AMREF) approved the DURE study. Informed written consent was obtained at the cluster level, while informed verbal consent was obtained at the individual level. The study adhered to the tenets of the Declaration of Helsinki and the principles of Good Clinical Practice.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

Additional notes on data collection

Trial documents such as registers, activity logs, minutes, diaries and field notes provided quantitative and qualitative data on field activities. Quantitative data was extracted on an Excel template by the study team and used to measure recruitment, reach, dose and fidelity. Qualitative data was extracted by two team members independently using thematic analysis and provided explanatory information on the quantitative parameters, as well as on adaptation and contextual factors.

Interviews with key informants were conducted by the primary investigator and captured through field notes written during the interviews. The data was not audio-recorded as field notes were considered sufficient for capturing the information, providing an audit trail and were easily accessible to the key informant during the interview for member-checking. Multiple coders carried out the analysis as explained in the paper. These factors helped to maintain objectivity and transparency, and minimize bias.

Additional notes on measurement of contamination in the DURE study

Before the study we identified processes that may lead to contamination. The intervention was delivered during DSG meetings. There were two main processes that could lead to contamination at DSG meetings. The first process was participants in the control arm attending meetings in the intervention arm. This might occur if PLWD in the control arm were visiting in the vicinity of an intervention DSG. The second process was peer supporters from the intervention arm delivering the intervention in the control arm, if they were responsible for more than one DSG.

Methods that were used to mitigate contamination are summarised in three categories: statistical design, trial conduct, and monitoring for contamination. In statistical design, we used

cluster randomisation, where the intervention was delivered within geographically dispersed clusters. This minimized the likelihood of members of different DSGs coming into close contact. Regarding trial conduct, the recruitment of peer supporters from each DSG ensured that each peer supporter was only responsible for delivering the intervention in one DSG. Visiting PLWD were not eligible for recruitment into the study. To monitor contamination, participants in all trial activities (such as attendance to DSG meetings) were carefully documented in trial registries, to identify any movement of participants between DSGs. We did not find evidence of contamination.

We measured self-efficacy in all participants before and after the intervention, as discussed in chapter 10. We found that self-efficacy was low in all arms at the start of the study, but increased in the intervention arm after the intervention. Self-efficacy remained low in the control arm. This indicated that there was no receipt of intervention in the control arm, and therefore that there was little evidence of contamination. During focus group discussions with participants and peer supporters at the end of the trial, we also enquired about exposure of the control group to the intervention. We had promised the DSG leaders that we would offer the intervention to the control arm at the end of the follow-up period. The follow-up period was short (180 days) and this may have safeguarded against contamination.

Chapter 10

Effectiveness of peer support to increase attendance at DR screening - a pragmatic cluster randomized clinical trial

Outcome evaluation of the DURE trial

10.1 Overview

Research paper 1 (chapter 4) provided a conceptual model on how interventions to strengthen knowledge, referral and self-efficacy of PLWD can improve uptake of eye examination. In settings that have diabetes support groups, innovative use of this resource to influence these factors may be effective in enhancing uptake of DRS uptake.

Research paper 5, which is the study protocol (chapter 7), provided further insights on how self-efficacy for taking a retinal examination might improve through peer support in the Uptake of Retinal Examination in Diabetes (DURE) study. The previous chapter (chapter 9) reported the process evaluation of the trial, which provided evidence that the intervention worked through the anticipated mechanism of the intervention.

This chapter consists of a research paper that describes the main trial results reporting the effectiveness of the intervention. The trial is reported in adherence to the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement: extensions for cluster trials and for pragmatic trials (www.consort-statement.org).

Research paper 8 (being submitted to Lancet Global Health) includes data on baseline characteristics of participants, self-efficacy scores, follow-up, attendance to DRS screening and time to screening. The data on effectiveness of the intervention is stratified by gender, as there was evidence of variability of effect between men and women.

This study demonstrated a significant early screening response following the intervention, and it offers a practical way to increase attendance at DRS screening, particularly in countries where DR is often detected late.

10.2 Research Paper 8

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Student	Nyawira Mwangi
Principal Supervisor	Professor Allen Foster
Thesis Title	Diabetic Retinopathy in Kenya: Assessment of services and interventions to improve access

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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Stage of publication	**Not yet submitted**

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. (Attach a further sheet if necessary)	I designed the study, conducted the research, analysed and interpreted the data, drafted the manuscript and prepared subsequent revisions in consideration of the comments from the co-athors and peer reviewers

Student Signature: Nyawira **Date:** 17 SEPT 2019

Supervisor Signature: [redacted] **Date:** SEPT 17, 2019.

Increasing attendance at screening for diabetic retinopathy: results of the DURE cluster-randomized trial in Kenya

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Abstract

Background

Diabetic retinopathy (DR) is a common complication of diabetes; it can occur without symptoms, so regular screening is essential to avoid vision loss. Access to screening for DR remains limited, particularly in low and middle-income countries (LMICs). We assessed whether combining usual care in diabetes support groups with a peer-led health education intervention was effective in increasing attendance at DR screening.

Methods

In a cluster randomised controlled trial, we randomly assigned 14 diabetes support groups (1:1) to receive a peer-led health education intervention (group talks, individual reminders and referral for screening) in addition to usual care (intervention group) or to receive usual care only (control group). The primary outcomes were proportion of participants who attended DR screening in each arm at 6 months, analysed in the intention to treat population.

[Pan African Clinical Trials Registry number: PACTR201707002430195, registered 15 July 2017].

Findings

Among 734 participants, 54.2% (200/ 369) in the intervention arm and 11.2% (41/365) in the control arm attended screening (Odds Ratio [OR] 9.4 95%CI 6.4–13.7; p<0.0001). Gender was an effect modifier (Men: OR 4.5 95%CI 2.5-7.1; Women: OR 19.5 95%CI 10.9-34.8, p<0.0001). Among those who attended screening, the median time to screening was 11 days (range 1-180) in the intervention arm and 90 days (range 1-180) in the control arm, p<0.0001. No unanticipated adverse events occurred.

Interpretation

This intervention increased attendance at DR screening in people who had not previously attended screening.

Research in context panel

Evidence before this study

Before this trial, we searched in PubMed, the Cochrane Library and trial registries on the International Clinical Trials Registry Platform for systematic reviews and randomised controlled trials (RCTs) using peer support (emotional, educational, motivational or practical assistance provided by non-professionals) to improve diabetes outcomes, including screening for retinopathy. We searched with the terms: "peer support", "diabetes", "diabetic retinopathy", "screening" and "retinal examination" for literature published in English by June 1, 2017.

We found three systematic reviews. Dale et al in 2012 included 14 RCTs and found that peer support improved clinical and behavioural outcomes in some adults with diabetes. Fisher et al in 2017 included 30 studies and found that peer support can reduce $_{HbA1c}$ levels. Gatlin et al in 2017 included seven studies and found that peer led self-management education can increase diabetes knowledge and reduce HbA_{1c}. None of the studies in these reviews included any outcome related to diabetic retinopathy screening (DRS) and none of the studies was conducted in LMICs. We searched the reference lists of included studies to identify additional relevant studies, but found none.

During our study, Lawrenson et al (2018), published a systematic review in January 2018 reporting that interventions targeting patients, health professionals, the healthcare system, or a combination of these may be effective in increasing access to DRS. None of the included studies were from LMICs, and none provided evidence on the effect of peer supporter-led interventions. Thus, before our study, there was no substantial evidence on whether peer-supporter-led interventions can increase attendance to screening in LMICs.

Added evidence

To our knowledge, this is the first published randomised trial to assess the effect of a peer-led intervention to increase uptake of DRS among members of diabetes support groups (DSGs). We provide evidence that attendance at DRS in similar settings can substantially and rapidly improve if peer supporters are empowered to provide an intervention that combines health education and referral. This finding is novel, and of considerable potential importance not only because the intervention is feasible and acceptable, but also because a mixed-methods process evaluation of the trial identified the active ingredients of the intervention. Our findings further add value to the existing evidence because the participants were people who had never had DRS hence they are the population who need screening most urgently.

What the whole evidence means

Increasing attendance to DRS is a key objective of DR screening programs in all countries. Our results showed that it is feasible to reach PLWD who have never had screening with a peer support intervention that increases initiation of DRS. Many countries may have untapped potential for improving health-care access using existing resources such as community groups. This highlights the importance of collaboration with DSGs in order to reach this highly vulnerable group in the real world settings.

The findings have important implications for public health programs, particularly in countries where DR is often detected late with the risk of resultant visual loss and blindness. In such resource-limited settings, DR control programs should give priority to potentially feasible and sustainable public health interventions like those suggested in our study. Future studies should investigate context-specific costs of the intervention, and whether the intervention leads to maintenance of annual DRS over the long term.

Background

Retinal changes due to diabetic retinopathy (DR) were first described by Jaeger in 1856.[1] It is estimated that there were 420 million people living with diabetes (PLWD) in 2017, with a third having DR.[2] Early detection and treatment are important for preventing vision loss associated with DR, therefore regular DR screening (DRS) for all PLWD is recommended.[3] Low uptake of DRS is well documented, particularly in low and middle-income countries (LMICs), where the majority of PLWD live. Lack of screening or low uptake contribute to increased risk of vision loss from DR.[4]

Given the need to increase coverage of screening, it is essential that attendance at DRS be maximized as far as resources allow. Finding low cost effective interventions that can increase uptake of screening in the real world setting is challenging for DR screening programs. Lawrenson in 2018, in a systematic review on attendance at DRS, provided evidence that various interventions targeting patients, healthcare professionals or the healthcare system are associated with meaningful improvements in DRS attendance.[5] However, the authors noted that the interventions were 'black box' whose active ingredients were not easily identifiable. All the 66 studies included in this review were conducted in high income countries, hence there is need for evidence from LMICs.[5] There is also need for evidence on interventions that are targeted to those who need DRS most— those who have never had screening, as they are highly vulnerable to vision loss from DR.

Improving the knowledge of PLWD about eye screening is essential if avoidable vision loss is to be prevented.[6] The lack of knowledge of PLWD on diabetes eye health is known to be a modifiable predictor of DRS uptake, especially in LMICs.[7, 8] Knowledge can raise PLWD's perception of vulnerability and severity of DR, hence building self-efficacy for adherence to screening recommendations. A recent systematic review of barriers and enablers for DRS reported higher odds of uptake of DRS when PLWD were provided health education.[7] The effect of health

education interventions led by peers within community-based diabetes support groups (DSGs) on attendance at DRS remains equivocal, although peer support is beneficial for other outcomes.[9-11]

The Uptake of Retinal Screening in Diabetes (DURE) trial was a two arm (1:1) pragmatic cluster-randomized clinical trial (cRCT) designed to test the hypothesis that the proportion of PLWD attending DRS would be higher in DSGs with the peer supporter-led intervention than in DSGs offering the usual standard of care in DSGs. The mechanism of effect of the intervention was predicted to be through increasing the self-efficacy of PLWD to adopt screening behaviour. The primary outcome was the proportion attending DRS in either arm during the six-month study period. We defined DRS as measurement of visual acuity and a retinal examination through a dilated pupil conducted by an eye care worker using either an ophthalmoscope, a slit lamp microscope or a retinal camera, which reflects current practice in Kenya.[12]

We chose a cRCT design instead of an individually randomised trial because peer support is normally provided at group level in DSGs, and to reduce the effect of intervention contamination, since patients in the same DSG often interact with one another. The trial design was guided by the United Kingdom's Medical Research Council framework for developing complex interventions.[13] Patient representatives were involved in the planning and implementation of the intervention. We anticipate that the trial findings will inform future strategies for improving screening services and subsequent early detection and treatment of vision threatening DR (VTDR).

Methods

Setting

Kenya is a LMIC, as defined by the World Bank[14], and the prevalence of diabetes is 2% in the 18-64 years age group.[15] Kirinyaga is a rural county located in central Kenya. Our formative research had established that only 12% of PLWD who are already attending diabetes services in Kirinyaga had ever taken DRS.[8] DRS services are available at the county hospital on a walk-in basis, but

they are under-utilized. An estimated 25%-30% of PLWD are registered members of DSGs, while an additional 20% of PLWD attend DSG meetings occasionally even though they are not members.

Study design and conduct

The study protocol was peer-reviewed and a favourable ethics opinion was received from the ethics committees of the London School of Hygiene and Tropical Medicine (LSHTM) and the African Medical Research Foundation. The trial was conducted in accordance with the principles of the International Conference on Harmonisation of Good Clinical Practice under the oversight of the study sponsor, LSHTM. Written informed consent was obtained at the cluster level, while participants gave verbal consent to receive the study interventions and follow-up.

The sample size was estimated using standard formulas for cRCTs recommended by Hayes and Bennett.[16] Based on the data from formative research, with 50 PLWD in each DSG and 12% of PLWD attending DRS services in the control arm, and using a coefficient of variation of 0.25, 14 clusters (7 in each arm, Fig 10-1) were required in order to have 80% power to detect a twofold increase in uptake in the intervention arm (with statistical significance at the 5% level).

A research nurse recruited the participants from each group through simple random sampling prior to randomization. Table 10-1 shows the eligibility criteria while Fig 10-2 (at the end of the chapter) shows the participant flow in the trial. Computer generated random numbers were obtained remotely by a statistician on STATA 15 (StataCorp 2017) and used for allocation of clusters to study arm. The allocation sequence was concealed from trial personnel until the moment of assignment.

For each cluster in the intervention arm, two peer supporters (1 male, 1 female) were selected according to the exclusion and inclusion criteria and received a two-day training to deliver the intervention. The content of the training is described in the trial protocol[17] and summarized in Box 1. In addition to usual care at DSGs, the intervention arm had three components: monthly

group talks on diabetes eye health, individual referral for DRS using a referral card and monthly individual telephone reminders to take DRS. Peer supporters received airtime to facilitate the telephone calls, as well as reimbursement for any logistical costs, but no other incentives. Research assistants monitored the implementation of the intervention. Self-efficacy to take a retinal examination (a participant's confidence in his ability to obtain a retinal examination, despite potential barriers) was assessed at baseline, after the first group talk and at the end of the study period, using a structured questionnaire. The primary outcome was attendance at DRS within six months. The records at Kerugoya County Hospital eye clinic were monitored daily and the identifier cards of participants that attended screening were deposited in a specific container by the eye care team. These cards were then collected and given to the outcome assessment nurse (not involved in recruitment or follow-up).

Table 10-1: Eligibility criteria for participants and peer supporters

Criterion	**Participants**	**Peer supporters**
Age > 18 years		
Member of a diabetes support group		
Will reside in the county for the next 12 months		
Has a mobile phone		
Willing to participate in the study		
Had not had a screening exam in the last 12 months		
Has had a screening exam in the preceding 12 months		
Willing to be a peer supporter		
Willing to commit two days for training		
Willing to commit many hours to peer support work		
Fluent in Kikuyu or Kiswahili		
Already attending DR screening		
Already receiving treatment for DR		
Has a debilitating illness		

KEY	Include	Exclude	Not applicable

The recruitment nurse, research assistants and the outcome assessor had no training in eye care, and were masked to the intervention allocation, to avoid contamination and bias. The eye care providers were also masked to the intervention allocation. It was not possible to mask the study participants or peer supporters in the intervention arm, because the peer supporters' activities within the DSG were overt. As the primary outcome was assessed from hospital records, we concluded that the lack of masking could not incentivise over-reporting or under-reporting in either arm.

Box 1: Trial Interventions

Domain		Intervention group	Control group
Usual care		Monthly group meetings with general diabetes education talks, blood sugar and blood pressure measurements	Monthly group meetings with general diabetes education talks, blood sugar and blood pressure measurements
Intervention			
	Peer-supporters training	Two days training following a structured curriculum regarding diabetes eye disease, retinal screening, role of peer-supporters, communication and other aspects specified in the protocol[17]	
	Group education	Monthly group education provided by trained peer-supporters, with structured content on diabetic eye disease and retinal screening as specified in the protocol[17]	
	Individual participant reminders	Monthly individual telephone reminder by peer-supporters to participants to take a screening exam as specified in the protocol[17]	

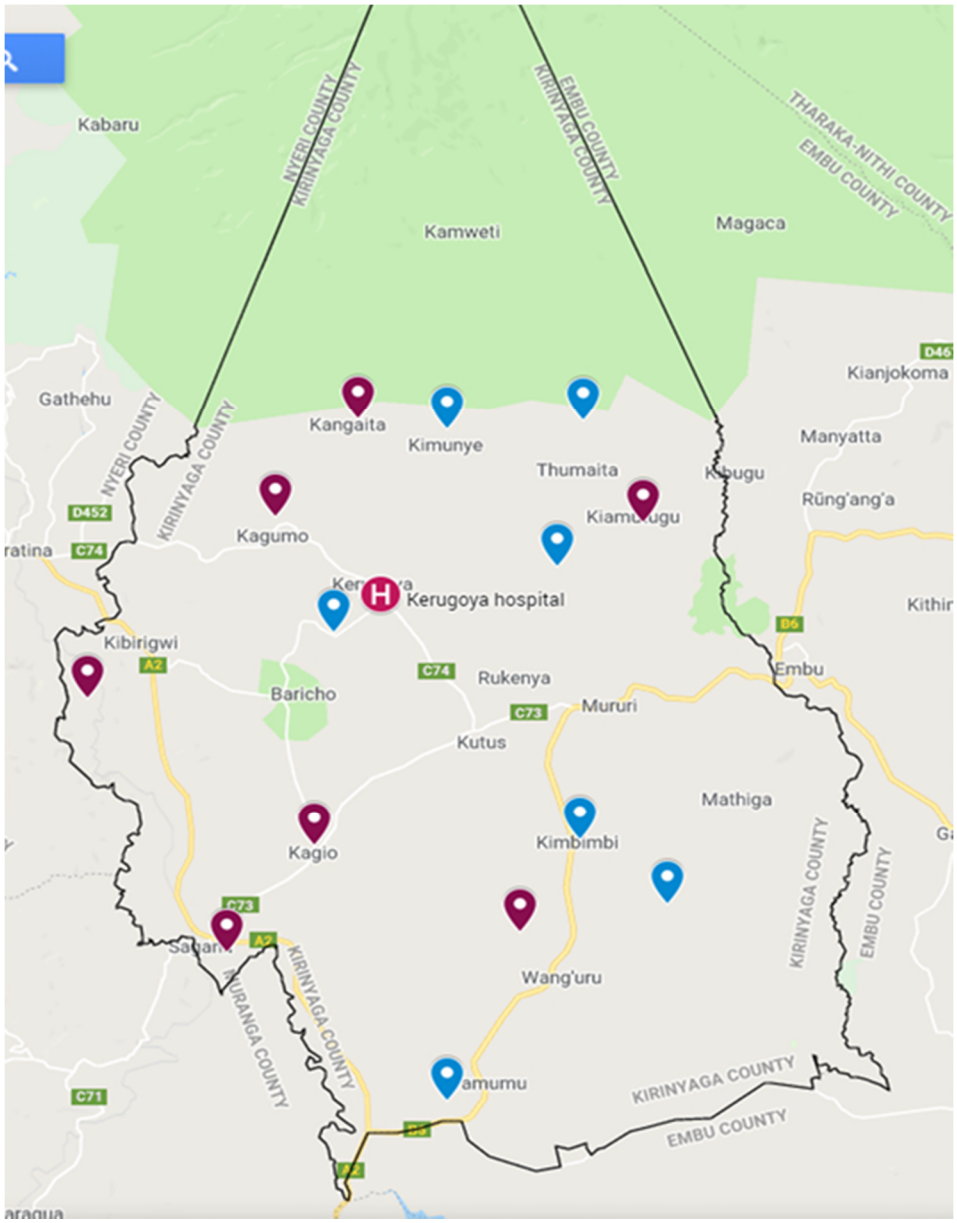
Statistical analysis and reporting

This study is reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement and its extensions to cluster randomized studies[18] and pragmatic

trials[19]. The CONSORT flow chart and the checklists are included as appendices. All data analysis was carried out using Stata 15 (StataCorp, College Station, Texas, USA 2017) and following a pre-specified analysis plan (Appendix 9).

We calculated descriptive statistics for participants' characteristics and compared the study arms. Continuous variables are summarised by mean and standard deviation, SD (if normally distributed), or median and inter-quartile range (IQR) if distribution was skewed. Categorical data are summarised as frequencies and percentages. We further analysed the intra-DSG correlation for these variables, to address a gap found in previous DRS studies.[5]

Our primary analysis was by intent-to-treat population, and we did not conduct interim analyses. The primary outcome (attendance at DRS) was binary, and analysed at the participant level as well as at cluster level. Tests of crude association with exposure to the intervention and with self-efficacy scores were performed. The measure of effect is presented as odds ratios (OR) with 95% confidence intervals (CI).



KEY H Kerugoya hospital eye clinic — Control DSGs — Intervention DSGs

Fig 10-1: Location of the clusters and the eye clinic within Kirinyaga county

We generated Kaplan-Meier survival curves to illustrate the difference in time-to-attendance between the two arms. We assessed the difference in time-to-attendance with hazard ratios (HRs) estimated by Cox regression. As the assumption for proportional hazards was not met, we estimated HRs for narrower time bands, within which the proportional hazard assumption holds.

We performed logistic regression for bivariate and multivariable analysis, while accounting for clustering, to identify which of the independent variables were predictors of attendance to DRS. We also constructed nested multivariable logistic models including all potential confounders and did not find any evidence of a confounding effect.

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 first author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Baseline characteristics

All the 14 DSGs completed the trial. Baseline data was collected for all 734 participants (369 in intervention and 365 in control arm). The two arms were balanced for baseline characteristics (Table 10-2). Appendix 8 shows the intra-cluster correlation coefficients (ICC) for the baseline anthropometric and clinical characteristics. The ICC is low for all the variables, indicating minimal clustering effect.

Table 10-2: Baseline characteristics of study participants (N=734)

Characteristic	**Control (N=365)**	**Intervention (N=369)**
Age (years) mean (SD)	59.6 (11.6)	56.5 (11.5)
Gender -Female n (%)	211 (57.8%)	208 (56.4%)
Duration of diabetes years, median (IQR)	4 (1 - 9)	4 (2-8)
Duration of DSG membership median (IQR)	2 (1-4)	2 (1-3)
Education (highest level completed) N, %		
Did not complete primary	108(29.6%)	84(22.8%)
Primary	167(45.8%)	171(46.1%)
Secondary	69(18.9%)	84(22.8%)
Post-secondary	21(5.8%)	30(8.1%)
Employed n (%)	294(80.1%)	297(80.5%)
Known comorbidity with hypertension (N, %)	34 (9.3%)	61(16.5%)
Body Mass Index mean (SD)	28.3 (5.0)	27.9 (5.1)
Waist circumference cm (mean, SD)	89.9 (8.5)	87.2 (9.6)
Random Blood Sugar mmol/l (mean, SD)	8.0 (3.2)	7.9 (3.0)
Systolic blood pressure mmHg (mean, SD)	137.8 (19.4)	134.3 (18.8)
Diastolic blood pressure mmHg (mean, SD)	76.6 (12.3)	77.4 (11)
Self-Efficacy (mean, SD)	13.4/50 (1.2)	13.5/50 (1.2)

Follow-up

Some 4.2% (n=31) participants were lost to follow-up (20/369 in intervention arm and 11/365 in control arm). They were lost to follow up relatively late in the study (median 150 days, inter-quartile range 96-156 days). The reasons for loss to follow-up were travel (Intervention 7, Control 2); illness, not related to the intervention (Intervention 2, Control 1); untraceable (Intervention 11, Control 8). No adverse reactions were reported among the 369 participants who received the

intervention. Participants who attended for retinal examination screening experienced temporary blurring of vision due to the effect of mydriatic eye drops, but this was anticipated and explained to the participants in advance. All of them described this effect as minor.

Proportion attending screening

In the intervention arm, 54.2% (200/ 369) and in the control arm 11.2% (41/365) PLWD attended DRS. Compared with usual care, the intervention quintupled the number of participants taking screening. Overall, participants in the intervention arm had 9.4 times the odds of taking screening compared to those in the control arm (Odds Ratio 9.4, 95% CI 6.4–13.7; $p<0.0001$). Given the apparent imbalance between trial arms at baseline in terms of age, education, known comorbidity with hypertension and waist circumference, adjusting for these covariates (Odds Ratio 9.4, 95% CI 6.3 – 14; $p<0.0001$).

We obtained similar results in both participant level and cluster level analysis, Fig 10-3 shows the attendance by cluster. The influence of clustering on attendance to screening was reflected in an ICC of 0.3, (95% CI 0.05-0.54, $p<0.0001$), meaning that 30% of the variation in attendance to screening can be explained by the variation between DSGs. Attendance at DR screening was markedly high in two of the intervention DSGs, as compared to the other DSGs. Process evaluation (chapter 9) showed that this was due to the exceptional performance of the peer supporters in the task of delivering the intervention.

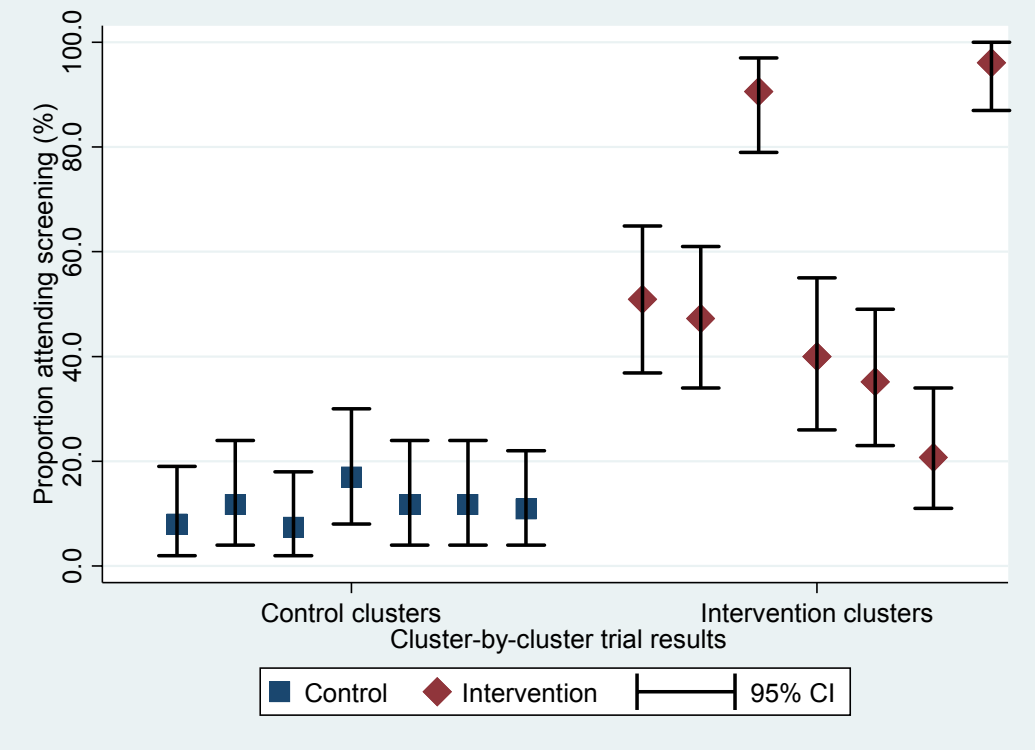


Figure 10-3: Proportion of PLWD that attended screening in each cluster

Although the intervention effect was high in both men and women, there was a more pronounced effect in women. The odds of taking screening in women was higher than in men (OR 19.5, 95% CI 10.9-34.9, p<0.001 compared to OR 4.2 95% CI 2.5-7.1, p<0.001), which was confirmed through logistic regression (interaction p<0.0001). Gender is thus an effect modifier. We did not find variability in the pooled effect estimates for other variables, hence there were no strong reason to perform subgroup analysis for other variables.

The scores for self-efficacy to take DRS at baseline did not differ between the two arms (median score 13/50, IQ z\d R 12-14 for both arms, p=0.2). After exposure to the first dose of the intervention there was strong evidence of a difference in self-efficacy scores, intervention arm (median 43/50, IQR 42-45) and control arm (median 14/50, IQR 13-15), p<0.0001) (Fig 10-4). This increase in self-efficacy in the intervention arm was associated with DRS (OR 9.4, 95% CI 6.4-13.7, p<0.0001).

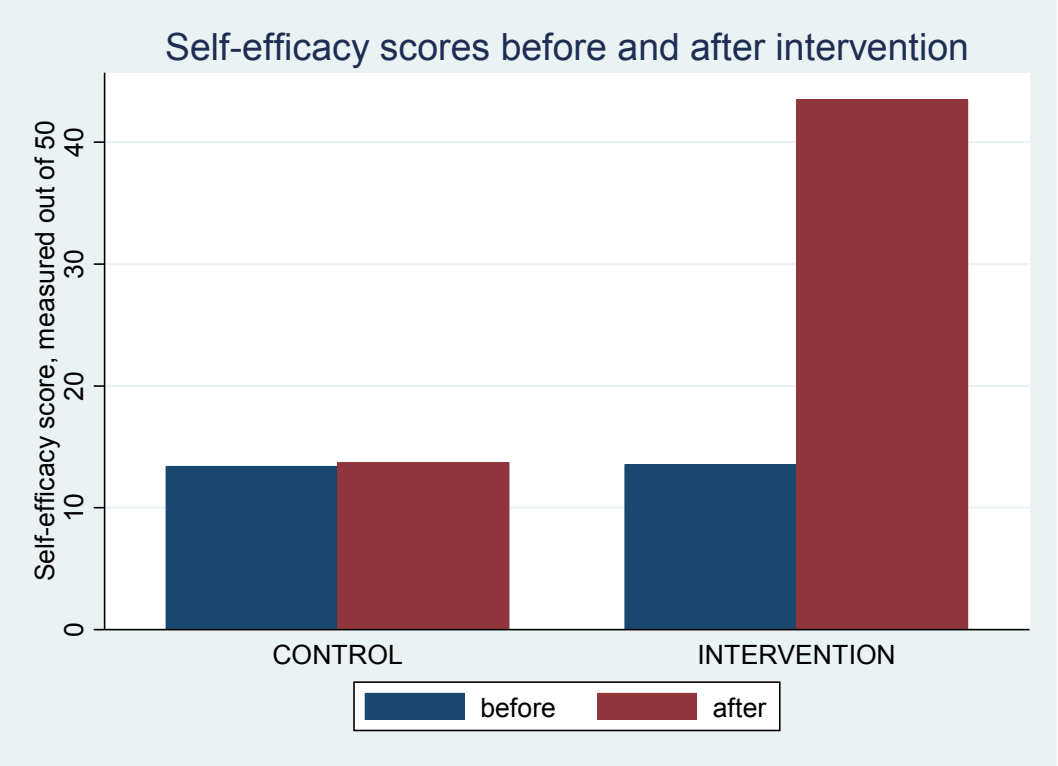
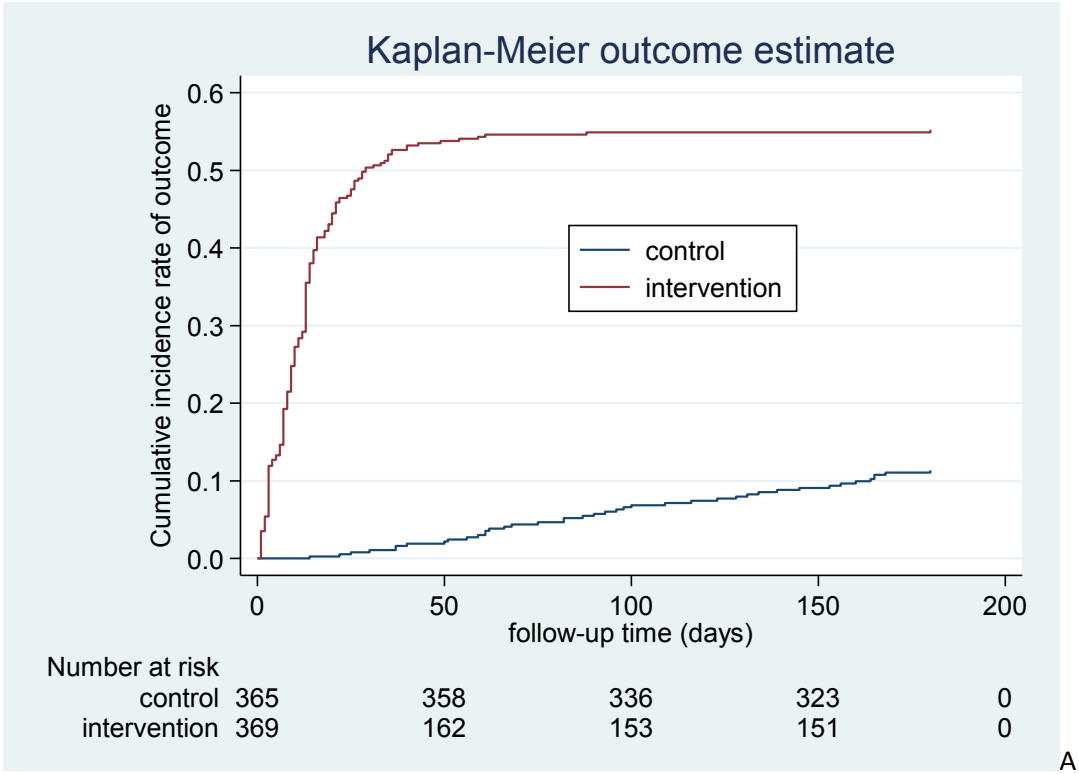


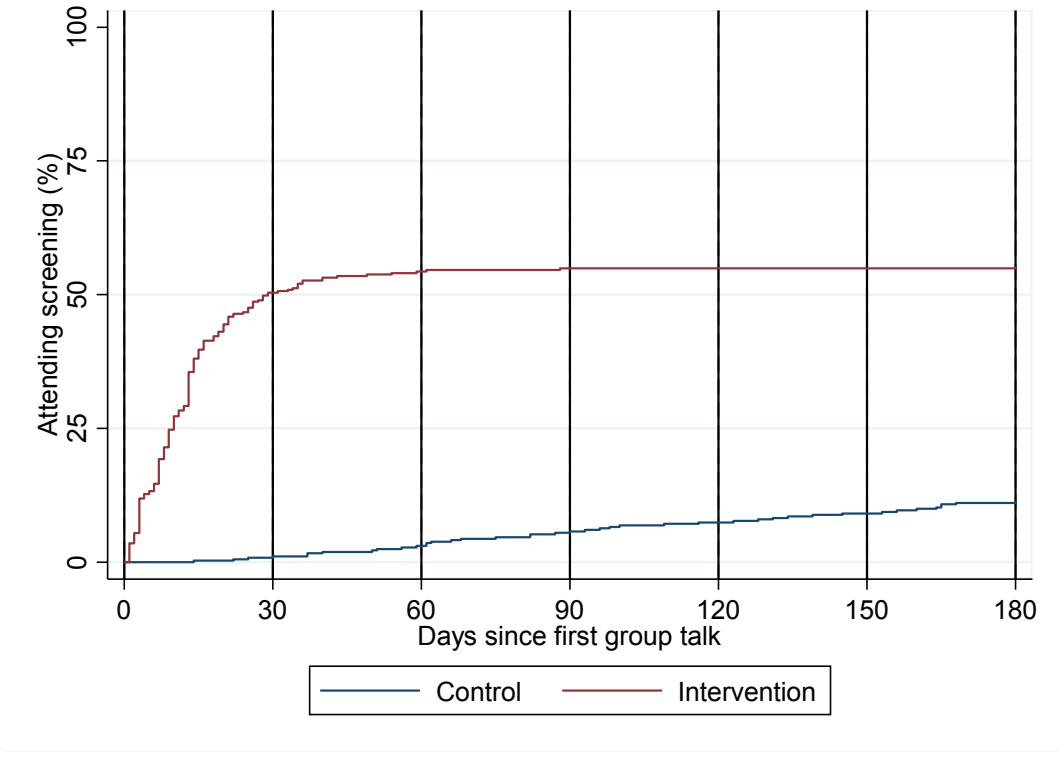
Fig 10-4 Self-efficacy scores in intervention and control arms

Time to screening

Trends in attendance to DRS over the study period were consistently higher in the intervention arm compared with the control arm, (Fig 10-5 and Table 10-3). However DRS was only taken up by 54% (200/369) of the intervention arm over the 6 months, of which 183 (50%) had their screening within the first 30 days of the trial after the first group talk and referral for screening. This indicates that the intervention had an early benefit for DRS attendance, but only an additional 16 (4%) attended DRS over the next five months of further exposure to the intervention. In the control arm, DRS attendance was spread more evenly across the follow-up period at 1-3% of control participants/ month. The median time to screening was 11 days (range 1-180) in the intervention arm and 90 days (range 1-180) in the control arm, $p<0.0001$.



A



B

Fig 10-5 Kaplan-Meier analysis of time from first group talk to attendance at DRS (A) and in relation to the group talks (B)

Table 10-3: Time period of trial in which attendance at DR screening occurred

	Proportion of participants attending screening			
Time period (days)	Intervention arm (n=369)	Control arm (n=365)	Hazard ratio [CI]	p value
0 -30	183(49.6%)	4 (1.1%)	63.0 [20.4 - 194.6]	<0.001
31-60	14 (3.8%)	7 (1.9%)	4.3 [1.6 - 11.8]	<0.001
61-90	2 (0.5%)	10 (2.7%)	0.4 [0.1 - 2.7]	<0.001
91-180	1 (0.3%)	20 (5.5%)	0.1 [0.02 - 2.6]	<0.001

Discussion

We found strong evidence that the intervention increased uptake of screening. To our knowledge, this is the first trial to investigate the effect of peer-led intervention on DR screening rates within diabetes support groups in any part of the world. The trial population was homogeneous in that they had not previously taken screening, hence they are the group particularly in need of screening.[6] The large effect of the intervention is likely to be because the intervention addressed known barriers to screening in this community, which are lack of referral and lack of knowledge on diabetes eye health.[8] Secondly, the high effect might be because the PLWD in our trial had never had screening, and other studies have reported that populations with low screening rates at baseline show the largest improvements.

We found an early response—PLWD exposed to the intervention tended to attend screening right after the first group talk and subsequent referral, and further group talks did not tend to increase the effect. This important finding has not been reported in the literature. In addition, similar to Zhang et al, we observed a ceiling effect, whereby additional reminders did not increase attendance at DR screening.[6] Given the relatively low probability of further improvement after exposure to the active ingredients, it may be appropriate to limit the intervention to a single

group talk and referral, and then repeat the intervention after six months. Additional intervention components are likely required to increase uptake among those who did not respond to this intervention.

In this population of African PLWD, diabetes was of short duration on average (median duration 4 years) and glycemic control at the time of study was poor. The demographic and anthropometric characteristics of this group are comparable to the characteristics of the national population 18-64 years, as described in the Kenya STEPwise survey for risk factors for non-communicable disease.[15] The results can be used to improve services in populations with a similar profile.

We envisaged that the intervention would cause effect by increasing PLWD's self-efficacy to initiate screening and this was confirmed. However, 46% of the PLWD in the intervention arm still did not take screening even though the overall self-efficacy in the group increased. This suggests that some participants face additional post-self-efficacy barriers that are not addressed by this intervention. Similar to other studies, our process evaluation (chapter 9) found that geographical barriers (for PLWD living in rural remote areas) as well as direct and indirect costs of screening are additional challenges for PLWD.[20] On the other hand, it is also possible that in some individuals there is a considerable time lag between improvement in self-efficacy and uptake of screening.

In the control arm, 11% attended DRS. This might be because all participants were asked if they have ever had a DR screening exam in the baseline assessment, which may have encouraged them to think about the need for DRS and motivated them to go for screening. Gender was an effect modifier with a more pronounced effect in women. This is fortunate, since women are known to have a higher burden of VI and lower use of eye care services, as compared to men.[21, 22]

Younger age and higher education were associated with increased odds of attendance to DRS. Considering the implications of DR-related vision loss on quality of life, and economic consequences such as lost productivity, it is of interest that young PLWD attend screening. In contrast, some studies have reported younger age to be associated with poor attendance to

screening.[20] There is consensus in most studies that higher education improves access to eye care services.[21, 23]

In women, known comorbidity with hypertension and poor control of blood pressure were associated with increased odds of attendance to DRS.[2] This is fortunate, since poor blood pressure control is a known risk factor for DR, and these women at high risk are more likely to attend DRS. However the same effect was not seen in men with hypertension.

In men, being employed was associated with reduced odds of attendance, perhaps because the DSG activities and the screening service are mostly available during regular working hours, when they are at work. We did not note a similar association for women, possibly reflecting different circumstances around employment. This is an indicator that there are additional barriers for men, and it might explain why the intervention effect in men was less pronounced than in women. It might be useful to target work spaces with additional interventions for men in employment.

Two DSGs in the intervention arm had higher performance than other DSGs, due to the high performance of peer supporters in their tasks. This shows the need for DR screening programs using this intervention to pay attention to the performance of peer supporters, and the factors that influence this performance. Peer supporters are volunteers and have different motivators for performance. Incentives that are responsive to their needs may sustain high performance.[24] These incentives may include formal employment with remuneration. However it is unclear whether employment would stifle the creativity, flexibility and sense of altruism that underpins this performance.[24, 25] Non-financial incentives including training and recognition through provision of badges, t-shirts or bicycles to help with transportation are appreciated by community volunteers in Kenya.[26, 27] The right package of incentives that is essential for program effectiveness and corresponds to the expectations of peer supporters will need to be determined.

The strengths of our study are the cluster randomised study design and robust study procedures that followed international guidance, with oversight from a registered clinical trials unit. It is a

pragmatic study, conducted in real world settings and using peer supporters to deliver the intervention, which facilitates sustainability and expansion to larger scale. The choice of intervention was based on barriers and enablers identified in literature review and formative research.[8] The follow up rate was high, and the primary outcome was measured objectively with data for the outcome being available for all participants. The trial steering team included a diabetes educator; this expertise is known to be particularly important in health education interventions for PLWD. The trial was also accompanied by a robust theory-driven process evaluation, hence it is not a 'black-box' intervention.[5, 28]

The trial provides an important example of task shifting to increase screening coverage. The task of providing health education on diabetes eye health was shifted from the clinic to the community, and from health workers to the peer supporters in DSGs. In turn the peer supporters referred the PLWD to the clinic, thus facilitating DRS. This linkage is important for reaching under-reached groups with screening interventions. Our study thus contributes to ongoing discussions on the role of task shifting in eye health.

Our study has limitations that also indicate directions for future research. We used a single geographic setting so the results may not be widely generalizable. However, they are likely to be replicable in LMIC settings with diabetes support groups and poor uptake of DRS. Longer-term follow-up studies are needed to determine the sustainability of the effect of peer support on attendance to regular annual screening, as opposed to a one-time effect. We did not collect data on socioeconomic status and did not measure cost-effectiveness.

The findings have important implications for clinical and public health policy, particularly in low-income countries where DR is often detected late. This peer supporter-led intervention may be effective in countries with similar health system structures, an opportunistic DR screening model and a low attendance to DRS. Many countries have diabetes support groups with peer supporters;

innovative use of this resource in enhancing uptake of DRS uptake may be implemented with minimum disruption to the existing health system.

This study may assist health workers understand the relationship between self-efficacy and DRS when attending to individual PLWD.[29] Our findings should assist policy makers in developing DRS strategies that utilise existing resources to improve coverage of screening. The next step in scaling up the intervention in Kenya would be for the Ministry of Health to collaborate with DSGs and train peer supporters to deliver the intervention in all 47 counties. We are presently planning this approach, which has stakeholder support.

Conclusion

The pragmatic DURE intervention resulted in a positive and early response for attendance at DRS offering a practical way to increase screening. The intervention was effective for both men and women, although it had a greater impact on women. Further research is needed to assess the best timing for repeating the intervention and the cost-effectiveness of this strategy.

Declarations

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from Ministry of Health, Kenya but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Ministry of Health.

Competing interests

The authors declare that they have no competing interests.

Abbreviations

CI	Confidence interval
cRCT	Cluster randomized clinical trial
DR	Diabetic retinopathy
DRS	Diabetic retinopathy screening
DURE	Uptake of Retinal Examination in Diabetes study
DSG	Diabetes support group
HbA_{1c}	Glycated haemoglobin
HIC	High income country
HR	Hazard ratio
IQR	Interquartile range
LMICs	Low and middle income countries
LSHTM	London School of Hygiene & Tropical Medicine
OR	Odds ratio
PLWD	People living with diabetes
RCT	Randomized clinical trial
SD	Standard deviation
VTDR	Vision-threatening diabetic retinopathy

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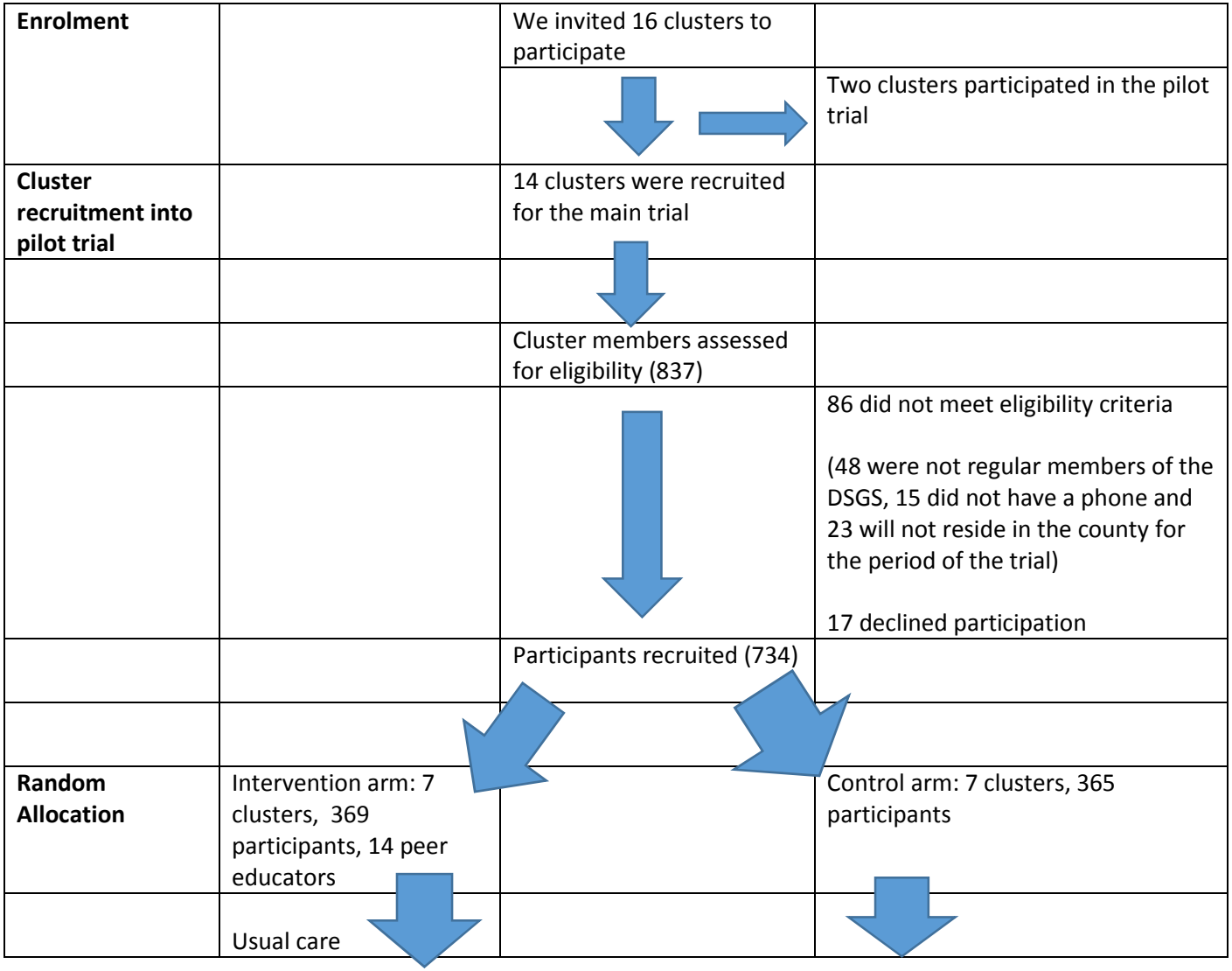
Fig 10-2 Trial flow chart



Intervention	Peer educators received a 2 day training All participants received the intervention (monthly group talk) Those who had not attended eye exam received a weekly individual reminder		All received usual care
Follow-up	349 participants and 13 peer educators were retained over 180-day follow-up period. 20 were lost to follow-up. 1 peer educator got a job in another county and was unavailable day 72 - 180		354 participants were retained over 180-day follow-up period. 11 were lost to follow-up
Interim estimate of primary outcome	369 participants included 0 participants excluded Intention to treat analysis		365 participants included 0 participants excluded Intention-to-treat analysis

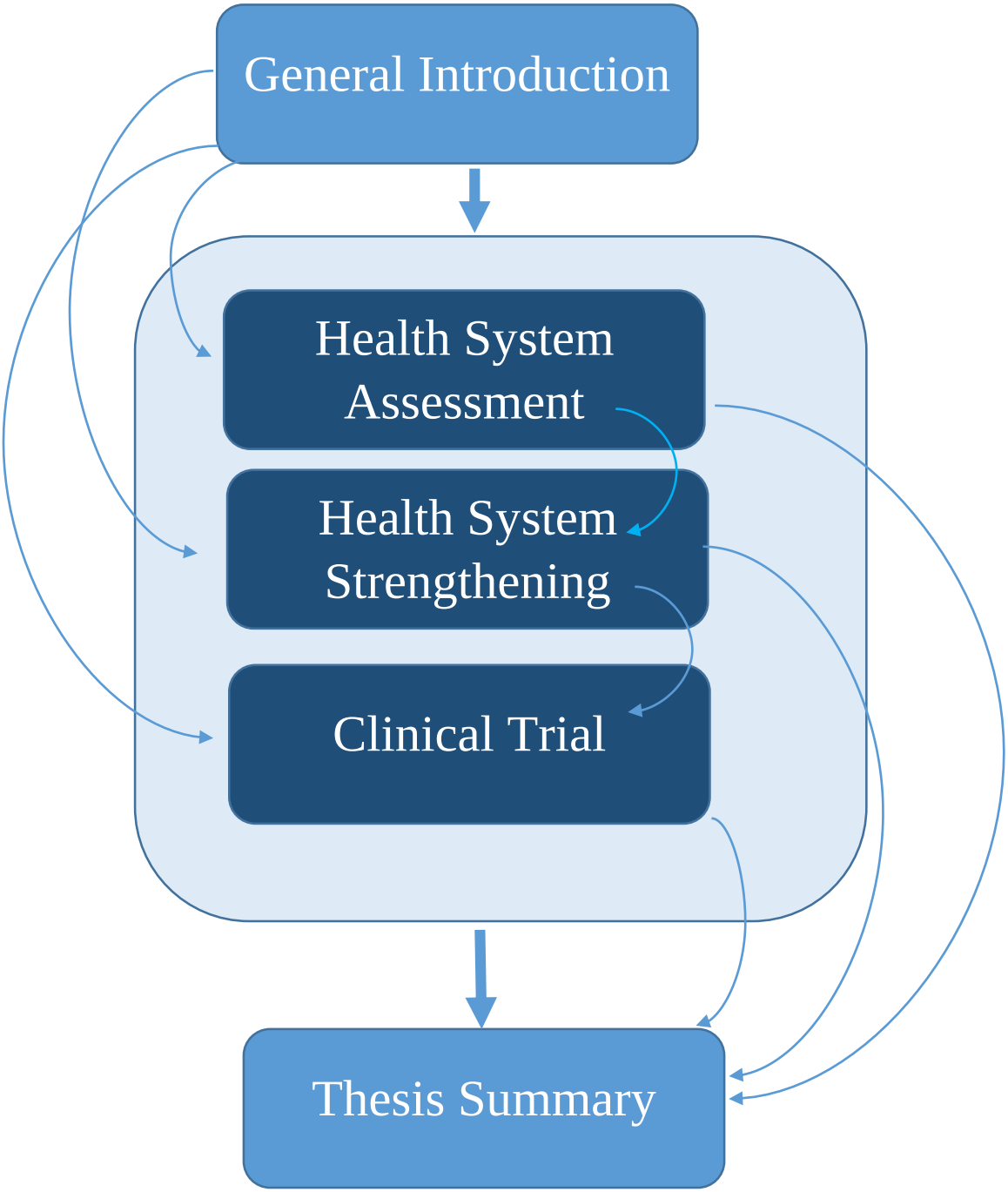
Figure 10-2: Flow diagram for the trial

Table 10-4: Predictors of attendance at DR screening

Variable	Attended screening (241)	Did not attend screening (493)	Odds Ratio	[95% Confidence Interval]	p value
			9.4	[6.4 - 13.7]	<0.001
Control	41	324	1		
Intervention	200	169	9.4	[6.4 - 13.7]	<0.001
Age (years)			0.5	[0.4 - 0.7]	<0.001
<45 years	48	45	1		
45-64 years	142	272	0.5	[0.3 - 0.8]	0.002
>65 years	51	176	0.3	[0.2 - 0.5]	<0.001
Gender			1.18	[0.9 - 1.6]	0.3
Male	97	218	1.00		
Female	144	275	1.18	[0.9 - 1.6]	0.3
Duration since diagnosis of diabetes			1.0	[0.9 - 1.2]	0.9
<6 years	158	313	1		

6-9 years	30	78	0.8	[0.5 - 1.2]	0.2
10-20 years	41	80	1	[0.7 - 1.5]	0.9
>= 20 years	12	22	1.1	[0.5 - 2.2]	0.8
Duration of membership to DSG			0.6	[0.5 - 0.9]	0.003
<3 years	165	287	1		
3-5 years	74	191	0.7	[0.5 - 0.9]	0.02
>=6 years	2	15	0.2	[0.05 - 1.02]	0.05
Education			1.5	[1.3 - 1.8[	<0.001
Did not complete primary	38	154	1		
Primary	116	222	2.1	[1.4 - 3.2]	<0.001
Secondary	64	89	2.9	[1.8 - 4.7]	<0.001
Post-secondary	23	28	3.3	[1.7 - 6.4]	<0.001
Employed			0.8	[0.5 - 1.1]	0.2
Unemployed	54	89	1		
Employed	187	404	0.8	[0.5 - 1.1]	0.2
Hypertension			2.0	[1.3-3.1]	0.001
Previously diagnosed with hypertension	45	50	2.0	[1.3-3.1]	
Not previously diagnosed with hypertension	196	443	1		
Body Mass Index			0.9	[0.8 - 1.1]	0.2

Normal	74	131	1		
Increased	167	362	0.8	[0.6 - 1.1]	0.2
Waist circumference			0.9	[0.7 - 1.3]	0.7
Normal	109	215	1		
Increased	132	278	0.9	[0.7 - 1.3]	0.7
Random Blood Sugar			1.01	[0.8 - 1.4]	0.9
Hypoglycaemia	6	14	1		
Normoglycaemia	129	263	1.14	[0.4 - 3.0]	0.8
Hyperglycaemia	106	216	1.14	[0.4 - 3.1]	0.9
Systolic blood pressure at baseline mmHg			0.9	[0.6 - 1.3]	0.5
Normal	54	101	1		
Elevated	187	392	0.9	[0.6 - 1.3]	0.5
Diastolic blood pressure at baseline mmHg			1.3	[1.0 - 1.8]	0.07
Normal	143	326	1		
Elevated	98	167	1.3	[1.0 - 1.8]	0.07
Visual Acuity			1.1	[0.8-1.6]	0.5
Normal	176	372	1		
Visual Impairment	65	121	1.1	[0.8-1.6]	0.5


General Introduction
Health System Assessment
Health System Strengthening
Clinical Trial
Thesis Summary

Section E

"I fully realize that I have not succeeded in answering all of your questions... Indeed, I feel I have not answered any of them completely. The answers I have found only serve to raise a whole new set of questions, which only lead to more problems, some of which we weren't even aware were problems. To sum it all up... In some ways I feel we are confused as ever, but I believe we are confused on a higher level, and about more important things."

Mary Ann Raywid, 1928-2010

Scholar, author and activist

Chapter Eleven: Thesis summary

11.0 Overview

This thesis documents lessons learned regarding the assessment of diabetic retinopathy (DR) services in Kenya and interventions to improve access to these services. In this chapter, we summarize the PhD narrative, including the overall strengths and limitations, highlight the key findings, consider the implications for policy, practice, research, and dissemination, and provide recommendations and conclusions.

11.1 The PhD narrative

The thesis is organized in five sections A-E and 11 chapters.

Section A provides an overview of the research (Chapter 1) and background information from the literature (Chapter 2).

Section B describes the health system assessment for diabetes and DR in three counties of Kenya (Chapter 3 and 4).

Section C describes the health system strengthening activities, mainly in knowledge translation of the evidence to develop clinical guidelines (Chapter 5) and a training program to address supply side gaps that hinder availability of DR services in the country (Chapter 6).

Section D describes the clinical trial, whether the DURE intervention increases attendance at screening in Kirinyaga county (Chapter 7-10).

Section E provides a summary discussion for the thesis (Chapter 11).

The strength of this research is the progression of thinking from an understanding of the global literature on DR services, assessment of the Kenyan health system, identification of a critical gap in services, and culminating in the design, implementation and evaluation of an intervention to increase access to DR screening. This progression of research, where each step informed the next step, made it possible to develop a significant knowledge base. In addition, each of those steps was based on a strong theoretical underpinning, which facilitated a deeper understanding of the findings.

The main limitation of the research concerns the generalizability of the findings. The findings may apply to the wider Kenyan population and possibly a wider African population with similar social, cultural and health system context, and a similar patient profile. However, the findings may not be generalizable to other settings.

11.2 Overview of DR services

The aim of DR services is to prevent DR-related vision loss. The growing increase in prevalence of diabetes in all parts of the world places the spotlight on these services, since a third of people living with diabetes (PLWD) at any point will have DR and one in 10 will require immediate treatment for vision-threatening DR (VTDR). The services encompass a broad approach consisting of: first, prevention of DR through metabolic control of diabetes; second, DR screening among PLWD, for early detection of DR; third, timely treatment of those with VTDR; and fourth, rehabilitation of those with significant sight loss. This comprehensive approach includes services provided in the community and in diabetes and eye care clinics,

although the extent of integration between these services varies in different parts of the world.

While high-income countries have successful DR programs that provide these services, sub-Saharan Africa (SSA) has a high level of unmet need for these services. The International Diabetes Federation reports that the projected increase in the prevalence of diabetes over the next two decades will be disproportionately concentrated in this region. We can expect a commensurate increase in the need for DR services, given that all PLWD are at risk of DR. As DR is asymptomatic until some sight is lost, early detection depends on the provision of regular screening for DR for all PLWD.

The first objective was a review of the literature on the epidemiology of both diabetes and DR globally and in Africa. In chapter two, the evidence from population-based studies, clinic-based studies and systematic reviews on the risk factors, prevention and treatment of DR was presented. It is notable that globally there is plenty of literature on these conditions, but the evidence from Africa is sparse. This was not a surprising finding, as this discrepancy is ubiquitous in global health research.

As explained in section 11.5, we did not conduct a systematic review. However, the principles of systematic review were applied to ensure robustness and breadth of the literature review. The population, intervention, comparator and outcomes (PICO) were defined, and the London School of Hygiene and Tropical Medicine provided access to a wide range of peer reviewed and grey literature. This made it possible to

perform a comprehensive and balanced synthesis of the evidence, as reported in chapter two. Important gaps were identified in the literature, which would be of interest to the academic and policy audience.

The literature review was useful for identifying the priorities and challenges in DR services. One such challenge is screening for DR. There is evidence that DR meets established criteria for a screening programme, and that such screening is cost-effective, at least in high-income settings that have well-established systematic screening programs and a higher prevalence of diabetes. A few papers reported that DR screening (or opportunistic case detection) in SSA is fragmented. It is not clear whether screening is cost-effective in SSA, but a first step would be to investigate this in a well-documented project within an African health system.

Kenya is one of the growing economies in SSA and the geographical context of this research, therefore the general health system in Kenya is described in chapter two.

11.3 DR services in Kenya

The prevalence of diabetes in Kenya is reported at 2% of the population 18-64 years (2015).[1] However, there are no population-based data on the prevalence of DR. The number of people requiring DR services can be estimated using existing evidence from the global literature, and this has been presented in chapter two in section A. Health systems influence the implementation and success of DR programs. Health systems research to improve DR services is thus an important area, in order to close existing gaps for PLWD.

The second objective of the thesis was to conduct a health system assessment. Section B describes the health system assessment for diabetes and DR in three counties of Kenya, representing rural, urban and semi-urban areas. The assessment employed mixed methods (quantitative and qualitative), was guided by the WHO health system approach and the tracer condition approach, and obtained patients' perspectives in the health system assessment. The use of these mixed methods and approaches provided a more comprehensive understanding of the health system.

Quantitative methods facilitated the analyses of patient-level predictors of use of DR services, such as duration of diabetes. Quantitative methods were also useful for identifying groups of PLWD who may be most at risk of not receiving screening services (e.g. those without symptoms, or those from a rural county), thereby contributing evidence to inform the design of targeted interventions to improve uptake in these groups. Barriers to access of services were also identified.

With qualitative methods (semi-structured interviews with service providers and key informants), strengths and weaknesses of the health system could also be explored. The use of the tracer approach alongside the WHO health systems approach facilitated the link of various health system indicators to the specific outcomes of interest in diabetes eye health, as discussed in section B.

Major gaps were found in the area of awareness and access. There were also gaps in availability and affordability of DR services, but the main barriers to entry to DR services were lack of awareness and lack of access. Although it is recommended that 100% of PLWD have an annual screening examination, only 25.6% of PLWD attending

diabetes clinics had ever had a DR screening examination in their lifetime, which demonstrates a need-demand mismatch (or a screening gap) in DR services. Only 13.3% had a screening examination in the preceding year as recommended in clinical guidelines. This 87% unmet need for screening (screening gap) emerged as the priority area for DR interventions, since it is a bottleneck in the continuum of DR services. The findings presented in this thesis support the findings of other studies that the uptake of DR screening is low in low-resource settings.

The PLWD in Kirinyaga (a rural county) were the least likely to have had an eye examination in the preceding 12 months, with PLWD in Nairobi (urban county) having 2.6 times (95% CI 1.1–7.1) and PLWD in Nakuru (semi-urban county) having approximately three times increased uptake (95% CI 1.1–8.0). The main predictors for attendance at screening were referral from diabetes services and knowledge of diabetes complications. Participants referred for an eye examination had almost eight times the odds of having attended an eye examination in the last 12 months compared to those who had not been referred (OR 7.9, 95% CI 3.7–16.4, $p < 0.001$). Participants who had a knowledge of diabetes eye complications had four times the odds (OR 3.9, 95% CI 1.6–9.1) of attending as compared to those who had no knowledge of eye complications.

The strong association of knowledge of diabetes complications and uptake of screening is suggestive of the influence of demand-side barriers to access. Only 24.4% of participants had ever been referred from the diabetes clinic for a retinal examination, which on the other hand reflects a supply-side barrier. Additional supply side barriers obtained from qualitative interviews were: the lack of local

clinical guidelines for DR; lack of mechanisms to ensure that patients referred for screening are not lost in the referral pathway between diabetes and eye care services; lack of point of care tools, such as checklists or protocols; lack of systematic patient education; and health workforce challenges such as lack of access to continuous professional development on DR.

This study helped to identify important opportunities in the health system. These include a high stakeholder interest in strengthening services, well-established support groups, a strong non-communicable disease strategy, and strong governance structures at national and county level. These strengths and gaps have been discussed in detail in section B the thesis.

In the papers from the health system assessment (research papers 1 and 2), these findings have been presented as the basis for exploring an approach to fill the health system gaps. Interventions to increase attendance to screening need to address the barriers and take the enablers in the health system into account.

11.4 Health system strengthening

As screening is the entry to DR services, and attendance at screening is low, our aim was to increase attendance to screening. However, it would be unethical and unnecessary to increase attendance at screening where existing supply-side barriers to DR services translate to the services being unavailable or of sub-optimal quality. Therefore there was need for health system strengthening (as a third objective) to facilitate the availability of an appropriate standard of care, including screening, treatment, referral and follow-up.

Stakeholders identified the priorities for health system strengthening at national level. The priorities identified were national clinical guidelines and easily accessible resources for continuous professional development for health workers. Both of these were important opportunities for knowledge translation informed by research evidence. The scientific evidence identified through our literature review and stakeholder engagement were useful for translating the evidence into clinical guidelines and a training programme that can be accessed easily.

Although several studies have pointed out the need for health system strengthening ahead of intervention research, most of the health system strengthening activities reported have not involved knowledge translation and have not been described in detail. In addition, there is limited literature on the processes and outputs from these health system strengthening activities. In order to address this gap, section C of the thesis provides a detailed description of these activities.

Clinical guidelines are an important governance tool in health systems. There is a paucity of literature on how context-relevant guidelines can be developed in Africa, despite the potential value of these guidelines. This study has provided methodological contributions on this process and contributed to expanding the literature on this subject. The process and outputs of guideline development are described in the research papers 3 and 4. The scope of the guidelines is screening, diagnosis, treatment and follow-up for DR. The guidelines have been implemented nationally, not just in the study area. An online training course on the control of DR has been developed, targeting multidisciplinary teams involved in DR care. The development of the course is described in chapter six.

The health system strengthening was done with significant input from stakeholders in both the diabetes and eye care services. This is important because it facilitates ownership and implementation by the stakeholders, as well as capacity building that can be applied in the health system. We have described the technical aspects of the health system strengthening that could aid replication of these interventions elsewhere.

11.5 Development of an intervention to increase uptake of screening

The fourth objective of the thesis was to develop an intervention to increase attendance at DR screening and to test it in a randomized controlled trial. This study involved a community-based intervention relevant for an LMIC setting, where the unmet need for DR screening is higher, and hence the intervention had the potential for significant health system benefits.

The intervention in this trial utilizes diabetes support groups (DSGs) and peer-supporters because they are existing resources in this context, a strength of the health system. The process of intervention development has been guided by the findings of the health system assessment, stakeholder consultation, review of the evidence and by the UK Medical Research Council's guidance on the development of complex interventions. The intervention fits the criteria for a complex intervention because it had several components, required different behaviours by PLWD, peer-supporters and eye care workers, and required implementation at multiple settings at community level and at eye clinics. Multiple stakeholders in diabetes and eye care services were involved in intervention development. It was important to combine

these approaches, as described in Section D of the thesis, in order to develop an intervention that could improve uptake of screening. The trial protocol for the trial is presented as research paper 5.

Before the trial, the literature on peer-support interventions to improve diabetes outcomes as well as the role of peer-support in other chronic conditions was reviewed. We did not conduct a systematic review, since previous systematic review evidence on peer-support for diabetes was already available and because of time limitations. This evidence has been presented in the thesis. The studies included in the systematic reviews were mainly conducted in high-income countries, while the peer-support models were mainly facility-based and led by health workers. In addition, the studies were mostly focused on other outcomes than DR screening.

11.5.1 Conceptual framework for the intervention

In developing the conceptual framework for the intervention it was hypothesised that a multi-faceted intervention delivered by peer-supporters would create awareness in PLWD regarding screening, build self-efficacy, link the PLWD with the eye clinic and provide reminders to attend screening. The basic principle behind the Self-Efficacy Theory by Albert Bandura is that individuals are more likely to engage in activities for which they have high self-efficacy in comparison to those in which they have low self-efficacy.[2, 3] Self-efficacy has been shown to be a strong and consistent predictor of health behaviours such as physical activity. However, self-efficacy is task specific, meaning that it is crucial to identify the mechanisms in which self-efficacy is

developed for a given behaviour, like attending DR screening. Self-efficacy had not been investigated previously in relation to uptake of DR screening services.

We developed the conceptual framework deductively using the self-efficacy theory. We also considered the barriers to attendance to screening identified by PLWD during the health system assessment. Our framework is thus novel and has not been validated in other populations. However, it could serve as a starting point for replication or expansion in future interventions.

11.6 Implementation of the intervention

This research has been conducted in the pragmatic context, which means the results are likely to be applicable to everyday practice and are important to policy makers looking for scalable interventions to increase access to DR screening in Kenya. The clinical trials unit at the London School of Hygiene and Tropical Medicine provided oversight of the trial.

The population included in the research were PLWD who are attending diabetes services but have never had eye screening for DR. Although this population is large in this context, in future screening programs will need to target a more heterogeneous population (PLWD that have previously been screened and those that have never been screened) hence these differences would need to be considered.

11.6.1 Pilot trial

Two clusters (DSGs) participated in a pilot trial to investigate the feasibility of the trial. The criterion for continuation to the main study was the feasibility of

recruitment of 50 participants in the trial, 80% monthly follow-up rates for individuals and no attrition of clusters. The pilot study met these success criteria, indicating that a full trial of the intervention was feasible. The pilot trial also provided additional benefits, such as documenting high acceptability and an interim measure of the effectiveness of the intervention. The findings of the pilot trial are described in research paper 6. The interpretation of these findings was that the full trial was feasible and we did not need to change the study procedures. We did not conduct a process evaluation for the pilot study, preferring to defer it to the main trial.

11.6.2 Full trial

11.6.2.1 Self-efficacy outcomes

The measurement of self-efficacy is particularly relevant for interventional studies aiming to improve specific health behaviours. The majority of studies evaluating the effects of interventions on health behaviour rely only on the distal outcome measures. The results of research that includes a measure that is proximal to the screening behaviour are relevant in that they provide insights on the intervention pathway; in this trial, that the intervention increased self-efficacy to take screening in the intervention arm. This increase occurred early in the intervention, corresponding to the first group talk and referral. Based on the findings of the process evaluation (chapter 9), evaluation of self-efficacy and the evaluation of the primary outcome (chapter 10), an association between the increase in self-efficacy and attendance at screening was inferred. However, some of the PLWD who had high self-efficacy after receiving the intervention did not attend screening, suggesting that there are additional barriers that were not addressed by the intervention.

11.6.2.2 Primary outcome evaluation

The intervention was highly effective for increasing uptake of DR screening, and this effect occurs early in the intervention, followed by a ceiling effect. Further, there was strong evidence of effect modification by gender, with women showing a more pronounced effect than men for exposure to the intervention and attendance at screening. This unusual effect was difficult to explain. However, it suggests that gender is a significant determinant of screening behaviour. It also corroborates the finding of other researchers that behaviour change and interventions to change behaviour are complex.[4]

These findings would suggest that the level of awareness of PLWD is a major driver of attendance to DRS. The intervention effect was primarily due to the first group talk, following which 50% of participants in the intervention arm took up screening. Only a further 4% took up screening in the following 5 months (making a total of 54%), hence it is clear that further group talks and telephone reminders to take screening have limited returns. Although the intervention increased self-efficacy in the intervention arm, 46% of participants exposed to the intervention did not go for screening over the follow-up period. This suggests that raised self-efficacy is necessary but not sufficient, as there are post-self-efficacy barriers to screening.

We found that 11% of the PLWD in the control arm took screening, which may have been because at baseline they were asked whether they had ever taken screening. It is worth considering how participation in the research itself (such as responding to the baseline questionnaire) may have influenced the results obtained. It is also possible that a similar effect may account for part of the response in the intervention

arm. This would suggest that the effect size might be smaller in a non-research setting. These results of the outcome evaluation are described in the research paper 8.

In this study, the primary outcome was the proportion of PLWD who attended DR screening by the end of the study period. This is an essential outcome indicator to chart progress in DR screening programs, and we have shown that it is possible to measure it easily and objectively. This measure also provides important evidence related to uptake, access and coverage of DR services. Screening programs in resource-restrained settings may benefit from identifying a single measure of intervention effect that can be used for monitoring, for which we would recommend this outcome. As gender is an effect modifier in this intervention, we would recommend that this outcome be routinely analysed by gender.

There were many additional questions on screening which were not addressed in this study. For instance, the cost-effectiveness of screening and the prevalence of DR in PLWD were not included as they were beyond the scope of the thesis. However, they are important input and impact factors that would further complete the understanding of the intervention. Given that screening programs are not uniform and they evolve over time, it is not possible to have a universal monitoring tool that provides a complete picture of a screening program. Each program needs to choose the priority indicators for monitoring and evaluation, considering the resources available.

11.6.3 Process evaluation

The Consolidated Framework for Implementation Research (CIFR) guided the mixed-methods process evaluation of the trial. This framework, linked with principles of Implementation Science, was useful in identifying how, why and for whom the intervention worked. The quantitative component enabled the evaluation of implementation outcomes, in terms of recruitment, retention, reach, dose and fidelity. These important process indicators may be used for monitoring this intervention, however their measurement is labour-intensive, requiring lots of documentation and time, especially when the intervention is delivered in its current form. The measurement of the indicators is more viable for routine settings, if the intervention is limited to just one group talk as we recommend later in this chapter.

Both quantitative and qualitative components of the process evaluation contributed to the investigation of potential influences on attendance at screening. Findings generated using different methods could therefore be synthesised, compared, and triangulated to increase the validity and facilitate a deeper understanding of how the intervention worked. The results indicated that all the elements of the CIFR had an influence on how the intervention worked. There was evidence of local adaptation of the intervention during implementation, to suit local contexts, which is described in research paper 7.

Participants who took up screening reported doing so soon after receiving the first group talk. This is attributable to the finding that the first group talk addressed the main barriers to screening attendance, which were lack of awareness and lack of referral. In addition, the influence of the culture of collective action led to the

majority of the PLWD attending screening together early in the intervention. These findings provide evidence that the first group talk and the referral are the most essential components of the intervention, as mentioned earlier. Research paper 7 describes these findings in detail.

11.7 Implications

11.7.1 Implications for research

Whilst the findings of this research contribute to evidence for improving DR screening services in Kenya, they also demonstrate that gaps remain and present opportunities for future research. As an example, further longitudinal research to enable greater understanding of the effect of the intervention on the future cycles of annual DR screening for the participants.

There is considerable social, cultural, and health system variation in different settings and the intervention may work differently in other settings. Further research is required to explore the extent to which the peer-led intervention is transferrable for use in other contexts and countries. We recommend that research interventions should be: preceded by a situation analysis to identify the existing forms of peer-support; robust in design; comprehensively described and process evaluations conducted to gain insights into their mechanism of action.

Priority research areas in the short-term period are:

1. How can the ceiling effect of the intervention be broken?
2. How feasible, cost-effective and sustainable is the scale-up of the intervention for the health system?

3. What is the long-term effect of the intervention on initiation and maintenance of screening for PLWD?
4. What is the effect of adding further components to the intervention (such as photography-based screening in diabetes clinics)?
5. Why is the intervention effect more pronounced in women?

11.7.2 Implications for DR programs

DR programs in Kenya

Given the implementation of the clinical guidelines that explicitly emphasise annual screening for all PLWD, it is anticipated that screening services will be developed and become available to all PLWD in all parts of the country.

This study has introduced a new intervention that is not already part of the existing DR program. The findings presented in this thesis suggest that the intervention components could feasibly be delivered as they were delivered in this trial, at community DSGs with DR screening being provided at the existing eye clinic with the required capacity. The intervention is acceptable to the PLWD, the peer-supporters, health-care providers and other stakeholders. This trial tested the effectiveness of the intervention for PLWD who have never had screening. However, the intervention could be offered to all PLWD, as envisaged in the DR guidelines. The intervention could be scaled up to other counties in Kenya that have DSGs in the current form and services to examine and treat patients with DR, though cost-effectiveness data is lacking.

The intervention could potentially be modified to just one group talk and referral to the eye clinic. The group talk could then be repeated after six months, and monitored to see if this repetition will increase uptake of screening. A further group talk should also be provided before the next screening cycle, at 12 months. The monthly group talks and monthly telephone reminders can be left out, as they did not seem to be critical ingredients for the effect of the intervention.

The 'bottom-up' approach to health education in this intervention is advantageous because it is delivered to the target audience that may benefit from it. It is a suitable model for use with other chronic conditions for which peer groups exist. The training curriculum for peer-supporters developed in this study is already being adopted by the Kenya Defeat Diabetes Association as part of their peer-support manual. The online DR course is already available for use by health workers, and it will continue to be available to support lifelong learning within and outside Kenya.

It is important to note that while this was a pragmatic study, the implementation phase required a lot of follow-up by the principal investigator (PI) and regular documentation by the peer-supporters. For example, the PI and peer-supporters had weekly telephone contact, which would not be considered standard 'real-world' practice in any context. When the programme is implemented in non-study conditions, it will be necessary to see if these roles are required and if so who may be suitable to fill them. In Kenya, this might be the focal person for NCDs or the focal person for eye care in each county. Thus during program scale-up it will be necessary for further health system strengthening to consider these questions. In addition, there will be a need for continuous engagement of the communities and

DSGs. Although the intervention is a 'low-hanging fruit', it is critical for policy makers and DR program implementers to invest adequately in the scale-up phase if the research finding is to be turned into a practical and effective health service activity.

DR programs outside Kenya

The Kenya model of national DR guidelines has already been used to develop the DR guidelines in Ghana through the DR Network. The online training program is open to participants in all parts of the world.

In principle, the DSG intervention can be implemented in other contexts that have similar DSG and health system structures, after adaptation to account for the local context. Funders of international DR programs may therefore wish to invest in such a process of adaptation before program implementation.

11.7.3 Implications for practice

Pocock and Stone[5] in their paper 'The primary outcome is positive —Is that good enough?' recommend that researchers reflect on the following questions to interpret whether the evidence from a clinical trial with positive results is sufficient to advance clinical practice (Table 11-1). These questions have provided a useful framework for appraisal and interpretation of the trial findings, and other researchers might find them useful.

Table 11-1: Is the evidence sufficient?

1. **Does a p value of <0.05 provide strong enough evidence?**

There is very strong evidence of a large intervention effect, which is not just based on an interpretation of the statistical significance of the p value

2. **What is the magnitude of the treatment benefit?**

Compared with usual care, the intervention quintupled the number of PLWD taking screening. Given that these are PLWD who had never taken screening, this effect has important implications for increasing screening among this unreached group. The literature suggests that 10 people need to be screened to find one person who requires treatment, however further research is needed to investigate if this is true in LMIC settings with no or limited previous screening programmes.

3. **Is the primary outcome clinically important (and internally consistent)?**

Yes, attendance to screening is important for early detection of DR. However, we did not investigate the prevalence of DR among those screened. The literature evidence indicates that a third of PLWD have DR and one in 10 VTDR.

4. **Are secondary outcomes supportive?**

Yes the secondary outcomes in our study were evaluated in the process evaluation, such as implementation outcomes (high acceptability, fidelity, reach and dose), and they support the findings of the outcome evaluation.

5. **Are the principal findings consistent across important subgroups?**

The intervention effect was high in both men and women. It was markedly higher in women.

6. **Is the trial large enough to be convincing?**

Although the sample size was sufficient for our study objectives, we recommend replication of the study with larger samples in different LMICs.

7. **Was the trial stopped early?**

   No

8. **Do concerns about safety counterbalance positive efficacy?**

   No

9. **Is the efficacy–safety balance patient-specific?**

   No, this intervention is considered safe for all participants.

10. **Are there flaws in trial design and conduct?**

    No the study design and conduct is robust, we have discussed the limitations of the study.

11. **Do the findings apply to my patients?**

    The findings are context-specific, hence generalizability is limited to similar contexts.

11.8 Dissemination

The findings contained in this thesis have been disseminated, and will further be disseminated to a local, national and international audience of PLWD, diabetes support groups, health workers, policy-makers, program implementers and researchers.

The findings have been shared in publications, conferences, stakeholders' feedback meetings, peer research meetings, pubic engagement activities, reports to funders, and knowledge translation activities. The specific forums where the findings have been shared are shown as an appendix. We have received positive feedback from our dissemination. This has prompted us to further reflect on the implications of our findings, and on the next steps. Some of the data on secondary outcomes is still being analysed and will be disseminated in similar forums.

11.9 Conclusion

The overall aim of the PhD study was to assess DR services and provide evidence to improve the services. The findings provide new evidence to further the discussion on health systems for diabetes and DR and targeted interventions to improve access to DR services.

We have introduced a peer-led health education intervention in community settings and showed that it is effective in increasing attendance to screening. The main findings show that the intervention had a positive effect on screening attendance. The positive results are largely due to the increased awareness resulting from one group talk given by a peer-supporter and the referral of PLWD for a screening eye clinic.

As this is the first study to document the role of peer-led interventions to increase attendance at DR screening, the results provide a useful contribution to the knowledge base on the use of community resources for DR care in LMICs, which often goes undocumented in practice.

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4. Kelly MP, Barker M. Why is changing health-related behaviour so difficult? Public Health. 2016;136:109-16.
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The Road Not Taken

Two roads diverged in a yellow wood,
And sorry I could not travel both

[...]

I shall be telling this with a sigh
Somewhere ages and ages hence:
Two roads diverged in a wood, and I—
I took the one less travelled by,
And that has made all the difference.

Robert Frost (1874-1963)
American poet

Appendix 1 Courses undertaken

	Modules	Organizer
Sept –Dec 2015 (10 weeks)	Statistics for Epidemiology	LSHTM module
Sept –Dec 2015 (10 weeks)	Extended Epidemiology	LSHTM module
Sept –Dec 2015 (10 weeks)	Principles of Social Research	LSHTM module
Sept 2016 (eight weeks)	Ophthalmic Epidemiology	LSHTM MOOC
June 2018 (one week)	Clinical Trials	LSHTM short course
May – July 2018 (eight weeks)	Implementation Research	World Health Organization TDR MOOC
Oct 2018 (four weeks)	Diabetic Eye Disease- Strengthening Services	LSHTM MOOC

	Transferable Skills courses	Organiser
Friday, 02 October 2015	UCL Careers Workshop: Academic Career Planning	Bloomsbury Postgraduate Network
Tuesday, 06 Oct 2015	An Introduction to Semi Structured Interviews	LSHTM
Wednesday, 07 Oct 2015	MS Excel 2013: Formulae, Functions and Formatting	LSHTM
Wednesday, 07 Oct 2015	Introduction to Qualitative Analysis	LSHTM
Friday, 09 Oct 2015	MS Excel 2013: Data Management	LSHTM
Wednesday, 14 Oct 2015	MS PowerPoint 2013: for academic presentations	LSHTM
Wednesday, 28 Oct 2015	Your PhD Part 1 - Reading for a PhD - The First Important Steps	Bloomsbury Postgraduate Network
Wednesday, 04 Nov 2015	Oral Presentations: What Makes it Good?	LSHTM
Thursday, 05 Nov 2015	Research Information Skills 1	LSHTM Library
Friday, 06 Nov 2015	UCL Careers Workshops – Academic Careers Planning	Bloomsbury Postgraduate Network
Thursday, 12 Nov 2015	MS Excel 2013: Graphs & Charts	LSHTM
Friday, 13 Nov 2015	Research Information Skills 2	LSHTM Library
Thursday, 26 Nov 2015	Your PhD Part 2 - Management Skills for Researchers	Bloomsbury Postgraduate Network
Friday, 04 Dec 2015	Introduction to Data Management in the Social Sciences	LSHTM
Monday, 07 Dec 2015	Oral Presentations: What Makes it Good?	LSHTM

Tuesday, 14 Jun 2016	Introduction to Working with NVIVO 10	LSHTM
Wednesday, 15 Jun 2016	Working with NVIVO 10	LSHTM
Wednesday, 15 Jun 2016	Making Your Thesis Legal - & Depositing it Online	LSHTM
Wednesday, 15 Mar 2017	Publication Workshop 2: Publication Ethics	LSHTM
Thursday, 23 Mar 2017	Journal Metrics and the Publishing Landscape – a talk from leading Scientific Publishers- Elsevier	Bloomsbury Postgraduate Network
Friday, 24 Mar 2017	Fundamentals of Giving A Poster Presentation	Bloomsbury Postgraduate Network
Tuesday, 28 Mar 2017	Introduction to Research Support and Integrity	Bloomsbury Postgraduate Network
Thursday, 30 Mar 2017	Using Social Media for research	Bloomsbury Postgraduate Network
Friday, 31 Mar 2017	Skills for Conflict Resolution	Bloomsbury Postgraduate Network
Monday, 03 Apr 2017	Travel Safety and Security	LSHTM
Wednesday, 19 Apr 2017	Writing up your Research for Publication and Social Media	LSHTM
Monday, 24 Apr 2017	Travel Procedures for Students	LSHTM
Tuesday, 25 Apr 2017	EndNote X7: managing your references and bibliographies	LSHTM
Tuesday, 02 May 2017	Sexual Aggression: Avoidance and Survival	LSHTM
Tuesday 09 May 2017	MS Excel 2016: Data Management	LSHTM
Thursday, 10 May 2016	Social Media for Research	LSHTM
Friday 02 Jun 2017	MS Excel 2016: Graphs and Charts	LSHTM
Tuesday, 13 June 2017	Conducting Systematic literature Search	LSHTM Library
Wednesday, 21 June 2017	Understanding Journal Metrics	University of London / LSHTM
Thursday, 23 June 2018	Peer Review	LSHTM
Monday, 21 January 2019	Peer Review	Elsevier Researcher Academy
Friday, 10 May 2019	Improving your Assertiveness	LSHTM
Wednesday, 22 May 2019	Preparing to Submit Your Thesis	LSHTM

Key: LSHTM-*London School of Hygiene and Tropical Medicine;* MOOC-*Massive Open Online Courses;* UCL-*University College London*

Appendix 2: PhD Timeline

ACTIVITY	2015				2016				2017				2018				2019				2020
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Award of Research grant																					
Registration for PhD																					
Literature review																					
Health system assessment																					
Health system strengthening																					
Clinical trial																					
Writing up																					
Viva																					

*Q=Quarter

Measuring Clinical and Anthropometric parameters

Weight

Participant should be weighed in light dress (remove all heavy items of clothing or items in pockets before being weighed) and without shoes.

Ensure the scale reads 'zero' before weighing the patient.

Use the same scale for all participants.

Record the weight to one decimal place in the enrolment form.

Inform the participant of the measurement findings

Height

Volunteer must remove his/her shoes and hat before having his/her height measured.

Record the height in cm to no decimal places in the enrolment form.

Inform the participant of the measurement findings

Waist circumference

To measure the waist:

- Participant in upright standing position
- Find the bottom of the ribs and the top of the hips
- Wrap a soft tape measure around the waist, midway between these points, usually at the level of the umbilicus
- Participant should breathe out naturally before taking the measurement
- Record the measurement to the nearest 0.5cm on the enrolment form

Inform the participant of the measurements

The cutoffs are 94cm and 80cm for men and women respectively (recommended by IDF for sub-Saharan Africa)*

*The metabolic syndrome--a new worldwide definition. Alberti KG, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group. Lancet. 2005 Sep 24-30; 366(9491):1059-62.

Blood pressure

Participant must rest for at least 5 minutes in the seated position before measuring blood pressure

Use a digital device for measuring blood pressure

Measure blood pressure in the seated position, at the upper arm, using an appropriate size of cuff

Record the systolic and diastolic blood pressure in the enrolment form

Inform the participant of the measurement findings

Patients with blood pressure >140/90mmHg or >90/60mmHg should be referred to the physician

Random blood sugar

Participant should be seated

Check that meter code and test strip code match

Apply single use disposable non sterile gloves

Using the single use lancet, obtain a blood sample from the side of the finger

Avoid using thumb or index finger

The finger may bleed without assistance, but may need 'milking' gently

Apply a drop of blood to the strip by holding the patient's finger to the edge of the strip until the yellow window is completely filled with blood

Dispose of used lancet into a sharps container

Apply digital pressure to stop bleeding

Remove test strip from meter and switch meter off

Remove gloves and dispose appropriately

Record the blood sugar on the enrolment form

If blood sugar is <=4.4mg/dl, give a glucose feed immediately

Inform the participant of the measurement findings

Visual acuity

Snellen chart is placed 6m away at eye level and in good lighting

Test each eye separately, starting with the right eye

Test visual acuity with glasses if participant uses glasses

Record the visual acuity on the enrolment form

Appendix 4

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility randomized trial

Item	Description	Reported on page number
Title	Identification of study as randomised pilot or feasibility trial	1
Authors	Contact details for the corresponding author	1
Trial design	Description of pilot trial design (e.g. parallel, cluster)	4 and 5
Methods		
Participants	Eligibility criteria for participants and the settings where the pilot trial was conducted	4
Interventions	Interventions intended for each group	5 and 6
Objective	Specific objectives of the pilot trial	3
Outcome	Prespecified assessment or measurement to address the pilot trial objectives	5
Randomization	How participants were allocated to interventions	5
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	5
Results		
Numbers randomized	Number of participants screened and randomised to each group for the pilot trial objectives	8
Recruitment	Trial status	8
Numbers analysed	Number of participants analysed in each group for the pilot objectives	8
Outcome	Results for the pilot objectives, including any expressions of uncertainty	8
Harms	Important adverse events or side effects	8
Conclusions	General interpretation of the results of pilot trial and their implications for the future definitive trial	11
Trial registration	Registration number for pilot trial and name of trial register	1
Funding	Source of funding for pilot trial	11

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

Appendix 5
Developing the competences and training content for peer supporter training

Context: The content of the training is incremental to the existing training manual for peer supporters.

Process

The following steps were completed:

1. Identification of a local gap. The health system assessment for diabetes and diabetic retinopathy identified that uptake of eye examination in three counties is low. A peer-led educational and referral intervention targets to address the demand side barriers to uptake of eye examination.
2. Literature review of peer support. This showed that peer support has been effective in contributing to education of PLWD and linkage with health care resources.
3. A review of the existing peer support training manual has been conducted. We noted that it does not have content on diabetes eye health.
4. Literature review on development of training programs identified the factors associated with greater impact of training initiatives to be: alignment to local needs and priorities, country ownership of the training program, competency-based training, and a sustainability strategy.
5. Competencies for peer supporters have been developed, based on the literature and the identified local need
6. Assessment of the social accountability of this training. Social accountability in medical education is defined as an education that responds to the requirements and expectations of the society. This training has been assessed for relevance, cost-effectiveness, quality and equity.

a. Relevance: The training is relevant because it addresses a need that has been identified in this community.
b. Cost-effectiveness: The training is cost-effective because it is low cost in terms of training resource. It requires only two days and hence it can easily be added to the existing training without causing significant disruption to the training arrangements during the scale up phase. In addition, if necessary a shorter version of the training can also be created.
c. Quality Assurance: The identification of concise competencies provides a consistent standard of knowledge and skill. The training will also consist of structured practical sessions and role modelling to aid application of knowledge.
d. Equity: The training contributes to enhancing equity because it empowers disadvantaged individuals and groups to obtain the eye examination that they require.

7. Stakeholder consultation: The draft competencies were reviewed by ophthalmologists, endocrinologists, physicians, diabetes educators, public eye health specialists and the umbrella body for peer supporters (Kenya Defeat Diabetes Association).
8. The curriculum was presented at a local workshop and a local conference for discussion. This was done to foster a sense of ownership among the stakeholders.

Appendix 6: CONSORT 2010 checklist for DURE cluster randomised trial

Section/Topic	Item No	Standard Checklist Item	Extension for Cluster Designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	Table 2 (below)	2
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the cluster level, the individual participant level or both	5
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	5,6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		**None**
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	Table 1
	4b	Settings and locations where the data were collected		**6**
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when	Whether interventions pertain to the cluster level, the individual participant level or both	6

		they were actually administered		
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons		**None**
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	6
	7b	When applicable, explanation of any interim analyses and stopping guidelines		**7**
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		**6**
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who	Replace by 10a, 10b and 10c	

		assigned participants to interventions		
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	6
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	6
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		**7**
	11b	If relevant, description of the similarity of interventions		**N/A**
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	7,8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		**7,8**
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	Fig 2

		were analysed for the primary outcome		
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	Fig 2
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Period of follow-up	8
	14b	Why the trial ended or was stopped		**N/A**
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	8
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	7,8
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		**8**
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		**8**
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		**8**

Discussion				9-11
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		**11**
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	11
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		**9-11**
Other information				
Registration	23	Registration number and name of trial registry		**2**
Protocol	24	Where the full trial protocol can be accessed, if available		**6**
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		**7**

** Note: page numbers optional depending on journal requirements*

Full bibliographic reference

Campbell MK, Piaggio G, Elbourne DR, Altman DG; for the CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. BMJ. 2012;345: e5661.

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[1] Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

[2] Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

[3] Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.

Appendix 7: Checklist of items for reporting pragmatic trials - DURE trial

Section	Item	Standard CONSORT description	Extension for pragmatic trials
Title and abstract	1	How participants were allocated to interventions (e.g., “random allocation,” “randomised,” or “randomly assigned”)	
Introduction			
Background	2	Scientific background and explanation of rationale	Describe the health or health service problem that the intervention is intended to address Page 5
Methods			
Participants	3	Eligibility criteria for participants; settings and locations where the data were collected	Eligibility criteria should be explicitly framed to show the degree to which they include typical participants and/or, where applicable, typical providers (e.g., nurses), institutions (e.g., hospitals), communities or localities (e.g., towns) and settings of care Table 1
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered	Describe extra resources added to (or resources removed from) usual settings in order to implement intervention. Indicate if efforts were made to standardise the intervention or if the intervention and its delivery were allowed to vary between participants, practitioners, or study sites Page 6
			Describe the comparator in similar detail to the intervention Page 6, detailed information is provided in the trial protocol
Objectives	5	Specific objectives and hypotheses	

Section	Item	Standard CONSORT description	Extension for pragmatic trials
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors)	Explain why the chosen outcomes and, when relevant, the length of follow-up are considered important to those who will use the results of the trial Page 5
Sample size	7	How sample size was determined; explanation of any interim analyses and stopping rules when applicable	If calculated using the smallest difference considered important by the target decision maker audience (the minimally important difference) then report where this difference was obtained Page 6
Randomisation—sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification)	
Randomisation—allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	
Randomisation—implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	
Blinding (masking)	11	Whether participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment	If blinding was not done, or was not possible, explain why Page 7
Statistical methods	12	Statistical methods used to compare groups for primary outcomes; methods for additional analyses, such as subgroup analyses and adjusted analyses	

Section	Item	Standard CONSORT description	Extension for pragmatic trials
Results			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended)—specifically, for each group, report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome; describe deviations from planned study protocol, together with reasons	The number of participants or units approached to take part in the trial, the number which were eligible, and reasons for non-participation should be reported Figure 2
Recruitment	14	Dates defining the periods of recruitment and follow-up	
Baseline data	15	Baseline demographic and clinical characteristics of each group	
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether analysis was by “intention-to-treat”; state the results in absolute numbers when feasible (e.g., 10/20, not 50%)	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision (e.g., 95% CI)	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating which are pre-specified and which are exploratory	
Adverse events	19	All important adverse events or side effects in each intervention group	
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes	

Section	Item	Standard CONSORT description	Extension for pragmatic trials
Generalisability	21	Generalisability (external validity) of the trial findings	Describe key aspects of the setting which determined the trial results. Discuss possible differences in other settings where clinical traditions, health service organisation, staffing, or resources may vary from those of the trial. This information is published in the process evaluation paper.
Overall evidence	22	General interpretation of the results in the context of current evidence	

1. Campbell MK, Piaggio G, Elbourne DR, Altman DG, for the CONSORT Group. Consort 2010 statement: extension to cluster randomised trials
BMJ. 2012;345
2. Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D, for the CONSORT and Pragmatic Trials in Healthcare (Practihc) group, [1]Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008; 337; a2390

Appendix 8: Intra-cluster correlation coefficients (ICC) for demographic, anthropometric and clinical variables

Variable	ICC	95% CI
Education	0.026	0.000 - 0.060
Occupation	0.021	0.000 - 0.081
Duration of diabetes	0.004	0.000 - 0.022
Duration of membership to diabetes support group	0.072	0.007 - 0.136
Weight	0.000	0.000 - 0.015
Height	0.003	0.000 - 0.020
Waist circumference	0.112	0.023 - 0.200
Random blood sugar	0.037	0.012 - 0.158
Systolic blood pressure	0.008	0.000 - 0.029
Diastolic blood pressure	0.035	0.000 - 0.075

Interpretation

The intra-cluster correlation coefficients for all the variables are very small, thus there is very little effect of clustering. This means that clustering did not reduce the power of the study to detect true differences between the study arms.

Appendix 9

DURE Statistical Analysis Plan (SAP)

Study title	Effectiveness of peer support to increase uptake of retinal examination for diabetic retinopathy: pragmatic cluster randomized clinical trial in Kirinyaga, Kenya
Acronym	DURE
Pan African Clinical Trials registration	PACTR201707002430195
Study Protocol	https://bmcpublichealth.biomedcentral.com/track/pdf/10.1186/s12889-018-5761-6
SAP version	1
Author	Nyawira Mwangi, supervisors and statisticians listed below
Principal investigator	Nyawira Mwangi
Supervisors	
	Allen Foster
	Covadonga Bascaran
	Lawrence Muthami
Statisticians	
	David Macleod
	Lawrence Muthami
	Min Kim
Advisory committee	
	Stephen Gichuhi
	Consuela Moorman

	David Macleod
	Min Kim
Aim	To evaluate, by means of a pragmatic cluster randomized controlled trial, the effectiveness of a peer supporter- led community education programme in Kirinyaga county, Kenya.
Hypothesis	The proportion of people living with diabetes (PLWD) having a retinal examination for DR is higher in diabetes support groups (DSGs) allocated to the peer supporter-led educational package than in DSGs randomized to the usual standard of care.
Research questions	1. To what extent can health education delivered by peer supporters increase the demand for annual retinal examination among PLWD? 2. What are the contextual factors that determine the effectiveness of the intervention?
Study design	Two arm (1:1) pragmatic cluster randomized clinical trial
Level of statistical significance	P<0.05, two-sided
Sample size	Based on standard formula for cluster randomized trials by Hayes and Bennett *There were no previous studies that assessed attendance to diabetic retinopathy screening (DRS) in DSGs, and hence there was no published literature on intracluster correlation for DRS. The health system assessment had shown that only 12.2% of the PLWD in Kirinyaga had ever taken a DRS. We based our sample size determination on this evidence, as well as on a discussion with experts

	about what magnitude of effect would be clinically relevant (two-fold increase in attendance to DRS) Power: 80%, alpha 5%, 50 participants in each group (including 15% loss) Pilot study: 2 clusters (DSGs), 50*2=100 participants Main trial: 14 clusters (DSGs), 50*14=700 participants
Reliability assessment for self-efficacy questionnaire	Cronbach alpha of 0.70
Baseline data	Demographic, clinical and self-efficacy data
Randomization	- Done after recruitment - Use computer generated random numbers generated on Stata 15 away from study site by statistician (DM) - Block randomization in groups of 4 clusters
Follow-up trial period	Six months
Stopping rules	None - no stopping rules for safety, futility, efficacy or lack of power. We do not expect to stop early, based on our findings at the pilot trial.
Population to be analysed	All those who were randomized, by intention to treat analysis
Interim analysis	Not planned
Primary Outcome	Attendance to DRS, measured at the end of 180 days
Secondary outcomes	These will be assessed as a part of the process evaluation at 6 months: 1. Contextual factors that affect the effectiveness of the intervention 2. Characteristics of peer supporters associated with uptake of eye examination

	3. Barriers to uptake of eye examination among PLWD.
Implementation outcomes	Acceptability, recruitment and retention, reach and dose delivered/received will be assessed during the process evaluation and reported as proportions and percentages
Timing of data analysis	Data cleansing will be performed upon completion of the 180-day follow-up of the last cluster/participant included in the study. The final analysis will be conducted thereafter.
Presentation of results	Data will be presented with their values, confidence intervals and p values.
Comparison of baseline characteristics	-We will list general patient characteristics in a baseline characteristics table. -Data will be presented as mean with standard deviation (SD) when normally distributed or as median with interquartile range in case of skewed data. -Dichotomous and categorical data will be presented in proportions. -Normality of the data will be assessed using histograms. -Linearity will be assessed using scatter plots. -Differences between continuous variables will be assessed using Student's t-tests or Mann-Whitney-U test, depending on normality, whereas the Chi-squared test or Fisher's exact will be used for categorical values.

Reference for interpretation of the anthropometric, clinical and metabolic parameters	-*Visual acuity*- WHO classification of Visual Impairment -*Blood sugar* – reference ranges from the World Health Organization -*Blood pressure* – reference ranges used by the Ministry of Health, Kenya: 60-90mmHg diastolic and 90-40mmHg systolic -*Body Mass Index*: standard international categories -*Waist circumference* cut offs used for sub-saharan Africa (80cm in women and 94cm in men)
Reporting primary outcome	Frequencies and percentages of those that attend DRS in each arm will be reported
Relationship between primary outcome and explanatory variables	We will conduct a linear regression analysis for continuous variables and a logistic regression for dichotomous variables. A univariable regression analysis will be conducted on demographic and clinical variables against the outcome variable. A univariable regression analysis will be conducted on all variables and all variables will be used for inclusion in the multivariable model. As there are no previous studies that include these variables into one model estimating effect on DRS, we will not include any variable on a theory driven basis. We will construct the multivariable model using backward stepwise regression by starting with all variables in the model, testing the removal of each variable in turn, and deleting variables whose loss gives the most statistically insignificant deterioration in the fit of the model. This process will be repeated until no further variables can be deleted without a statistically significant loss of fit.

Adjustment for multiplicity	We will control for Type 1 errors by adjusting our primary outcomes for different confounders.
Subgroup analysis	We will conduct analysis for these subgroups as they reflect the perspective from which a patient approaches DRS: age, gender, education, occupation, current diabetes treatment, comorbidity with hypertension, and current challenges with diabetes services
Survival analysis	Analysis of time-to-DRS data will be done (participants will be censored at 180-days of follow-up). Categorical variables will be analysed using the log-rank test and continuous variables will be assessed using a univariable Cox proportional hazard regression analysis. Analysis of survival data will be presented by Kaplan-Meier survival curves when independent variables are dichotomous or categorical. A univariable Cox regression analysis will be conducted on clinical and demographic variables with 180-day DRS attendance as the dependent variable. Covariates with a of $p < 0.25$ in the univariable analysis will be included in the multivariable model
Reporting guidelines	CONSORT 2010 statement and its extensions to abstracts, cluster randomized clinical trials and pragmatic trials
Missing data	In our pilot trial we collected baseline data and primary outcome data, and obtained some insight into the likelihood of missing data in our main trial. We expect to have no missing data for the baseline variables. For survival data, any participant lost to follow up before DRS is considered censored from the last day of follow-up.

Statistical software Statistical analyses will be performed using Stata version 15 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA http://www.stata.com)

Publication of results We aim to publish three results papers

1. The pilot trial results
2. The primary outcome
3. Process evaluation

Appendix 10: Research Dissemination

Category	Audience	Venue	Date
Research meetings			
	CEHC/QEDJT meeting	London	October 2019
	ICEH research meeting	ICEH	May 2019
	CEHC/QEDJT research meeting	London	March 2019
	Publications (see papers in thesis)	-	-
	Kenya DR working group	Nairobi	Diverse dates
Conferences			
	Ophthalmological Society of Kenya Conference	Nairobi, Kenya	November 2018
	COECSA 2018	Addis Ababa, Ethiopia	August 2018
	Nordic Ophthalmology Congress	Oslo, Norway	August, 2018
	UNESCO 'Open Education for a Better World' Workshop	Vipava, Slovenia	July, 2018
	World Ophthalmology Congress	Barcelona, Spain	June 2018
	Fourth Global Forum on Human Resource for Health	Dublin, Ireland	November 2017
	COECSA 2017	Kampala, Uganda	August 2017
	COECSA 2016	Naivasha, Kenya	August 2016
Public Engagement			
	World Diabetes Day	Nairobi, Kenya	Nov, 2017
	World Health Day	Nairobi, Kenya	April 2017
	Three Minute thesis competition	London	May 2017
	Three Minute thesis competition	London	May 2018

	Lay persons visiting LSHTM for public engagement	London	May 2017
	World Diabetes Day	Nairobi	Nov 2016
Implementation partners			
	Kenya DR Stakeholders meeting	Nairobi	August 2017
	Kenya DR Research Group meeting	Nairobi	February 2018
	KDDA strategic planning meeting	Embu	Sept 2018
	KDDA strategic planning meeting	Nairobi	Sept 2017
	Kenya DR Stakeholders meeting	Nairobi	May 2016

CEHC - Commonwealth Eye Health Consortium
COECSA - College of Ophthalmology of Eastern, Central and Southern Africa
DR - Diabetic Retinopathy, ICEH-International Centre for Eye Health
KDDA - Kenya Defeat Diabetes Association
LSHTM - London School of Hygiene and Tropical Medicine
QEDJT -Queen Elizabeth Diamond Jubilee Trust
UNESCO - United Nations Educational, Scientific and Cultural Organization

REF: AMREF – ESRC P227/2016 April 20, 2016

Nyawira Mwangi
London School Hygiene and Tropical Medicine/KMTC
Email: nyawiramwangi@yahoo.com
Phone: +254722727839

Dear Dr. Nyawira,

RESEARCH PROTOCOL: SITUATION ANALYSIS OF THE HEALTH SYSTEM FOR DIABETES AND DIABETIC RETINOPATHY IN KENYA

Thank you for submitting your research protocol to the AMREF Ethics and Scientific Review Committee (ESRC).

This is to inform you that the ESRC has approved your protocol. The approval period is from April 20, 2016 to April 19, 2017 and is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.

b) All changes (amendments, deviations, violations etc) are submitted for review and approval by AMREF ESRC before implementation.

c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the ESRC immediately.

d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to AMREF ESRC immediately.

e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period (attach a comprehensive progress report to support the renewal).

f) Clearance for export of biological specimen or any form of data must be obtained from AMREF ESRC, NACOSTI and Ministry of Health for each batch of shipment/export

g) Submission of an executive summary report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

Please do not hesitate to contact the ESRC Secretariat (esrc.kenya@amref.org) for any clarification or query.

Yours sincerely,

[redacted]

Prof. Mohamed Karama
Chair, AMREF ESRC

CC: Dr. George Kimathi, WASH Programme Manager, AMREF Kenya and Vice Chair AMREF ESRC
Samuel Muhula, Monitoring & Evaluation and Research Manager, AMREF Kenya

REF: AMREF – ESRC P301/2016

14th February 2017

Mwangi Nyawira
Kenya Medical Training College
P.O. Box 2 – 00202
Kenyatta National Hospital, Nairobi
Tel: +254722727839
Email: nyawiramwangi@yahoo.com

Dear Dr Nyawira,

RESEARCH PROTOCOL: DIABETIC RETINOPATHY IN KIRINYAGA COUNTY, KENYA: UPTAKE OF RETINAL EXAMINATION IN PATIENTS WITH DIABETIS MELLITUS STUDY

Thank you for submitting your research protocol to the Amref Ethics and Scientific Review Committee (ESRC).

This is to inform you that the ESRC has approved your protocol. The approval period is from 14th February 2017 to 14th February 2018 and is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.

b) All changes (amendments, deviations, violations etc) are submitted for review and approval by Amref ESRC before implementation.

c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the ESRC immediately.

d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to Amref ESRC immediately.

e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period (attach a comprehensive progress report to support the renewal).

f) Clearance for export of biological specimen or any form of data must be obtained from Amref ESRC, NACOSTI and Ministry of Health for each batch of shipment/export.

g) Submission of an executive summary report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

Please do not hesitate to contact the ESRC Secretariat (esrc.kenya@amref.org) for any clarification or query.

Yours sincerely,

[redacted]

AMREF - ESRC
14 FEB 2017
P.O. Box 30125 - 00100, NAIROBI

Prof. Mohamed Karama
Chair, Amref ESRC

CC: Dr. George Kimathi, Director Capacity Development Institute, Amref Health Africa and Vice Chair Amref ESRC
Samuel Muhula, Monitoring & Evaluation and Research Manager, Amref Health Africa in Kenya

REF: AMREF – ESRC P301/2016

January 25, 2018

Nyawira Mwangi
P.O Box 2, 00202, Nairobi, Kenya
Email: nyawiramwangi@yahoo.com
Tel: +254722727839

Dear Dr. Mwangi,

RESEARCH PROTOCOL: DIABETIC RETINOPATHY IN KIRINYAGA COUNTY, KENYA: UPTAKE OF RETINAL EXAMINATION IN PATIENTS WITH DIABETES MELLITUS

Thank you for submitting your protocol to the Amref Health Africa Ethics and Scientific Review Committee (ESRC). Your protocol was reviewed during a meeting held on January 25, 2018.

This is to inform you that the ESRC has approved the annual renewal of your protocol. The approval period is from January 25, 2018 to January 24, 2019 and is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc.) will be used.
b) All changes (amendments, deviations, violations etc.) are submitted for review and approval by Amref ESRC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the ESRC immediately.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to Amref ESRC immediately.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period (attach a comprehensive progress report to support the renewal).
f) Clearance for export of biological specimen or any form of data must be obtained from Amref ESRC, NACOSTI and Ministry of Health for each batch of shipment/export.
g) Submission of an executive summary report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

Please do not hesitate to contact the ESRC Secretariat (esrc.kenya@amref.org) for any clarification or query.

Yours sincerely,

[redacted]

AMREF - ESRC
02 FEB 2018
P. O. Box 30125 - 00100, NAIROBI

Prof. Mohamed Karama
Chair, Amref Health Africa ESRC

CC: Dr. George Kimathi, Director Institute of Capacity Development, Amref Health Africa and Vice Chair Amref Health Africa ESRC
Samuel Muhula, Monitoring & Evaluation and Research Manager, Amref Health Africa in Kenya

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United Kingdom
Switchboard: +44 (0)20 7636 8636

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Observational / Interventions Research Ethics Committee

Dr Nyawira Mwangi
LSHTM

25 May 2016

Dear Nyawira

Study Title: Assessment of health system performance for Diabetes and Diabetic Retinopathy in Kenya in order to recommend and implement a package of interventions to strengthen DR services'

LSHTM Ethics Ref: 10904

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Protocol / Proposal	Nyawira_Project_ Proposal_Feb2016	21/02/2016	final
Protocol / Proposal	Patient interview (Diabetes)	21/02/2016	final
Protocol / Proposal	Patient interview (DR)	21/02/2016	final
Protocol / Proposal	Service provider interview (Diabetes)	21/02/2016	final
Protocol / Proposal	Service provider interview (DR)	21/02/2016	final
Investigator CV	CURRICULUM VITAE	21/02/2016	final
Information Sheet	Consent to Participate in the Study	21/02/2016	final
Information Sheet	Information sheet for service providers	21/02/2016	final
Investigator CV	CV Foster 2015	27/02/2016	final
Investigator CV	Covadonga Bascaran CV 2016	01/03/2016	final
Covering Letter	Cover letter for clarifications	23/05/2016	1
Information Sheet	Information sheet Kiswahili	23/05/2016	update
Information Sheet	Information sheet for participants	23/05/2016	update

Information Sheet	Consent to Participate in the Study	23/05/2016	update
Information Sheet	Consent Form- Kiswahili	23/05/2016	update
Local Approval	AMREF Approval letter	23/05/2016	final
Protocol / Proposal	Semi-structured interview guide for key informants for diabetes services_240516	24/05/2016	updated
Protocol / Proposal	Semi-structured interview guide for key informants for diabetic retinopathy services_240516	24/05/2016	update

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Professor John DH Porter
Chair

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Observational / Interventions Research Ethics Committee

Dr. Nyawira Mwangi
LSHTM

5 June 2017

Dear Dr. Nyawira Mwangi,

Study Title: Diabetic Retinopathy in Kenya: Uptake of Retinal Examination in patients with Diabetes Mellitus (DURE) study

LSHTM ethics ref: 11853

Thank you for your application for the above research, which has now been considered by the Interventions Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Investigator CV	Covadonga Bascaran CV 2016	21/08/2016	1
Investigator CV	CV Foster 2015	21/08/2016	1
Investigator CV	Nyawira_LSHTM_CV	21/08/2016	1
Protocol / Proposal	Information sheet for participants	01/11/2016	1
Protocol / Proposal	Information sheet Kiswahili	01/11/2016	1
Protocol / Proposal	Consent to Participate in the Study	01/11/2016	1
Protocol / Proposal	Kiswahili_Consent_Form	01/11/2016	1
Protocol / Proposal	Recruitment Form	01/11/2016	1
Protocol / Proposal	OUTCOME EVALUATION FORM	01/11/2016	1
Protocol / Proposal	TOPIC GUIDE FOR PARTICIPANTS	01/11/2016	1
Protocol / Proposal	TOPIC GUIDE FOR FOCUS GROUP DISCUSSION WITH PEER SUPPORTERS	01/11/2016	1
Protocol / Proposal	TOPIC GUIDE FOR INDEPTH INTERVIEWS WITH EYE CARE PROVIDERS	01/11/2016	1
Protocol / Proposal	Evaluation of peer supporters training	01/11/2016	1
Advertisements	RECRUITMENT PROCEDURE	01/11/2016	1
Safety Information	SAFETY INFORMATION	01/11/2016	1

Protocol / Proposal	Nyawira_CRT_Proposal_FINAL	17/11/2016	final
Information Sheet	Information sheet for team leaders of patient support groups	20/02/2017	final
Information Sheet	Consent to Participate in the Study_team lead	20/02/2017	final
Information Sheet	Information sheet Kiswahili	20/02/2017	final
Information Sheet	Information sheet for participants	20/02/2017	final
Information Sheet	Consent to Participate in the Study	20/02/2017	final
Information Sheet	Kiswahili_Consent_Form	20/02/2017	final
Local Approval	Approval Letter P301-2016	20/02/2017	final
Sponsor Letter	QA973_Sponsor confirmation_22.02.17	22/02/2017	final
Covering Letter	Cover letter-Nyawira Mwangi	24/05/2017	May 2017
Protocol / Proposal	Nyawira_CRT_Proposal_May2017	24/05/2017	May 2017
Protocol / Proposal	Information sheet for team leaders of patient support groups	24/05/2017	May 2017
Protocol / Proposal	Information sheet for participants	24/05/2017	May 2017
Protocol / Proposal	Information sheet for participants (Kiswahili)	24/05/2017	May 2017
Protocol / Proposal	Consent to Participate in the Study	24/05/2017	May 2017
Protocol / Proposal	Consent form for participants (Kiswahili)	24/05/2017	May 2017
Protocol / Proposal	Participant Recruitment Form	24/05/2017	May 2017
Protocol / Proposal	Topic guide for FGD with participants	24/05/2017	May 2017
Protocol / Proposal	Topic guide for focus group discussion with peer supporters	24/05/2017	May 2017
Protocol / Proposal	Topic guide for indepth interviews with eye care providers	24/05/2017	May 2017
Protocol / Proposal	Peer Support Training Programme evaluation	24/05/2017	May 2017
Information Sheet	Consent to Participate in the Study	24/05/2017	May 2017
Information Sheet	Consent form for participants (Kiswahili)	24/05/2017	May 2017
Information Sheet	Information sheet for participants	24/05/2017	May 2017
Information Sheet	Information sheet for participants (Kiswahili)	24/05/2017	May 2017
Information Sheet	Information sheet for team leaders of patient support groups	24/05/2017	May 2017
Advertisements	Participant Recruitment Procedure	24/05/2017	May 2017

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Chair

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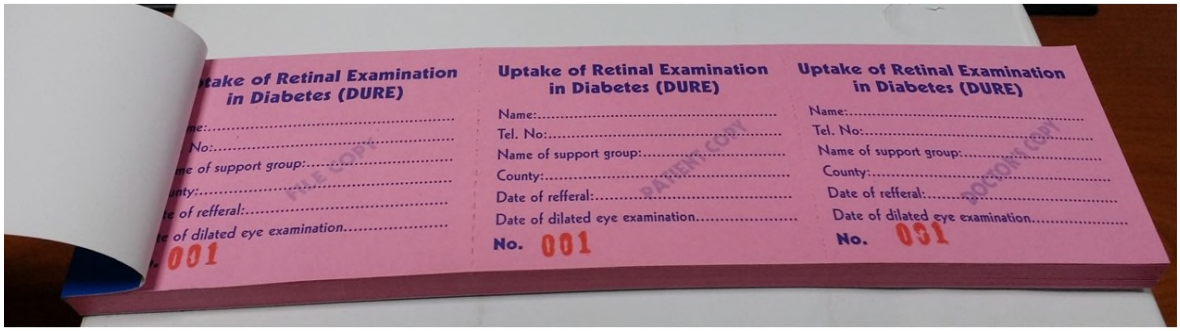

To the glory of God and for the good of our people.