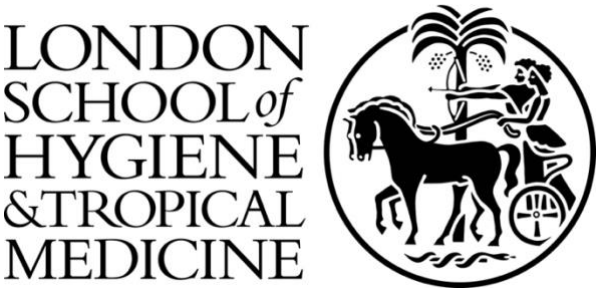

Advances in the conceptualisation and measurement of maternal morbidity and mortality

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STATEMENT OF OWN WORK

I, Ursula Maria Gazeley, confirm the work presented in this thesis is my own. Where information derives from other sources, I confirm that this has been indicated in the thesis.

Signed: Ursula Maria Gazeley

Date: 9th October 2024

Abstract

Progress to improve maternal survival has stalled in the first five years of the Sustainable Development Goal (SDG) era. In the context of this stagnation and the rapidly changing epidemiological profile of maternal health, this thesis examines the reasons for, and limitations of, the focus of the international maternal health agenda on survival up to 42 days postpartum. Specifically, it advances the conceptualisation and measurement of maternal morbidity and mortality (1) in the extended postpartum period beyond 42 days; and (2) the cumulative burden across the reproductive life course.

Part 1: The postpartum period is defined as the first 42 days following the termination of pregnancy. This definition influences the upper limit of the WHO's recommended postpartum care schedule and serves as the cut-off for identifying maternal deaths. I interrogate this timeframe by examining women's risk of death, causes of death, and recovery trajectories in the extended postpartum period and beyond. The findings support the need to re-envision models of postpartum care and the measurement of mortality beyond 42 days.

Part 2: Existing measures of maternal morbidity estimate the obstetric risk associated with an individual pregnancy. However, risk accumulates across a woman's life course, depending on repeated exposure (fertility levels) and reproductive age survival (mortality levels). I develop the methodology and derive the first cross-country estimates for two new measures of cumulative risk: the lifetime risk of maternal near miss and the lifetime risk of severe maternal outcome (near miss or maternal death). These metrics offer new perspectives on global inequity in maternal outcomes.

Based on these findings, this thesis advocates for an ambitious expansion of the maternal health agenda. A reorientation towards the neglected medium- to long-term consequences of pregnancy and childbirth, and the cumulative burden of maternal morbidity across the reproductive life course, is essential in the post-SDG era.

Acknowledgements

First, I am immensely grateful to my supervisor Veronique Filippi, for her unwavering support and mentorship. Veronique has been instrumental in my growth as a researcher and is a continual source of inspiration. Thank you for all the doors you have opened for me and for believing in me throughout. Our relationship has been integral to how much I have loved doing this PhD, and I could not have wished for a better supervisor.

A special thanks to my co-supervisor, Georges Reniers, for encouraging me to attend the European Doctoral School of Demography (absolutely the right decision!), perseverance with HDSS data access, and for providing invaluable input on my work. I am grateful to Julio Romero Prieto for his generosity and patience in helping me with technical problems over the years. To Clara Calvert, for many thoughtful discussions about HIV and pregnancy and for guiding me through the complexities of verbal autopsy data. To Hallie Eilerts and Antonino Polizzi, for all their support when I've been stuck in the weeds with code and analysis. And to José Manuel Aburto, who has taught me so much, and made me laugh even more.

It has been a pleasure to be part of the PRECISE Network throughout my PhD, where I have been surrounded by excellent researchers and exposed to many new ideas in reproductive health. To Peter von Dadelszen and Laura Magee especially, I am thankful for their mentorship and the many hours spent discussing the difficulties of near miss measurement. To Sergio Silverio, for showing me the power and purpose of qualitative research. To Marleen Temmerman, Angela Koech, Marvine Ochieng, and Onesmus Wanje, for their collaboration in Kenya, which was one of the most formative experiences of my PhD. To the PRECISE Central team, including Hiten Mistry, Malou Volvert, and Joseph Waiswa, for all their help with PRECISE data. And to all the PRECISE PhD students with whom I have shared the ups and downs of doctoral research.

I am hugely grateful to my colleagues and mentors at the WHO Human Reproduction Programme – Jenny Cresswell, Sahar Ahmed, and Lale Say. Working in the team has been instrumental in developing my understanding of maternal mortality measurement challenges. I have learned so much from you all and have benefited immensely from this experience.

The demographic training I received during the EDSD prior to my PhD has been invaluable to this thesis and my growth as a researcher. I am profoundly grateful to the organisers, teachers and students who made this experience so enriching, despite the curveball that COVID-19 threw at us.

Thank you to all my co-authors and colleagues at LSHTM (including the MRC Unit The Gambia, and members of the Maternal & Neonatal Health Group and the Population Studies Group), the University of Oxford, King's College London, Aga Khan University Kenya, and multiple HDSS sites, for the motivating discussions, guidance, and input on my work.

Above all else, my deepest gratitude goes to my family and friends for their love and support, as always.

Preface

This thesis is presented in research article format, with published papers presented in their published version. These research papers are accompanied by an introduction, background, discussion, and conclusion to provide an overall rationale for this thesis, situate the topic, and explain the cross-cutting implications of my work. Ethical approval and supplementary material for each paper is available in the Appendices.

Chapter 1 introduces the rationale for this PhD, my aims and objectives, and the contribution of the thesis.

Chapter 2 situates this PhD within the international maternal health agenda, the 'measurement trap', and its relevance for the relative neglect of maternal outcomes beyond 42 days postpartum and maternal morbidity across the life course.

Chapter 3 is a published paper: Women's risk of death beyond 42 days postpartum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa. *The Lancet Global Health.*

Chapter 4 is a published paper: Pregnancy-related mortality up to 1 year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries. *BJOG: An International Journal of Obstetrics & Gynaecology*.

Chapter 5 is a published paper: Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: A Grounded Theory of recovery trajectories beyond 42 days. *BMJ Global Health*.

Chapter 6 is a published paper: Lifetime risk of maternal near miss morbidity: A novel indicator of maternal health. *International Journal of Epidemiology.*

Chapter 7 is an accepted paper (in press): The lifetime risk of maternal near miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis. *The Lancet Global Health*.

Chapter 8 synthesises the findings of each paper**,** discusses the limitations of this thesis, and its implications for research, policy, and practice.

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Acronyms and Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ALPHA	African Population-based HIV Data
ARR	Annual Rate of Reduction
ART	Antiretroviral Therapy
BJOG	British Journal of Obstetrics and Gynaecology
BMJ	British Medical Journal
CBT	Cognitive Behavioural Therapy
CCVA	Computer Coded Verbal Autopsy
CEMD	Confidential Enquiry into Maternal Deaths
CI	Confidence Interval
CHW	Community Health Worker
COD	Cause of Death
CRVS	Civil Registration and Vital Statistics
DHIS2	District Health Information Software 2
DHS	Demographic and Health Survey
EmOC	Emergency Obstetric Care
EPMM	Ending Preventable Maternal Mortality
HDSS	Health and Demographic Surveillance System
HIC	High Income Country
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information System
ICD	International Statistical Classification of Diseases and Related Health Problems
IHME	Institute for Health Metrics and Evaluation
INDEPTH	International Network for the Demographic Evaluation of Populations and their Health
IJE	International Journal of Epidemiology
IPT	Interpersonal Therapy
LMIC	Low- and Middle-Income Country
LTR-MD	Lifetime Risk of Maternal Death
LTR-MNM	Lifetime Risk of Maternal Near Miss
LTR-SMO	Lifetime Risk of Severe Maternal Outcome
MCH	Maternal and Child Health
MDG	Millenium Development Goal
MMEIG	United Nations Maternal Mortality Estimation Inter-Agency Group
MMR	Maternal Mortality Ratio
MMWG	WHO's Maternal Morbidity Working Group

MNM	Maternal Near Miss
MNMR	Maternal Near Miss Ratio
MPDSR	Maternal and Perinatal Death Surveillance and Response
NCD	Non-communicable Diseases
NICE	National Institute for health and Care Excellence
PCVS	Physician Coded Verbal Autopsy
PHC	Primary Health Care
PLTC	Potentially Life-Threatening Condition
PMTCT	Prevention of Mother to Child Transmission
RAMOS	Reproductive Age Mortality Survey
SCI	Symptom-cause Information
SDG	Sustainable Development Goal
SRB	Sex Ratio at Birth
SRH	Sexual and Reproductive Health
TB	Tuberculosis
TFR	Total Fertility Rate
UHC	Universal Health Coverage
UI	Uncertainty Interval
VA	Verbal Autopsy
WHO	World Health Organization
WPP	World Population Prospects

Glossary

Table G.1 Definitions and associated metrics of maternal health

Indicator	Definition	Source
Existing metrics of maternal health used in this thesis		
Live birth	"The complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life. Each product of such a birth is considered a live born."	Say et al. (2009) (1)
Maternal death	"The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from unintentional or incidental causes."	ICD-11 (2)
Late maternal death	"The death of a woman from direct or indirect obstetric causes, more than 42 days but less than one year after termination of pregnancy." Specific codes capturing deaths occurring beyond 42 days are included in ICD-10 (O96 and O97) and ICD-11 (JB61 and JB62)	ICD-MM (3) ICD-11 (2)
Direct obstetric death	"Resulting from obstetric complications of the pregnant state (pregnancy, labour and puerperium), and from interventions, omissions, incorrect treatment, or from a chain of events resulting from any of the above."	ICD-11 (2)
Indirect obstetric death	"Resulting from previous existing disease or disease that developed during pregnancy, and that were not due to direct obstetric causes but were aggravated by the physiologic effects of pregnancy."	ICD-11 (2)
HIV-related indirect maternal death	"Deaths to HIV-positive women caused by the aggravating effect(s) of pregnancy on HIV; the interaction between pregnancy and HIV becomes the underlying cause of death. These are counted as indirect maternal deaths. There is an ICD code for HIV disease complicating pregnancy, childbirth and the puerperium (O98.7 in ICD-10; JB63.7 in ICD-11) for identifying HIV-related indirect maternal deaths."	ICD-MM (3) ICD-11 (2)
Incidental (non-maternal) HIV death	"Deaths caused by HIV/AIDS that occur to women who happen to be pregnant, in labour or postpartum (also defined as "HIV-related deaths to women during pregnancy, delivery or puerperium; these are not maternal deaths and are not included in the numerator of MMR."	WHO Trends in Maternal Mortality (2023) (4)
Comprehensive maternal death	The summation of maternal deaths and late maternal deaths	ICD-11 (2)
Pregnancy-related death	"The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death (obstetric and non-obstetric)" *(1)*; this definition includes unintentional/accidental and incidental causes."	ICD-11 (2)
Maternal mortality ratio (MMR)	The number of maternal deaths during a given time period per 100000 live births during the same time period	WHO Trends in Maternal Mortality (2023) (4)
Maternal mortality rate (MMRate)	The number of maternal deaths (in a given time period) divided by person-years lived by women of reproductive age in a population (within the same time period). This captures both the obstetric risk and level of fertility in a population.	WHO Trends in Maternal Mortality (2023) (4)
Pregnancy-related mortality ratio (PRMR)	The number of pregnancy-related deaths during a given time period per 100,000 live births during the same time period	WHO Trends in Maternal Mortality (2023) (4)

Pregnancy-related mortality rate (PRMRate)	The number of pregnancy-related deaths (in a given time period) divided by person-years lived by women of reproductive age in a population (within the same time period).	DHS Program (5)
Lifetime risk of maternal death (LTR-MD)	"The probability that a 15-year-old girl will eventually die from a maternal cause in her lifetime (before age 50)."	WHO Trends in Maternal Mortality (2023) (4)
Maternal near miss (MNM)	"A woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy"	Say et al. 2009 (1)
Severe maternal outcome (SMO). Also known as Women with life-threatening conditions (WLTC)	All women who either qualitied as having maternal near miss or who died. Summation of MNM and maternal deaths (mutually exclusive life-threatening conditions).	Say et al. 2009 (1)
Potentially life-threatening condition (PLTC)	Haemorrhagic disorders (abrupio placentae, accreta/increta/percreta placenta, ectopic pregnancy, postpartum haemorrhage, ruptured uterus); hypertensive disorders (severe pre-eclampsia, eclampsia, severe hypertension, hypertensive encephalopathy, HELLP syndrome); Other systemic disorders (endometritis, pulmonary oedema, respiratory failure, seizures, sepsis, shock, thrombocytopenia <100,000, thyroid crisis); severe management indicators (blood transfusion, central venous access, hysterectomy, ICU admission, prolonged hospital stay > 7 days, non-anaesthetic intubation, return to operating room, surgical intervention. Summary list defined as: severe haemorrhage, severe pre-eclampsia, eclampsia, uterine rupture, sepsis	Say et al. 2009 (1) WHO 2011 (6)
Severe maternal morbidity (SMM)	The summation of maternal near miss (MNM) cases and women with potentially life-threatening conditions (PLTC) [SMM = MNM + PLTC]	Say et al. 2009 (1)
MNM incidence ratio (MNMR)	The number of maternal near miss cases per 1000 live births, (MNMR = MNM/LB)	Say et al. 2009 (1)
SMO Ratio	The number of women with life threatening conditions per 1000 live births (SMOR = (MNM + MD)/LB)	Say et al. 2009 (1)
Maternal near miss: mortality ratio	The ratio of maternal near miss cases and maternal deaths. Higher ratios indicate better care. (MNM: 1 MD)	Say et al. 2009 (1)
Mortality index (MI)	The number of maternal deaths divided by the number of women with life threatening conditions, expressed as a percentage. The higher the index the more women with life-threatening conditions die (low quality of care) (MI = MD/(MNM + MD))	Say et al. 2009 (1)
Maternal morbidity	"Any health condition attributed to and/or complicated by pregnancy and childbirth that has a negative impact on the woman's wellbeing and/or functioning."	Chou et al. (2016) (7)
Definitions and metrics proposed in this thesis		
Late pregnancy-related death	The death of a woman, more than 42 days but less than one year after termination of pregnancy, irrespective of the cause of death (obstetric and non-obstetric)". This definition includes unintentional/accidental and incidental causes.	Chapter 3
Maternal near miss rate (MNMRate)	The number of maternal near miss cases divided by person-years lived by women of reproductive age in a population	Chapter 6
Lifetime risk of maternal near miss (LTR-MNM)	The probability that a 15-year-old girl will eventually experience a maternal near miss in her lifetime (before age 50).	Chapter 6
Lifetime risk of severe maternal outcome (LTR-SMO)	The probability that a 15-year-old girl will eventually experience a severe maternal outcome (a maternal near miss or die from a maternal cause) in her lifetime (before age 50).	Chapter 6

Chapter 1 Introduction

1.1 Thesis rationale

Rapid progress was made to reduce maternal mortality during the Millenium Development Goal (MDG) era from 2000-2015. The most recent WHO and Joint UN Agency report estimated that the global Maternal Mortality Ratio (MMR) fell from 339 maternal deaths per 100,000 live births in 2000 to 227 per 100,000 by 2015 (4). This corresponds to an average annual rate of reduction (ARR) of 2.7% (80% uncertainty interval 2.0% to 3.2%) (4). However, ending preventable maternal mortality remains one of the world's most critical development challenges, and numerous obstacles confront the maternal health community in 2024 (8). Previous declines in the MMR during the MDG period have stalled during the first five years of the Sustainable Development Goal (SDG) era (2016-2030, estimates until 2020 only) (4). Globally, the maternal mortality ratio stagnated at 223 maternal deaths per 100,000 live births from 2016 to 2020. This corresponds to 287,000 maternal deaths per year and almost 800 women dying of maternal causes every day (4).

Global trends obscure significant inequities in maternal outcomes that persist both between and within countries. The burden of maternal mortality is highest in sub-Saharan Africa, including three countries with an extremely high MMR above 1000 per 100,000 live births in 2020 (Sudan, Chad, and Nigeria). Ten additional countries, all but one in sub-Saharan Africa, had a high MMR between 500-999 (4). Sub-Saharan Africa accounted for 70% of all maternal deaths in 2020, of which Nigeria alone contributed 29% (4). Maternal deaths largely affect the most socioeconomically disadvantaged women within a population (9,10), and almost all are preventable (10). Such 'diversity and divergence' continues to characterise maternal mortality in the SDG era (11).

Tackling maternal mortality is a key commitment of the SDG: SDG 3.1 is to reduce the global MMR to less than 70 maternal deaths per 100,000 live births. Considerable and sustained course correction is required if the world is to achieve this goal by 2030 (4,12). Maternal deaths are defined in the International Classification of Diseases 11th edition (ICD-11) as, "*the death of a woman while*

pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from unintentional or incidental causes" (2). SDG target 3.1 therefore orients the global maternal health agenda towards a primary focus on improving survival within 42 days postpartum.

This global target is set amid fundamental shifts in the epidemiological profile of maternal health as countries progress through the obstetric transition (10,13). Parallel to the concept of the epidemiological transition, the obstetric transition describes the secular shift from high to low maternal mortality, and direct obstetric to indirect obstetric causes of death (10,13). Stages in the obstetric transition correspond to levels of the MMR, and can provide guidance on priority areas for health system improvement (10,13). As maternal mortality is closely correlated with stillbirth and neonatal mortality, these transitions can be analysed together in an integrated model to benchmark countries' progress and enhance understanding of the common drivers of mortality change (14).

Progression through the stages of obstetric transition requires health systems strengthening to mitigate the individual factors and social determinants of maternal mortality (10,13,15). Countries require the capacity to prevent and appropriately manage direct obstetric causes of maternal morbidity and mortality alongside indirect obstetric causes from infectious and non-communicable diseases that are aggravated by pregnancy (10,13,15). Tackling these dual challenges emphasises the need for a health systems approach to improve the coverage and quality of obstetric care, in addition to closer integration of obstetric and non-obstetric care providers (10,13,15). Reducing the persistent inequities in maternal outcomes demands more than direct investment in vertical interventions that target biomedical causes (15,16). A multipronged approach includes Universal Health Coverage (UHC), women's empowerment, and climate adaptation and mitigation (10,15).

Stagnating progress and persistent inequity in maternal survival demands continued global investment and political prioritisation to confront these challenges, with funds falling in recent years

(17). However, the focus of the maternal health agenda on maternal survival up to 42 days postpartum has recently been challenged on two counts.

First, the focus on survival within the first 42 days postpartum may cause us to underestimate the true burden of maternal mortality and morbidity. Rather, many conditions may persist for far longer or manifest later than the 42-day postpartum threshold (18). Recognition is growing, therefore, that the standard 42-day postpartum period following termination of pregnancy does not fully represent the timing and diversity of postpartum challenges women face (18–20). The 2023 Lancet series 'Maternal health in the perinatal period and beyond' suggests that a paradigm shift is underway, towards adopting a longer-term lens to postpartum health and maternal outcomes beyond 42 days (9,18,21).

Second, an exclusive focus on survival causes us to underestimate the true burden of maternal ill-health and the myriad ways maternal morbidity affects women's wellbeing (10,22–25). Relative to other causes, the absolute number of maternal deaths is small (26). Acute or chronic conditions during pregnancy or the postpartum period may affect many more women than death (27), often with long-term sequelae for their physical, mental, and sexual health and functioning (18,20,28–30). Akin to the global response to maternal mortality, a forceful commitment to expand the maternal health agenda towards the prevention and treatment of maternal morbidity is required (18–20,22,28,31). A more ambitious agenda reoriented towards non-fatal outcomes should adopt a life cycle approach that recognises the risk of recurrence of complications, the risk of pregnancy on exacerbation of underlying conditions, and its effects on later life health (19). It should also include recognition of non-life-threatening maternal morbidity that still negatively affects women's wellbeing despite a low risk of death (19,20). To do so underscores global calls for better, population-level metrics with which to understand its epidemiological profile and monitor progress (7,19,20,28,31).

These two challenges to the maternal health agenda determine the objectives of this thesis, as described below.

1.2 Aims and objectives

This thesis aims to contribute to advances in the conceptualisation and measurement of maternal morbidity and mortality, in (1) the extended postpartum beyond 42 days; and (2) the burden over the female reproductive life course. I determined these aims iteratively, informed by the findings of each consecutive paper:

For aim 1, specific objectives are as follows:

a) Determine the duration of an elevated risk of death following childbirth and delivery up to one year postpartum in sub-Saharan Africa.
b) Determine the causes of death following childbirth and delivery during the postpartum and extended postpartum periods in sub-Saharan Africa.
c) Develop a theory of women's recovery in the extended postpartum period following severe maternal morbidity in Kilifi, Kenya that can be validated in other contexts.

For aim 2, specific objectives are as follows:

a) Develop summary indicators to quantify the cumulative risk of maternal near miss morbidity across the female reproductive lifespan: the 'lifetime risk of maternal near miss' (LTR-MNM) and 'lifetime risk of severe maternal outcome' (LTR-SMO).
b) Apply the new indicators to develop the first cross-country comparable estimates of the LTR-MNM and LTR-SMO.

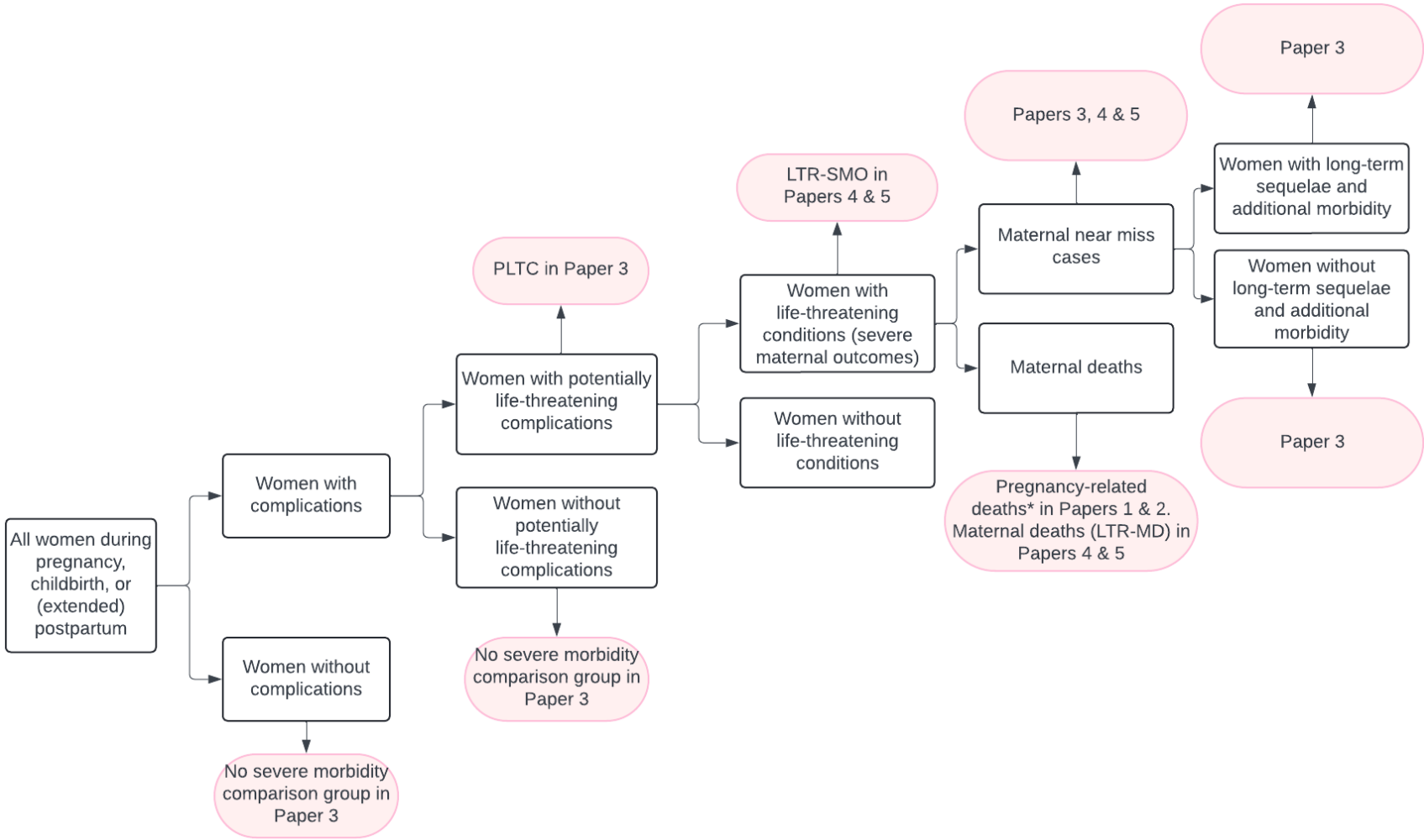
1.3 Obstetric continuum focus area by paper

The focus of this PhD is predominantly on the severe end of the maternal continuum, including potentially life-threatening conditions (PLTC), maternal near miss events (MNM), and maternal deaths. For most of the work presented in this thesis, I limited the substantive focus to these severe outcomes because they are likely to have the most significant long-term effects on women's health and wellbeing in the extended postpartum and have the clearest case definitions required for

monitoring. Measurement and conceptualisation of less severe forms of morbidity that are not potentially life-threatening was therefore largely beyond the scope of this PhD, except for Paper 3.

Figure 1.1 (below) shows the obstetric continuum focus area by paper.

Figure 1.1 Obstetric continuum focus area by paper



Note: Figure 1.1 adapted from Say et al (2009).

1.4 Thesis structure

Chapter two provides background to situate this thesis research within the maternal health 'measurement trap'. I describe how issues in conceptualisation, indicators, data sources, and measurement techniques contribute to a lack of information and relative neglect of maternal outcomes beyond 42 days postpartum and the burden of maternal morbidity across women's lives.

Chapter three presents a research paper published in The Lancet Global Health, which examines the duration of women's risk of death after childbirth in sub-Saharan Africa. This paper pooled Health and Demographic Surveillance System (HDSS) data from 30 sites across 12 countries to calculate the risk ratios of death by postpartum interval.

Chapter four presents a research paper published in The British Journal of Obstetrics and Gynaecology (BJOG), and examines the causes of pregnancy-related deaths, comparing the causes for women who died during pregnancy and within the 42-day postpartum period, with women who died from 43 days to one year postpartum. This paper used HDSS data and verbal autopsy data from 10 HDSS sites across six countries, and two algorithms (InterVA5 and InSilicoVA) to attribute the most likely cause of each pregnancy-related death.

Chapter five presents a research paper published in The British Medical Journal (BMJ) Global Health, where I developed a Grounded Theory of women's postpartum recovery after severe maternal morbidity Kilifi, Kenya. This paper used the PRECISE Network prospective cohort as a sampling frame to identify women with severe maternal morbidity, from which I purposively selected women across a range of diverse characteristics to understand differences in women's recovery trajectories.

Chapter six presents a research paper published in the International Journal of Epidemiology (IJE), where I proposed and demonstrated two new cumulative risk metrics – the LTR-MNM and LTR-SMO

– to quantify the burden of maternal near miss morbidity and severe maternal outcomes across women's reproductive lives. This paper used population-level MNM surveillance data from Namibia to demonstrate the calculation of this novel metric.

Chapter seven presents an accepted research paper, in press at The Lancet Global Health, where I computed LTR-MNM and LTR-SMO for 40 countries across five regions, to quantify global inequity in reproductive outcomes across the reproductive life course. I conducted a systematic review to identify eligible MNM prevalence data, and for countries with more than one available estimate, I conducted a meta-analysis to estimate a pooled MNM ratio, which was used in computation of the of the LTR-MNM (and LTR-SMO) for each country.

Chapter eight provides an overview of how each research paper met the objectives of this PhD and synthesises the main findings. I discuss the cross-cutting limitations of my research, before describing the study-specific implications for measurement, health systems, guidelines, and future research, and finally, address the cross-cutting implications of this PhD thesis.

1.5 PhD Publications

The following list contains the full citations for the published and accepted work included in this thesis.

PhD published papers

(1) **Gazeley U**, Reniers G, Eilerts-Spinelli H, Prieto JR, Jasseh M, Khagayi S, Filippi V. Women's risk of death beyond 42 days postpartum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa. The Lancet Global Health. 2022 Nov 1;10(11):e1582-9.

(2) **Gazeley U**, Reniers G, Romero-Prieto JE, Calvert C, Jasseh M, Herbst K, Khagayi S, Obor D, Kwaro D, Dube A, Dheresa M. Pregnancy-related mortality up to 1 year postpartum in

sub-Saharan Africa: an analysis of verbal autopsy data from six countries. BJOG: An International Journal of Obstetrics & Gynaecology. 2024 Jan;131(2):163-74.

(3) **Gazeley U**, Ochieng MC, Wanje O, Etyang AK, Mwashigadi G, Barreh N, Kombo AM, Bakari M, Maitha G, Silverio SA, Temmerman M. Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: a grounded theory of recovery trajectories beyond 42 days. BMJ Global Health. 2024 Jun 1;9(6):e014821.

(4) **Gazeley U**, Polizzi A, Romero-Prieto JE, Aburto JM, Reniers G, Filippi V. Lifetime risk of maternal near miss morbidity: a novel indicator of maternal health. International Journal of Epidemiology. 2024 Feb 1;53(1):dyad169.

PhD accepted papers (in press)

(5) **Gazeley U**, Polizzi A, Romero-Prieto JE, Aburto JM, Reniers G, Filippi V. The Lifetime Risk of Maternal Near Miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis. The Lancet Global Health.

1.6 Thesis contribution

I identify two major contributions of this thesis.

First, this thesis contributes to a growing body of research that questions the justification for the 42-day postpartum period. The standard definition is entrenched with far reaching implications for the measurement of maternal health outcomes and the provision of postpartum care. I believe my research has contributed to a paradigm shift that is currently underway which seeks to reorient how we consider postpartum maternal health and address the historical neglect of adverse outcomes that occur beyond the 42-day threshold. This contribution was achieved through Paper 1, Paper 2, and Paper 3, which provide evidence of the duration of postpartum risk, causes of pregnancy-related

death beyond 42 days, and recovery trajectories throughout the extended postpartum following severe maternal morbidity, respectively.

The second contribution of this thesis is the conceptual and methodological innovation of proposing new population-level metrics of maternal morbidity – the LTR-MNM and LTR-SMO. This is a novel contribution, and for the first time, extends the measurement of maternal morbidity into a cumulative risk framework. Papers 4 and 5 demonstrate how these new metrics can help us to better quantify the burden of maternal morbidity across women's lives, and the magnitude of cross-country inequity in reproductive outcomes. My hope is that these new metrics could be used to re-establish maternal health on the development agenda and reorient commitment towards ending all forms of preventable maternal morbidity and mortality, beyond the exclusive focus on women's survival up to 42 days postpartum.

1.7 Role of the candidate

I, the candidate, designed the studies in this thesis with the guidance of my supervisors (Veronique Filippi and Georges Reniers). I managed the data acquisition for those sources requiring requests for approval (certain HDSS sites, PRECISE Network data). I conducted all data analyses, prepared outputs including visualisations, interpreted findings, and wrote the first drafts of each manuscript. I incorporated revisions from my supervisors and co-authors for each paper. I led the submission process to each journal and the responses to peer reviewer comments and revisions.

1.8 Ethical clearance

Three studies presented were approved by the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Advisory Board (Chapters 3 and 4: reference 26603 & Chapter 5: reference 27267). The study presented in Chapter 5 was also approved by Aga Khan University Ethics Committee. The

studies presented in Chapters 6 and 7 were exempt from ethical approval as they only used open-access data available in the public domain. Ethical approval certificates are available in Appendix A.

1.9 Collaborating institutions

Collaborations with multiple academic and research institutions have been instrumental to this thesis research. First, I worked closely with colleagues at several HDSS sites, who played key roles in the collection, cleaning, and management of surveillance data, and provided critical input on my analyses and the interpretation of results. Second, I collaborated with members of the PRECISE Network throughout my PhD, including the PRECISE central team at Kings College London, and PRECISE partner institutions in Kenya (Aga Khan University) and The Gambia (The MRC Unit The Gambia). Membership of this consortium, which includes scientists across all areas of reproductive and child health, exposed me to new ideas and collaborations outside of my specific focus area. Finally, colleagues from several institutions, including from LSHTM, Kings College London, the University of Oxford, the University of Liverpool, Aga Khan University Kenya, and The MRC Unit The Gambia, are co-authors on the research papers presented in this thesis.

1.10 Funding

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Chapter 2 Background

This chapter situates my PhD research, by describing how global targets continue to establish maternal survival up to 42 days postpartum as the primary focus of the maternal health agenda. I argue that the absence of targets concerning maternal outcomes beyond 42 days, and the impact of maternal morbidity on women's wellbeing across the life course, can be understood as an extension of the maternal health 'measurement trap'. Adapting and expanding upon Graham and Campbell's original 1992 description, I explain how the lack of information on these outcomes and their relative neglect from the maternal health agenda are mutually reinforcing. Each of the four components of the trap and their implications for conceptualisation and measurement of maternal morbidity and mortality are described in turn.

2.1. Global goals, targets and the international maternal health agenda

Global goals and targets simultaneously embody and determine the established maternal health agenda. In doing so, global goals and targets are intricately linked to policy, programmes, measurement, and the galvanising of funds for those activities (32). The axioms 'what you count is what you target' and 'governance through goals' continue to characterise much of the maternal health agenda (32,33).

The MMR has long been recognised and promoted as an important indicator of women's health and development more generally (34). Maternal mortality was the primary reproductive health outcome of the Millenium Development Goals (MDGs) (35,36). The inheritance of this goal in the Sustainable Development Goal (SDG) era (2016-2030) both reflects and reinforces the continued prioritisation of improving maternal survival up to 42 days postpartum. SDG target 3.1 is to reduce the global MMR below 70 per 100,000 by 2030. This primary SDG target is supplemented with additional targets to reduce inequities in outcomes (37). These are set out in the Ending Preventable Maternal Mortality (EPMM) strategy: that by 2030, every country should reduce its MMR by at least two-thirds from their 2010 baseline, and no country should have an MMR higher than 140 maternal deaths per 100,000 live births (twice the global target) (8,38). The EPMM cross-cutting strategy to "*improve metrics, measurement systems, and data quality to ensure all maternal and newborn deaths are counted*" (8) (p.9) also orients the prioritisation of global action to the prevention of maternal mortality up to 42 days.

To achieve these maternal mortality goals, policies and programmes have largely focused on key vertical interventions in the provision of basic and emergency obstetric care (10,15). Global coverage targets have also largely reflected this focus on vertical interventions, including skilled attendance at birth, institutional delivery, antenatal care coverage, and access to emergency caesarean section (10,15). The EPMM coverage targets for 2025 span the obstetric continuum, from antepartum to postpartum care, and include coverage of four or more antenatal contacts; births attended by skilled

personnel; coverage of early routine postpartum care (within 2 days of delivery); the proportion of the population within 2 hours' travel time of an Emergency Obstetric Care (EmOC) facility; and women aged 15-49 years able to make empowered decisions about their own reproductive health (38).

Some global goals, targets, and coverage indicators have broadened this focus. The Global Strategy for Women's, Children's, and Adolescents' Health (2016-2030) incorporates three overarching objectives: 1. Survive – to reduce the global MMR below 70; 2. Thrive – which includes ensuring universal access to sexual and reproductive health (SRH) services; and 3. Transform – which includes the broader social determinants of health (39). Similarly, in addition to coverage indicators that overlap with EPMM, Countdown to 2030 also includes indicators that track the integration of communicable diseases and maternal health (e.g., preventive treatment for pregnant women with malaria, pregnant women living with HIV on antiretroviral therapy (ART)) (40). Finally, recent efforts to advance the measurement of 'effective coverage' – defined by Marsh et al. (2020) as "*the proportion of a population in need of a service that had a positive health outcome from the service*" – have promoted an extension of monitoring beyond mortality to include a focus on the quality of care (41) (p.e732). Effective coverage has not yet been adopted in any international goals, however.

These global mortality goals and coverage targets have constrained, and been constrained by, the priorities of the maternal health agenda. Yet, against the backdrop of a small absolute number of maternal deaths relative to other causes, stalling progress to further reduce maternal mortality, and an evolving epidemiological profile of maternal health, recognition is growing that this historic focus of the maternal health agenda has become overly restrictive. This includes global goal setting: across all global mortality goals and coverage targets, maternal outcomes beyond 42 days, and the reduction and prevention of maternal morbidity more generally, are absent.

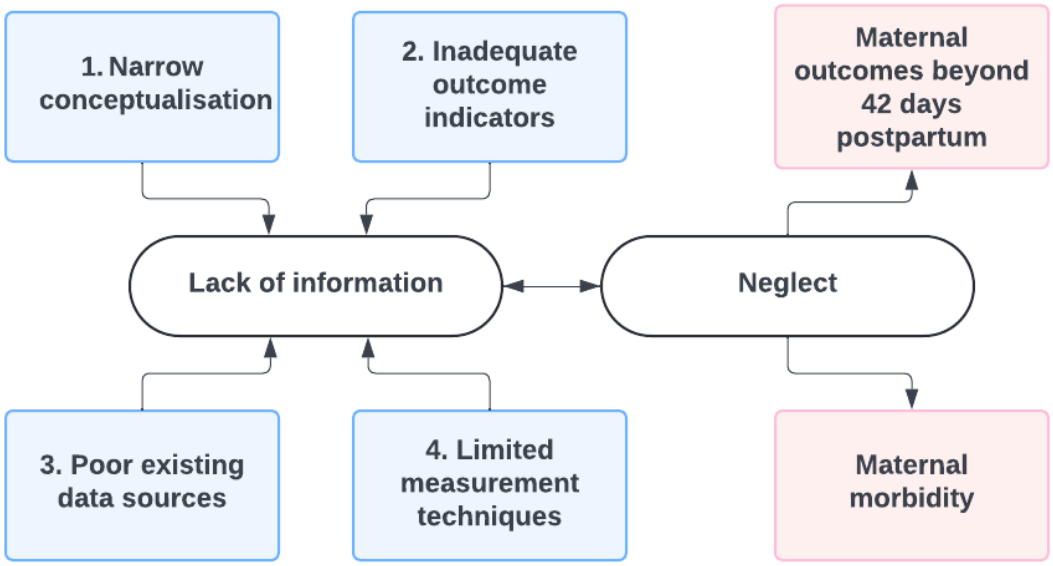
2.2 Maternal health measurement trap

The reasons for the absence of these outcomes in global priorities may be understood as an extension of the 'maternal health measurement trap'. Originally proposed by Graham and Campbell in 1992 (34), they argued that decisions and actions on maternal health are often based on inadequate information at the level of both individuals and populations. A lack of information and comparatively low prioritisation of maternal health are mutually reinforcing and result from four interrelated problems:

1. Narrow conceptualisation of maternal health
2. Inadequate outcome indicators
3. Poor existing data sources
4. Limited measurement techniques

These measurement challenges still apply today and, I argue, may help explain the continued narrow focus on improving maternal survival up to 42 days postpartum. The lack of information about maternal outcomes (fatal and non-fatal) occurring beyond 42 days postpartum, and the burden of maternal morbidity on women's wellbeing more generally, results in their relative neglect from the global maternal health agenda. The absence of these objectives in global targets not only reflects but also reinforces this information gap. Figure 2.1 shows a modified version of Graham and Campbell's measurement trap, adapted in relation to the focus of this thesis.

Figure 2.1 Adapted maternal health measurement trap



Each of the four components of the measurement trap for maternal outcomes beyond 42 days and maternal morbidity across the reproductive life course are discussed in turn. I then describe the contribution of this thesis in relation to these challenges.

2.3 Narrow conceptualisation of maternal health

2.3.1 Postpartum period

First, a narrow conceptualisation of the postpartum period has affected the measurement of maternal mortality and the schedule of postpartum care. A critical re-evaluation of the postpartum period and adequate recognition of its implications for the provision of care and measurement of key metrics have been so far under-prioritised and under-researched. This is not to imply a time frame is not required for indicators, but there is a need to recognise the exclusion this creates and its consequences for the relative prioritisation of maternal outcomes occurring after 42 days postpartum.

Inconsistency in terminology

'Postpartum' describes the period that begins after the termination of pregnancy (regardless of pregnancy outcome – live birth, stillbirth, miscarriage, or abortion) (42). The use of the terminology

‘postpartum’ is not universal. The World Health Organization (WHO) has alternated between ‘postpartum’ to ‘postnatal’ over time, and since 2010 has used ‘postnatal’ (42,43). Others prefer the term ‘puerperal’. Although sometimes used interchangeably, the terminology used to describe this period varies between countries and organisations, with different connotations (42). Consistent with ICD-11, where ‘postnatal’ exclusively refers to the health of the baby after delivery, and ‘postpartum’ refers to the health of the woman after delivery (42), I have used the term ‘postpartum’ to refer to this period throughout this thesis. This term is also more commonly used across scientific research (42), and was primarily adopted in the 2023 Lancet Series ‘Maternal health in the perinatal period and beyond’ that focused on the needs of women (9,10,18). Inconsistency in terminology causes ambiguity about the provision of care and the need to centre the woman’s care, not just her baby’s (42).

Inconsistency in duration of the postpartum period

There is no consensus on the duration of the postpartum period, as demonstrated by an analysis of postpartum guidelines from international and national-level institutions (42). As defined by the WHO, it begins immediately after the end of pregnancy and extends up to 42 days (six weeks) after birth (43). This period is typically divided into three phases: the immediate postpartum, which covers the first 24 hours after birth; the early postpartum period, from day two until day seven after birth; and the late postpartum period, from day 8 to day 42 (43). However, the WHO’s categorisation of these postpartum phases is not universally accepted (44,45), with some differences in the timing of transition from immediate to the early to the late postpartum phases, as well as differences in the 42-day duration (42).

Maternal mortality was initially defined in the ICD as deaths up to one year postpartum (46). This timeframe was reduced to 42 days in the ninth revision (ICD-9), first implemented in 1979 (46). Justification for this 42-day upper limit of the postpartum period is unclear and does not appear to be based on empirical studies of the risk of death by time since delivery (47). Data on the progression of physiological changes in the puerperium is limited. It is possible that the decision to reduce the

timeframe to 42 days was retrofitted based on clinical knowledge rather than empirical data. For example, it is often claimed that six weeks coincides with the return of the uterus to its pre-pregnancy size (48,49), but longitudinal ultrasound data on the duration of uterine involution is scarce. Descriptions of 'normal' postpartum uterine involution highlight considerable variability between women and by measurement method (50–52), which may explain why so little data exists (53).

Six weeks may also roughly coincide with the resumption of menses for non-lactating women (47). However, for women who are partially or exclusively breastfeeding, lactational amenorrhea can last much longer than 42 days (54), with an average duration of 5.5 months (55). Sub-Saharan African populations typically experience among the longest durations of lactational amenorrhea (56,57). Some changes in the genitourinary system may take up to six months to resolve, while others may never fully revert to their pre-pregnancy state (44,58). The ability of the body to recuperate from pregnancy and delivery within 42 days may also be hindered by direct obstetric complications, and infectious or non-communicable morbidities (47,59).

The origin of the 42 day puerperium may have historical religious and cultural underpinnings, including Ambrahamic traditions of postpartum confinement (47,60). These traditions may have influenced the medical convention of considering the first six weeks postpartum as the critical period of recovery. However, contemporary postpartum cultural practices are highly heterogeneous (61), suggesting the cultural legacy of a 42-day cut-off may no longer apply. For example, a systematic review from 2007 found that the duration of a postpartum period of rest varied between 21 and 40 days, while the period of abstention from sexual activity ranged from 20 to 100 days (61).

Implications of the narrow conceptualisation of the postpartum period

This entrenched conceptualisation of the postpartum period is vitally important.

First, it determines the recommended schedule for the provision of routine services. The WHO's recommended schedule of postpartum care according to the 2022 guidelines states that: "*A minimum*

of four postnatal care contacts is recommended. If birth is in a health facility, healthy women and newborns should receive postnatal care in the facility for at least 24 hours after birth. If birth is at home, the first postnatal contact should be as early as possible within 24 hours of birth. At least three additional postnatal contacts are recommended for healthy women and newborns, between 48 and 72 hours, between 7 and 14 days, and during week six after birth" (25) (p.xiv). The web annex includes the following research question on the number of postpartum contacts: "*For postpartum women and term infants (without complications), do more frequent postnatal care contacts, compared with less frequent postnatal care contacts, improve maternal, newborn and infant outcomes?*" (62) (p.6). However, there is no discussion on the rationale for final the visit occurring in week six, and no explicit research agenda on postpartum visits beyond 42 days (62). This 2022 guidance mirrors the schedule in the WHO's 2013 guidance, described as a "*strong recommendation…based on low quality evidence for mothers*" (63) (p.3). Earlier WHO documentation does acknowledge that "*the model recognises that additional contacts may be required depending on individual circumstances*" (24) (p.3), but not as routine care.

The WHO's 2022 recommendations for a positive postnatal experience also include guidance on the content of routine postpartum care services at each visit, including physical assessments of the mother (and baby), mental health screening, family planning, intimate partner violence screening, and counselling on the resumption of sexual intercourse, breastfeeding, and nutrition (25). However, there is no guidance for postpartum care or the provision of services beyond six weeks postpartum (25,64).

Except in health systems which depart from WHO guidelines, women with ongoing or unresolved morbidity beyond this time point must self-elect to seek care. This approach directs the prioritisation of healthcare providers toward the management and treatment of morbidity within, but not necessarily beyond, this time point. A comparison of international and national guidelines identified that South Africa (65), India (66), and Canada (67) align with the WHO, indicating 42 days as the upper limit for postpartum contact (42). In contrast, three high-income countries (HICs) have

guidelines that depart from WHO recommendations: Australian guidelines indicate one year (68), the American College of Obstetricians and Gynecologists (ACOG) recommends 12 weeks (69), and the UK National Institute for Health and Care Excellence (NICE) suggest eight weeks (70). Few low- and middle-income countries (LMICs) have guidelines specifying the duration of the postpartum period for health service provision, indicating that LMICs may rely more heavily on WHO guidelines to inform national policy (64).

Second, the WHO's use of the 42-day definition of the postpartum period is integral to the ICD-11 (and earlier ICD-10) definitions of maternal death and pregnancy-related death (2). Only maternal deaths within 42 days are included in the numerator of the MMR. This has far-reaching implications for international surveillance of maternal mortality. The United Nations Maternal Mortality Estimation Inter-Agency Group (MMEIG) MMR estimates used to benchmark global progress against SDG 3.1 do not report on late maternal deaths, as inconsistency in reporting hinders comparability (4). Late maternal deaths occurring from 43 days to one year postpartum are not included in any supplementary SDG or EPMM mortality targets, and the provision of care beyond 42 days is not included in coverage indicators.

2.3.2 Maternal morbidity

The conceptualisation of maternal morbidity has been a significant challenge for the maternal health community. Maternal deaths account for only a small proportion of adverse maternal outcomes; many more women may experience acute or chronic maternal morbidity, often with long-term sequelae for their physical, mental, and sexual health and functioning (18,20,28–30). Conceptual challenges have resulted in a lack of standard, comparable indicators and significant information evidence gaps on the true prevalence of many types of maternal morbidity (71). Modelled global estimates of the burden of maternal disorders produced by the Institute for Health Metrics and Evaluation (IHME) are a notable exception (27,72), but they estimate only a limited number of

conditions, ignoring common conditions such as postpartum depression and urinary incontinence (71). This information gap, in turn, has contributed to its relative neglect as a policy priority.

The term 'maternal near miss' to describe women who survive a life-threatening maternal complication was first proposed by Stones et al. in 1991 (73). This constituted an important theoretical advancement in the obstetric continuum, where life-threatening complications (near miss or death) are the final stage. Stones et al. argued that, as MNM cases share many clinical characteristics with women who died, and since they are more frequent, the clinical review of these cases is useful for improving the quality of obstetric care (73). After twenty years of conceptual development (73,74), WHO published their own definition of MNM in 2009 (1). Agreed upon at the international level, this definition marked a significant step forward in the conceptualisation of the most severe form of maternal morbidity. The WHO MNM definition was reconciled with the ICD-10 definition of maternal death (see Glossary) and was defined as "*a woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy*" (1). Defining uniform diagnostic criteria was an essential step in advancing the use of this concept and ensuring comparability in its measurement (see section 2.4) (1).

Progress has also been made in the conceptualisation of maternal morbidity more generally, with the WHO's Maternal Morbidity Working Group (MMWG) leading efforts to reconceptualise maternal morbidity since 2012. The MMWG's work highlighted the need to expand the narrow conceptualisation of maternal morbidity to acknowledge women's diverse experiences of morbidity and wellbeing (7). Their definition of maternal morbidity is defined broadly as "*any health condition attributed to and/or complicated by pregnancy and childbirth that has a negative impact on the woman's wellbeing and/or functioning"* (7) (p.1).

As part of the WHO MMWG, Filippi et al. (2018) developed a new conceptual framework for maternal morbidity, reflecting six principles: 1. There is a need to adopt a woman-centred approach,

foregrounding the experiences women feel are important to them; 2. Maternal risks are cyclical because many women become pregnant more than once, and sequelae from one pregnancy may occur in the subsequent pregnancy; 3. Maternal morbidity may affect women for far longer than 42 days postpartum; 4. Maternal health is not just a clinical phenomenon but is also social and economic in nature; 5. The context and environment in which women live influence the experience of morbidity; 6. Morbidity has strong linkages to WHO guidance, including the quality of care (19). This extends previous conceptualisations of maternal morbidity beyond distal and intermediate determinants to encompass the lived experience of maternal morbidity, including non-severe forms (19).

In parallel to this reconceptualisation, Firoz et al. (2018) developed a framework for healthcare interventions to address maternal morbidity (20). This stresses the need to move beyond a focus on emergency obstetric care towards a health systems approach, to improve the integration of maternal health with existing services, especially NCD programmes. Beyond the historical focus on interventions primarily around the time of delivery, this framework situates maternal health within the life cycle, viewing reproductive episodes as entry points to improve women's health more generally (20).

Despite this recent progress with reconceptualisation of maternal morbidity, there is still a long way to go to operationalise these conceptualisations and measure the burden of its different forms at the population level (as discussed in section 2.4.3 below).

2.4 Inadequate outcome indicators

Intricately linked to conceptualisation, indicators used to monitor trends and progress in maternal health reflect and reinforce the narrow prioritisation of survival during pregnancy and up to 42 days postpartum. As the second component of the measurement trap, I identify three main challenges with the indicators currently available: first, most measure obstetric risk without adequately

accounting for exposure (pregnancy); second, there is an 'indicator gap' in metrics available to measure deaths occurring beyond 42 days postpartum if cause of death information is not available; and finally, operationalising the indicators of maternal morbidity remains challenging.

2.4.1 Obstetric risk

The primary indicator used to measure trends in maternal health and progress towards SDG 3.1 is the MMR – the number of maternal deaths per 100,000 live births. This is a measure of obstetric risk only. It does not quantify the probability of maternal death because the probability is composed of both (i) the probability of being pregnant or within 42 days postpartum (i.e., exposed to the risk of pregnancy-related death), and (ii) the probability of dying from maternal causes, given being pregnant or within 42 days postpartum (34). Live births are not commensurate with exposure to risk because women are at risk of maternal mortality not only for pregnancies that end in a live birth but also for pregnancies that end in miscarriage, abortion, and stillbirth, and up to 42 days thereafter. All else equal, using live births as the denominator therefore inflates the MMR and overestimates the probability of death. This problem affects all relevant ratios that use live births as the denominator, including the Pregnancy-related Mortality Ratio (PRMR) and Maternal Near Miss Ratio (MNMR). There is a trade-off between the difficulties with and biases inherent in pregnancy reporting (75,76) (see section 8.2.3) and remedying the incongruence between the numerator and denominator in these measures.

Relatedly, most widely used measures of maternal risk of mortality or morbidity (all rates and ratios) used for global monitoring quantify the obstetric risk associated with an individual pregnancy, depending on the period of observation. The lifetime risk of maternal death (LTR-MD) is the only metric of mortality that moves beyond the risk associated with an individual pregnancy to account for repeated exposures (indexed by the Total Fertility Rate (TFR)). Similarly, this measure does not account for pregnancies that do not end in a live birth. It is a synthetic cohort probability: a period population average of the cumulative risk of dying from a maternal cause over women's reproductive

lives, accounting for both fertility and survival across reproductive ages. Before the development of the LTR-MNM made in this thesis, no corresponding indicator for maternal morbidity existed.

2.4.2 Inadequate indicators for deaths after 42 days

There is an indicator gap for fatal outcomes beyond 42 days postpartum when cause of death information is lacking. Pregnancy-related mortality captures deaths within 42 days postpartum where cause of death information is absent: *"the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death"* (2). For deaths occurring beyond 42 days, where cause of death information is available, late maternal deaths are defined as "*the death of a woman from direct or indirect obstetric causes, more than 42 days but less than one year after termination of pregnancy"* (2). However, no corresponding definition exists for what could be termed 'late pregnancy-related deaths', occurring beyond 42 days, irrespective of cause.

In contexts where cause of death information is incomplete (see section 2.5 below), these deaths bypass maternal health surveillance efforts: they are excluded from reported statistics of pregnancy-related mortality and late maternal deaths. This definitional omission may be because, in principle, the underlying cause of death should be recorded along with the timing of death (pregnancy checkbox from 43 days to one year postpartum) on the death certificate in Civil Registration and Vital Statistics (CRVS) systems (77). However, depending on the data source, there may be instances where information on the timing of death is available, but the cause of death is not. A definition compliant with ICD-11 of 'late pregnancy-related death' is needed to produce comparable statistics on the magnitude of mortality beyond 42 days.

2.4.3 Maternal morbidity

As maternal mortality falls and more countries progress through the obstetric transition, measuring maternal morbidity becomes essential to monitor the quality of maternal health care (7,78). However, the frequently cited statistic that maternal morbidity affects 20-30 women for every maternal death

is "*not based on standard, well-documented, and transparent methodologies*" (7) (p.1). Appropriate outcome indicators for measuring maternal morbidity are critical to establishing its reduction as a key global target.

Severe maternal morbidity

Since the 1990s, following the conceptualisation of MNM, attempts have been made to develop criteria to distinguish between severe and less severe maternal complications. Examples of standardised criteria to identify MNM include those developed by Stone et al. in 1991 (73), followed by Mantel et al. in 1998 (79), and Waterstone et al. in 2001 (80). The WHO's 2009 criteria for identifying potentially life-threatening conditions (PLTC) and MNM further advanced the international standardisation of criteria for measuring severe maternal morbidity (1). The WHO MNM criteria comprise 25 clinical, laboratory, and management-based indicators of organ dysfunction (1). This includes failure or dysfunction of any vital organ system (circulatory, respiratory, cardiac, renal, hepatic, central nervous, metabolic, and haematological) (1). However, the difficulty applying these criteria in many low-resource contexts has been widely documented (81–88). In health systems lacking laboratory or management capacity, the WHO criteria may miss true near miss cases (low sensitivity) and underestimate the prevalence of near miss morbidity. As a consequence, several modifications to the WHO criteria have been proposed to reflect these health system constraints, including the Global Network criteria (89), Haydom criteria (82), and Tura criteria for sub-Saharan Africa (84).

Very few high income countries use the standard WHO maternal near miss criteria (90,91), with modifications including the ACOG criteria (92), Canadian criteria (93), France's Epidemiology of Severe Maternal Morbidity (EPIMOMS) criteria (94), the United Kingdom's English Maternal Morbidity Outcome Indicator (EMMOI) (95), the Australian Maternal Morbidity Outcome Indicator (AMMOI), Ireland's National Perinatal Epidemiology Centre (NPEC) Severe Maternal Morbidity criteria (96), and the Netherlands' criteria (97). Identification of MNM and/or severe maternal morbidity ranges from 26 criteria in the UK, including 17 diagnoses and 9 management procedures,

to only 5 criteria in the Netherlands (90). The WHO criteria are not integrated with ICD morbidity codes used in many high-income countries' Health Management Information Systems (HMIS), which may contribute to low compliance (91).

Therefore, despite substantial progress in the identification of MNM, this lack of compliance with the WHO standard criteria in both high- and low-resource settings means data are often not comparable across populations (22,91). This may have contributed to the omission of MNM in the SDGs and EPMM targets.

Non-life-threatening maternal morbidity

A wide variety of definitions and measurement approaches for non-life-threatening maternal morbidity (98–100) have resulted in a lack of consensus about its prevalence (78,101). Progress in standardisation was made during the five-year WHO MMWG project, through which a matrix of 121 criteria for the identification of non-life-threatening maternal morbidity was developed (7). The matrix incorporates three dimensions: morbidity categories with associated ICD-10 codes, self-reported functioning and disability, and an evaluation of physical and mental health history (7). Overall, the matrix includes 58 symptoms, 29 signs, 44 investigations, and 35 management strategies (7). This led to the development of measurement tools designed to be applied in primary health care (PHC) settings, in antenatal care and postnatal care; women's poor recall of complications and low specificity of self-reports (102–104) means these tools were purposely not designed for use by lay fieldworkers doing retrospective interviews in the community (7). However, despite these efforts to develop a comprehensive list of maternal morbidity conditions and pilot in three countries (78), the tool has not yet been widely used (105), in part because of its length (106), and requires further validation in other settings. A systematic review of systematic reviews found that there was no systematic review available for 71% of the conditions listed in the matrix (71).

2.5 Poor data sources

The third aspect of the maternal health measurement trap is the inadequacy of data sources to measure maternal outcomes beyond 42 days and maternal morbidity at the population-level. This contributes to a lack of accurate, reliable information on these outcomes and reinforces their relative neglect from the international maternal health agenda. National-level data sources to measure mortality beyond 42 days postpartum are inadequate in many LMICs, meaning we are reliant on subnational surveillance data and verbal autopsy data to understand deaths in the extended postpartum. Morbidity data are predominantly facility-based, with few population-level data sources.

2.5.1 Inadequate national-level data sources to measure mortality beyond 42 days postpartum in LMICs

Maternal mortality data sources are affected by two types of reporting errors, which may occur simultaneously (77):

(i) Incompleteness: the extent to which deaths are recorded in the data collection system.

(ii) Misclassification: whether the cause of death is classified as maternal or non-maternal. This is expressed as sensitivity (true maternal death) and specificity (true non-maternal death). Accurate classification depends on both pregnancy status reporting and coding of cause compliant with ICD.

These reporting errors affect all types of data sources and maternal death reporting regardless of timing. They may, however, present even greater challenges for measuring deaths occurring beyond 42 days postpartum, as discussed below.

Challenges for the measurement of deaths beyond 42 days using Civil Registration and Vital Statistics (CRVS) data

CRVS systems are the preferred source of data for producing comparable, nationally representative maternal mortality statistics because they generate data continuously for the entire country (77,107).

These systems should include the date of death and its registration, the cause of death, timing of death in relation to pregnancy, and type of certification (77).

In LMICs, deficiencies in countries' CRVS systems pose significant challenges for the monitoring of late maternal deaths and their causes. Many countries still do not have complete CRVS systems (77,108–111). This is despite increased international momentum and notable progress since the 2007 Lancet series 'Who counts?' drew attention to the 'scandal of invisibility' of the births, deaths, and causes of death that go unregistered and uncounted (109,110,112–115). In 2021, nearly 40% of deaths were never registered globally, and death registration was as low as 10% in Africa (116). Certification of the cause of death was available for only 8% of registered deaths in low-income countries in 2021 (116). For maternal mortality, this means maternal death statistics are often most incomplete in the countries with the highest burden of these deaths (107). Completeness may be further compromised for deaths occurring beyond 42 days because late maternal deaths are more likely to occur outside of facilities and are less likely to be observed (77). Many CRVS systems are passive as they rely on family members to report the death (115). Where they do exist, active notification procedures through community key informants, village authorities, etc., may be slow and incomplete (77).

Deaths may be misclassified within the CRVS if the person reporting the death is unaware of the deceased's pregnancy status and this is incorrectly recorded on the death certificate. The inclusion of a pregnancy checkbox on the 2016 WHO International Medical Certificate of Cause of Death is intended to help improve the recording of pregnancy status. However, for deaths beyond 42 days postpartum, pregnancy status misreporting may be more likely than for deaths occurring during pregnancy or within 42 days (2,107). Second, maternal deaths should be coded according to ICD-Maternal Mortality (ICD-MM) principles (77). Indirect causes of maternal death, which are more likely for deaths occurring beyond 42 days (117), are subject to more coding errors than other causes because deaths require two codes: one to denote the maternal cause (O code in ICD-10 or JB code in ICD-11), and the infectious or NCD cause (77). Without the maternal code, these deaths are not

identifiable as late maternal in the CRVS system. Ad hoc coding that is non-compliant with the principles of ICD-MM is a particular concern in sub-Saharan Africa, where coding of the cause of death frequently falls short of international standards (110,111).

Finally, although the WHO recommends that countries' CRVS systems collect data and report on late maternal deaths, many do not (4,77). For the MMEIG's 2020 maternal mortality estimates, only 54% of the 120 countries that reported CRVS data to the WHO Mortality Database recorded deaths occurring beyond 42 days postpartum (4). Countries not reporting this data to WHO most likely do not collect it in the first place.

Alternative national-level data sources rarely monitor deaths beyond 42 days in LMICs

Other national data sources in LMICs rarely monitor deaths beyond 42 days, including Confidential Enquires into Maternal Death (CEMD); Maternal and Perinatal Death Surveillance and Response (MPDSR); censuses; and survey data, such as Reproductive Age Mortality Surveys (RAMOS) and population-based household surveys (e.g., Demographic and Health Surveys, (DHS)). As a result, we are predominantly reliant on subnational data to measure the burden and cause distribution of deaths in the extended postpartum in many low-resource contexts.

Even in countries with well-functioning, complete CRVS systems, special investigations such as CEMD can be used to investigate misclassification and identify the true burden of (late) maternal mortality (77). Within CEMD, maternal deaths are notified by the health workers involved in the deceased's care. Anonymised medical records and death certificates are reviewed by a specialist team, away from the hospital. CEMD also gathers information on the timing of death (antepartum, intrapartum, postpartum, extended postpartum) that informs policy but is rarely available within the CRVS. These features make CEMD a valuable source of data for late maternal mortality (e.g., the UK CEMD (118)). However, few countries in sub-Saharan Africa have conducted national confidential enquiries, except South Africa (facility-based only) (119,120), Malawi (facility-based only) (121), Kenya (deaths extracted from DHIS2) (122), and Namibia (123); a subnational CEMD

was conducted in Nigeria (Ondo state only) (124). Although possible in principle, none of these CEMDs included deaths occurring beyond 42 days.

By contrast, many countries in Africa now have MPSDR systems (125). These are facility-based audits conducted with multidisciplinary panels of providers involved in the woman's care, typically notified from the individual facility to the district-level administration (125). While MPDSR should not be limited to obstetric wards, review is seldom conducted for deaths occurring beyond 42 days postpartum, unlike CEMD in high-income countries (107). The linkages required to identify these deaths in facility records (i.e., to trace an earlier obstetric admission or birth record for a death occurring on a non-obstetric ward beyond 42 days) may not be present in high-burden countries that conduct MPDSR. Therefore, although theoretically possible, the current implementation of MPDSR does not readily facilitate the investigation of late maternal deaths.

Finally, nationally representative data on maternal mortality may also come from censuses, specialist Reproductive Age Mortality Surveys (RAMOS) (for example, conducted in Malawi (126) and Zimbabwe (127)), and population-based household surveys (e.g., DHS). However, although feasible, none of these routinely collect data on deaths occurring beyond 42 days postpartum (5). For the DHS, the sisterhood method estimates mortality only up to 2 months postpartum for pregnancy-related deaths and 42 days to approximate maternal deaths (not consistent with WHO/ICD definitions because violence and accidents are excluded, but incidental causes are not) (5).

2.5.2 Reliance on subnational data to measure deaths beyond 42 days postpartum

Challenges with national-level data sources in LMICs mean subnational data are often the only available sources to measure deaths beyond 42 days postpartum. Health and Demographic Surveillance Systems (HDSS) are geographically defined, subnational surveillance areas, designed to provide detailed, prospective longitudinal data on the health status of a given population (128,129).

Originating in the 1940s, HDSS have a long history of facilitating the evaluation of health interventions in sub-Saharan Africa and South Asia (130). At regular intervals – usually between two and four times per year – the population in the surveillance area is interviewed about all births, deaths, and migrations that have occurred in the household since the preceding round (128). Verbal autopsy interviews are conducted to ascertain the cause of death (see section 2.5.3 below). Populations of HDSS in Africa vary in size, ranging from 38,000 in Bandiagara (Mali) to 266,000 in Navrongo (Ghana) (131). Particularly in contexts where most deaths do not occur in a facility and where death registration and certification are poor, HDSS are a critical source of population-level, longitudinal data on mortality in the community (128,132).

The International Network for the Demographic Evaluation of Populations and their Health (INDEPTH) is an affiliated group of HDSS sites across Africa and South Asia. Founded in 1998, INDEPTH aimed to increase collaboration between sites. By 2018, it included 49 HDSS sites from 19 countries, covering a total population of over three million individuals (131). INDEPTH sought to strengthen the capacity of member sites to measure priority outcomes, including maternal mortality (131). It provides consolidated data files that include surveillance data from all member sites to aid usage. Similarly, the Network for Analysing Longitudinal Population Based HIV/AIDS Data on Africa (ALPHA) was founded in 2005 to foster research collaboration on HIV epidemiology in sub-Saharan Africa (133). It comprises 10 HDSS sites in Kenya, Uganda, Tanzania, Malawi, Zimbabwe, and South Africa and is administered by LSHTM (134).

However, although HDSS are a critical source of population-based data on deaths in the (extended) postpartum period, they are not designed to be nationally representative of the countries in which they are located (129,132). Findings from an HDSS site represent only a geographically defined area and may not correspond to national estimates (129,132). Without additional triangulation of HDSS data with additional data sources, such as ad hoc specialist surveys or facility data, it is challenging to derive national-level conclusions on the burden and risk factors for late pregnancy-related deaths from HDSS data alone.

2.5.3 Reliance on verbal autopsy data to estimate causes of death beyond 42 days postpartum

Where most deaths occur outside of health facilities and where medical certification of the cause of death is not available, verbal autopsy (VA) is a vital, though imperfect, source of cause of death information and a pragmatic approach to determine cause-specific mortality levels (115,135). This method involves a trained enumerator interviewing a close relative or caregiver who was present prior to the deceased's death to gather information about their signs and symptoms before the death. Verbal autopsy engages the communities most affected by a lack of cause of death information (135).

In 2007, the WHO published the first international verbal autopsy standards to ascertain causes of death, including an instrument for adult deaths aged 15 years and above (136,137). This standardisation aimed to address the proliferation of locally developed instruments in use (136). In 2012, the WHO introduced a new tool to enhance compliance of VA cause of death categories with the ICD standards to improve data comparability (135,136). The most recent WHO tool, released in 2022, is compliant with ICD-11 (136,138).

The use of verbal autopsy is mainly confined to cause of death attribution within HDSS sites (135). Since 2016, the WHO has led efforts to integrate verbal autopsy within CRVS and sample registration systems (115,135–137,139). This integration serves as an interim health systems strengthening strategy to provide cause of death data until medical certification becomes more widely available (115,135,136,139,140). CRVS verbal autopsy integration is at various stages of pilot or demonstration in Nepal, Morocco, Senegal, Ghana, Tanzania, Kenya, and Zambia (139). Currently these data are not nationally representative.

Methods to process verbal autopsy data to assign the cause of death

Responses to verbal autopsy questionnaires can be processed to assign the most likely underlying cause of death either using expert physician review (physician coded VA – PCVA), or automated algorithms (computer coded verbal autopsy – CCVA). Algorithms assign the cause of death based on signs and symptoms reported in a series of closed questions, considering each sign or symptom individually rather than in combination. By contrast, physicians can evaluate the significance of multiple co-occurring symptoms and use the narrative report which details the sequence of events leading to death. Research is ongoing into using machine learning and natural language processing models to analyse VA narratives at scale (141,142). However, the negative impact of open narratives on respondent distress means their inclusion must be carefully justified (143).

Variability in physician training and potential biases in the interpretation of VA data can make PCVA results less reproducible (136,140). Additionally, shortages of physicians and the associated costs often render PCVA infeasible or unaffordable (144). This also raises ethical questions about the allocation of physician time between the interpretation of VA data and patient care. Automated models not only free up physician time, but also provide a more cost-effective and consistent method for assigning causes of death (136,140). Efficiency, cost-effectiveness, and consistency mean CCVA is crucial for addressing uncertified deaths at scale, especially through the integration of VA with CRVS systems (140).

Multiple algorithms have been developed to process verbal autopsy data and assign causes of death, including: SmartVA/Tariff (145), InSilicoVA (146), and InterVA (147). A specific model designed to classify pregnancy-related deaths, InterVA-M (100), was later integrated with the full InterVA model, with the latest version being InterVA5 (136,140). All three algorithms utilise a set of symptom-cause information (SCI). For SmartVA/Tariff, the SCI is derived from a reference mortality dataset that contains VA data and causes of death assigned by facility-based medical certification (136). However, because SmartVA relied on a different questionnaire until 2016 that was not widely used in ALPHA network sites (136), I did not use this algorithm in Paper 2.

For both InterVA and InSilicoVA, the SCI are conditional probabilities for the presence of each sign or symptom associated with a given cause of death. This is known as the probability base ('probbase'), which is based on epidemiological evidence and expert physician opinion. InterVA assigns letter grades to the likelihood of observing each sign or symptom for a particular cause, translating these rankings into numeric probabilities (e.g., A+ = almost always = 0.8, A = common = 0.5) (146). InSilicoVA estimates numeric probabilities within a Bayesian hierarchical model (146,148). Additional differences include: InterVA5 utilises only symptoms present for an individual; it assigns a cause based solely on positive signs or symptoms, disregarding those which are negative, and it does not account for missing symptoms (136,146,148). By contrast, InSilicoVA considers both negative signs or symptoms (e.g., a negative HIV test), and missing symptoms (146,148). Consequently, InSilicoVA can provide a measure of uncertainty for cause-specific mortality fractions, which InterVA cannot (146,148). For both algorithms, underlying causes of death are aggregated to calculate cause-specific mortality fractions.

In addition to questions about the signs and symptoms of the deceased prior to death, since 2012, the WHO VA instrument has included questions regarding the social and health system circumstances surrounding the death. These are known as the Circumstances of Mortality Categories (COMCATs) and are processed using InterVA5 (140,149,150). The aim is to understand the health system failures and social factors contributing to deaths, thereby informing decision-making (135,149,150). These questions address aspects such as travel to a health facility, issues during admission, difficulties accessing medications or diagnostic tests, use of traditional medicine, mobile phone use, and out-of-pocket healthcare costs. They correspond to seven circumstantial categories: traditions, emergencies, recognition, resources, health systems and inevitability (i.e., death occurred in circumstances that could not reasonably have been averted, such as terminal illness) (149).

Misclassification of cause of maternal death in VA data

There is limited information on the accuracy of VA data for deaths occurring from days 43 to one year postpartum. However, for maternal deaths within 42 days, the ability of VAs to accurately identify specific causes of maternal death has been studied (100,151–155), and more recently, questioned (156). For all pregnancy-related deaths, the accuracy of VA is constrained by the informant's knowledge of the deceased's pregnancy status, their symptoms preceding death, and the skill of the interviewer (156). Second, compared to the gold standard of medical certification by a specially trained physician, both PCVA and CCVA have inherent biases and may misclassify the true underlying cause of death (126). Concordance between the two methods may be low for maternal causes: for instance, InterVA5 might more frequently assign obstetric haemorrhage and less often assign non-obstetric causes compared to physician coding (157). Additionally, when the burden of communicable diseases is high, misclassification is more likely to occur, especially for HIV and TB (100,158). Finally, without triangulation with other data sources or medical records, VA data alone cannot be used to differentiate which indirect causes of pregnancy-related death are true indirect maternal deaths and which are coincidental to the pregnancy. For example, a death from HIV within 42 days postpartum could be either a true HIV-related indirect maternal death or an incidental death (59,158,159). This issue also applies to 'late pregnancy-related deaths' occurring beyond 42 days postpartum.

2.5.4 Lack of population-level data on maternal morbidity

A key challenge in measuring non-fatal maternal outcomes is the lack of population-level data on maternal morbidity. Although increasing institutional deliveries have mitigated this issue to some extent (16,160–162), it remains a significant problem in many low-resource settings. In sub-Saharan Africa, institutional delivery rates remain especially low, and only 23% of births were in facilities in Chad in 2015 (160). In such contexts, the selectivity of facility attendance affects the representativeness of maternal morbidity data obtained from registers or medical records (16,34). This can result in either underestimation if women avoid seeking care for certain conditions, or overestimation if those with severe morbidity are more likely to seek facility care (71). With approximately one-third of all maternal morbidity prevalence estimates based solely on facility-level

data, the true population-level prevalence of many maternal morbidities remains unclear (71). Defining the denominator for data deriving from facilities and/or using HMIS data presents further challenges (71,163).

Although a valuable source of population-level data on mortality, HDSS data are less useful source of data on maternal morbidity, except for some data on HIV diagnosis and treatment and NCD history in the Alpha HDSS sites (164).

2.6 Limited measurement techniques

The final component of the maternal health measurement trap are the limited measurement techniques available. This is a product of narrow conceptualisation and the availability of appropriate data sources.

2.6.1 Longitudinal data to adopt a life cycle approach

Recent reconceptualisations of maternal health have emphasised the need to take a life cycle approach: to embed recurrent reproductive episodes of women's lives within their life course (19,20). This approach recognises that women's health during pregnancy and the postpartum period are influenced by their health during pre-pregnancy phases earlier in life and that pregnancy and postpartum influence their later life health during post-reproductive phases (19,20).

However, adopting a life cycle approach has stringent data requirements. Longitudinal data are more appropriate to identify recurrence of maternal morbidity in subsequent pregnancies. This may necessitate record linkage or expensive, specially designed cohort studies across multiple levels of the health system (34). The PRECISE (PREgnancy Care Integrating Translational Science Everywhere) prospective, facility-based cohort is an example of a study that provides detailed information on the trajectories of women's health from pregnancy to the extended postpartum in The Gambia, Kenya, and Mozambique (165,166). This cohort is designed to phenotype placental

disorders in sub-Saharan Africa and follows all women until six weeks postpartum, with a subset followed until three years postpartum in the PRECISE-DYAD sub-study (167). For pregnant women recruited into the cohort, clinical data and biological samples were collected at multiple intervals throughout pregnancy, intrapartum, and the postpartum period (65). The total sample of the PRECISE cohort was approximately 9,000 women across the three countries, recruited from rural primary health centres, district hospitals, subcounty hospitals, and a tertiary referral centre (65,66).

The logistical and financial costs associated with this type of approach mean that we are often reliant on cross-sectional data to approximate risks across the reproductive life course in LMICs. For example, full birth and full pregnancy histories in cross-sectional household surveys such as the DHS go some way towards providing retrospective data on recurrence of adverse pregnancy outcomes such as stillbirth (168). Yet, the DHS collects very little data on maternal complications or episodes of maternal morbidity (168). In the study of maternal mortality, the lifetime risk of maternal death is a synthetic cohort measure that accounts for women's repeated exposure to pregnancy and the cumulative risk this entails (169). This period measure utilises cross-sectional data that are much more frequently available than longitudinal data. Synthetic cohort measures are limited, however, in that they cannot help us understand trajectories across the reproductive life course at the individual level, such as the risk of maternal near miss or death after a prior episode of morbidity (170–172).

2.6.2 Woman-centred approach to the lived experience of morbidity

In 2003, the WHO's Beyond the Numbers argued that the preoccupation of the maternal health community with the numbers of maternal deaths contributed to a lack of understanding of the underlying factors that led to the deaths (173). There is much to learn from each death to provide practical recommendations to improve the quality of care and improve programmes. Although critically important, the narrowness of methodological focus on estimating trends reinforces the measurement trap by obscuring the reasons why women die (173).

The same argument applies in the case of maternal outcomes beyond 42 days, as well as women's lived experience of maternal morbidity throughout their reproductive lives. Monitoring the numbers of deaths beyond 42 days is an essential, and so far overlooked task, as is estimating the prevalence of maternal morbidity throughout pregnancy and the extended postpartum. But these numbers can only provide part of the information needed to truly understand the conditions that cause these outcomes and prevent them from occurring (173).

Woman-centred, in-depth qualitative research is an essential methodology to better understand the lived experience of adverse maternal outcomes beyond 42 days and the many ways in which maternal morbidity affects all areas of women's lives. Grounded Theory is increasingly being used in cross-disciplinary women's health research to foreground testimonies of women's lived experiences, beyond a narrow clinical conceptualisation of morbidity (174,175). Due to the small samples typically required, following participants longitudinally to understand women's recovery trajectories can also be more feasible in qualitative studies (30,176,177).

2.7 Implications of the measurement trap for this thesis

All four components of the measurement trap I have described contribute to a lack of information and the relative neglect of (1) maternal outcomes beyond 42 days postpartum and (2) the burden of maternal morbidity across women's lives, from the international maternal health agenda. The challenges around conceptualisation, indicators, data sources, and measurement techniques are complex, multifaceted, and often mutually reinforcing.

Through the specific objectives outlined in Chapter 1, the five studies presented in this thesis target each component of the maternal health measurement trap:

1. **Narrow conceptualisation**: Contribute to reconceptualising the postpartum period as extending far beyond 42 days postpartum; enhance understanding of the burden of maternal morbidity across women's life course through new metrics of cumulative risk.

2. **Inadequate indicators:** Develop new indicators of adverse outcomes beyond 42 days ('late pregnancy related mortality') and new metrics for the cumulative burden of maternal morbidity across the reproductive lifespan (LTR-MNM and LTR-SMO).
3. **Poor data sources:** Demonstrate the utility of existing data sources (HDSS and verbal autopsy) in addressing the evidence gap on risk and causes of death beyond 42 days postpartum; demonstrate the adjustment of facility-based maternal morbidity data to provide population-level estimates of lifetime risk.
4. **Limited measurement techniques:** Adopt a woman-centred, Grounded Theory methodology to understand women's experiences of recovery following severe maternal morbidity; utilise cross-sectional data to estimate the cumulative risk of maternal morbidity in the absence of longitudinal data.

Chapter 3 Research paper 1

Women's risk of death beyond 42 days postpartum: a pooled analysis of Health and Demographic Surveillance System data in sub-Saharan Africa

Summary of chapter

In Chapter 3 I present the first paper of this thesis, as published in The Lancet Global Health. This includes the rationale for the study, the study setting, methods, results and discussion.

Supplementary material for this paper is available in Appendix B. Please note, in the following typeset text, page references for supplementary tables and figures refer to the online appendices for The Lancet Global Health, rather than this thesis.

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Student ID Number	2005281	**Title**	Ms
First Name(s)	Ursula		
Surname/Family Name	Gazeley		
Thesis Title	Advances in the conceptualisation and measurement of maternal morbidity and mortality		
Primary Supervisor	Professor Veronique Filippi		

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?	The Lancet Global Health This work was published open access under a Creative Commons Attribution License (CC BY).		
When was the work published?	November 2022		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	NA		
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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	In consultation with my supervisors, I proposed the idea for this study during my year of demographic training at the European Doctoral School of Demography. I analysed the data, prepared the visualisations, and wrote a complete first draft of the paper for co-authors to review. I led the submission process and responses to reviewers.

SECTION E

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Date	20th March 2024

Supervisor Signature	Veronique Filippi
Date	20th March 2024

Women's risk of death beyond 42 days post partum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa

Ursula Gazeley, Georges Reniers, Hallie Eilerts-Spinelli, Julio Romero Prieto, Momodou Jasseh, Sammy Khagayi, Veronique Filippi

Summary

Background WHO's standard definitions of pregnancy-related and maternal deaths only include deaths that occur within 42 days of delivery, termination, or abortion, with major implications for post-partum care and maternal mortality surveillance. We therefore estimated post-partum survival from childbirth up to 1 year post partum to evaluate the empirical justification for the 42-day post-partum threshold.

Methods We used prospective, longitudinal Health and Demographic Surveillance System (HDSS) data from 30 sites across 12 sub-Saharan African countries to estimate women's risk of death from childbirth until 1 year post partum from all causes. Observations were included if the childbirth occurred from 1991 onwards in the HDSS site and maternal age was 10–54 years. We calculated person-years as the time between childbirth and next birth, outmigration, death, or the end of the first year post partum, whichever occurred first. For six post-partum risk intervals (0–1 days, 2–6 days, 7–13 days, 14–41 days, 42–122 days, and 4–11 months), we calculated the adjusted rate ratios of death relative to a baseline risk of 12–17 months post partum.

Findings Between Jan 1, 1991, and Feb 24, 2020, 647 104 births occurred in the HDSS sites, contributing to 602 170 person-years of exposure time and 1967 deaths within 1 year of delivery. After adjustment for confounding, mortality was 38·82 (95% CI 33·21–45·29) times higher than baseline on days 0–1 after childbirth, 4·97 (3·94–6·21) times higher for days 2–6, 3·35 (2·64–4·20) times higher for days 7–13, and 2·06 (1·74–2·44) times higher for days 14–41. From 42 days to 4 months post partum, mortality was still 1·20 (1·03–1·39) times higher (ie, a 20% higher risk), but deaths in this interval would be excluded from measurement of pregnancy-related mortality. Extending the WHO 42-day post-partum threshold up to 4 months would increase the post-partum pregnancy-related mortality ratio by 40%.

Interpretation This multicountry study has implications for measurement and clinical practice. It makes the case for WHO to extend the 42-day post-partum threshold to capture the full duration of risk of pregnancy-related deaths. There is a need for a new indicator to track late pregnancy-related deaths that occur beyond 42 days, which are otherwise excluded from global maternal health surveillance efforts. Our results also emphasise the need for international agencies to disaggregate estimates by antepartum, intrapartum, postpartum, and extended post-partum periods. Additionally, the schedule and content of postnatal care packages should reflect the extended duration of post-partum risk.

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Introduction

Improving survival in the post-partum period—defined as the first 42 days following birth, termination of pregnancy, or miscarriage—as well as in the extended post-partum period up to 1 year is crucial. Data from high-income countries, where maternal mortality is low, indicate that the majority of maternal deaths occur post partum.[1] In sub-Saharan Africa, which accounts for two-thirds of maternal deaths wordwide,[2] 2013 data indicate that 48% of maternal deaths occurred between 24 h and 42 days post partum, and a further 13% occurred between 43 days and 1 year (authors' own calculation).[3] More evidence is needed, although there are indications that improvements in post-partum survival have not kept pace with the rapid decline in antepartum and intrapartum mortality in recent decades.[3,4] Consistent with the epidemiological transition, deaths in the extended post-partum period will continue to increase in relative importance in sub-Saharan Africa.[3]

The primary indicator used to monitor maternal survival up to 42 days post partum is the maternal mortality ratio (MMR)—the number of maternal deaths per 100 000 live-births. The MMR is the key indicator reported by international agencies and is used to track progress towards Sustainable Development Goal 3.1.1. Identifying maternal deaths, however, requires information on both the cause and time of death. A maternal death must occur within 42 days of the end of pregnancy, from any direct

Research in context

Evidence before this study

We searched MEDLINE and Embase for studies that analysed the risk of death (maternal or pregnancy-related) in the extended post-partum period. We used the following search terms: ("pregnancy-related" or "maternal" or "postpartum" or "postnatal" or "late maternal") and ("mortality" or "death" or "risk") and ("over time" or "time since delivery" or "time since birth" or "six weeks" or "42 days") and (MEDLINE expert search for all low-income and middle-income countries) for articles published from inception up to May 26, 2022, without language or date restrictions. We noted 141 publications, only four of which were relevant upon screening of title and abstract. These four studies showed that women's risk of death could remain elevated until 3–6 months post partum, casting doubt on the empirical basis for the 42-day post-partum threshold.

Added value of this study

This existing research is now outdated, mostly from observation periods before the millennium. Most studies were also based on relatively small cohorts, and only one article was based on a population in sub-Saharan Africa. In our study, we provide a long-overdue update on the evidence of women's risk of death following delivery, on the basis of an unparalleled sample size, from multiple countries in sub-Saharan Africa where the burden of maternal mortality remains the highest.

Implications of all the available evidence

Our finding that women's risk of death remains 20% elevated until 4 months post partum questions the empirical justification of the 42-day postpartum threshold, integral to WHO's standard definitions of maternal, late maternal, and pregnancy-related death. Based on post-partum pregnancy-related mortality, this study reaffirms calls for the 42-day post-partum threshold to be revised to better capture the full duration of elevated mortality risk. It also implies that the schedule and content of postnatal care visits should be reconsidered. Finally, in contexts where the availability of cause-of-death data are poor, the definition and measurement of late pregnancy-related mortality beyond 42 days postpartum is crucial.

(obstetric) or indirect (non-obstetric) cause related to or aggravated by the pregnancy.[5] Deaths that occur from direct or indirect causes beyond 42 days but within 1 year are classified as late maternal deaths. Maternal and late maternal deaths are jointly termed "comprehensive maternal deaths" in the International Classification of Diseases 11th revision (ICD-11).

In the absence of cause of death (COD) information, however, the number of pregnancy-related deaths and estimates of the pregnancy-related mortality ratio (PRMR) are used. Pregnancy-related deaths occur within 42 days of pregnancy, irrespective of the cause, and include causes incidental to the pregnancy.[5] Surveillance of pregnancy-related mortality is particularly crucial in sub-Saharan Africa, where medical certification of the cause of death (COD) is rare[6] and measurement of maternal mortality is often not possible.[7] Without COD information, the Demographic and Health Surveys,[5] Multiple Indicator Cluster Surveys,[5] and population censuses[8] estimate pregnancy-related mortality, and are key inputs into WHO global maternal mortality modelling.

Whichever definition is applicable, depending on the presence or absence of COD information, the definitions of maternal, late maternal, and pregnancy-related deaths are all contingent on the 42-day post-partum threshold. Explanations for this cut-off often invoke the timing of physiological changes that occur post partum, such as the return of the uterus to its new post-pregnancy size and the resumption of menstruation for non-lactating women.[9] However, for women who are partially or exclusively breastfeeding, lactational amenorrhoea can last much longer.[10] The ability of the body to recuperate from the trauma of pregnancy and childbirth by 42 days might also be hindered by direct obstetric complications, and infectious or non-communicable comorbidities.[3,11]

In an era where indicators govern global health priorities, the 42-day post-partum threshold has implications for mortality surveillance, maternal health interventions, and post-partum care policy and practice.

Surveillance of maternal survival beyond the 42-day post-partum threshold is often poor when COD information is available,[4] and virtually non-existent when it is not. WHO recommends countries monitor late maternal mortality, but deaths are not coded uniformly according to ICD (code JB61 in ICD-11, previously O96 in ICD-10[12]), resulting in measures that are often not comparable between countries.[4] There exists no official definition of what could be called late pregnancy-related deaths—ie, those that occur beyond 42 days but within 1 year post partum. Where COD is not available, these deaths will not be counted. A reliance on the MMR and PRMR to track progress might therefore lead to an overestimation of improvement in maternal survival if mortality reduction is more rapid for antepartum, intrapartum, and early post-partum periods than beyond 42 days.[3,13]

The 42-day post-partum threshold might itself also directly affect estimates of the distribution of direct, indirect, or incidental causes of death within 1 year post partum. Whether a woman's death occurred within 42 days of delivery, termination, or miscarriage is a question in the WHO 2022 verbal autopsy instrument.[14] This timing field is used as an input for both physician coding and automated coding of verbal autopsy data to assign the likely COD where medical certification of COD is lacking. Accurate estimates of the disease burden

are a vital component of public health policy and programme prioritisation.[15]

Finally, the 42-day post-partum threshold is also integral to post-partum care policy and practice, an often-neglected aspect of quality maternal care.[16] Current WHO guidelines recommend postnatal contacts within the first 24 h, and follow-up contacts on day 3, between 7 days and 14 days, and 6 weeks after birth.[17] There are no guidelines for visits scheduled beyond the 6-weeks' post-partum period, despite WHO's acknowledgement that some physiological or psychological changes could take longer than 6 weeks to manifest.[16] Accurate estimates of the duration of the elevated risk following pregnancy and delivery are necessary to inform post-partum care practices and ensure the effective transfer between maternity services and primary or secondary health care for women who need longer term management.[18,19]

Research that analyses the risk of death over an extended post-partum period in low-income and middle-income countries (LMICs) is scarce. The few studies that do exist suggest that mortality risk might remain elevated far beyond 42 days.[11,20–22] All but one of these studies are based on cohorts with small sample sizes,[11,20] and one study is a case review with no exposure sample.[21] Only one study is based on a population in sub-Saharan Africa.[11] The three cohort studies are also extremely outdated,[11,20,21] with the last observation period ending in 2001.[21] Given maternal survival has improved substantially since then,[5] the duration of post-partum risk must be revisited.

We aimed to estimate the duration of post-partum risk after the end of pregnancy. Based on an analysis of the risk of post-partum (late) pregnancy-related mortality up to 1 year, we assess the validity of the WHO's 42-day post-partum threshold.

Methods

Data and sample

We used prospective, longitudinal data from 30 Health and Demographic Surveillance System (HDSS) sites, across 12 sub-Saharan African countries (Tanzania, Ethiopia, Kenya, Malawi, Mozambique, South Africa, Nigeria, The Gambia, Burkina Faso, Cote d'Ivoire, Senegal, and Ghana). Data from 28 of these sites are open access from the INDEPTH Network's iShare database,[23] whereas access to the data from two additional sites (Basse in The Gambia and Siaya in Kenya) was arranged through data-sharing agreements with the principal investigators of these sites. HDSSs collect data on births, deaths, and migrations that occur within a small geographical area. Households and individuals residing within the radius of the site are visited between quarterly and annually, depending on the site, and all vital events that occurred since the last visit are recorded.[23] Further detail about HDSS data is documented elsewhere.[24,25]

All individuals in the HDSS sites are assigned a unique identification code, which facilitates data linkage across HDSS datasets to estimate post-partum survival. Childbirths were identified using the HDSS delivery file (at the level of the female, the event of a pregnancy ending after 28 weeks' gestation, including livebirths and stillbirths, although stillbirths are likely to be under-reported).[26] The birth outcome (livebirth or stillbirth), records of pregnancies ending before 28 weeks' gestation (miscarriage or abortion), and obstetric history before residency in the site, are not recorded universally across sites and therefore not included in the consolidated HDSS data.

Childbirths before 1991, before most sites were fully operational, were excluded (n=13 274). Return migrants or new in-migrants were included in the sample if site entry preceded the end of pregnancy. Observations were included as long as the woman gave birth in the site and their age at childbirth was between 10 and 54 years, inclusive. Based on the calendar year the childbirth occurred, observations were grouped into 5-year child-birth cohorts. The London School of Hygiene and Tropical Medicine ethics committee approved the study. Each HDSS site had their own consent procedure (either written or verbal), but in most sites informed consent was at the household level.[24]

Statistical analysis

For each childbirth, exposure time (person-years) was calculated as the time between a delivery (n) and start date of the next pregnancy (n+1 delivery date minus 281 days), outmigration from the HDSS, death, or the end of the first year post partum, whichever occurred first. In the case of multiple births (eg, twins), exposure was counted only once. The distribution of deaths by days since childbirth was adjusted to correct for the overestimation of days until death when calculated using calendar days (eg, a woman who survived less than 24 h but who died on the next calendar day would be misattributed to day 1), splitting deaths between the calendar day of occurrence and the day before.

To estimate the risk of death, we moved from individual-level data to an aggregate model of maternal survival, approximated using a Piecewise Constant Hazard Model (PCHM). The standard 42-day post-partum period was split into risk intervals (0–1 day, 2–6 days, 7–13 days, and 14–42 days). In the PCHM, the risk of death is assumed to be constant for the duration of each interval, and so intervals were closely spaced where the risk of death declines rapidly, and more widely spaced as the risk of death changes more slowly (appendix p 4). Beyond 42 days, we incrementally estimated the point at which women's risk of death remains elevated at 95% significance. We estimated this to be up to 122 days, and hence the remainder of the first year post partum was split accordingly (42–122 days and 4–11 months). Within each risk interval, counts of deaths and person-years were aggregated. The period 12–17 months was used as the baseline risk of death, to

See Online for appendix

	Alive or censored by the end of the 1-year post-partum follow-up (n=645 137 births)*	Died within the 1-year post-partum follow-up (n=1967 births)
Childbirth cohort		
1991 to 1995	20 203 (3·1%)	81 (4·1%)
1996 to 2000	47 339 (7·3%)	204 (10·4%)
2001 to 2005	81 419 (12·6%)	382 (19·4%)
2006 to 2010	182 158 (28·2%)	575 (29·2%)
2011 to 2015	270 817 (42·0%)	641 (32·6%)
2016 to 2020	43 201 (6·7%)	84 (4·3%)
Country		
Burkina Faso	65 817 (10·2%)	97 (4·9%)
Côte d'Ivoire	10 460 (1·6%)	17 (0·9%)
Ethiopia	67 287 (10·4%)	169 (8·6%)
The Gambia	105 382 (16·4%)	286 (14·5%)
Ghana	82 126 (12·7%)	200 (10·2%)
Kenya	67 716 (10·5%)	194 (9·95)
Malawi	100 (<0·1%)	0 (0)
Mozambique	13 331 (2·1%)	46 (2·3%)
Nigeria	22 836 (3·5%)	53 (2·7%)
Senegal	48 578 (7·5%)	176 (8·9%)
South Africa	73 810 (11·4%)	364 (18·5%)
Tanzania	87 695 (13·6%)	365 (18·6%)
Parity in HDSS†		
1	375 498 (58·2%)	1214 (61·7%)
2–3	212 279 (32·9%)	586 (29·8%)
4–5	50 559 (7·9%)	150 (7·6%)
6+	6801 (1·1%)	22 (1·1%)
Maternal age at time of childbirth‡		
<15 years	3285 (0·5%)	11 (0·6%)
15–24 years	269 459 (41·8%)	639 (32·5%)
25–34 years	271 648 (42·1%)	897 (45·6%)
35+ years	100 745 (15·6%)	425 (21·6%)

Data are n (%). HDSS=Health and Demographic Surveillance System. *Some women gave birth multiple times within the HDSS site. Multiparous women might contribute to multiple categories. †Parity is likely to be poorly recorded in the HDSSs, as often only births to women resident in the site are recorded, rather than full obstetric histories. ‡Observations where maternal age at the end of pregnancy was <10 years or >54 years were excluded (n=1108, 0·17% of the sample), in line with the Global Burden of Disease protocol.[14] These observations will be mostly, though not exclusively, caused by HDSS sites erroneously recording the maternal date of birth or the date of childbirth.

Table 1: **Frequency distribution for births within the HDSS**

	Death distribution*	Person-years	Crude death rate per 1000 person-years
0 to 1 day	306	3541	86·6
2 to 6 days	118	8841	13·4
7 to 13 days	101	12 354	8·2
14 to 41 days	223	49 145	4·5
42 to 122 days	363	139 387	2·6
4 to 11 months	856	388 903	2·2
12 to 18 months	574	263 592	2·2

*Adjusted death distribution to correct for misattribution of deaths to the next calendar day (eg, women who survive less than 24 h but die on the next calendar day would be misattributed to day 1). Half of deaths are assumed to occur on the calendar day, and half on the day before. A comparison of adjusted and unadjusted distributions can be found in the appendix (p 3).

Table 2: **Crude death rates by interval up to 1·5 years post partum**

represent women's unexposed state.[11] Following Høj and colleagues,[11] we chose this interval as it occurs after the cut-off for late maternal death after the first year post partum, and is long enough to provide stable statistical estimates.[11] For subsequent births (n+1) that occurred before the end of 17 months post partum, we adjusted the person-years as half of the exposure time between birth n and n+1.

As we were working with aggregated counts of deaths and person-years, we estimated the PCHM using negative binomial regression, which also corrects for overdispersion in the data by adjusting the standard error. We accounted for the effect of potential confounders that were available in the HDSS data (maternal age at childbirth, parity in the HDSS, and delivery cohort). The final multivariable model was specified as follows: the dependent variable was the death count; the independent variable was the time interval from childbirth; and the additional predictors were maternal age at the time of birth, parity in the HDSS, and childbirth cohort. Person-years was the offset variable to weight the death counts by the exposure. We also included HDSS site dummies to estimate aggregate-level fixed effects to control for unobserved heterogeneity between sites.

Finally, in the absence of COD information, and with exposure beginning from the date of childbirth onwards, we estimated the postpartum pregnancy-related mortality ratio (life table analysis available in the appendix p 5).

Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 1, 1991, and Feb 24, 2020, 647 104 births occurred in the HDSS sites, contributing 602 170 total person-years-at-risk, among 386 318 women (multiparous women contributed more than one post-partum exposure period). The sample characteristics for women who delivered in the HDSS sites are described in table 1. There were 1967 deaths within 1 year post partum, of which 748 deaths occurred within 42 days of childbirth, and 363 between 42 days and 4 months. Deaths, person-years, and crude deaths rates for each interval are summarised in table 2.

After adjustment for confounding, mortality was 38·82 (95% CI 33·21–45·29) times higher than baseline on days 0–1 after childbirth, 4·97 (3·94–6·21) times higher for days 2–6, 3·35 (2·64–4·20) times higher for days 7–13, 2·06 (1·74–2·44) times higher for days 14–41, and

1·20 (1·03–1·39) times higher from 42 days to 4 months post partum (table 3, figure).

Women who gave birth for the first time in the HDSS face 1·30 (95% CI 1·17 to 1·44) times the risk of death relative to second or third birth in the HDSS (table 3). Women aged 15–24 years had lower mortality (0·63 [0·57 to 0·70] times that of women aged 25–34 years), whereas women aged 35 years and older had higher mortality (1·32 [1·18 to 1·48] times that of women aged 25–34 years). Relative to births in the HDSS between 1996 and 2000, from 2006 to 2010 onwards successive cohorts have a lower risk of pregnancy-related death, indicating improving mortality conditions. Further analysis of the decline in post-partum pregnancy-related mortality from 1991–95 to 2016–20 versus sample heterogeneity can be found in the appendix (p 2).

The Wald test of joint significance confirms that aggregate-level fixed effects for HDSS site are significant. Relative to the site in Basse, five sites in South Africa, Tanzania, Kenya, and Senegal had a higher risk of death; nine sites in Tanzania, Senegal, Kenya, Ghana, Ethiopia, Cote d'Ivoire, and Burkina Faso had a lower risk of death; and there was no significant effect in 15 sites in South Africa, Tanzania, Senegal, Nigeria, Mozambique, Malawi, Kenya, The Gambia, Ghana, and Ethiopia. The full results for HDSS site heterogeneity are available in the appendix (p 6).

For deaths within 42 days, the approximate post-partum PRMR was 117 per 100 000 births for the period 1991–2020. Extending the limit to 4 months post partum results in an estimate of 174 per 100 000 births, a 40% increase (ln [174/116]). This illustrates the sensitivity of the PRMR to the choice of the threshold, and hence the implications of WHO's standard definition of maternal mortality to mortality surveillance.

Given the lack of consistency between studies in the choice of the risk period beyond 42 days, we tested the sensitivity of the effect size to the choice of the interval. The shorter the risk period after 42 days, the higher the mortality risk. This strengthens the case that the risk of death is not constant at prepregnancy levels by 42 days. We also tested the sensitivity of the results to the choice of the post-partum period used as the baseline (12–17 months), using the periods 12–23 months and 12–35 months instead. Our main result is robust to the choice of the baseline, with the risk of death from 42–122 days being 1·17 (95% CI 1·01–1·33) and 1·15 (1·01–1·30) when a 12–23 month or 12–35 month baseline period was used, respectively. The full set of results from sensitivity analyses is available in the appendix (pp 4–6).

	Univariable analysis		Multivariable analysis (negative binomial)	
	Rate ratio (95% CI)	p value	Rate ratio (95% CI)	p value
Interval				
0–1 day	39·78 (34·63–45·70)	<0·0001	38·82 (33·21–45·29)	<0·0001
2–6 days	6·16 (5·06–7·51)	<0·0001	4·97 (3·94–6·21)	<0·0001
7–13 days	3·78 (3·06–4·66)	<0·0001	3·35 (2·64–4·20)	<0·0001
14–41 days	2·09 (1·79–2·44)	<0·0001	2·06 (1·74–2·44)	<0·0001
42–122 days	1·20 (1·05–1·36)	0·0078	1·20 (1·03–1·39)	0·016
4–11 months	1·01 (0·91–1·12)	0·83	1·02 (0·90–1·15)	0·76
12–18 months‡	1·0	..	1·0	..
Parity (within HDSS)†				
1	1·18 (1·08–1·29)	<0·0002	1·30 (1·17–1·44)	<0·0001
2–3‡	1·0	..	1·0	..
4–6	1·02 (0·87–1·20)	0·79	0·86 (0·71–1·03)	0·095
7+	1·19 (0·83–1·71)	0·35	0·74 (0·48–1·10)	0·15
Maternal age at childbirth				
<15 years	1·05 (0·62–1·77)	0·87	0·86 (0·48–1·41)	0·58
15–24 years	0·73 (0·67–0·80)	<0·0001	0·63 (0·57–0·70)	<0·0001
25–34 years‡	1·0	..	1·0	..
≥35 years	1·28 (1·16–1·42)	<0·0001	1·32 (1·18–1·48)	<0·0001
Childbirth cohort				
1991 to 1995	0·91 (0·73–1·14)	0·40	0·95 (0·74–1·22)	0·71
1996 to 2000‡	1·0	..	1·0	..
2001 to 2005	1·07 (0·92–1·24)	0·38	0·99 (0·83–1·17)	0·88
2006 to 2010	0·73 (0·64–0·84)	<0·0001	0·81 (0·69–0·96)	0·015
2011 to 2015	0·57 (0·50–0·66)	<0·0001	0·69 (0·58–0·82)	<0·0001
2016 to 2020	0·58 (0·46–0·72)	<0·0001	0·64 (0·48–0·87)	0·0027

HDSS=Health and Demographic Surveillance System. *HDSS site aggregate level fixed-effects results available in the appendix (p 6). †No adjustment for correlated data is made. Although exposure for women who survive can be clustered, the outcome (death) is an absorbing state, and hence cannot be clustered by woman. ‡Reference category.

Table 3: **Univariable and multivariable results: risk of death by time since childbirth, with predictors and HDSS site fixed effects*†**

Discussion

To our knowledge, this study is the first to estimate the duration of an elevated risk of all-cause mortality during the extended post-partum period in a large dataset compiled of sub-Saharan African HDSSs. With an exposure size of almost 650 000 births and 1967 deaths within 1 year of childbirth, we find that women remain at 20% higher risk of death from day 42 until 4 months post partum. This result is robust to the choice of the post-partum reference period (ie, 12–17 months, 12–23 months, or 12–35 months post partum) and is substantial, with the increased risk of the post-partum period exceeding any general increase in mortality with age. We also estimate that including deaths up to 4 months post partum would increase the post-partum PRMR by 40%. These results strengthen the evidence that the 42-day post-partum threshold does not to capture the full duration of post partum risk of death.

These results of the duration of an increased risk of post-partum pregnancy-related mortality are consistent with previous research on maternal mortality (where COD was ascertained), although the magnitude of the risk is lower than in other studies. In Guinea-Bissau, the risk of maternal death remained elevated until 91 days relative to 12–17 months post partum (risk ratio 2·8,

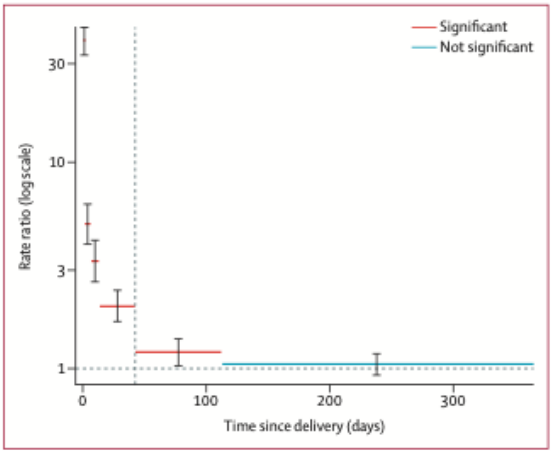

Figure: **Rate ratios of death by time interval since childbirth for the estimated Piecewise Constant Hazard Model**

95% CI 1·4–5·4);[11] in Bangladesh, the risk remained elevated until 180 days (adjusted risk ratio 1·5, 95% CI 1·3–2·1),[21] relative to the third and fourth year post partum. Conversely, our estimate of the effect of an upward revision of the 42-day threshold on the post-partum PRMR is higher than an estimate of the effect on the MMR: in Guinea-Bissau, extending the measurement of maternal death up to 3 months would increase the MMR by 10–15%.[11] However, differences in methodology mean these estimates are not directly comparable: the post-partum threshold differs and as deaths during pregnancy are not included in this HDSS data, the relative contribution of an extension in the post-partum threshold will be greater.

Deaths during the first year post partum can either be direct maternal, indirect maternal, or coincidental. Without COD information to exclude coincidental causes, our results question the justification of the 42-day threshold for pregnancy-related deaths. The contribution of coincidental causes to the pregnancy-related deaths might be substantial, estimated as 46% in one study in sub-Saharan Africa.[7] But since maternal deaths are more likely to be misclassified as non-maternal in the later post-partum period,[3] this is likely an overestimate. The causes that are coincidental or accidental are likely to be constant over the pregnancy and post-partum period because they are not aggravated or caused by pregnancy. Yet, since we see an increased risk of death between 42 days and 4 months, this is most plausibly explained by causes that are aggravated or caused by pregnancy. The increased risk is more likely related to conditions that could manifest later than 42 days post partum (eg, direct late maternal deaths from suicide[1] or cardiomyopathy[4]), or unresolved chronic conditions and infectious disease (eg, indirect late maternal deaths). Evidence on the causes of late maternal deaths in sub-Saharan Africa is sparse. However, studies up to 42 days post partum suggest that indirect causes (from HIV,[27,28] tuberculosis,[29] malaria,[7] pneumonia,[7] and cardiovascular disease[7]) might be substantial in the extended post-partum period.

Our results emphasise a need to revisit the schedule and content of post-partum care. The proportion of women who receive routine post-partum care up to 42 days in sub-Saharan Africa is not as high as it should be.[29] But the provision of care for women who experience chronic morbidity in the extended post-partum period must also be prioritised to improve maternal health. Patient transfer from maternity services to higher level care beyond 42 days in sub-Saharan Africa requires further research.

The implications of our findings for tracking progress in maternal survival are four-fold. First, our results reaffirm calls for a review of the 42-day post-partum threshold to better capture the full duration of increased risk of death after birth.[11,22] Although an upward revision of the 42-day post-partum threshold would complicate comparisons of the MMR and PRMR over time, a change to the standard definition could, in turn, help to improve awareness of the duration of the post-partum risk women face.

Second, our results also expose the need to define and count what could be called late pregnancy-related deaths over an extended post-partum period, particularly in sub-Saharan Africa, where medical certification of COD remains uncommon.[6] Until medical certification of COD is routine in sub-Saharan Africa, an internationally agreed indicator to monitor the burden of late pregnancy-related mortality is essential. Without an indicator, these deaths will continue to fall through the cracks of global efforts to monitor maternal health outcomes—captured neither in statistics on pregnancy-related mortality, nor in estimates of late maternal death. In a world where indicators continue to govern global health prioritisation, late pregnancy-related deaths must be officially defined and counted. As a start, the availability of data would be greatly improved if the Demographic and Health Surveys extended the sisterhood method from 8 weeks to 1 year post partum.

Third, in contexts where COD information is available, our results suggest that monitoring of late maternal deaths requires renewed dedication and institutionalisation.[4,29] To plan interventions and prevent late maternal deaths, we urgently need to know the reasons for maternal mortality beyond 42 days in LMICs. Data from the UK Confidential Enquiries suggest the majority of late maternal deaths fall into one of four causes: cardiovascular, cancer, suicide, or thromboembolism,[30] but audits of the causes of late maternal deaths in LMICs are lacking.[4] The relative contribution of causes is likely to differ in LMICs due to differences in the disease burden affecting populations, as well as the capacity of health systems to identify underlying conditions during antenatal care and unresolved conditions during the post-partum period. Even in the rare instances that the cause of late maternal deaths are reported, egregious inconsistencies, particularly

in LMICs, around the ad-hoc coding of deaths from suicide as an indirect cause of maternal death or incidental to the pregnancy mean that data are often not comparable.[3,4] Improved surveillance of late maternal deaths will therefore require better compliance with ICD-11, which might require increased WHO support. It might also require improved linkage of childbirth and other health records to better identify women's post-childbirth status in health information systems. Ultimately, the dearth of data on the causes of late maternal deaths in LMICs leads to missed opportunities to address causes and reduce preventable mortality.

Fourth, incentivising and institutionalising international reporting on late maternal and late pregnancy-related deaths in the extended post-partum period beyond 42 days will only be achieved once international agencies disaggregate their reports of maternal and pregnancy-related deaths by time—the antepartum, intrapartum, post-partum, and extended post-partum (up to 1 year) periods.

There are several important limitations to this analysis. First, because we consolidated HDSS data that do not include pregnancy status reports, this study only considered post-partum risk from the date of the childbirth. The exclusion of antepartum and some intrapartum deaths is likely to substantially underestimate maternal risk (eg, deaths from unsafe abortion, ectopic pregnancy, and eclampsia before childbirth).[7] The underestimation of mortality, however, does not invalidate this study's main conclusion that mortality remains elevated beyond WHO's 42-day post-partum threshold. Second, there might be additional confounders that could affect women's post-partum survival not available in HDSS data that we were unable to adjust for. Third, analysis of date heaping suggests that date imputation is standard practice in many HDSS sites (examples can be found in the appendix pp 10–11). Bias from imputation error is a concern, but these results are still valuable when the alternative is an absence of evidence. Fourth, HDSSs cover small, geographically concentrated, and often rural populations. Whether findings from HDSSs are generalisable to broader or national populations is unclear.[25]

In summary, our results suggest that the global community and sub-Saharan African countries are underestimating the number of deaths associated with pregnancy. It is likely, therefore, that women who should receive routine and specialist care are not receiving the support they need. We call for revisions to the definitions of maternal and pregnancy related deaths and for research on the implications of a longer duration of increased risk of death following childbirth for postnatal care.

Contributors
UG, VF, and GR conceived the idea and developed the study design. UG and HE-S analysed the data. HE-S and JRP provided methodological support. UG reviewed the literature and wrote the initial draft of the manuscript. MJ and SK were responsible for data acquisition. All authors were involved in commenting on subsequent revisions. All authors are the guarantors. All authors had full access to all relevant data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests
We declare no competing interests.

Data sharing
Data for 28 of the HDSS sites included in this analysis are open access via the INDEPTH Network and the microdata are available upon application on the website.

For **the INDEPTH Network** see www.indepth-network.org

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Chapter 4 Research paper 2

Pregnancy-related mortality up to 1 year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries

Summary of chapter

In Chapter 4, I present the second paper of this thesis, as published in British Journal of Obstetrics and Gynaecology (BJOG). This includes the rationale for this study, the study setting, methods, results and discussion.

Supplementary material for this paper is available in Appendix C. Please note, in the following typeset text, page references for supplementary tables and figures refer to the online appendices for BJOG rather than this thesis.

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Thesis Title	Advances in the conceptualisation and measurement of maternal morbidity and mortality		
Primary Supervisor	Professor Veronique Filippi		

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SECTION B – Paper already published

Where was the work published?	British Journal of Obstetrics and Gynaecology This work was published open access under a Creative Commons Attribution License (CC BY).		
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SECTION E

Student Signature	Ursula Gazeley
Date	20th March 2024

Supervisor Signature	Veronique Filippi
Date	20th March 2024

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RESEARCH ARTICLE

Epidemiology

Pregnancy-related mortality up to 1 year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries

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Abstract

Objective: To compare the causes of death for women who died during pregnancy and within the first 42 days postpartum with those of women who died between >42 days and within 1 year postpartum.

Design: Open population cohort (Health and Demographic Surveillance Systems).

Setting: Ten Health and Demographic Surveillance Systems (HDSS) in The Gambia, Kenya, Malawi, Tanzania, Ethiopia and South Africa.

Population: 2114 deaths which occurred within 1 year of the end of pregnancy where a verbal autopsy interview was conducted from 2000 to 2019.

Methods: InterVA5 and InSilicoVA verbal autopsy algorithms were used to attribute the most likely underlying cause of death, which were grouped according to adapted International Classification of Diseases-Maternal Mortality categories. Multinomial regression was used to compare differences in causes of deaths within 42 days versus 43–365 days postpartum adjusting for HDSS and time period (2000–2009 and 2010–2019).

Main outcome measures: Cause of death and the verbal autopsy Circumstances of Mortality Categories (COMCATs).

Results: Of 2114 deaths, 1212 deaths occurred within 42 days postpartum and 902 between 43 and 365 days postpartum. Compared with deaths within 42 days, deaths from HIV and TB, other infectious diseases, and non-communicable diseases constituted a significantly larger proportion of late pregnancy-related deaths beyond 42 days postpartum, and health system failures were important in the circumstances of those deaths. The contribution of HIV and TB to deaths beyond 42 days postpartum was greatest in Southern Africa. The causes of pregnancy-related mortality within and beyond 42 days postpartum did not change significantly between 2000–2009 and 2010–2019.

Conclusions: Cause of death data from the extended postpartum period are critical to inform prevention. The dominance of HIV and TB, other infectious and non-communicable diseases to (late) pregnancy-related mortality highlights the need for better integration of non-obstetric care with ante-, intra- and postpartum care in high-burden settings.

KEYWORDS

causes of death, maternal health, pregnancy-related mortality, verbal autopsy

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1 | INTRODUCTION

Globally, remarkably little is known about the causes of death (COD) for women who die beyond the standard 42-day postpartum period,[1] despite the need for this evidence to inform policy and programming to prevent these deaths. This evidence gap is particularly apparent in sub-Saharan Africa. Of five relevant studies on the causes of deaths in the extended postpartum, two did not disaggregate deaths within 42 days postpartum from those that occurred after 42 days;[2,3] two had small samples and are now outdated;[4,5] and one study in South Africa identified HIV and TB as the primary causes of deaths beyond 42 days postpartum.[6]

The reasons for the lack of data on deaths beyond 42 days are twofold. First, although late maternal deaths occurring beyond 42 days but within 1 year of the end of pregnancy are defined ('any cause related to or aggravated by the pregnancy or its management but not from unintentional or incidental causes'[7]) only maternal deaths within 42 days are included in the numerator of the Maternal Mortality Ratio (MMR) – the primary indicator used to monitor trends in maternal survival between countries and over time. For pregnancy-related deaths ('a female death occurring within 42 days of termination of pregnancy, irrespective of cause'[7]), there is no corollary definition of what could be called 'late pregnancy-related mortality' for deaths between 43 and 365 days postpartum, despite recent evidence that the risk of pregnancy-related mortality remains elevated until 4 months after delivery.[8] Many countries, therefore, either do not monitor or do not report estimates of mortality levels and causes beyond 42 days postpartum.

Secondly, cause of death information and analyses in sub-Saharan Africa frequently falls short of international standards.[9] Civil Registration and Vital Statistics systems and medical certification of the cause of death are often incomplete,[9,10] and though many African countries have Maternal and Perinatal Death Surveillance and Response (MPDSR) with a national policy for maternal deaths notification,[11] MPDSR systems rarely review deaths beyond 42 days postpartum. Deaths that occur outside of the labour or postnatal ward or cases that were referred to higher-level facilities may also be less likely to be captured and reviewed through MPDSR.[12] Finally, MPDSRs are primarily facility-based; community deaths during pregnancy and the extended postpartum period may be missed when community reporting mechanisms are weak.[12] These concerns may be particularly salient for deaths occurring after 42 days postpartum.

For these reasons, population-based HDSS and verbal autopsy (VA) data are essential to estimate the causes of pregnancy-related deaths up to 1 year postpartum in data-scarce contexts. Our objective was to compare the causes of pregnancy-related deaths occurring during pregnancy and within 42 days postpartum with 'late' pregnancy-related deaths occurring 43 days to 1 year postpartum to provide much-needed evidence on the causes of death in the extended postpartum in sub-Saharan Africa.

2 | METHODS

2.1 | Data

This study pooled longitudinal, prospective data from 10 Health and Demographic Surveillance Systems (HDSS) across six countries in sub-Saharan Africa: Basse and Farafenni (The Gambia), Nairobi, Kisumu and Kilifi (Kenya), Agincourt and uMkhanyakude (South Africa), Karonga (Malawi), Kersa (Ethiopia), and Kisesa (Tanzania). HDSS are open population cohorts and collect data on births and deaths that occur within a small geographical area quarterly to biannually. Each HDSS had their own informed consent procedure (either written or verbal), which in most sites was at the household level.[13] Access to data for Agincourt, Basse, Farafenni, Kersa, Kisesa and Kisumu was arranged through data-sharing agreements with the London School of Hygiene and Tropical Medicine (LSHTM). Access to data for Karonga, Kilifi, Nairobi and uMkhanyakude was granted through the sites' online data repositories. The LSHTM ethics committee approved this study.

2.2 | Study population

Deaths that occurred in the 20-year period from 2000 to 2019 (inclusive) were included. Deaths pre-2000 were excluded because only a few sites were operational; deaths occurring between 2020 and 2022 were excluded to limit the effect of COVID-19 misclassification, with COVID-19 only introduced to the WHO verbal autopsy tool in 2022.[14]

We identified all deaths of women aged 10–54 years that occurred up to 1 year postpartum in two ways. First, we identified postpartum deaths for whom the date of the end of pregnancy was available in the HDSS delivery file and for whom a VA interview was conducted. In all 10 sites, this included pregnancies ending in a live birth or stillbirth after

28 weeks' gestation. In Basse, Farafenni, Kilifi and Nairobi, pregnancy terminations before 28 weeks' gestation (miscarriage or abortion) were also included. We then identified which of these women died within 1 year postpartum. Secondly, we identified all additional deaths where the proxy respondent reported in the VA interview that the woman was either currently pregnant or in labour at the time of death, or died within 42 days of pregnancy termination, but for whom no delivery was recorded in the HDSS delivery file.

2.3 | Procedures

Deaths were grouped as occurring during pregnancy and within the standard 42-day postpartum period or between 43 days and 1 year postpartum. Where a discrepancy existed between the timing of death in the VA data and HDSS delivery data ($n=41$), priority was given to the VA data if it was possible that a repeat pregnancy had occurred that had not yet been recorded in the HDSS delivery file. Maternal age at death was grouped by 5-year intervals from 10–14 to 50–54 years.

For each death, we estimated the single most likely underlying COD using the InterVA5 algorithm. We grouped deaths according to the four types and nine adapted International Classification of Diseases-Maternal Mortality (ICD-MM) categories[15,16] as follows:

Obstetric (1. Pregnancy with abortive outcome, 2. Hypertensive disorders, 3. Obstetric haemorrhage, 4. Pregnancy-related infection, 5. Other obstetric complications, 6. Unanticipated complications of management);

Non-obstetric (7a. HIV & TB, 7b. Other infectious diseases, 7c. Cardiovascular diseases, 7d. Other NCDs);

Unspecified (8. Undetermined);

External (9. Accidents & violence).

Exact replication of the ICD-MM categories was not possible because we analysed pregnancy-related deaths (i.e. defined only by time of death) and not maternal mortality. From VA data alone, it is not possible to differentiate which non-obstetric pregnancy-related deaths were indirect maternal deaths and which were coincidental; this would require a clinical COD expert reviewing a patients' medical records to ascertain whether the underlying condition (e.g. HIV, carcinoma or cardiovascular disease) was 'aggravated by pregnancy' – as is required for the death to be considered maternal. This was not possible without further record linkage and data triangulation, and hence we modified the ICD-MM categories to apply to pregnancy-related mortality (Figure S1). *Obstetric* and *Unspecified* groups replicate the ICD-MM categories. *Non-obstetric* includes all non-obstetric causes without an attribution whether the death was indirect maternal death or coincidental to the pregnancy. *External* includes deaths from accidents and violent injuries only.

Finally, for each death, we processed the Circumstances of Mortality categories (COMCATs) using InterVA5 and COMCAT version 1.0 to attribute the most likely circumstance of mortality: traditions, emergencies, recognition of serious disease, resources, health systems, inevitability and multiple.

2.4 | Statistical analyses

Based on the classification of death type and adapted ICD-MM category, we estimated the relative COD distribution by age group and whether the death occurred within or beyond 42 days postpartum. Multinomial logistic regression was used to calculate the predictive margins (potential-outcome means) for deaths occurring within and after 42 days postpartum, to adjust for potential confounders – maternal age at death, time period and HDSS. As each ICD-MM category is a competing cause of death, we estimated one enclosing multinomial model for all causes.

We tested the sensitivity of the results to the choice of VA algorithm, comparing InterVA5 with InSilicoVA. We also compared the concordance between algorithm- and physician-coded VA for the underlying cause, adapted ICD-MM categories, and type (Kisumu, Nairobi and Karonga, only), and the concordance of InterVA5 and InSilicoVA algorithms for all 10 HDSS.

3 | RESULTS

Between 3 January 2000 and 21 December 2019, there were 2114 deaths during pregnancy and up to 1 year postpartum in the HDSS, of which 902 (42.7%) occurred beyond 42 days postpartum.

The background characteristics of these deaths are presented in Table 1. For each HDSS, the years of the earliest to last death are presented in parentheses. Except in Agincourt and uMkhanyakude, more deaths occurred during pregnancy and within 42 days than from 43 to 365 days postpartum. Almost two-thirds of deaths from 43 to 365 days postpartum occurred between the years 2000 and 2009.

Table 2 shows the full results for InterVA5, with the breakdown of deaths by type, adapted ICD-MM category and underlying cause. There were no deaths attributed to unanticipated complications of management in the data. Most other direct obstetric deaths were unspecified maternal causes; malaria and pneumonia were the leading causes of other infectious diseases; and digestive neoplasms were the leading cause of other NCDs.

Figure 1A shows the proportion of pregnancy-related deaths for each COD type for data from all 10 HDSS pooled together. Across all age groups, for deaths occurring during pregnancy and within 42 days postpartum, direct obstetric causes were the leading COD, whereas for deaths beyond 42 days, non-obstetric causes were dominant. Undetermined and external causes constituted a small proportion of deaths across all age groups and each period.

Figure 1B shows the proportion of pregnancy-related deaths for each type disaggregated by adapted ICD-MM category for all 10 HDSS. For deaths occurring within 42 days, obstetric haemorrhage was the dominant cause, followed by HIV and TB. The proportion of deaths from hypertensive disorders was comparable to deaths from other infectious diseases and cardiovascular diseases. For late pregnancy-related deaths occurring from 43 to 365 days postpartum, HIV and TB were the

TABLE 1 Background characteristics.

Characteristic	Pregnancy-related deaths	
	Deaths during pregnancy and within 42 days (inclusive) postpartum, $n=1212$	Deaths from 43 to 365 days postpartum, $N=902$
HDSS[a] (earliest to last death in sample)		
Agincourt, South Africa (2000–2019)	127 (10.5%)	131 (14.5%)
Basse, The Gambia (2006–2018)	143 (11.8%)	62 (6.9%)
Farafenni, The Gambia (2000–2018)	74 (6.1%)	15 (1.7%)
Karonga, Malawi (2003–2017)	58 (4.8%)	31 (3.4%)
Kersa, Ethiopia (2008–2019)	36 (3.0%)	23 (2.5%)
Kilifi, Kenya (2008–2019)	160 (13.1%)	69 (7.7%)
Kisumu, Kenya (2003–2013)	328 (27.1%)	281 (31.1%)
Magu, Tanzania (2000–2016)	71 (5.9%)	23 (2.6%)
Nairobi, Kenya (2003–2016)	88 (7.3%)	57 (6.3%)
uMkhanyakude, South Africa (2000–2019)	127 (10.5%)	210 (23.3%)
Age at death		
10–14	1 (0.1%)	1 (0.1%)
15–19	134 (11.1%)	50 (5.6%)
20–24	304 (25.1%)	205 (22.7%)
25–29	289 (23.8%)	270 (29.9%)
30–34	247 (20.4%)	196 (21.7%)
35–39	155 (12.8%)	126 (14.0%)
40–44	69 (5.7%)	44 (4.9%)
45–49	11 (0.9%)	10 (1.1%)
50–54	2 (0.2%)	0 (0.0%)
Year of death		
2000–2009	679 (56.0%)	556 (61.6%)
2010–2019	533 (44.0%)	346 (38.4%)

[a]Health and Demographic Surveillance System.

dominant causes, followed by other NCDs and other infectious diseases. All obstetric causes constituted a small proportion of the late pregnancy-related deaths. The timing of obstetric deaths from 43 days to 1 year postpartum is shown in Figure S2.

Multinomial logistic regression confirmed that the predicted proportions for all direct obstetric causes of pregnancy-related deaths were significantly larger for deaths occurring within (versus beyond) 42 days postpartum, adjusting for HDSS and time period (2000–2009 and 2010–2019). Maternal age at death was not significant and was dropped from the final model. After adjusting for time period and HDSS heterogeneity, HIV & TB, other infectious diseases and other NCDs were significantly more likely causes of pregnancy-related deaths occurring beyond (versus within) 42 days postpartum. For full multinomial results see Table S1 and Figure S3.

Sensitivity analyses show that the results for InSilicoVA were broadly consistent, although within 42 days postpartum, the contribution of pregnancy-related infection was slightly higher and that of cardiovascular disease was lower compared with InterVA5; replication of the main results can be found in Figure S4. Concordance between physician-coded VA and algorithm-assigned results can be found in Table S2 for the three HDSS with available physician-coded VA data; concordance of physician-coded VA results was low for both the underlying cause of death (ranging from 25% to 43%) and adapted ICD-MM category (from 33% to 55%), but was higher for broad type (from 82% to 83%). Agreement between InterVA55 and InSilicoVA was high for all 10 HDSS (from 47% for underlying cause to 93% for broad cause type).

3.1 | Causes of pregnancy-related deaths from 2000–2009 and 2010–2019

Figure 2 shows the causes of pregnancy-related deaths from 2000–2009 and 2010–2019 for InterVA5. The CSMFs are similar across both time periods; however, univariable analyses suggest a slight decrease in HIV and TB, and a marginal increase in hypertensive and cardiovascular causes of deaths within 42 days. For deaths from 43 days to 1 year postpartum, univariable analyses indicate a slight decrease in other infectious diseases and increase in other NCDs. However, after accounting for HDSS heterogeneity, no changes in the predicted proportions were significant at 95%. Multinomial results for the differences by time period (2000–2009 and 2010–2019) are available in Tables S3 and S4, and Figures S5 and S6.

3.2 | Causes of pregnancy-related deaths by HDSS

Figure 3 shows substantial heterogeneity in the causes of pregnancy-related deaths between HDSS for InterVA5. Within 42 days postpartum, obstetric haemorrhage was the leading cause of death for all sites except Basse, The Gambia and uMkhanyakude, South Africa, where other infectious diseases and HIV and TB were dominant, respectively. For deaths beyond 42 days postpartum, HIV and TB were the leading causes of death in all HDSS except Basse, The Gambia, though the contribution was greatest in Southern Africa. After adjustment for time period, multinomial predicted proportions indicate significant (non-overlapping CIs) in the CSFM between HDSS for all causes of pregnancy-related death. Full multinomial results for HDSS are available in Table S5 and Figure S7.

3.3 | Circumstances of Mortality categories (COMCATs)

Figure 4 shows that hypertensive and haemorrhagic disorders, as well as other infectious diseases, were most frequently emergencies. Deaths from HIV and TB were most frequently related to health system failures (difficulty in receiving care and

TABLE 2 Underlying causes and ICD-MM cause categories, InterVA5.

Adapted ICD-MM[a] group	Underlying cause	Deaths within 42 days	Deaths from 43 to 365 days
Obstetric causes		728	63
1. Abortive	Abortion-related death	46	8
	Ectopic pregnancy	17	0
2. Hypertensive	Pregnancy-induced hypertension	96	15
3. Obstetric haemorrhage	Obstetric haemorrhage	456	18
	Ruptured uterus	12	1
4. Pregnancy-related infection	Pregnancy-related sepsis	53	8
5. Other direct obstetric	Anaemia of pregnancy	15	2
	Intentional self-harm	0	11
	Obstructed labour	3	0
	Other and unspecified maternal cause	30	0
6. Unanticipated complications of management	N/A	0	0
Non-obstetric causes	422	758	
7a. HIV/tuberculosis	HIV-related death	110	317
	Tuberculosis	61	125
7b. Other infectious diseases	Acute respiratory infection including pneumonia	36	41
	Diarrhoeal diseases	2	18
	Haemorrhagic fever (non-dengue)	0	2
	Malaria	32	34
	Meningitis and encephalitis	13	19
	Other and unspecified infectious disease	3	11
7c. Cardiovascular diseases	Acute cardiac disease	11	9
	Other and unspecified cardiac disease	72	35
	Stroke	6	9
7d. Other NCDs[b]	Acute abdomen	11	16
	Asthma	4	3
	Breast neoplasms	0	7
	Diabetes mellitus	7	7
	Digestive neoplasms	10	30
	Epilepsy	6	6
	Liver cirrhosis	7	5
	Oral neoplasms	1	0
	Other and unspecified NCD	4	6
	Other and unspecified neoplasms	1	11
	Renal failure	2	8
	Reproductive neoplasms	14	25
	Respiratory neoplasms	7	11
	Severe malnutrition	0	2
	Sickle cell with crisis	2	1
Unspecified cause		37	43
8. Undetermined	Undetermined	37	43

(Continues)

TABLE 2 (Continued)

Adapted ICD-MM[a] group	Underlying cause	Deaths within 42 days	Deaths from 43 to 365 days
External causes		25	38
9. Accidents & violence	Accidental drowning and submersion	3	3
	Accidental exposure to smoke fire & flame	0	4
	Accidental fall	0	2
	Assault	9	11
	Road traffic accident	13	18
Total		1212	902

[a]International Classification of Diseases – Maternal Mortality.
[b]Non-communicable diseases.

adhering to treatment) and knowledge factors (lack of recognition of the severity or seriousness of disease). Cardiovascular and other NCDs were mostly related to health systems. As a result, more deaths within 42 days were emergencies, and more deaths from 43 days to 1 year postpartum were related to health system failures and knowledge (Figure S8).

4 | DISCUSSION

4.1 | Main findings

To our knowledge, this is the first study to compare CODs for women who died during pregnancy and within 42 days postpartum with those who died between 43 and 365 days postpartum for multiple countries in sub-Saharan Africa.

Our results indicate the important role of infectious diseases in pregnancy-related mortality up to 1 year postpartum. For all 10 HDSS pooled together, HIV and TB were the second largest COD occurring within 42 days and were the dominant cause for deaths occurring from 43 days to 1 year postpartum. Though also important causes of pregnancy-related mortality within 42 days postpartum, deaths from HIV and TB, other infectious diseases and other NCDs constituted a significantly higher proportion of late pregnancy-related deaths beyond 42 days (versus within 42 days), and health system failures were important in the circumstances of those deaths. These results corroborate the limited existing research on the causes of pregnancy-related deaths within 42 days postpartum[17–19] and late pregnancy-related deaths beyond 42 days in sub-Saharan Africa.[2–5] Women's repeated contacts with the health system throughout pregnancy and postpartum provides multiple opportunities to optimise management of infectious and non-communicable diseases. New strategies may require an improved health system approach and include better training of midwives and obstetricians to identify and treat non-obstetric conditions, better integration of non-obstetric care within maternity, postpartum and extended postpartum care[18,20] and improved referral pathways between obstetric and non-obstetric care-providers. While obstetric and non-obstetric causes of pregnancy-related mortality remain high, African health systems require the capacity and preparedness to respond to both types of maternal health challenges simultaneously.

Our results highlight significant inter- and intra-country heterogeneity between the 10 HDSS, across six countries with different underlying epidemiology and health systems. For deaths within 42 days, obstetric haemorrhage was the cause of over half of all deaths in Karonga (Malawi), Kisesa (Tanzania) and Kisumu (Kenya), compared with less than a quarter of deaths in uMkhanyakude (South Africa). HIV and tuberculosis were the leading causes only in uMkhanyakude HDSS. For deaths beyond 42 days, HIV and tuberculosis were the leading causes in all HDSS except for Basse (The Gambia) and accounted for over three-quarters of deaths in uMkhanyakude (South Africa). In Basse, other infectious diseases were the leading cause of deaths from 43 days to 1 year postpartum. This heterogeneity highlights an urgent need for more data on causes of pregnancy-related deaths up to 1 year postpartum across more countries in sub-Saharan Africa to inform preventative strategies and policy.

For all 10 HDSS pooled, there were no significant differences in the causes of pregnancy-related mortality between 2000–2009 and 2010–2019. This finding corroborates existing evidence that the causes of maternal mortality are slow to change over time,[23] and the obstetric transition theory which hypothesises that causes are similar until the MMR falls below 50 per 100 000 live births.[21] For pregnancy-related deaths within 42 days and from 43 days to 1 year postpartum, there were no significant declines in the contribution of HIV and TB, despite expansions in access to ART and reductions in mother-to-child transmission in sub-Saharan Africa.[22] This may be due to one or more of the following reasons: (i) true persistence of HIV and TB relative to other causes: the proportion of deaths from HIV and TB will not decline if other causes fall more quickly. The high contribution of HIV and TB to pregnancy-related mortality up to 1 year postpartum also corroborates existing VA evidence on deaths within six months postpartum in sub-Saharan Africa in the post ART-era[17]; (ii) overestimation of HIV and TB in 2010–2019: unlikely, as other evidence suggests VA

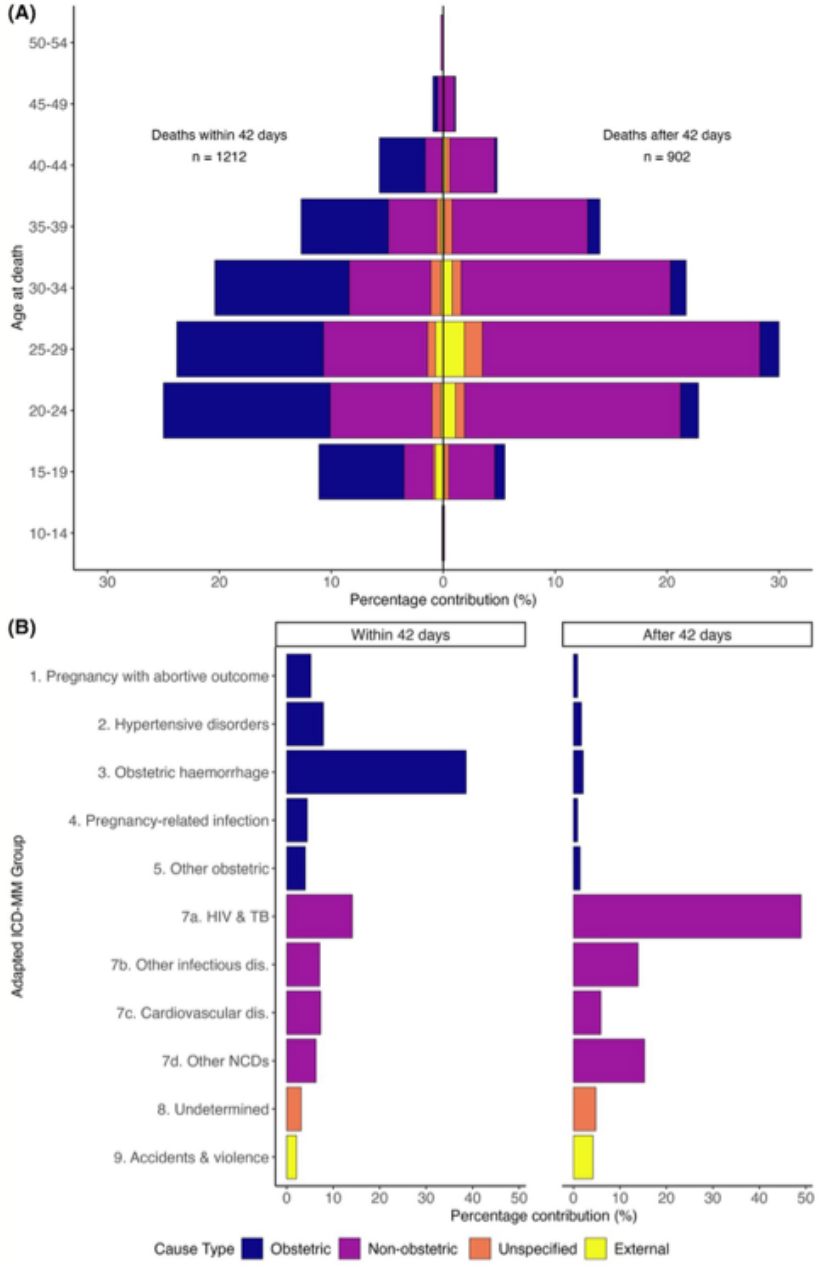

FIGURE 1 Panel A: Causes of pregnancy-related deaths up to 1 year postpartum by timing and age;Panel B: Causes of pregnancy-related deaths up to 1 year postpartum by timing and ICD-MM category. There were no deaths attributed to ICD-MM category 6. Unanticipated complications of management, so this category is not shown.

algorithms may even underestimate HIV and TB-related mortality[24,25] and misclassification would affect both 2000–2009 and 2010–2019 periods; (iii) a lack of power to detect a true change over time: power was limited by the imbalance of the sample biased towards the 2000–2009 period, especially for deaths occurring beyond 42 days postpartum. Potential explanations for this imbalance include: the time period of data contributed by the larger HDSS (e.g. Kisumu up to 2013 only); declines in VA coverage over time in some HDSS (Figure S9) and/or changes in the selection of deaths investigated with a verbal autopsy interview that prioritised deaths to recently pregnant women; or declines in mortality levels for late pregnancy-related deaths.

While recognising these competing explanations for the persistence of HIV and TB, COMCATs emphasise the contribution of health system factors (difficulty in receiving care and adhering to treatment) and knowledge factors (lack of recognition of the severity or seriousness of disease). These findings suggest ANC and PNC programmes in high-prevalence contexts require more emphasis on facilitating treatment

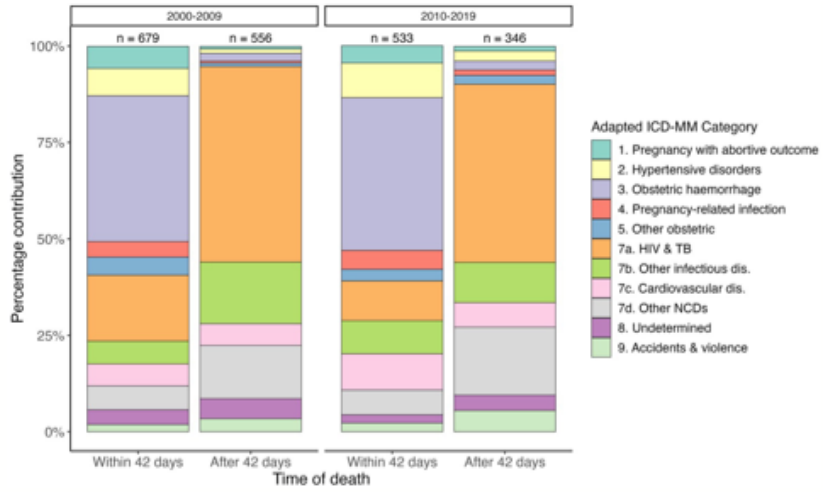

FIGURE 2 Cause of pregnancy-related deaths up to 1 year postpartum from 2000–2009 and 2010–2019, InterVA5. *Note*: There were no deaths attributed to ICD-MM category 6. There were unanticipated complications of management, so this category is not shown.

adherence during pregnancy and postpartum, and also echo earlier calls for complication readiness programmes to include postpartum monitoring of HIV-positive women,[26] which – for some high-risk women – should extend beyond 42 days.[8]

Consistent with other research[16,27] our analysis reveals low concordance between physician-assigned and algorithm-determined underlying cause of death and adapted ICD-MM category, though concordance is high for the type of death (obstetric or non-obstetric). Unlike the algorithms, physicians can use the VA narrative report that describes the sequencing of events that led to death to help attribute an underlying cause, but the quality of training affects the accuracy of physician-coded VA. Previous research has demonstrated 50% or lower concordance of physician-coded VA with hospital-based autopsy.[28]

Finally, from VA data alone, it is not possible to identify which non-obstetric deaths were maternal (i.e. were aggravated by pregnancy). Our results emphasise the urgent need for better linkage and triangulation of data sources so that maternal deaths can be accurately identified and classified in sub-Saharan Africa.[10]

4.2 | Strengths and limitations

A strength of this study is the large sample size of deaths during pregnancy and up to 1 year postpartum across 10 HDSS in six different African countries. The use of VA data for deaths that occur in the community, moreover, means our findings on the COD distribution during pregnancy and the extended postpartum period are more generalisable to the communities where COD attribution is most urgently needed. We also evaluated COD by broad type and adapted ICD-MM categories, and by InterVA5, InSilicoVA and physician review where available.

The limitations of this study are threefold. First, the time period covered is broad, and substantial changes in the burden of disease and health system responses occurred throughout this period that were beyond the scope of this study to explore in detail. Secondly, COD may be misclassified. Both InterVA5 and InSilicoVA algorithms have a weighting factor that make attribution of an obstetric cause more likely if the death occurred within 42 days. Our results may therefore overestimate obstetric causes within 42 days and underestimate obstetric causes after 42 days postpartum. Thirdly, HDSS data are often incomplete; VA interviews were not completed for all reproductive-age deaths in every HDSS (Table S6), and not all pregnancies and births were recorded in the delivery file – e.g. early pregnancy outcomes such as ectopic pregnancy, miscarriage or abortion were only recorded in the delivery file in four HDSS. Across all sites, recording of stillbirths may be incomplete if stigma or cultural taboos precluded disclosure of the birth to enumerators. Some pregnancy-related deaths may also have been missed if respondents did not report that the deceased was recently pregnant during the VA interview and if the algorithm did not identify signs or symptoms of recent pregnancy. These problems of misclassification and incompleteness may bias our results.

4.3 | Interpretation

Despite the difficulty in attribution, available evidence indicates the potential plausibility of women's heightened vulnerability to infectious disease beyond 42 days postpartum. Postpartum immune recovery and its effect on susceptibility to infectious disease is poorly understood, but normal cellular function may take 3–4 months to recover.[29] Sleep deprivation, lactation and recovery from labour and delivery drive a pro-inflammatory state[30] or 'immune reconstitution', which might contribute to an exacerbation of latent infection in the postpartum period. In sub-Saharan Africa in particular, the high prevalence of anaemia among women of reproductive age[31] might further increase susceptibility to infectious disease.

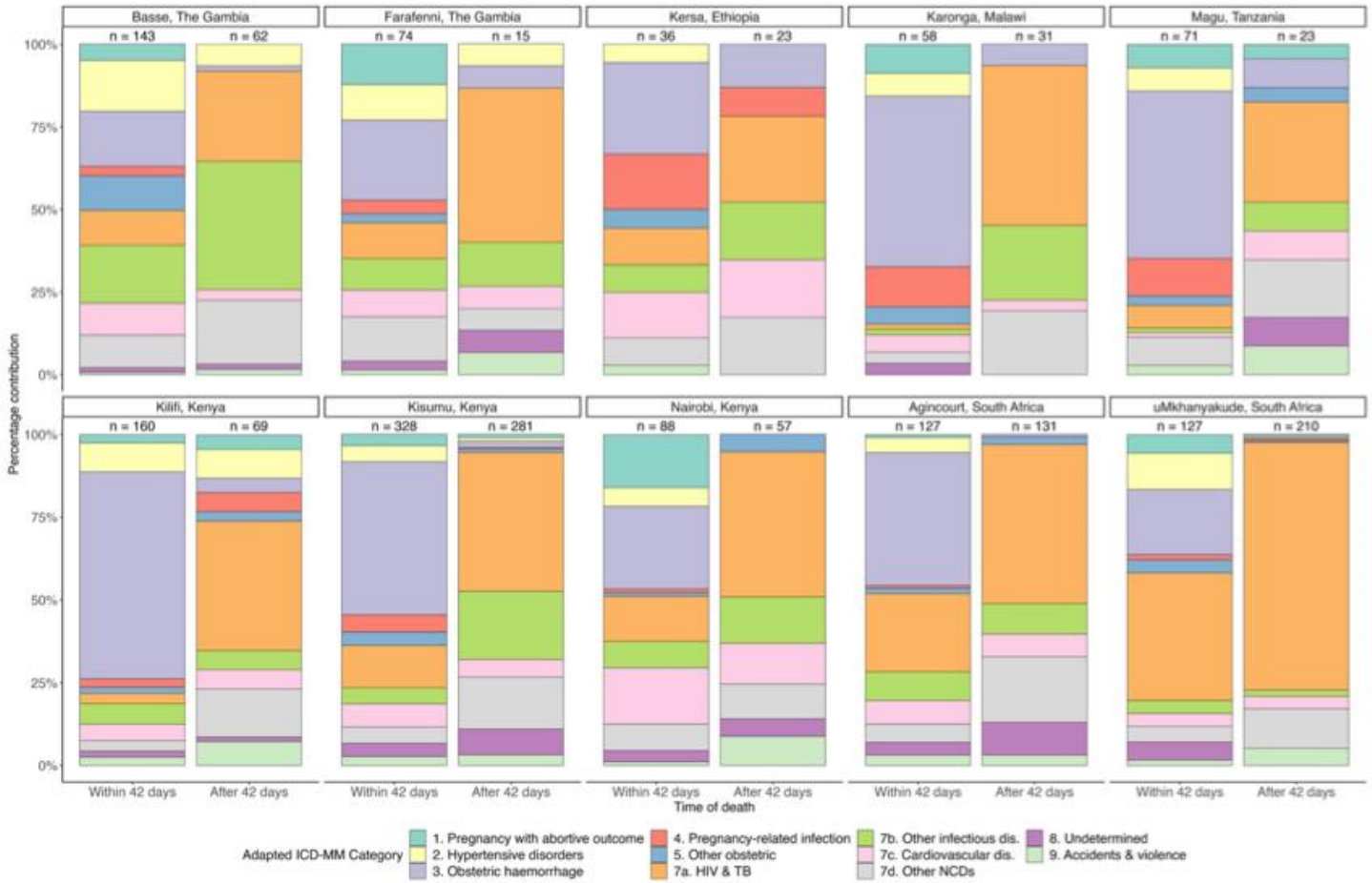

FIGURE 3 Cause of pregnancy-related deaths up to 1 year postpartum by timing and HDSS, InterVA5. *Note*: There were no deaths attributed to ICD-MM category 6. There were unanticipated complications of management, so this category is not shown.

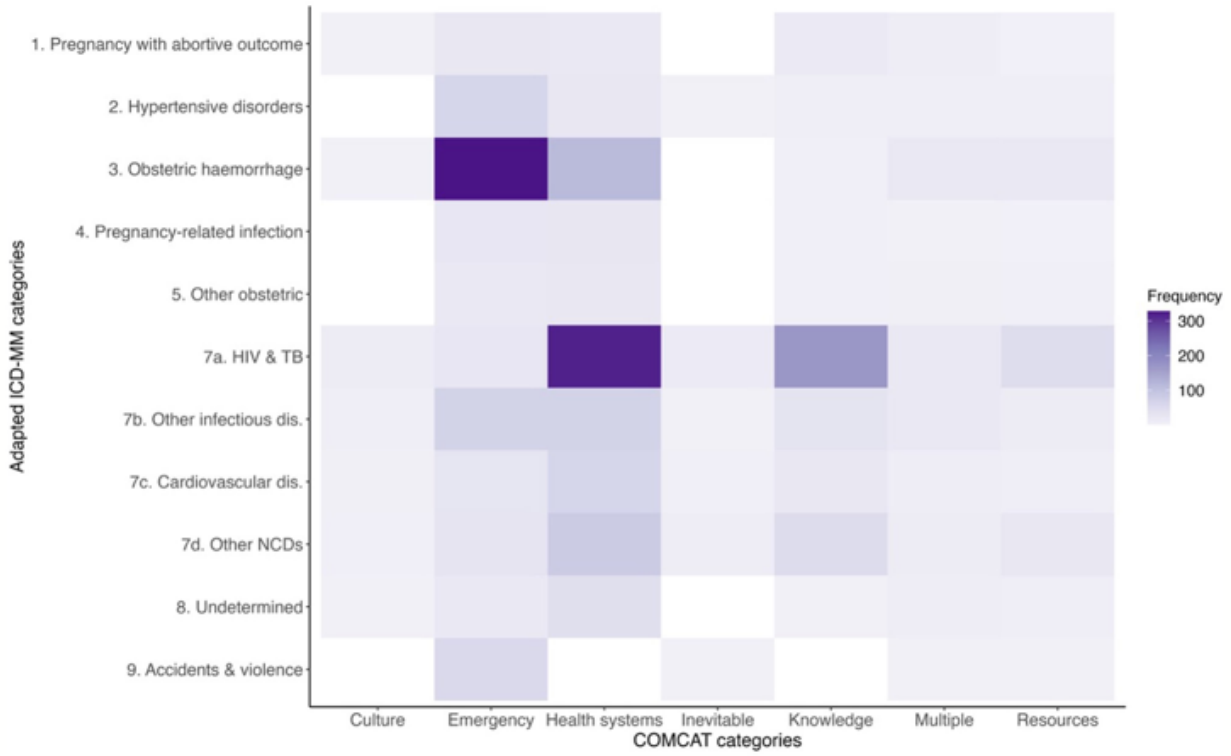

FIGURE 4 Circumstances of Mortality (COMCATs) by adapted ICD-MM category, InterVA5. *Note*: There were no deaths attributed to ICD-MM category 6. There were unanticipated complications of management, so this category is not shown.

There is a need for further research into women's vulnerability to infectious disease (and co-infection) during the extended postpartum period.[18] Though evidence is scarce, coincidental deaths from HIV during the postpartum period might be less likely because very sick women with advanced HIV infection are unlikely to get pregnant.[32] Rather, pregnancy might accelerate HIV progression, or HIV might cause heightened vulnerability to other postpartum complications. In the WHO maternal mortality estimation models, the fraction of pregnancy-related HIV deaths assumed to be HIV-related indirect maternal deaths (i.e. not coincidental) is 0.3.[7] There is an urgent need to update the evidence for this assumption and, in particular, its applicability to pregnancy-related deaths beyond 42 days postpartum. Pregnancy and postpartum recovery may also aggravate tuberculosis (co-)infection, through an acute worsening of active TB or an exacerbation of latent infection.[19,33] An increased risk of active TB may continue up to 6 months postpartum. Finally, available evidence on the women's susceptibility to malaria infection postpartum is contradictory[34,35] and even less is known about susceptibility to infection or its severity in the extended postpartum period.

5 | CONCLUSION

Infectious diseases are the predominant cause of late pregnancy-related deaths from 43 to 365 days postpartum, followed by NCDs, in Kenya, The Gambia, Malawi, Tanzania, Ethiopia and South Africa, and this was the case in both time periods (2000–2009 and 2010–2019). Further research is urgently required to understand women's potentially heightened vulnerability to infectious and non-communicable diseases in the extended postpartum period.

AUTHOR CONTRIBUTIONS

UG (guarantor): Conceptualisation, methodology, formal analysis, visualisation, writing – original draft. GR: Conceptualisation, methodology, writing – review and editing. JERP: Formal analysis, methodology, writing – review and editing. CC: Methodology, writing – review and editing. MJ, KH, SK, DO, DK, AD, MD, CWK, KK, MU, AN: Data acquisition & preparation, writing – review and editing. MT: Clinical interpretation, writing – review and editing. LAM: Clinical interpretation, methodology, writing – review and editing; PvD: Clinical interpretation, writing – review and editing. VF: Conceptualisation, methodology, interpretation, writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Each HDSS manages access to their microdata. Prospective users can apply for access to data for Karonga, Kilifi, Nairobi and uMkhanyakude from the HDSS online repositories and contact site managers at the remaining HDSS to request access. The data are not publicly available due to privacy or ethical restrictions.

ETHICS APPROVAL

This study was approved by the London School of Hygiene and Tropical Medicine ethical review committee (reference 26603, original approval date 13 December 2021; amendment approval date 5 June 23).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Chapter 5 Research paper 3

Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: a grounded theory of recovery trajectories beyond 42 days

Summary of chapter

In Chapter 5, I present the third paper of this thesis, as published in the BMJ Global Health. This includes the rationale for this study, a description of the PRECISE study setting and participant characteristics, Grounded Theory methodology, results and discussion.

Supplementary material for this paper is available in Appendix D. Please note, in the following typeset text, page references for supplementary tables and figures refer to the online appendices for BMJ Global Health rather than this thesis.

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Primary Supervisor	Professor Veronique Filippi		

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Where was the work published?	BMJ Global Health This work was published open access under a Creative Commons Attribution License (CC BY).		
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SECTION E

Student Signature	Ursula Gazeley
Date	1st July 2024

Supervisor Signature	Veronique Filippi
Date	1st July 2024

BMJ Global Health

Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: a grounded theory of recovery trajectories beyond 42 days

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ABSTRACT

Introduction The burden of severe maternal morbidity is highest in sub-Saharan Africa, and its relative contribution to maternal (ill) health may increase as maternal mortality continues to fall. Women's perspective of their long-term recovery following severe morbidity beyond the standard 42-day postpartum period remains largely unexplored.

Methods This woman-centred, grounded theory study was nested within the Pregnancy Care Integrating Translational Science Everywhere (PRECISE) study in Kilifi, Kenya. Purposive and theoretical sampling was used to recruit 20 women who experienced either a maternal near-miss event (n=11), potentially life-threatening condition (n=6) or no severe morbidity (n=3). Women were purposively selected between 6 and 36 months post partum at the time of interview to compare recovery trajectories. Using a constant comparative approach of line-by-line open codes, focused codes, super-categories and themes, we developed testable hypotheses of women's postpartum recovery trajectories after severe maternal morbidity.

Results Grounded in women's accounts of their lived experience, we identify three phases of recovery following severe maternal morbidity: 'loss', 'transition' and 'adaptation to a new normal'. These themes are supported by multiple, overlapping super-categories: loss of understanding of own health, functioning and autonomy; transition in women's identity and relationships; and adaptation to a new physical, psychosocial and economic state. This recovery process is multidimensional, potentially cyclical and extends far beyond the standard 42-day postpartum period.

Conclusion Women's complex needs following severe maternal morbidity require a reconceptualisation of postpartum recovery as extending far beyond the standard 42-day postpartum period. Women's accounts expose major deficiencies in the provision of postpartum and mental healthcare. Improved postpartum care provision at the primary healthcare level, with reach extended through community health workers, is essential to identify and treat chronic mental or physical health problems following severe maternal morbidity.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The burden of severe maternal morbidity on women, their families and health systems is significant.
⇒ Severe maternal morbidity increases the likelihood that women experience long-term adverse physical, mental, economic and social outcomes.

WHAT THIS STUDY ADDS

⇒ We develop a grounded theory of women's recovery following severe maternal morbidity based on women's accounts of their experience, represented by three themes of 'loss', 'transition' and 'adaptation to a new normal'.
⇒ This recovery is (1) multidimensional, affecting women's physical, mental, social, sexual and economic well-being; (2) cyclical across the female reproductive life course, from repeat pregnancies and recurrent episodes of maternal morbidity; and (3) protracted far beyond 42 days post partum.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Women's long-term, complex needs after severe maternal morbidity demand a reconceptualisation of the postpartum period of recovery as continuing far beyond 42 days after childbirth.
⇒ Women's postpartum experience after severe maternal morbidity highlights the need for better communication from healthcare workers about the morbidity event that women experienced; improved access to postpartum and mental healthcare at the primary healthcare level; and specialist care for chronic problems in the extended postpartum period.

INTRODUCTION

There is growing recognition that the focus of the global maternal health community should expand beyond survival.[1] For every woman who dies from a maternity-related

cause, maternal morbidity affects many more women, their families, communities and health systems.[2] As countries advance through the obstetric transition[3]—where maternal mortality declines and shifts from direct obstetric to indirect causes—the relative contribution of maternal morbidity to maternal ill health will continue to increase.

Adopting WHO terminology, severe maternal morbidity includes potentially life-threatening conditions (PLTCs) and maternal near-miss (MNM) events—life-threatening complications so severe that women would probably have died without receiving emergency obstetric care.[4] Severe maternal morbidity may occur before, during or after birth, and recovery post partum is physical, emotional, sexual, social and economic in nature. Although 'postpartum' is defined as the 42 days after birth, during which time the WHO recommends routine clinical contacts,[5] some women will not fully recover within this time frame. Compared to women with uncomplicated pregnancies, women who experience severe morbidity are more likely to experience adverse outcomes in the years following birth, such as chronic hypertension[6] or mental health problems,[7] economic hardship and sexual violence,[8] impaired functioning,[9] lower quality of life[10] and elevated mortality.[11] These women's needs may be diverse and context specific, requiring tailored packages of support after hospital discharge.[12]

There is a dearth of women-centred, in-depth research which seeks to understand women's lived experience of postpartum recovery beyond 42 days. An exclusive focus on clinical and biomedical aspects of postpartum recovery overlooks women's personal, interpersonal and cultural interpretation of their morbidity.[13 14] It is vital to understand the diverse ways that women may experience recovery from severe pregnancy-related morbidity, and how their experiences are shaped by individual, cultural and societal influences.[14]

This study aims to develop a grounded theory of women's experience of postpartum recovery trajectories after severe maternal morbidity in Kilifi County, Kenya—a theory which can be tested in other contexts and among different populations.

METHODS

The Consolidated Criteria for Reporting Qualitative Research checklist[15] guided the reporting of our methods (see online supplemental table S2).

Study design

Straussian grounded theory methodology, rooted in interpretivist ontology and epistemological contextualism,[16] was used to generate a new theory about women's recovery trajectories after severe maternal morbidity. Grounded theory is ideal for use when the evidence base is limited,[17] and it is an increasingly popular methodology for cross-disciplinary research on women's health.[13 18]

Setting

The study was conducted in Kilifi County, Kenya, which has a high burden of maternal morbidity, with facility-based MNM ratio estimates of 7.2[19]–10.4[20] per 1000 live births. In Kilifi, >80% of women deliver in a health facility; 83% of mothers receive a postpartum check during the first 2 days after birth; >50% have not been employed in the previous 12 months; >50% do not have drinking water on their premises; and only 12% of households have any form of health insurance.[21] Antepartum, intrapartum and postpartum care is provided through a government scheme ('Linda Mama') for women without health insurance. De jure postpartum services included in this scheme include analgesics, vitamin supplementation, family planning, sexually transmitted infection (STI) testing, insecticidal net provision, and treatment or referral for complications.[22]

This qualitative research was nested within the Pregnancy Care Integrating Translational Science Everywhere (PRECISE) multidisciplinary prospective cohort study in Kenya, designed to phenotype pregnancies in women with placental disorders in sub-Saharan Africa.[23 24] The PRECISE participating facilities in Kilifi County are Mariakani (semiurban) and Rabai (rural) Sub-County Hospitals. Both facilities now offer Comprehensive Emergency Obstetric and Newborn Care services, although Rabai offered only Basic Emergency Obstetric Care before 2022. Neither hospital has maternal intensive or high-dependency care units. Women requiring higher level care may be referred to the Kilifi County Teaching & Referral Hospital, if ambulances are available.

Participants

Three groups of participants (n=20) who were at least 6 months post partum were purposively selected, including women who experienced an MNM event (n=11); women who experienced a PLTC (n=6); and women who had no severe morbidity (n=3). The study timelines of the PRECISE cohort, which began enrolling women in November 2019, set the upper limit on how many months postpartum participants were at the time of interview. Purposive sampling was used to include women from diverse backgrounds (education, age, parity, type of morbidity, live birth/perinatal death, child health) and at different postpartum stages. Since the postpartum experiences of women who had experienced either an MNM or a PLTC were the primary research question, we kept the numbers of women with no maternal morbidity deliberately small. However, the women with no maternal morbidity were selected to reveal women's recovery trajectories in the absence of severe morbidity, to understand whether women experience commonalities in their postpartum recovery, despite morbidity.

MNM was defined by WHO standard criteria of organ dysfunction,[4] or modified criteria for low-resource settings (ie, Haydom[25] and Tura[26 27] criteria), as many of the WHO criteria were not applicable in the study sites. These modifications include some severe conditions and

interventions as sufficient for MNM. PLTC was defined by WHO criteria[4] (for detailed definitions of MNM and PLTCs, see online supplemental tables S3 and S4). Participant recruitment was iterative to explore emerging codes, super-categories and themes which required further validation (ie, theoretical sampling).

Table 1 presents participant characteristics for the 20 women interviewed.

Materials

The research team collectively reviewed and modified the semistructured interview guide in both English and Swahili, to ensure questions were accurately conveyed and culturally appropriate. The English interview guide is available in online supplemental table S3.

Data collection

Eligible participants were first invited to participate in the study, by telephone, by a PRECISE community engagement team member, with whom they were familiar. In person, before participation, interested individuals received detailed written and verbal information, which emphasised that participation is voluntary, they have a right to withdraw, to confidentiality, and to data anonymisation. One individual declined due to scheduling conflicts. All participants provided written informed consent.

Face-to-face interviews were conducted in Swahili (April to May 2023), by clinical and non-clinical, experienced qualitative researchers (MCO, NB, MB, AMK, GMa). Best practices for sensitive interviews were followed,[28] including a choice of private interview locations, conducted away from their partner. All participants chose to be interviewed at the facility. Some women brought their infants to the interview, to breastfeed or because of childcare constraints. 20 interviews were conducted, each lasting 35–70 minutes. There were no repeat interviews. Theoretical saturation was considered to have been reached when new data no longer provided additional insights, so that the resulting theory was adequately grounded in the data.[29]

Women were 6–36 months post partum at the time of interview to facilitate an analysis of recovery trajectories. Participants with ongoing physical or psychological problems were offered referral and counselling information. Five attended a group session with a psychotherapist following, but not as a result of, the interview; no women took up the offer of referral. Participants were reimbursed for transport costs and refreshments were provided. To support research staff, team members received two group debriefs with a trained psychotherapist during the data collection period.[28]

Data analysis and interpretation

With consent, interviews were audio recorded and transcribed verbatim in Swahili to preserve non-lexical elements capturing participants' emotions when talking. Transcripts translated into English were reviewed by bilingual team members (MCO, OW) for accuracy.

We followed an established approach to conducting grounded theory analysis[18] using inductive, 'bottom-up' coding derived directly from the data. First, transcripts were 'open coded' by hand to capture the phrase or word which best reflected each line of discourse. 'Open codes' were then grouped into focused codes applied to multiple sentences or whole paragraphs. Through a process of constant comparative analysis within and between transcripts and fieldnotes,[30] focused codes were aggregated into super-categories, and finally into themes. Relationships between themes were used to generate a grounded theory—a testable hypothesis derived from and grounded in the qualitative data. Data interpretation was an iterative exercise within the research team which continued until we reached consensus.

The lead researcher (UG) coded and analysed all transcripts. Two members of the research team (MCO, OW) coded and analysed a subset (20%) of the transcripts chosen purposively. When differences in interpretation arose, those of Kenyan researchers were prioritised, given their greater understanding of local context, including cultural customs in Kilifi.

Positionality statement

Our research team is multinational and multidisciplinary: of 14 coauthors, 9 are based in Kilifi, 8 are Kenyan nationals and 6 have a clinical background (further detail is available in our Reflexivity Statement in the online supplemental file 2). As a combination of cultural insiders and outsiders, we were able to leverage both groups' strengths in conducting qualitative research, with adequate scrutiny of potential insider-outsider biases.[31] Each interviewer kept fieldnotes to document their experience of the interview, including participants' emotional responses to interview prompts. These memos were triangulated with the transcripts to better capture the full contextual picture of participants' responses. We adopted a relative approach to reflexive judgement, considering how our perspectives and biases (subjectivity) are relative and historically situated within the broader social, cultural and contextual factors of the study. This recognises reflexivity as a continuous process and was implemented through cross-team discussions during tool design, data collection, analyses and interpretation.

RESULTS

The following three themes emerged from interconnected super-categories and represent women's experience of recovery following severe maternal morbidity throughout the extended postpartum period:

1. Loss: (a) of understanding, (b) functioning and (c) autonomy.
2. Transition: (a) in identity and (b) relationships.
3. Adaptation: (a) physical, (b) psychosocial and (c) economic recovery beyond 42 days.

Table 1 Participants' background characteristics

Participant code	Age group at enrolment	Relationship status at enrolment	Occupation at enrolment	Parity at enrolment	MNM criteria* met	Morbidity, intervention and organ dysfunction (WHO only)	Delivery type	Months between childbirth and interview
MNM and neonatal death								
Woman 1	40–44	Married	Market trader	Nulliparous	WHO, Haydom and Tura	Severe pre-eclampsia; hepatic dysfunction	Caesarean	24
Woman 2	20–24	Single	Professional services	Nulliparous	Tura only	Severe sepsis	Unassisted vaginal without episiotomy	16
MNM and live birth								
Woman 3	15–19	Cohabiting	Housewife	Nulliparous	Haydom and Tura	Severe PPH; RBC transfusion	Caesarean	6
Woman 4	25–29	Married	Professional services	1	WHO, Haydom and Tura	Severe pre-eclampsia; hepatic dysfunction	Unassisted vaginal without episiotomy	24
Woman 5	20–24	Single	Student	Nulliparous	WHO, Haydom and Tura	Eclampsia; hepatic and neurological dysfunction	Caesarean	24
Woman 6	30–34	Married	Housewife	3	Tura only	Severe pre-eclampsia and pulmonary oedema	Unassisted vaginal with episiotomy	30
Woman 7	35–39	Married	Factory worker	4	Haydom and Tura	Eclampsia	Caesarean	24
Woman 8	30–34	Married	Small business owner	3	Haydom and Tura	Severe sepsis	Unknown	28
Woman 9	25–29	Married	Casual labourer	1	WHO, Haydom and Tura	Severe pre-eclampsia; haematological dysfunction	Unassisted vaginal without episiotomy	5
Woman 10†	35–39	Married	Market trader	4	WHO, Haydom and Tura	Blood transfusion; respiratory dysfunction	Caesarean	15
Woman 11‡	30–34	Married	Housewife	2	N/A	Retained placenta; PPH; emergency referral	Unassisted vaginal without episiotomy	36
Woman 12	25–29	Married	Housewife	10	Haydom and Tura	Ruptured uterus	Unassisted vaginal without episiotomy	36
Woman 13	25–29	Married (polygamous)	Housewife	2	Tura only	Severe pre-eclampsia; laparotomy	Unassisted vaginal without episiotomy	15
Woman 14	30–34	Married	Retailer	1	Haydom only	Severe PPH; RBC transfusion; laparotomy	Unassisted vaginal with episiotomy	10
PLTC and stillbirth								
Woman 15	35–39	Single	Housewife	1	N/A	Severe pre-eclampsia	Caesarean	6
PLTC and live birth								
Woman 16	15–19	Married	Housewife	Nulliparous	N/A	Severe PPH	Unassisted vaginal without episiotomy	20
Woman 17	30–34	Married (polygamous)	Housewife	Nulliparous	N/A	Severe pre-eclampsia	Unassisted vaginal without episiotomy	13
No severe morbidity								

Continued

Table 1 Continued

Participant code	Age group at enrolment	Relationship status at enrolment	Occupation at enrolment	Parity at enrolment	MNM criteria* met	Morbidity, intervention and organ dysfunction (WHO only)	Delivery type	Months between childbirth and interview
Woman 18	15–19	Single	Student	Nulliparous	N/A	N/A	Unassisted vaginal without episiotomy	17
Woman 19	25–29	Married	Professional services	Nulliparous	N/A	N/A	Unassisted vaginal without episiotomy	16
Woman 20	30–34	Married	Housewife	2	N/A	N/A	Unassisted vaginal without episiotomy	14

*Further detail can be found in online supplemental tables S3 and S4. For WHO criteria, please refer to Say *et al*[4]; for Tura criteria for sub-Saharan Africa, please refer to Tura *et al* (2017); for Haydom criteria, please refer to Nelissen *et al*.[26]
†For this participant only, we identified child developmental problems—measured using the Malawi Developmental Assessment Tool (MDAT).
‡This participant's medical records were mostly missing because she delivered when PRECISE data collection was suspended due to COVID-19 regulations in 2020. During her interview, she described experiencing a retained placenta, severe haemorrhage, loss of consciousness and an emergency referral to Mariakani Hospital. She was admitted to hospital for 4days, which was longer than most women in our sample. We therefore considered this participant in the MNM group.
MNM, maternal near miss; PLTC, potentially life-threatening condition; PPH, Postpartum haemorrhage; PRECISE, Pregnancy Care Integrating Translational Science Everywhere; RBC, Red blood cell.

Figure 1 presents the conceptual mapping of these themes and super-categories and illustrates how recovery may be non-linear and cyclical (in the case of repeat pregnancy).

Illustrative quotations are found by way of analysis below, but additional supporting quotations for refined super-categories and themes can be found in online supplemental table S5.

Theme 1: loss

Women described multifaceted dimensions of 'loss' which incorporated both biomedical dimensions of a MNM or PLTC (ie, loss of blood or consciousness, or their baby's death), but also psychosocial dimensions (ie, loss of understanding of her health, functioning or autonomy).

Loss of understanding (of her own health)

Women's comprehension about the causes, consequences and treatment of their PLTC or MNM event varied greatly. While some women received and understood explanations from doctors, nurses or midwives, others received explanations they did not understand, and many women did not recall receiving any explanation from providers involved in their care. Lack of understanding affected women's ability to process their experience, compounded trauma and silenced their experience. For some women, this exacerbated confusion over whether postpartum symptoms were 'normal', and eroded trust in the healthcare services. The need to improve providers' health communication emerged as a key recommendation for improved quality of care:

> They didn't tell me anything. They said you are badly torn inside, I heard that only reaching the theatre. I couldn't tell how I got there. I don't know what happened… I would like to ask because now I can talk and say 'mmmh what was done to me, was it surgery or what?' I mean I don't know… I gave birth in the hospital, but I can't really tell what happened. That's the area to be improved, like they should at least write a report so that even if they won't tell the patient, whoever comes in the morning can read the report. Like in my case, whenever I touched inside I could only feel strings but I didn't know anything and I didn't know who I could ask. (Woman 12)

Women whose severe morbidity coincided with stillbirth or neonatal death also received poor communication, particularly around the cause of their babies' death:

> Upon giving birth, they never explained what had transpired, I was just discharged. I went home, and I haven't been called. (Woman 2)

However, for one woman whose baby died, her feelings towards understanding the biomedical causes were more complicated, and intertwined with spiritualism and fatalism:

> Aaa I don't want to know [what happened] because that won't bring back my baby to the world. The baby did not die in anyone's stomach, he died in my own stomach, and

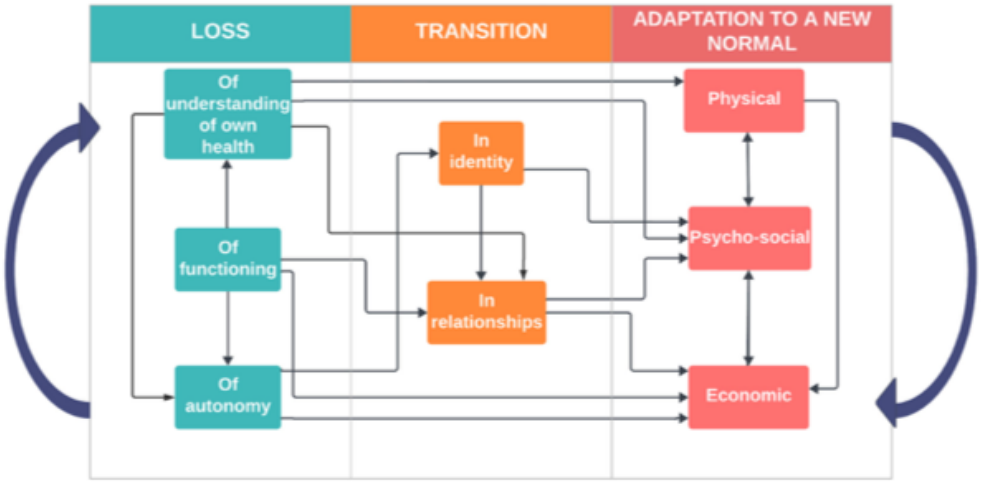

Figure 1 Conceptual mapping of grounded theory: 'Loss', 'transition' and 'adaptation to a new normal'.

> God himself is the one who knows why he took the child. Neither me nor the doctor knows. (Woman 15)

For some women, the severe morbidity they experienced coincided with a loss of consciousness or distorted memory. In these cases, the channel of communication first between the health worker and birth companion, and later between companion and women themselves, was critical for women to understand what happened. It was common in Kilifi for women to be accompanied to the facility by a female family member (typically her mother or mother-in-law), rather than her partner. However, a few women saw the absence of their partner as key to their poor understanding, and held him accountable:

> I was told he [the doctor] used to explain but there was a time I had lost my memory…I left crying and told my partner 'I went through a difficult situation and I escaped death, but you [her partner] failed to explain to me.' (Woman 7)

> It bothers me because I don't know what procedures were done to me. You see and I insist a lot, if my partner would have been there, then he's have known if his wife had been taken to theatre and known what was done to her. (Woman 12)

Loss of functioning

All women in our sample experienced a loss of functioning across multiple physical and psychosocial domains during the (extended) postpartum period which compromised their ability to carry out daily activities. This was typically more protracted for women with severe morbidity, and in some instances impaired their ability to care for their new baby:

> I cried… because I asked myself which situation is this? The child is required to be carried, me myself I cannot sit well… just give me strength God remove all these difficult situations so that I can at least carry my child. (Woman 13)

Loss of physical and cognitive functioning was at times profound enough that women experienced dissociation from their body:

> I was feeling a lot of pain… I didn't understand my body. I felt I couldn't do anything. (Woman 3)

A loss of functioning at times caused social isolation in the extended postpartum period:

> I couldn't meet up with people. I used to lock myself up in the house, because you can go to that place but maybe it is an activity now you cannot do, so I wasn't getting out of the house. (Woman 14)

An inability to carry out daily tasks was a cause of anxiety for women and their partners. While some partners responded to women's loss of functioning with love, empathy and a willingness to help, it was common for women to express sadness and disappointment at their partners' response. In some relationships, this led to conflict:

> He told me 'You should go and help mother', I would tell him 'Aaa right now I don't have strength to help mother, it will reach a time that I will help her' so he was just getting angry. (Woman 14)

With only a few exceptions, it was women's mother or mother-in-law who played the most substantial role in the provision of household and personal care during the (extended) postpartum period, often for many months. This reflects gendered expectations of support deemed to be a woman's role, but also practical considerations—with many partners working away from home (eg, in Mombasa), and perceived benefits of learning from mothers' first-hand experience of pregnancy and postpartum recovery:

> She [her mother-in-law] supported me well. She used to take care of the baby. As a first-time mother I didn't know

how to bathe a baby, but she did all that for me. (Woman 19)

Women's and/or their families' expectations of partners post partum primarily related to financial support. However, in a few cases, especially where maternal support was unavailable (mother was deceased or living far away), partners were more closely involved in the provision of household and personal care. Conversely, for single mothers or where the event precipitated the breakdown of the relationship, refusal of the baby's father to provide financially for the baby meant their own mothers often assumed roles as both caregiver and financial provider:

After delivery I had broken up with my partner. My mother was the one helping me with pampers, everything that the baby needed my mother was the one providing, everything—pampers, clothing, basins, and everything. She used to support in food also washing the baby and looking after me. (Woman 9)

Loss of autonomy

A loss of functioning affected women's autonomy to choose where, and from whom, she received care. For some, this meant living with their mother or mother-in-law for several months, at times, against her wishes. While this postpartum loss of autonomy is evident among all women in our sample, it affected women with severe morbidity more acutely, as she was expected to stay away to recover for longer:

I was upset because they forced me to go there [to the mother-in-law's] and there was no way I was going to stay with them. He [the participant's partner] forced me to go there… When the child started to sit, I came back to my place. (Woman 16)

For some women who were in paid work, pregnancy initiated a loss of financial autonomy, particularly for women working in the informal sector without maternity leave entitlement. Disruption in formal employment was typically more protracted for women with severe morbidity:

[Before the event] I was working and my partner was working too. I was used to catering to my own needs, so it was a challenge because I was not used to depending on him for everything. It was difficult for me to ask him for the children's needs… Sometimes I was even afraid to ask him because I thought he had no money. (Woman 7)

Theme 2: transition

In identity

As part of a normal postpartum course, pregnancy precipitated complex transitions in women's identity. For younger mothers, the birth of a child signified her own transition from childhood to adulthood. Many women expressed happiness at their transition to motherhood (for nulliparous women) or to a larger family size (for parous women):

I am just happy when I see my baby. Honestly the baby is my source of happiness… I feel at peace with my baby. (Woman 16)

Particularly after earlier pregnancy losses, the birth of a first child fulfilled some families' perceptions that the woman had finally become a 'true' wife.

When they [her partner's family] heard I lost the first pregnancy they started to say, 'she is not a wife, she is just playing, she is playing with your mind' so when I got this one [first live birth] even if it really hurt me they themselves told me 'Now come home we know now that you are a wife.' (Woman 14)

For women whose child died, and who had no surviving children, the loss led to complicated feelings towards motherhood and their identity as a woman:

Among mothers I was being referred to as a mother, but I felt like my womanhood wasn't complete without a child. (Woman 1)

In relationships

Severe maternal morbidity initiated multifaceted transitions in women's relationships, especially with their partner. For many women, it affected their desire for sexual intimacy in the extended postpartum period:

I was afraid I was going to get pregnant again, and afraid of seeing death come back. (Woman 6)

Some women preferred delaying sexual intimacy for emotional and physical healing post partum. While some partners were understanding, others were not, and one resorted to coercive behaviour to resume sex:

'If affected him because he wanted us to do the act of marriage and I couldn't because I was worried he can make those stitches tear, when they open I would have to be stitched again, or he can make us get another baby when this child is still young.' [After how long did he ask you?] 'Just two weeks' [Okay and how did he feel?] 'He got very angry… he got angry until he said, 'I will marry another woman.' (Woman 14)

The experience of severe maternal morbidity also affected women and their partners' plans for their future family size, although the impact on fertility intentions was sometimes discordant within couples. Motivated by a need to regain strength after the event, many women expressed a desire to space or postpone future childbearing:

I should take a rest. I am not thinking about having another baby until this baby reaches the 5 years, then I will see. [Why?] The pain I felt. (Woman 11)

Some women expressed a desire to stop childbearing altogether:

I said this should be the last born, I won't give birth again. Because of economics and the problem [morbidity] I went through. (Woman 8)

As witnesses to the event and their wife's long postpartum recovery, some partners changed their attitudes towards future pregnancies:

> I am not worried. The worries were left to my partner maybe, to me I did not have any problem. When he saw the report about the pressure, and when he remembered the previous miscarriage, let's say the truth is it hurt him mentally…he said he did not wish us to have another baby. (Woman 4)

For two nulliparous women whose child did not survive, anxiety around childbearing differed depending on whether she conceived again – fear that the baby who died was the only one they would ever have, or fear that their next baby would also die:

> Maybe I have the problem that I was privileged with that one child, we won't know where the problem is. Pressure is on both sides [to conceive again]. (Woman 2)

> When I got pregnant for the second time, I was afraid… will my child live or die. (Woman 1)

Finally, the impact of severe maternal morbidity on the stability of women's relationships differed depending on whether their baby survived. For some couples with a surviving baby, the baby was a source of joy that helped redefine aspects of their relationship, and cope with other challenges surrounding recovery from morbidity:

> It [my life] has changed a lot. There has been happiness inside the house. It has been filled with happiness… When he comes and hears his child calling him, then there is happiness. At first, he would come home angry, very angry. But now he sees my child, and when you ask something from him, he does not hesitate to bring it to you. (Woman 14)

However, under strain from unwanted pregnancy, acute and chronic morbidity, social destabilisation or bereavement, it was not uncommon for women to experience the breakdown of their relationship post partum. For two couples whose baby died, their grief and a lack of understanding of the reasons for their baby's death led to suspicion and allegations that eroded the foundations of their relationship:

> After the birth, he had changed. As for care, let's just say, I didn't really experience any at all. After the burial, he went back home, continued working and just like that we were not on good terms as partners…he started laying accusations that I had killed the child. He said, 'There's no way a child can just pass on like that, he was born healthy, I am sure you killed that child. Period.' (Woman 2)

Theme 3: adaptation to a new normal

Women's lives were profoundly affected by severe maternal morbidity, and for three women, the double hardship of morbidity and bereavement. Recovery during the extended postpartum period entailed adaptation to a new normal rather than a return to their pre-pregnancy and premorbidity selves. Although many women expressed gratitude to healthcare providers for the intrapartum care that likely saved their life, most received little clinical care for chronic physical, psychological or sexual health problems in the extended postpartum period. Some women were invited for postpartum visits at the hospital or primary health centre but could not afford to go back. Only one woman received a home visit from community health workers, and for most women, leaving the hospital marked the end of their medical care. Rather, women employed various coping mechanisms to navigate ongoing challenges and rebuild their lives. The duration of this adjustment period varied, with no set time frame and many women still experiencing difficulties at the time of the interview. Dimensions of adaptation to a new normal are discussed below.

Physical adaptation

Women described their physical recovery in the extended post partum primarily in relation to adapting to their postpartum body. This was described as regaining functioning to resume household responsibilities, and/or the absence of pain, rather than a return to their pre-pregnancy and premorbidity physical state. Women often invoked their ability to carry water again, especially after a caesarean:

> Let's say the energy I had from the beginning now it's like my health has gone a bit down. After three months I was fine, I could carry water, and now I can carry up to ten jericans without feeling pain. (Woman 17)

For all women, with and without severe maternal morbidity, regaining functioning took significantly longer than 42 days post partum. The duration women reported ranged from 3 months to 12 months and was typically more protracted for women who experienced severe morbidity:

> I am back to normal though sometimes I get body aches, I feel my entire body aching, but I assume it's normal. It [physical recovery] took time, around nine months. (Woman 16)

Psychosocial adaptation

Women's emotional recovery after severe morbidity often meant managing persistent or prolonged postpartum mental health challenges.

> If I remember the thoughts, especially the delivery situation, and the bad situation I was in with my child…. Let's just say the thoughts are still there. They are still running in my mind, they haven't ceased. (Woman 10)

For several women, fragmented memories of the complication or MNM event caused distress. Attempting to suppress traumatic memories was a common coping strategy:

> I just erased them… I knew if I think of them continuously, they will confuse me. (Woman 3)

To manage chronic postpartum mental health challenges, some women focused on the health and needs of their child. For three women who experienced suicidal ideation during the postpartum period, their surviving children helped moderate those thoughts:

I was thinking I should just kill myself, what good do I have. But when I look at my children I say aaa when I kill myself who will remain with them. (Woman 14)

However, all women whose baby did not survive or had developmental problems expressed chronic distress. These women continued to endure grief from bereavement or child ill health:

So I've been asking myself why? Why did he [God] do that to me? Having stayed so long without a child just to kill my child, did he deem me unfit to take care of a child or I was to beg him to help me raise my child. That's what has been bothering me and it stressed me out. (Woman 1)

I don't have peace like in the beginning… the women I had given birth with have their children. I have no peace at all. I have no peace at all. (Woman 2)

Until I witness my child walking, that's when some of these thoughts will disappear, but until then, when I look at the baby I still remember. (Woman 10)

Although women's ongoing physical health problems, poor child health outcomes or bereavement following severe maternal morbidity were common triggers for chronic postpartum mental health problems, some women without severe morbidity also experienced symptoms of postpartum depression. Their accounts exposed significant deficiencies in postpartum mental healthcare and a lack of recognition from women's social networks:

It took me time [to recover] and I wasn't getting help. I'm trying to tell someone that I have a problem, but I don't know how people treat postpartum depression. At home people think it's a white man's problem, you see?…There was a time I thought I would die because when this child was crying when he was small I felt like things were crying in my mind until I knock myself on the wall. (Woman 20)

For this participant, social isolation in the extended postpartum period was an adaptive strategy used to conceal ongoing mental health challenges:

I needed alone time and didn't want to reveal anything to anyone because I was like this, and they could not understand. If anyone would ask for anything from me, I would chase them away, and shout at them, I didn't want them to see me and say 'That one has changed.' (Woman 20)

Economic adaptation

Many women had to adapt financially to the economic shocks of out-of-pocket antepartum, intrapartum and postpartum care. The costs associated with severe morbidity were unplanned, and many couples did not have the financial capacity to withstand these costs without resorting to loans or limiting treatment:

It is something you don't plan for so it's a challenge. Maybe they might ask for money that you don't have, then you are forced to ask for loans from your friends, for you to solve the problem…I wasn't able to buy medicine because my partner was looking out for money. He would tell me, 'buy half the dose and finish the rest the next day.' (Woman 12)

However, among many women who experienced morbidity, especially single mothers, women highlighted the effect of motherhood and exit from the labour market on her economic recovery, more than the morbidity per se. Adapting often meant finding ways to resume paid employment:

I had to close it [grocery business] because I had no one to take care of the baby… My hope is for my baby to grow fast for me to get back into my hustles. (Woman 6)

DISCUSSION

Based on in-depth interviews with 20 women in Kilifi, Kenya, we provide evidence suggesting women progress through three phases of recovery after severe morbidity represented in the themes 'loss', 'transition' and 'adaptation to a new normal'. Our grounded theory posits that this phased postpartum recovery process is (1) multidimensional; (2) cyclical across the female reproductive life course, through repeat pregnancies and recurrent episodes of maternal morbidity; and (3) protracted, far beyond 42 days post partum. These features of the recovery process support Filippi *et al*'s conceptual framework for maternal morbidity[32] and recent reconceptualisations of postpartum vulnerability.[33 34]

Our grounded theory was developed based on the accounts of women with severe maternal morbidity, as well as three women who experienced the double hardship of severe maternal morbidity and perinatal death, and three women who experienced neither severe maternal morbidity nor perinatal death. This allowed us to test the limits of our theory and its applicability to women with different experiences. First, women whose severe morbidity coincided with the death of her baby experienced all features of 'loss', 'transition' and 'adaptation to a new normal', with this double burden profoundly affecting all areas of their lives. However, unlike women whose baby survived the complication, 'adaptation' focused on coping with grief, and recovery from morbidity became a secondary concern. Second, although based on a small sample, women without severe morbidity shared most, but not all, core experiences of 'loss', 'transition' and 'adaptation to a new normal', but not to the same degree. This suggests that severe maternal morbidity exacerbates and accelerates changes in women's lives associated with childbearing more generally.

Finally, often presenting the first opportunity for women to discuss their experience after severe maternal morbidity, women's accounts tended to focus on what they found challenging in the extended postpartum period, with few women divulging more positive experiences. Our analytical focus on these accounts should not obscure that positive and negative experiences can coexist during recovery from severe maternal morbidity.

Loss

Women with severe maternal morbidity encountered multifaceted losses in the extended postpartum

period.[35–37] Distorted memory after the event, when exacerbated by inadequate communication from healthcare providers and the absence of her partner at key treatment stages, affected women's understanding of their morbidity and whether postpartum symptoms were 'normal'. Prolonged and severe loss of functioning necessitated reliance on familial support for chores, personal care and childcare for many months,[35] mainly from their mother/mother-in-law.[38] Partners' postpartum support was often primarily financial,[38] leaving some women saddened at a lack of emotional support. Finally, for some women, severe maternal morbidity precipitated a loss of autonomy over decisions related to their care and increased financial dependence on their partner.

Transition

The experience of pregnancy, severe maternal morbidity and, in some cases, perinatal death precipitated complex transitions in women's identity as a woman, a partner and a mother. The transition to motherhood for nulliparous or to a larger family for parous women often brought joy and happiness that at times coexisted with more negative experiences. Challenges during pregnancy, delivery and the post partum initiated transitions in family structures and in women's relationships with her partner.[39] Relationship breakdowns were often linked to conflicts over partner support and empathy for ongoing physical, mental and sexual health problems. Many women whose child survived the event expressed a desire to space, postpone or stop future childbearing.[40]

Adaptation

Postpartum recovery after severe maternal morbidity required women to adapt to a new normal state, rather return to their pre-pregnancy and premorbidity selves. Physical recovery focused on regaining functioning to resume household tasks and/or the absence of pain, took all participants far longer than the 42 day postpartum period and was longer for women who had experienced severe morbidity.[6] Psychosocial adaptation required women to deploy their own coping mechanisms[35] to manage chronic postpartum mental health problems, and for three women with perinatal death, cope with grief.[41] High out-of-pocket treatment costs and loss of paid employment demanded adaptive coping strategies to withstand, such as halving doses or sourcing loans.

Implications for research, policy and practice

Women's accounts of their lived experience of postpartum recovery after severe maternal morbidity in Kilifi, Kenya, exemplify deficiencies in the provision of intrapartum and postpartum care. First, improved communication between providers, women and their families about the morbidity experienced, treatment received and aftercare required before hospital discharge, is important for recovery and retaining trust in health services.[42] Second, with many women unable to afford to return to the hospital for routine postpartum care,[35 39 43] provision must be improved at the primary healthcare level with community health workers to extend its reach.[44 45] Women who experienced severe maternal morbidity (and their children who survived) may also face chronic mental and physical health outcomes that require referral to specialist services in the extended post partum.[46 47] With care required in some cases for many months, or even years post partum, improving outcomes for women who experienced severe morbidity is an important consideration for universal health coverage. Finally, women's descriptions of mental health disorder after severe morbidity and/or perinatal death are consistent with the high prevalence of postpartum depression in other regions of Kenya and depict a mental healthcare system in Kilifi County that is yet to be fully fit for purpose.[48–50] Perinatal mental health support must be integrated within maternal and child health services,[51] with its own budget allocation[48 52] to improve its accessibility and acceptability within communities.

Strengths and limitations

Strengths lie in the inclusion of women from diverse backgrounds (education, age, parity, type of morbidity, live birth/perinatal death, child health), to better capture the diversity of postpartum experience. As we were unable to interview women more than once during their postpartum period, we included participants at different postpartum stages at the time of interview to better understand recovery trajectories over time. The inclusion of two additional subpopulations—of double hardship (morbidity and perinatal death) and women without severe morbidity—helped test the limits and validity of our grounded theory. Finally, our multidisciplinary and multinational team provided a broader epistemic lens.

Our study has limitations. First, our grounded theory derives from the experiences of a small group of women with a varied set of morbidities and requires validation in other populations. Further, some of the most critically ill women could not be included in our study if they were referred to higher level tertiary facilities. These women may have had worse experiences, and their recovery trajectories may differ. Second, we were unable to fully explore the effect of child developmental outcomes on women's social, emotional and economic recovery and this requires further research. Third, due to competing workloads in the research team, five individuals conducted the interviews. Differences in interviewers' gender, age and (non-)clinical background may have introduced some heterogeneity in interview style and women's responses. Finally, it was not possible to analyse transcripts concurrently with data collection, and we relied on team debriefs and field memos to assess theoretical saturation.

CONCLUSION

Our grounded theory reaffirms the need for research, policy and practice to reconceptualise the postpartum period as extending far beyond 42 days, to better reflect the time needed for women to recover, particularly after severe maternal morbidity.[46] Further research is required to validate our grounded theory in other contexts and provide a richer picture of women's postpartum recovery after severe morbidity in other settings.

Patient and public involvement

Patients were not included in the design of this study and were not directly involved in the review of transcripts or results. However, with open-ended sections of the interview tool, and prompts for participants to discuss anything else they wanted to share, the data collected were informed by their priorities, experience, and preferences. A panel of maternal health experts, including researchers based in Kilifi, ratified the study objectives, design, and the interview schedule. Our findings were presented at the Kilifi County 2nd Scientific Symposium for feedback from Kilifi-based health workers.

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Chapter 6 Research paper 4

Lifetime risk of maternal near miss morbidity: a novel indicator of maternal health

Summary of chapter

In Chapter 6, I present the fourth paper of this thesis, as published in the International Journal of Epidemiology (IJE). This includes the need for new metrics of maternal morbidity, development of the new indicators, demonstration for Namibia, and discussion.

Supplementary material for this paper and an accompanying IJE blog post I wrote are available in Appendix E. Please note, in the following typeset text, page references for supplementary tables and figures refer to the online appendices for IJE rather than this thesis.

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Student ID Number	2005281	**Title**	Ms
First Name(s)	Ursula		
Surname/Family Name	Gazeley		
Thesis Title	Advances in the conceptualisation and measurement of maternal morbidity and mortality		
Primary Supervisor	Professor Veronique Filippi		

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SECTION B – Paper already published

Where was the work published?	International Journal of Epidemiology This work was published open access under a Creative Commons Attribution License (CC BY).		
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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I proposed the idea for this new measure of maternal near miss morbidity. I developed the methodology, wrote the code, prepared the visualisations, and wrote a complete first draft of the paper for co-authors to review. I led the submission process to IJE and the responses to reviewers.

SECTION E

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Lifetime risk of maternal near miss morbidity: a novel indicator of maternal health

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Abstract

Background: The lifetime risk of maternal death quantifies the probability that a 15-year-old girl will die of a maternal cause in her reproductive lifetime. Its intuitive appeal means it is a widely used summary measure for advocacy and international comparisons of maternal health. However, relative to mortality, women are at an even higher risk of experiencing life-threatening maternal morbidity called 'maternal near miss' (MNM) events—complications so severe that women almost die. As maternal mortality continues to decline, health indicators that include information on both fatal and non-fatal maternal outcomes are required.

Methods: We propose a novel measure—the lifetime risk of MNM—to estimate the cumulative risk that a 15-year-old girl will experience a MNM in her reproductive lifetime, accounting for mortality between the ages 15 and 49 years. We apply the method to the case of Namibia (2019) using estimates of fertility and survival from the United Nations World Population Prospects along with nationally representative data on the MNM ratio.

Results: We estimate a lifetime risk of MNM in Namibia in 2019 of between 1 in 40 and 1 in 35 when age-disaggregated MNM data are used, and 1 in 38 when a summary estimate for ages 15–49 years is used. This compares to a lifetime risk of maternal death of 1 in 142 and yields a lifetime risk of severe maternal outcome (MNM or death) of 1 in 30.

Conclusions: The lifetime risk of MNM is an urgently needed indicator of maternal morbidity because existing measures (the MNM ratio or rate) do not capture the cumulative risk over the reproductive life course, accounting for fertility and mortality levels.

Keywords: Maternal health, maternal near miss, maternal morbidity, maternal mortality, lifetime risk, demographic methods.

Introduction

The lifetime risk of maternal death (LTR-MD) is a widely used summary measure of maternal health. As most commonly measured, this denotes the probability of that 15-year-old girl will die from a maternal cause in her reproductive lifetime, accounting for other competing causes of mortality.[1] Its intuitive appeal means it is used to compare differences between countries and changes over time in World Health Organization (WHO) and United Nations agency joint maternal mortality estimates.[2] However, maternal deaths are just the tip of the iceberg of poor maternal health outcomes. For every woman who dies from a maternal cause, as many as 20 women may experience a life-threatening 'maternal near miss' (MNM) complication,[3] defined as a 'woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy'.[4] For the WHO definition, cases are identified based on clinical, laboratory and management-based criteria of organ dysfunction; these criteria are selected such that women would die without emergency care in hospitals.[4]

Substantial reductions in maternal mortality have occurred in the last two decades[2] as countries advance through the obstetric transition—the secular shift from high to low maternal mortality and direct obstetric to indirect causes of maternal death.[5] Expansions in access to and improvements in the quality of emergency obstetric care mean that many more women who experience a life-threatening complication now survive pregnancy and the immediate 42-day post-partum period.[5] The ratio of MNM cases to maternal deaths can be interpreted as a measure of the quality of obstetric care: the higher the ratio, the better the capacity of a health system to manage obstetric emergencies.[4] Nonetheless, experiencing a complication of this severity may have significant sequelae far beyond 42 days post-partum, including for women's long-term survival, physical and mental health outcomes, and ability to perform economic and social functions.[3,6–11] Given the substantial relative contribution of maternal morbidity to adverse pregnancy outcomes, better indicators are needed for maternal health monitoring and advocacy.

Analogous to the concept of LTR-MD, we propose a new indicator—the lifetime risk of MNM (LTR-MNM)—to measure the probability that a 15-year-old girl will experience a

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Key Messages

- The global burden of life-threatening maternal near miss (MNM) complications is higher than the burden of maternal death.
- Analogous to the concept of lifetime risk of maternal death (LTR-MD), we propose a new measure of MNM morbidity—labelled the 'lifetime risk of maternal near miss (LTR-MNM)'—to estimate the cumulative risk of MNM morbidity across the female reproductive life course.
- The LTR-MNM is a novel indicator that estimates the probability that a 15-year-old girl will experience a life-threatening maternal complication during her reproductive lifetime.
- The LTR-MNM is needed because no existing measure of MNM morbidity prevalence (ratio or rate) estimates the cumulative risk over the reproductive age range, accounting for repeated exposures (fertility levels) and background mortality.
- There is utility in comparing trends in the lifetime risk of MNM morbidity alongside trends in the lifetime risk of maternal mortality to better understand changing dynamics of maternal health.

life-threatening MNM complication during her reproductive lifetime. This novel metric is required because existing measures of the frequency of MNM in relation to either the number of live births (MNMRatio) or the female population of reproductive age (MNMRate) do not quantify the cumulative risk of maternal morbidity over a woman's reproductive life from repeated exposures to pregnancy and childbirth. Nor do they capture how the risk of experiencing an MNM during the reproductive life course is dependent upon surviving from ages 15 to 49 years (i.e. all-cause mortality levels, including maternal causes). Hence, the significance of introducing this new indicator is the need to move beyond measuring the discrete risk of a near miss event and instead capture the cumulative impact of MNM morbidity across the female reproductive life course. As a function of the MNM ratio, fertility and mortality levels, the LTR-MNM addresses this deficit and captures potentially countervailing dynamics.

Using the equation for the LTR-MD as a starting point, we present two methods for the calculation of the LTR-MNM, the choice of which depends on the availability of age-disaggregated MNM data. We describe the step-by-step calculation of the LTR-MNM for Namibia—a country that has achieved a substantial reduction in maternal mortality since 2000,[2] but where the burden remains 'high' at 223 maternal deaths per 100 000 live births.[2,5] The calculation combines the national-level estimate of the MNM ratio from 2019[12] with fertility and survival data from the United Nations World Population Prospects.[13] Finally, we discuss the strengths and limitations of our proposed indicator.

Development of the indicator

To calculate the LTR-MNM, we adapt the established method for calculating the LTR-MD. As described by Wilmoth *et al.*,[1] the LTR-MD can be calculated by using the Maternal Mortality Ratio (i.e. the number of maternal deaths per 1000 live births) or the Maternal Mortality Rate (i.e. the number of maternal deaths per 1000 woman-years lived) as follows:

$$LTR_{MD} = \sum_{x}^{x+n} {}_nMMRatio_x \cdot {}_nf_x \cdot \frac{{}_nL_x}{l_{15}} = \sum_{x}^{x+n} {}_nMMRate_x \cdot \frac{{}_nL_x}{l_{15}} \quad (1)$$

where ${}_nf_x$ is the fertility rate between ages x and $x+n$ (where n is the length of the age interval), ${}_nf_x = \frac{{}_nB_x}{{}_nW_x}$, ${}_nB_x$ is the number of live births for women aged x to $x+n$, and ${}_nW_x$ is the number of woman-years of exposure for ages x to $x+n$, in the observed population; ${}_nL_x$ is the number of woman-years of exposure to the risk of dying from maternal or other causes between ages x and $x+n$, and l_{15} is the probability that a girl will survive to age 15 years. Both ${}_nL_x$ and l_{15} can be obtained from a female-population life table. To calculate the cumulative risk of maternal death across the female reproductive life course, all values are summed from x to $x+n$, where x is age 15 years, n is an interval of 35 years, and hence x to $x+n$ denotes age 15 to the end of the 49th year. Using period data, the LTR-MD quantifies the risk of death from a maternal cause in a synthetic cohort, conditional on survival to age 15 years, accounting for competing causes of mortality.

Analogously, the LTR-MNM can be calculated by using either (i) the MNM ratio (MNMRatio: the number of MNMs per 1000 live births) or (ii) the MNM rate (MNMRate: the number of MNMs per 1000 woman-years lived). As the MNMRatio is more frequently available, we use this to calculate the LTR-MNM as follows:

$$LTR_{MNM} = \sum_{x}^{x+n} {}_nMNMRatio_x \cdot {}_nf_x \cdot \frac{{}_nL_x}{l_{15}} \quad (2)$$

Equation (2) measures the risk of experiencing an MNM during the reproductive life course, conditional on survival to age 15 years and accounting for mortality between the ages 15 and 49 years. As with the LTR-MD, the LTR-MNM is a population average that accounts for age-specific fertility, and hence a women's repeated exposure to near miss morbidity, but does not account for parity-specific risks because these data are so rarely available.

Where available, the MNMRatio used to estimate the LTR-MNM should be both nationally representative and population-based. As women with an MNM would likely have died without receiving care at the facility, a facility-based estimate of the numerator of the MNMRatio should closely approximate the true number of cases in a community. However, in settings with low levels of institutional delivery, facility-based estimates of live births are likely to underestimate total births in the community, and hence overestimate the MNMRatio. To better approximate the LTR-MNM, a facility-based MNMRatio estimate can be adjusted using the institutional delivery rate to account for births

occurring at home; this adjustment is more accurate when facility-based estimates encompass all levels of care (primary, secondary and tertiary). Caution is advised when interpreting the LTR-MNM in cases in which institutional delivery is low and live birth estimates derive solely from tertiary hospitals. See the Appendix for further details.

Below we describe two methods to calculate the LTR-MNM depending on the availability of age-disaggregated estimates of the MNMRatio. All procedures were conducted using R[14] and are fully reproducible from open data. Our code is posted in a public code repository, available at doi.org/10.17605/OSF.IO/UYZ5H.

Calculation when (abridged) age-specific MNM data are available

Where age-specific MNM data are available, estimates of the LTR-MNM should use the age-specific MNMRatio. In practice, as the MNMRatios for single-year age groups are virtually never available, the MNMRatio for 5-year age groups is likely the optimum age-disaggregated near miss data. Calculation of the LTR-MNM by 5-year age groups assumes that the MNMRatio, fertility and survival are constant throughout each 5-year age interval.

To demonstrate the calculation of the LTR-MNM in Namibia in 2019 with abridged MNMRatio data, we used a summary MNMRatio for ages 15–49 years of 8.03 per 1000 live births.[12] This estimate derives from a national MNM surveillance study in Namibia from 2019 that identified MNM events across all hospitals in the country and live births from the Namibian National Health Information System.[12] As age-disaggregated data for the MNMRatio were not available for Namibia, we simulated possible age patterns of the MNMRatio by 5-year age intervals as follows: we used an estimate of the number of total births by 5-year age group in Namibia from the United Nations World Population Prospects 2019, adjusted for a stillbirth rate of 17.68 per 1000,[15] and then simulated possible age distributions of MNM cases, for an observed MNMRatio for ages 15–49 years of 8.03. Following evidence on the MNMRatio by age group from Brazil[16] and global evidence on the risk of maternal death by age,[17] we hypothesized that a 'J-shaped' risk profile might be most plausible and this was used for the worked example: a slightly higher risk for adolescent ages 15–19 years, falling to a minimum at ages 20–24 years and increasing with maternal age thereafter. Finally, we test the sensitivity of the LTR-MNM to the assumed age pattern of the MNMRatio.

In addition to the MNMRatio, we also used open-access estimates of age-specific fertility rates, ${}_nf_x$, survivors to age 15 years, l_{15}, and the number of woman-years lived in the interval, ${}_nL_x$, by 5-year age group from the United Nations World Population Prospects abridged life tables for Namibia in 2019[13] to calculate the LTR-MNM.

Applying Equation (2), the steps are as follows:

i) For each age group, the MNMRatio is multiplied by the age-specific fertility rates, ${}_nf_x$.
ii) This is then multiplied by $\frac{{}_nL_x}{l_{15}}$, which is the expected number of years lived in the age interval for a girl who survived to her 15th birthday.
iii) Estimates of the LTR-MNM for each 5-year age group are summed to get the final LTR-MNM.
iv) Reciprocating this total expresses the LTR-MNM as a risk of 1 in n.

Calculation when only summary estimates of MNM for all ages 15–49 years combined are available

Age-disaggregated MNM estimates—even by 5-year age group—are often not available. Rather, an estimate of the MNMRatio is often calculated for all reproductive ages combined from ages 15 to 49 years. The LTR-MNM can be calculated using this summary estimate, although this assumes that the risk of MNM is constant throughout the reproductive ages. This is a simplifying assumption that is most appropriate for data-scarce contexts or when data aggregation results in a loss of detail. Equation (2) becomes:

$$LTR_{MNM} = {}_{35}\ MNMRatio_{15} \cdot \sum_{x}^{x+n} \frac{{}_nL_x}{l_{15}} \cdot\ {}_nf_x \qquad (3)$$

where ${}_{35}\ MNMRatio_{15}$ denotes the summary estimate of the MNMRatio between ages 15 and 49 years (age 15 plus an interval of 35 years). Equation (3) can be further simplified to remove age-specific mortality:

$$LTR_{MNM} = {}_{35}\ MNMRatio_{15} \cdot NRR \cdot \left(\frac{SRB}{100}+1\right) \cdot \frac{l_0}{l_{15}} \qquad (4)$$

where l_0 is the initial female-population radix (100 000), NRR is the net reproduction rate and SRB is the sex ratio at birth. As the NRR is expressed in terms of female births only, this must be adjusted using the SRB to account for both male and female births included in the fertility rate, ${}_nf_x$. The observed SRB in Namibia in 2019 was 101 boys to 100 girls,[13] hence Equation (4) becomes:

$$LTR_{MNM} = {}_{35}\ MNMRatio_{15} \cdot NRR \cdot 2.01 \cdot \frac{l_0}{l_{15}} \qquad (5)$$

Note that, for most countries with a typical SRB of 105 boys to 100 girls, the scaling factor would be 2.05; for countries with high sex selection at birth, it could be much higher.

The steps in this calculation are as follows:

i) The summary MNMRatio is multiplied by the NRR and the SRB scaling factor.
ii) This is then multiplied by $\frac{l_0}{l_{15}}$, which is the inverse probability of surviving from birth to age 15 years.
iii) Reciprocating this total expresses the LTR-MNM as a risk of 1 in n.

Lifetime risk of severe maternal outcome

The concept of LTR-MNM can be used in addition to the LTR-MD to estimate the lifetime risk of severe maternal outcome (LTR-SMO). As SMO is the summation of MNMs and maternal deaths, the LTR-SMO becomes:

$$LTR_{SMO} = LTR_{MD} + LTR_{MNM} \qquad (6)$$

Uncertainty

Where estimates of the MNMRatio derive from surveys, the LTR-MNM is subject to sampling variability. In frequentist

models, the 95% CI for the MNMRatio could be used to calculate corresponding uncertainty in the LTR-MNM. In Bayesian models, an 80% uncertainty interval for the MNMRatio and LTR-MNM could be estimated using the 10th and 90th percentiles of the posterior distribution.[2]

Application

Calculation when (abridged) age-specific MNM data are available

Table 1 presents the simulated age-disaggregated MNMRatio data, the United Nations World Population Prospects fertility and survival data, and the calculation of the LTR-MNM by each 5-year age group when a 'J-shaped' distribution of MNMRatio was assumed.

In this application, the resulting LTR-MNM was 1 in 35, such that, conditional upon surviving to age 15 years, a girl will face a 1 in 35 chance of experiencing an MNM complication during her reproductive lifetime, accounting for survival from ages 15 to 49 years. This compares with a LTR-MD of 1 in 142 (see 'Lifetime risk of severe maternal outcome', below).

Sensitivity of the LTR-MNM estimate to the age pattern of the MNMRatio

For the worked example above, we assumed a 'J-shaped' age profile for the MNMRatio. In reality, for a given level of maternal morbidity for reproductive ages 15–49 years combined (8.03 per 1000 live births), the age pattern of the MNMRatio could adopt a variety of shapes (e.g. U-shaped, Increasing, N-shaped, Constant, Decreasing—though N-shaped, Constant and Decreasing are less likely, given what is known about risk of maternal death by age[17]). Figure 1 shows simulated MNM age distributions and Table 2 shows the corresponding estimates of the LTR-MNM. Despite substantial differences in the underlying MNMRatio by age group, the resulting LTR-MNMs are similar. Full calculations for each age distribution can be found in Supplementary Table S1 (available as Supplementary data at *IJE* online).

Calculation when only summary estimates of MNM for all ages 15–49 years combined are available

By using the observed NRR of 1.554 (WPP Namibia 2019)[13] and applying Equation (4), the LTR-MNM becomes:

$$LTR_{MNM} = 0.00803 \cdot 1.554 \cdot 2.01 \cdot \frac{100\ 000}{95\ 283} = 0.0263\ (2.63\%)\ \text{or}\ 1\ \text{in}\ 38 \quad (7)$$

This summary estimate of the LTR-MNM for ages 15–49 years combined falls within the results for the different possible age distributions above (1 in 40 to 1 in 35), which suggests that Equation (4) is a reasonable approximation where age-disaggregated MNM data are not available.

Lifetime risk of severe maternal outcome

Using an estimated MNMRatio of 223 per 100 000 live births for Namibia in 2019,[2] the LTR-MD is 0.00702 or 1 in 142 (using Equation (4) with the MNMRatio). Using the aggregate estimate of the LTR-MNM (0.0263), Equation (6) for the LTR-SMO becomes:

$$LTR_{SMO} = 0.00702 + 0.0263 = 0.0333\ (3.33\%)\ \text{or}\ 1\ \text{in}\ 30 \quad (8)$$

This means that, in 2019, there was a 1 in 30 risk that a 15-year-old girl in Namibia would experience either a maternal death or an MNM complication during her reproductive lifetime. MNM morbidity accounts for 79% of the LTR-SMO in this example. The relative contribution of near miss morbidity will vary depending on a country's position in the obstetric transition.

Discussion

Life-threatening MNM morbidities are complications so severe that the woman almost died.[4] Relative to maternal mortality, MNM complications and their sequelae affect many more women, their families, communities and health systems.[18,19] As countries progress through the obstetric transition, emergency obstetric care saves more women's lives after

Table 1 Lifetime risk of maternal near miss in Namibia in 2019: calculation assuming 'J-shaped' age distribution of the maternal near miss ratio

Age (years)	MNM cases[a]	Live births[b]	MNMRatio[a,b] per 1000	${}_nf_x$ per 1000 women[c,d]	${}_nL_x$[d]	l_{15}[d]	${}_nL_x/l_{15}$	LTR-MNM
15–19	68	7939	8.57	66.9	474 931.6	95 283	4.98	0.0029
20–24	82	18 050	4.57	154.3	470 667.4		4.94	0.0035
25–29	107	18 241	5.86	160.0	464 275.4		4.87	0.0045
30–34	143	12 772	11.19	140.9	455 466.6		4.78	0.0075
35–39	91	7492	12.19	103.9	443 928.0		4.66	0.0059
40–44	44	2895	15.06	45.6	429 401.3		4.51	0.0031
45–49	11	612	17.57	11.2	411 688.2		4.32	0.0008
Total	546	68 001	8.03[e]					0.0282 (2.8%) 1 in 35

[a] Simulated data.
[b] Data from United Nations World Population Prospects Namibia 2019 total births,[13] adjusted by stillbirth rate of 17.68 per 1000.[15]
[c] Values expressed per 1000 are divided by 1000 before calculation.
[d] United Nations World Population Prospects Namibia 2019.
[e] Maternal near miss ratio for ages 15–49 years combined = 546/68 001 = 8.03 per 1000 live births.
LTR-MNM, lifetime risk of maternal near miss; MNM, maternal near miss.

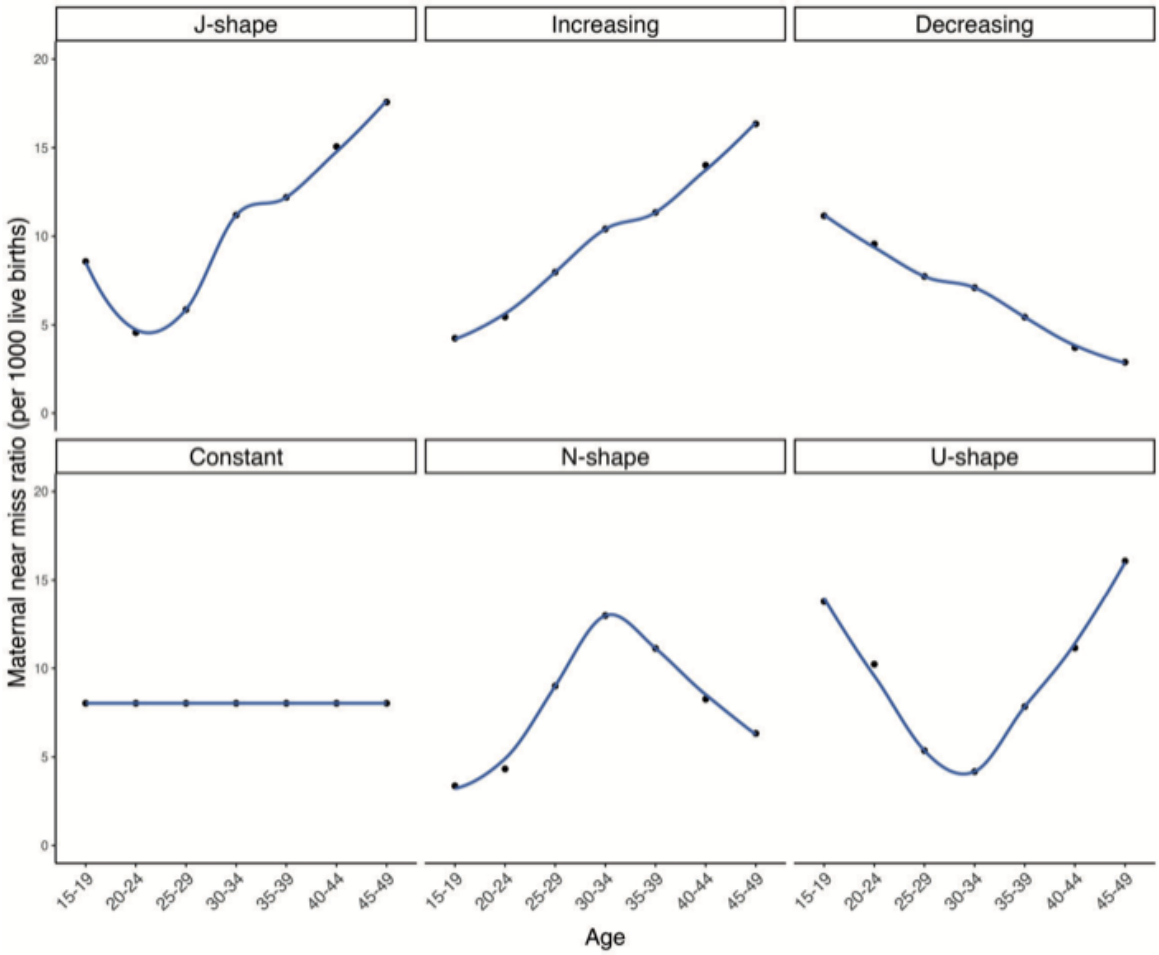

Figure 1 Simulated age distributions of the maternal near miss ratio in Namibia 2019. All distributions have a maternal near miss ratio for ages 15–49 years combined of 8.03 per 1000 live births

Table 2 Sensitivity of lifetime risk of maternal near miss for Namibia 2019 to the age pattern of the maternal near miss ratio

Age distribution of MNM	LTR-MNM	LTR-MNM 1 in *n*
J-shape	0.0282	1 in 35
N-shape	0.0274	1 in 36
U-shape	0.0261	1 in 38
Constant	0.0262	1 in 38
Decreasing	0.0252	1 in 40
Increasing	0.0278	1 in 36

LTR-MNM, lifetime risk of maternal near miss; MNM, maternal near miss.

life-threatening complications and the relative contribution of maternal morbidity to maternal (ill)health increases.[5] This makes MNM an important indicator for advocacy and surveillance, and to identify approaches to improve quality of care.[20]

We propose an extension to the concept of lifetime risk of maternal death (LTR-MD) to MNM morbidity—called the lifetime risk of MNM (LTR-MNM)—to address the deficit of comparable indicators that measure the cumulative impact of maternal morbidity across the female reproductive life course.[11,21] The LTR-MNM is a novel indicator to estimate the risk that a 15-year-old girl will experience an MNM complication in her reproductive lifetime. Unlike existing measures of near miss prevalence (e.g. ratio or rate), the LTR-MNM uses fertility rates to account for women's repeated exposure to the risk of MNM morbidity and adjusts for survival from ages 15 to 49 years. Akin to the LTR-MD, the intuitive appeal of the LTR-MNM may contribute to improved recognition of the global burden of maternal morbidity and strengthen advocacy for its prevention.[22]

Aside from the MNMRatio, the calculation of LTR-MNM uses the same inputs as required for the LTR-MD, increasing the usability of the LTR-MNM. Though the availability of age-disaggregated MNMRatio estimates is often poor, especially in low-resource settings where the burden of maternal morbidity is highest, we have shown that the summary-level estimate of the LTR-MNM falls within the range of estimates derived from age-specific data. If the risk of near miss increases after a certain age, as is the case with the risk of maternal death,[17] the summary estimate of LTR-MNM may be an underestimate and is therefore best interpreted as a lower bound on the true cumulative risk of near miss morbidity.

There is scope for future research to decompose differences in the LTR-MNM into changes in (i) the risk of near miss associated with each pregnancy (MNMRatio); (ii) the number of times women are exposed (fertility levels, ${}_nf_x$) and (iii) all-

cause mortality (${}_nL_x$). Disentangling these dynamics can improve our understanding of the global burden of maternal morbidity across the female reproductive life course.

Limitations

As with (period) life expectancy and the LTR-MD, the LTR-MNM is a synthetic cohort measure of population health in which rates observed in a particular year are assumed to be constant for future cohorts. It cannot be interpreted as a prediction of the lifetime risk of an MNM in a real cohort because the MNM, mortality or fertility rates may change in the future. Second, heterogeneity may cause us to over- or underestimate the LTR-MNM: women who experience an MNM may face elevated mortality risks (from maternal and other causes[3]) and therefore have a lower ${}_nL_x$ schedule; they may have either a lower ${}_nf_x$ schedule if women delay or limit future childbearing after an initial near miss[23] or a higher ${}_nf_x$ if the near miss coincided with a perinatal death.[8] Third, experiencing a near miss is a potentially repeating, non-independent event because having an initial near miss may increase a woman's future risk of experiencing a subsequent near miss. Our calculation does not account for this clustering but amounts to a population average. Finally, estimates of the MNMRatio often derive from surveys of tertiary facilities. These may underestimate live births (thereby overestimating the MNMRatio) even after adjustment using the institutional delivery rate and makes national-level estimation of the LTR-MNM difficult. Further work is required to inform the aggregation of MNM data to produce nationally representative estimates of the LTR-MNM.

Conclusion

We propose the lifetime risk of MNM as a much-needed new summary measure of maternal health, in addition to mortality. Comparability of estimates would benefit from improvements in the national-level aggregation of MNM, especially in high burden settings.

Ethics approval

Ethics approval was not required to demonstrate our new indicator as we used population-level data available in the public domain (United Nations World Population Prospects).

Data availability

All data used in this article are freely available for download from the United Nations World Population Prospects Download Center at https://population.un.org/wpp/Download/Standard/CSV/. All code is available at http://doi.org/10.17605/OSF.IO/UYZ5H.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

U.G. conceived the idea, performed the computations, developed the code and drafted the initial manuscript. J.R.P., J.M.A., A.P., G.R. and V.F. supported the interpretation of results and the refinement of the simulations. A.P. developed the code and built the code repository. J.R.P., J.M.A., A.P., G.R. and V.F. revised the article.

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Conflict of interest

None declared.

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Chapter 7 Research paper 5

The Lifetime Risk of Maternal Near Miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis

Summary of chapter

In Chapter 7, I present the fifth paper of this thesis. This work has been accepted for publication in The Lancet Global Heath and is currently in press, so I have included the accepted version of this paper. This includes the rationale for this study, the study setting, methods, results and discussion.

Supplementary material for this paper is available in Appendix F. Please note, in the following text, page references for supplementary tables and figures refer to the appendices submitted to the Lancet Global Health rather than this thesis.

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Primary Supervisor	Professor Veronique Filippi		

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Stage of publication	**In press**

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 proposed the idea for this comparative paper on the lifetime risk of maternal near miss. I conducted the literature search, extracted the raw maternal near miss prevalence data, wrote the code for the meta-analysis, prepared all tables and visualisations, and wrote a complete first draft of the paper for co-authors to review. I led the submission process to The Lancet Global Health and the responses to reviewers.

SECTION E

Student Signature	Ursula Gazeley
Date	22nd July 2024

Supervisor Signature	Veronique Filippi
Date	22nd July 2024

The Lifetime Risk of Maternal Near Miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis

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Abstract

Background

Life-threatening maternal near miss (MNM) morbidity can have long-term consequences for women's physical, psychological, sexual, social, and economic wellbeing. The lifetime risk of MNM (LTR-MNM) quantifies the probability that a 15-year-old girl will experience a near miss before age 50, given current mortality and fertility levels. We compare LTR-MNM globally to reveal inequities in the cumulative burden of severe maternal morbidity across the reproductive life course.

Methods

We estimated the LTR-MNM for 40 countries with multi-facility, regional, or national data on the prevalence of MNM morbidity measured using World Health Organization (WHO) or modified WHO criteria of organ dysfunction from 2010 onwards (Central and Southern Asia=6, Eastern and South-Eastern Asia=9, Latin America and the Caribbean=10, Northern Africa and Western Asia=2, sub-Saharan Africa=13). We also calculated the lifetime risk of severe maternal outcome (LTR-SMO) as the lifetime risk of maternal death or MNM.

Findings

The LTR-MNM ranges from a 1 in 269 risk in Vietnam (2010) to 1 in 6 in Guatemala (2016), while the LTR-SMO ranges from a 1 in 201 risk in Malaysia (2014) to 1 in 5 in Guatemala (2016). The LTR-MNM is a 1 in 20 risk or higher in nine countries, seven of which are in sub-Saharan Africa. The LTR-SMO is a 1 in 20 risk or higher in 11 countries, eight of which are in sub-Saharan Africa. The relative contribution of the LTR-MNM to the LTR-SMO ranges from 42% in Angola to 99% in Japan.

Interpretation

There exists substantial global and regional inequity in the cumulative burden of severe maternal morbidity across the reproductive life course. The LTR-MNM is an important indicator to advocate for further global commitment to end preventable maternal morbidity. Finally, the LTR-SMO can be used to highlight variation in the relative and important contribution of morbidity to the overall burden

of maternal ill-health across the female reproductive life course, depending on countries' stage in the obstetric transition.

Funding

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Research in Context

Evidence before this study

We searched Embase, MEDLINE, and Global Health for English language studies reporting national, regional, or multi-facility estimates of the prevalence of life-threatening maternal morbidity (i.e., "maternal near miss" events), published from 2010 until 15 July 2024. Search terms included (1) "maternal near miss"/"severe (acute) maternal morbidity"/"life-threatening condition/complications" and (2) "prevalence"/"incidence"/ "ratio"/ "surveillance". Our search revealed a dearth of population-level estimates: most existing prevalence data derive from (single) facility-based studies without accounting for births that occur outside of the facility. This bias may be substantial where institutional delivery rates are low. Second, existing global comparisons of the Maternal Near Miss Ratio indicate differences in the level of obstetric risk associated with an individual pregnancy only. But since women are at risk of experiencing a life-threatening complication with each pregnancy, existing data fail to account for differences in cumulative risk from repeat pregnancy.

The Lifetime Risk of Maternal Near Miss is a new indicator oriented to address these deficits in the existing evidence and aiming to better understand global inequities in the burden of maternal near miss morbidity across women's reproductive lives.

Added value of this study

We provide the first cross-country estimates of the lifetime risk of maternal near miss for 40 countries with multi-facility, regional, or national data on the prevalence of maternal near miss. We also calculate how the lifetime risk of maternal near miss compares to the lifetime risk of maternal death for a given country-year, and the relative contribution of morbidity to the lifetime risk of severe maternal outcome (the risk of death or near miss morbidity). This is the first study to do so.

Implications of all the available evidence

First, there is substantial global inequity in the risk of severe maternal morbidity across women's reproductive lifetimes. By accounting for the cumulative risk from repeat pregnancy and reproductive age survival, the lifetime risk of maternal near miss presents a clearer picture of cross-country

disparities in the burden of near miss morbidity than prevalence data alone might suggest. Second, the composite risk that a girl will either die from a maternal cause or experience near miss morbidity during her lifetime is extremely high in many countries, particularly in sub-Saharan Africa. These findings provide a new lens through which to understand reproductive injustice, and a new opportunity to advocate for increased global commitment to end preventable maternal morbidity and mortality.

Introduction

A maternal near miss (MNM) case is defined as "a woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy".[1] The World Health Organization (WHO) identifies MNM cases based on clinical, laboratory, and management-based indicators of organ dysfunction.[1] These criteria are not, however, used universally and some countries use complication- or management-based criteria instead.[2] Sharing many characteristics with the review of women who die from maternal causes, clinical audit of women who survive life-threatening complications is an effective tool to improve quality of maternal health care.[3,4] Maternal near miss events reflect the ability of a healthcare system to save a woman's life when life-threatening complications arise, and are testament to the importance of expanding access to and the quality of emergency obstetric care.[3,4] However, surviving a complication of this severity can also lead to long-term physical, psycho-social, sexual, and economic sequelae.[5,6] As countries progress through the obstetric transition,[7,8] from high to low maternal mortality and direct obstetric to indirect (infectious and non-communicable diseases (NCD) causes of maternal death, a greater proportion of adverse maternal outcomes are cases of near miss morbidity.

Existing measures of maternal near miss morbidity typically estimate the level of obstetric risk associated with an individual pregnancy only – for example, the MNM ratio (MNM cases per 1000 live births)[1], MNM rate (MNM cases per 1000 women of reproductive age). Few standard measures of non-life-threatening maternal morbidity exist at all.[9] In response to global calls for comparable, population-level estimates of maternal morbidity,[9,10] Gazeley et al (2023) proposed a new summary measure called the "lifetime risk of maternal near miss" (LTR-MNM) to estimate the risk (1 in N chance) that a 15-year-old girl will experience a maternal near miss complication before age 50.[11] The LTR-MNM extends metrics of maternal morbidity to a cumulative risk framework. This conceptual shift recognises that women face repeated exposure to the risk of maternal morbidity with each recurrent pregnancy they have, and that this risk accumulates across their reproductive lives.

Measurement of the LTR-MNM is analogous to lifetime risk of maternal death (LTR-MD) – a widely-used metric to compare maternal mortality across countries and changes over time.[12] As a composite measure, its computation requires three components: (i) the MNM ratio (the level of obstetric risk); (ii) fertility levels (a proxy for the number of times women are exposed) ; and (iii) all-cause mortality (to experience a MNM one must not die from a maternal cause or something else).[11] When two lifetime risks – of death or MNM – are combined, the 'lifetime risk of severe maternal outcome' (LTR-SMO) denotes the risk that a 15-year-old girl will either die from a maternal cause or experience a MNM during her reproductive lifetime. This is an important tool that may help to strengthen global advocacy to reduce preventable maternal mortality and morbidity.[11]

To our knowledge, no global estimates of the LTR-MNM or LTR-SMO currently exist. Our objective is to produce the first, population-level estimates of the LTR-MNM and LTR-SMO for countries with available data, to better understand global inequities in reproductive outcomes.

Methods

We used the GATHER statement to guide the reporting of our methods.[13] All procedures were conducted using R version 4.4.1[14] and are reproducible from open data (code available at: https://osf.io/n3uwx/?view_only=649efa0029ab4285b3f7a3e0143c5f95).

Calculation of the Lifetime Risk of Maternal Near Miss

We calculated the LTR-MNM using the Maternal Near Miss (MNM) ratio for all reproductive ages 15-49 combined, following the procedure described in Gazeley et al. (2023),[11] where age-specific data on the MNM ratio are not available. The LTR-MNM is a composite measurement which depends on the level of obstetric risk, fertility, and mortality, as indicated in Equation 1. The first input is the MNM ratio for all ages 15-49, ${}_{35}MNMRatio_{15}$. The second input is expected fertility, as a function of the Net Reproduction Rate (NRR) – the number of daughters that would be born to a woman if she experienced current fertility and mortality rates over her lifetime, and the Sex Ratio at Birth (SRB) – the number of male births per one hundred female births. Jointly, the two terms incorporate

women's repeat exposure to the risk of MNM (fertility levels) and survival across the reproductive ages 15-49 (mortality levels). Finally, the third input conditions the LTR-MNM on survival to age 15, using the radix of the life table (100,000), l_0, divided by the number of female survivors to age 15, l_{15}:

$$(1) \qquad LTR_{MNM} = {}_{35}MNMRatio_{15} \cdot NRR \cdot \left(\frac{SRB}{100} + 1\right) \cdot \frac{l_0}{l_{15}}$$

We also calculated the lifetime risk of maternal death (LTR-MD) analogously, as shown in Equation 2. This was used to estimate the lifetime risk of severe maternal outcome (LTR-SMO) (Equation 3). Since SMO are the summation of maternal deaths and MNM cases[1], the LTR-SMO is the summation of the two lifetime risks – of death or morbidity:

$$(2) \qquad LTR_{MD} = {}_{35}MMRatio_{15} \cdot NRR \cdot \left(\frac{SRB}{100} + 1\right) \cdot \frac{l_0}{l_{15}}$$

$$(3) \qquad LTR_{SMO} = LTR_{MD} + LTR_{MNM}$$

Data inputs

1. Maternal near miss data

a. Systematic search for MNM prevalence estimates

Our objective was to derive population-level estimates of the LTR-MNM for each country with available MNM data (i.e., 'country-related' estimates, which may not represent the national lifetime risk). To do so required data on the frequency of MNM. However, as the fertility and mortality data used to calculate the LTR-MNM are national, we included only multi-facility, regional, or nationally representative data on the MNM ratio, excluding estimates deriving from a single facility only.

To identify eligible studies, we implemented two search strategies. First, we searched Embase, MEDLINE, and Global Health for studies reporting the prevalence of maternal near miss from 2010 onwards (full search strategy available in Table S1, Appendix p.2). This yielded 1285 results, of which 787 remained once duplicates were removed, and 130 were eligible for full text review. Second, we searched recent systematic reviews for multi-facility, regional, or national studies of MNM prevalence. [2,15–18] In total, from these two search strategies we identified 43 studies (with 80 separate

estimates from 40 countries) eligible for inclusion. See Table S2 (Appendix pp.3-8) for the included studies, and Figure S1 and Table S3 (Appendix pp.9-10) for which countries' MNM data were national only (n=18), subnational only (n=12), or both (n=10). Only two studies were a national audit of all facilities; other 'national' studies aimed to improve representation by randomly sampling multiple regions and facilities within regions; subnational data derived from one region only.

b. Heterogeneity in the MNM criteria

There is little consistency in the criteria used to identify severe maternal morbidity cases.[2,19] In 2009, the WHO developed a set of 25 clinical, laboratory, and management-based criteria of organ dysfunction to standardise the measurement of MNM[1]. In health systems where laboratory or management capacity is lacking, however, the full WHO criteria can be hard to implement, and may miss true positive MNM cases (i.e., high specificity but low sensitivity). [2,19–21] Many studies therefore apply adaptations to the WHO organ dysfunction criteria to improve sensitivity in LMICs, such as lowering the units of blood transfused, including admission to ICU, and certain severe conditions.[20–22]

Very few high-income countries use the WHO or modified organ-dysfunction criteria, and instead often apply disease- and/or management-based criteria that are more readily available from routine administrative records.[2,23] With higher sensitivity but lower specificity, disease- and/or management-based criteria typically result in higher estimates of the MNM ratio.[2,19,24]

These differences in the measurement criteria can introduce substantial heterogeneity in the MNM ratio estimates. To mitigate this, we only included studies which applied either the WHO criteria of organ dysfunction or modified versions adapted for low resource settings (see Table S4, Appendix pp.11-12). This aimed to ensure we are including estimates of the same severity of morbidity into the calculation of the lifetime risk. However, this restriction also resulted in more conservative estimates of the MNM ratio and led to the exclusion of numerous studies from high-income countries.

In instances where multiple organ dysfunction-based criteria were applied in the same study, we included each separate MNM estimate.

c. Denominator adjustment

The denominator of the MNM ratio, as specified in WHO guidelines, is live births.[1] For studies which used deliveries (n=4), pregnant women (n=1), or obstetric admissions (n=1) as the denominator, we approximated live births using (i) global data on the twin birth rate per 1000 deliveries from 2010-15 to partially account for multiple births,[25] and (ii) open access data on the stillbirth rate from UNICEF.[26]

Second, most MNM ratio estimates derive from facilities. Since MNM cases require emergency intervention in a facility, facility-level estimates may approximate the true number of MNM cases in a given geographic area. The accuracy of this approximation depends on the proportion of facilities included and how referrals are accounted for. However, in countries with low institutional delivery rates, facility-based estimates of live births in the MNM ratio denominator risk under-estimating live births in a population. This potential bias is even greater if the MNM ratio derives only from tertiary referral facilities. To avoid over-estimating the MNM ratio and the LTR-MNM, we adjusted facility-based estimates of live births using open access data from the WHO on the institutional delivery rate from the closest available year to studies' reference period to derive a population-level estimate of total live births (facility live births multiplied by the inverse of the institutional delivery rate).[11]

d. Deriving estimates for countries with available data

To derive estimates of the LTR-MNM for each country with available data, we first required a single, population-level estimate of the MNM ratio for each country. MNM input data may not be nationally representative, which means resulting LTR-MNM estimates are 'country-related'. For 26 out of 40 countries, only a single MNM ratio estimate was available, and hence this was used as the input to the LTR-MNM. For the remaining 14 countries with multiple studies, we used a random effects meta-analysis model to derive a pooled MNM ratio estimate (R package 'metafor').[27] Studies were weighted by their sample size. A random effects only model was used to partially account for the

heterogeneity in study designs, study populations and MNM criteria.[18] Our population-level MNM estimates for each country are available in the Supplementary Material (Table S5, Appendix pp.13-15). For the 14 countries where meta-analysis was used, sensitivity to the weighting procedure is available in Table S6 (Appendix p.16); heterogeneity by country is available in Table S7 (Appendix p.17-19). Univariable and multivariable meta-regression suggests the type of MNM criteria was a significant source of heterogeneity in estimates of the MNM ratio (see Tables S8 and S9, Appendix pp.19-22).

2. Additional data inputs on fertility and mortality levels

We used open-access estimates of the NRR, SRB, and I_{15} from the 2022 United Nations World Population Prospects (13) to calculate the LTR-MNM for each country with eligible MNM ratio data. To estimate the LTR-MD (and consequently the LTR-SMO), we used the latest WHO and Joint United Nations estimates of the maternal mortality ratio (MMR)[12], alongside survival and fertility data from the World Population Prospects for consistency with the LTR-MNM.

Uncertainty

We estimated uncertainty in the LTR-MNM deriving from variation in the pooled MNM ratio estimate, excluding other sources of uncertainty (i.e., from WPP fertility and mortality estimates). We computed the 95% confidence intervals of the MNM ratio and the corresponding upper and lower bounds of the LTR-MNM. Uncertainty in the LTR-MNM is substantial where there is a large degree of variability in the MNM ratio across studies (Table S10, Appendix pp.23-24).

Role of the funder

The funder of the study had no role in study design, data collection, data analysis, interpretation, or writing of the report.

Results

We estimated population-level estimates of the LTR-MNM, LTR-MD, and LTR-SMO for 40 countries with multi-facility, regional, or national data on the MNM ratio. **Table 7.1** presents the country-related estimates by Sustainable Development Goal (SDG) regional grouping.

In Central and Southern Asia, the LTR-MNM ranges from 1 in 206 (Nepal in 2012) to 1 in 17 (Pakistan in 2016); in Eastern and South-Eastern Asia from 1 in 269 (Vietnam in 2010) to 1 in 35 (Cambodia in 2010); in Latin America, from 1 in 174 (Paraguay in 2010) to 1 in 6 (Guatemala in 2016); in Northern Africa and Western Asia, from 1 in 109 (Lebanon in 2010) to 1 in 59 (Iraq in 2010); in sub-Saharan Africa, from 1 in 69 (South Africa in 2014) to 1 in 8 (Democratic Republic of Congo in 2016). The LTR-MNM is almost 45 times higher in Guatemala (the highest risk) than in Vietnam (the lowest risk).

Global variation in the LTR-MD is substantially greater than for the LTR-MNM, and ranges from 1 in 12,778 (Japan in 2010) to 1 in 17 (Nigeria in 2012), representing over a 750-fold higher risk. Variation in the LTR-SMO – of experiencing either a MNM event of dying from a maternal cause – is still substantial, but less than for either the LTR-MNM or the LTR-MD. However, 11 countries had a LTR-SMO of at least 1 in 20 risk or higher; eight of these countries are in sub-Saharan Africa.

Table 7.1 Global estimates of the lifetime risk of maternal near miss, maternal death, and severe maternal outcome

Country	Year[a]	MNM data type)[b]	No. of MNM estimates[c]	Total fertility rate[d]	Maternal near miss ratio[e]	Maternal mortality ratio[f]	LTR-MNM 1 in N[g]	LTR-MD 1 in N[h]	LTR-SMO 1 in N[i]	Contribution of LTR-MNM to LTR-SMO (%)[j]
Central and Southern Asia										
Afghanistan	2010	National only	1	6.1	7.1	898.7	24	19	11	44.3
India	2014	Both	7	2.3	8.5	134.9	52	326	45	86.3
Iran	2014	Subnational only	4	2.0	8.2	20.9	61	2,372	59	97.5
Nepal	2012	Both	2	2.4	2.1	287.7	206	148	86	41.7
Pakistan	2013	Both	2	4.1	14.8	206.1	17	120	15	87.8
Sri Lanka	2010	National only	1	2.2	4.0	37.3	114	1,234	104	91.6
Eastern and South-Eastern Asia										
Cambodia	2010	National only	1	2.8	10.6	276.4	35	134	28	79.3
China	2015	Both	6	1.7	4.1	26.0	148	2,321	140	94.0
Japan	2010	National only	1	1.4	5.9	5.7	122	12,788	121	99.1
Laos	2020	Subnational only	1	2.5	9.8	126.1	41	316	36	88.6
Malaysia	2014	Subnational only	1	2.1	2.2	22.5	222	2,146	201	90.6
Mongolia	2010	National only	1	2.5	8.2	65.5	49	616	45	92.6
Philippines	2010	National only	1	3.3	1.7	105.0	186	295	114	61.4
Thailand	2010	National only	1	1.6	5.7	35.3	112	1,811	106	94.2
Vietnam	2010	National only	1	1.9	2.0	87.6	269	608	186	69.3
Latin America and the Caribbean										
Argentina	2012	Both	2	2.3	5.0	45.0	87	958	80	91.7
Brazil	2011	Both	3	1.8	10.0	61.9	56	904	53	94.2
Ecuador	2010	National only	1	2.6	2.6	76.2	150	507	116	77.2
Guatemala	2016	Subnational only	1	3.0	61.9	103.1	6	330	5	98.4
Honduras	2014	Subnational only	1	2.6	11.8	68.3	33	561	31	94.5
Mexico	2010	National only	1	2.3	11.1	51.2	39	841	37	95.6
Nicaragua	2010	National only	1	2.6	13.2	97.8	30	397	28	93.1
Paraguay	2010	National only	1	2.7	2.1	100.5	174	369	118	67.9
Peru	2010	National only	1	2.6	10.0	76.4	40	515	37	92.9
Suriname	2018	National only	3	2.4	12.9	97.6	32	428	30	93.0
Northern Africa and Western Asia										

Table 7.1 Global estimates of the lifetime risk of maternal near miss, maternal death, and severe maternal outcome

Country	Year[a]	MNM data type)[b]	No. of MNM estimates[c]	Total fertility rate[d]	Maternal near miss ratio[e]	Maternal mortality ratio[f]	LTR-MNM 1 in N[g]	LTR-MD 1 in N[h]	LTR-SMO 1 in N[i]	Contribution of LTR-MNM to LTR-SMO (%)[j]
Iraq	2010	Subnational only	1	4.4	3.9	114.9	59	200	46	77.2
Lebanon	2010	National only	1	2.1	4.3	18.0	109	2,630	105	96.0
Sub-Saharan Africa										
Angola	2010	National only	1	6.2	2.6	367.3	65	46	27	41.5
Democratic Republic of Congo	2013	Both	2	6.5	19.7	584.6	8	28	6	77.2
Ethiopia	2018	Subnational only	10	4.3	12.8	311.9	19	76	15	80.4
Ghana	2016	Subnational only	1	3.9	26.9	258.1	10	103	9	91.2
Kenya	2015	Both	3	3.8	4.5	483.0	62	57	30	48.0
Namibia	2018	Both	3	3.5	9.6	218.0	31	138	25	81.5
Niger	2010	National only	1	7.5	5.5	593.9	26	24	12	47.9
Nigeria	2014	National only	3	5.7	11.3	1,135.3	17	17	8	49.9
South Africa	2014	Subnational only	3	2.4	6.2	141.2	69	303	56	81.4
Tanzania	2012	Subnational only	1	5.1	22.3	393.7	9	52	8	85.0
Uganda	2012	Both	2	5.8	13.6	334.4	13	54	11	80.2
Zambia	2016	Subnational only	1	4.7	13.0	155.4	17	142	15	89.3
Zimbabwe	2016	Subnational only	1	3.8	9.3	399.8	30	69	21	69.9

[a] Year is the average of the reference period midpoints across the studies for that country.

[b] Data type is classified as 'national' if the input data aimed towards national representation of the MNM ratio by using multistage/random sampling to select facilities from multiple regions, provinces, or states in the country, and 'subnational' if facilities were selected from one region or from regions without random sampling.

[c] The number of MNM estimates corresponds to the number of separate studies and separate estimates within a single study (e.g., if two different MNM criteria were applied, both estimates were extracted). Full details of all MNM input data are available in Table S1 (Appendix pp.3-8).

[d] Total fertility rate is expressed as births per woman and is the total number of children that would be born to a woman if she were to live to the end of her childbearing years based on observed age-specific fertility rates. We use estimates of the TFR from World Population Prospects.

[e] Maternal near miss ratio is the number of MNM per 1000 live births. This is the denominator adjusted MNM ratio where facility-based estimates have been adjusted using the institutional delivery rate. For countries with multiple studies, this is the pooled (adjusted) MNM ratio from the random effects meta-analysis. Full meta-analysis results can be found in Table S5.

[f] Maternal mortality ratio is the number of maternal deaths per 100 000 live births. We used the WHO and UN Joint Agency estimates of the MMR, according to closest year.

[g] LTR-MNM expressed as a reciprocal (1 in N risk).

[h] Authors' calculation of LTR-MD using WHO and UN Joint Agency MMR estimate for the given country-year and Equation 2 for summary estimates of the MMR. These estimates may differ from WHO and UN Joint Agency LTR-MD estimates.

[i] LTR-SMO expressed as a reciprocal (1 in N risk).

[j] This is the LTR-MNM as a proportion of the LTR-SMO, expressed as a percentage (i.e., LTR-MNM/ (LTR-MNM + LTR-MD)).

The relationship between a countries' LTR-MNM and their fertility level can show whether a high LTR-MNM is driven by a high obstetric risk, high fertility level, or both. Figure 7.1 shows the LTR-MNM and Total Fertility Rate (TFR, from World Population Prospects) according to three quantile classes for each indicator, i.e., high, medium, and low LTR-MNM (>1 in 32, 1 in 32-65, <1 in 65 lifetime risk) and high, medium, and low TFR (>3.77, 2.42-3.77, <2.42 births per woman). Although most countries with a high LTR-MNM have a high TFR (dark magenta, e.g., Democratic Republic of Congo) and vice versa (light violet, e.g. Japan), there are some countries with a high LTR-MNM despite low fertility (dark red, e.g., Nicaragua).

Global inequity in the LTR-SMO of death or MNM morbidity is substantial. Figure 7.2 shows that the cumulative burden of these two maternal outcomes across women's reproductive lifetimes is the highest among countries in sub-Saharan Africa, and some parts of Central and Southern Asia (Afghanistan and Pakistan, in particular).

The contribution of the LTR-MNM to the LTR-SMO varies according to countries' positions in the obstetric transition. Figure 7.3 shows that for most countries in sub-Saharan Africa in Stage 1 or Stage 2 of the obstetric transition (MMR >500 or 300-499 per 100,000 live births, respectively), the contribution of near miss morbidity to the LTR-SMO is relatively low. However, as countries progress through the obstetric transition and mortality declines, the relative contribution of morbidity to the LTR-SMO increases. There are some exceptions: the proportion of lifetime risk from near miss morbidity is greater than expected in Tanzania and Guatemala given their mortality levels, and lower than expected in Vietnam and Ecuador.

The relationship between countries' LTR-MNM and their LTR-MD is available in the Supplementary Material (Figure S2, Appendix pp.25-26). On a log-log scale, there is a positive association between a countries' LTR-MNM and their LTR-MD: countries with a high burden of maternal near miss morbidity are likely to also have a high burden of maternal mortality across the female reproductive life course.

Figure 7.1 Global variation in the Lifetime Risk of Maternal Near Miss (LTR-MNM) by the Total Fertility Rate (TFR)

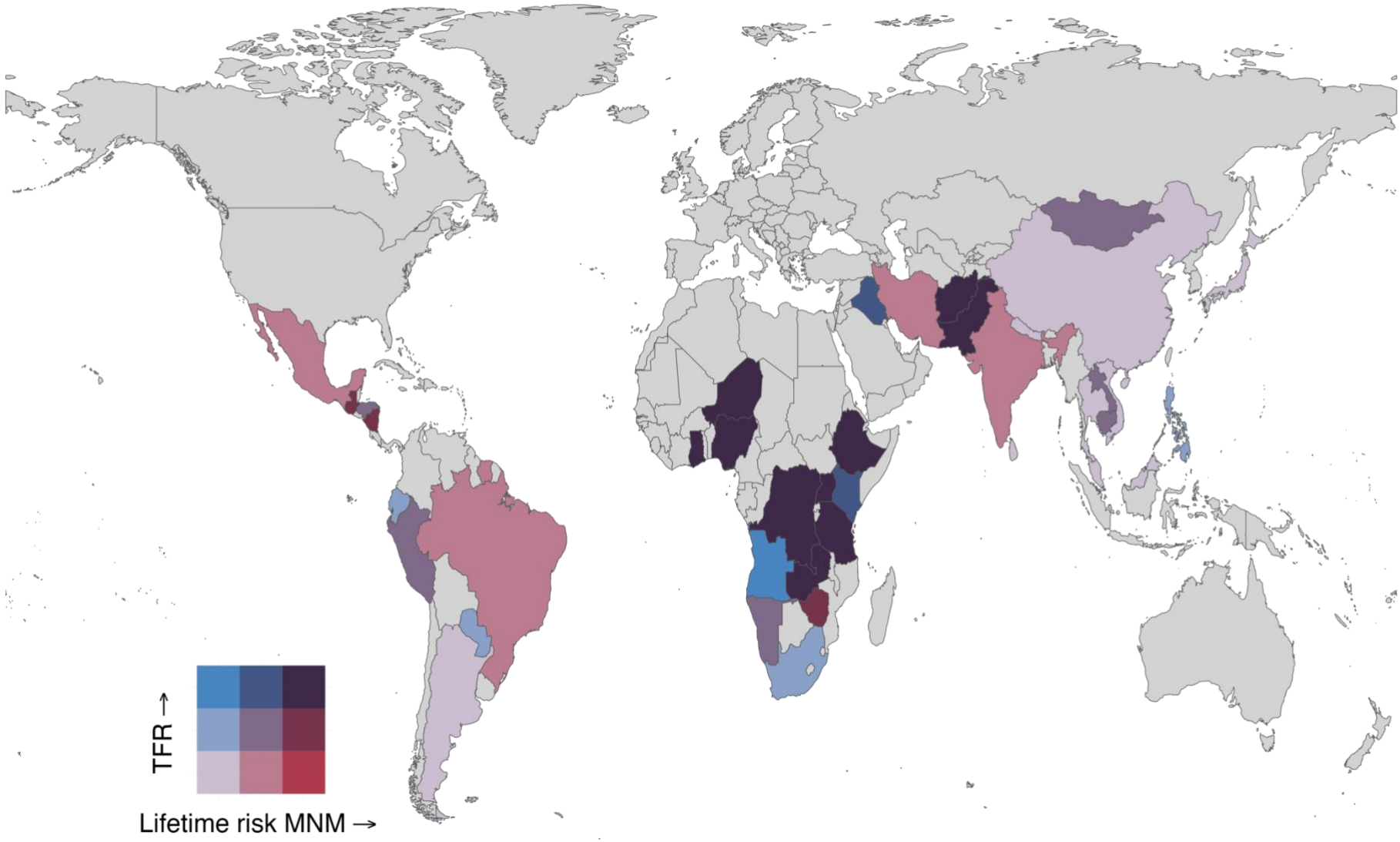


Figure 7.2 Global variation in the Lifetime Risk of Severe Maternal Outcome (LTR-SMO)

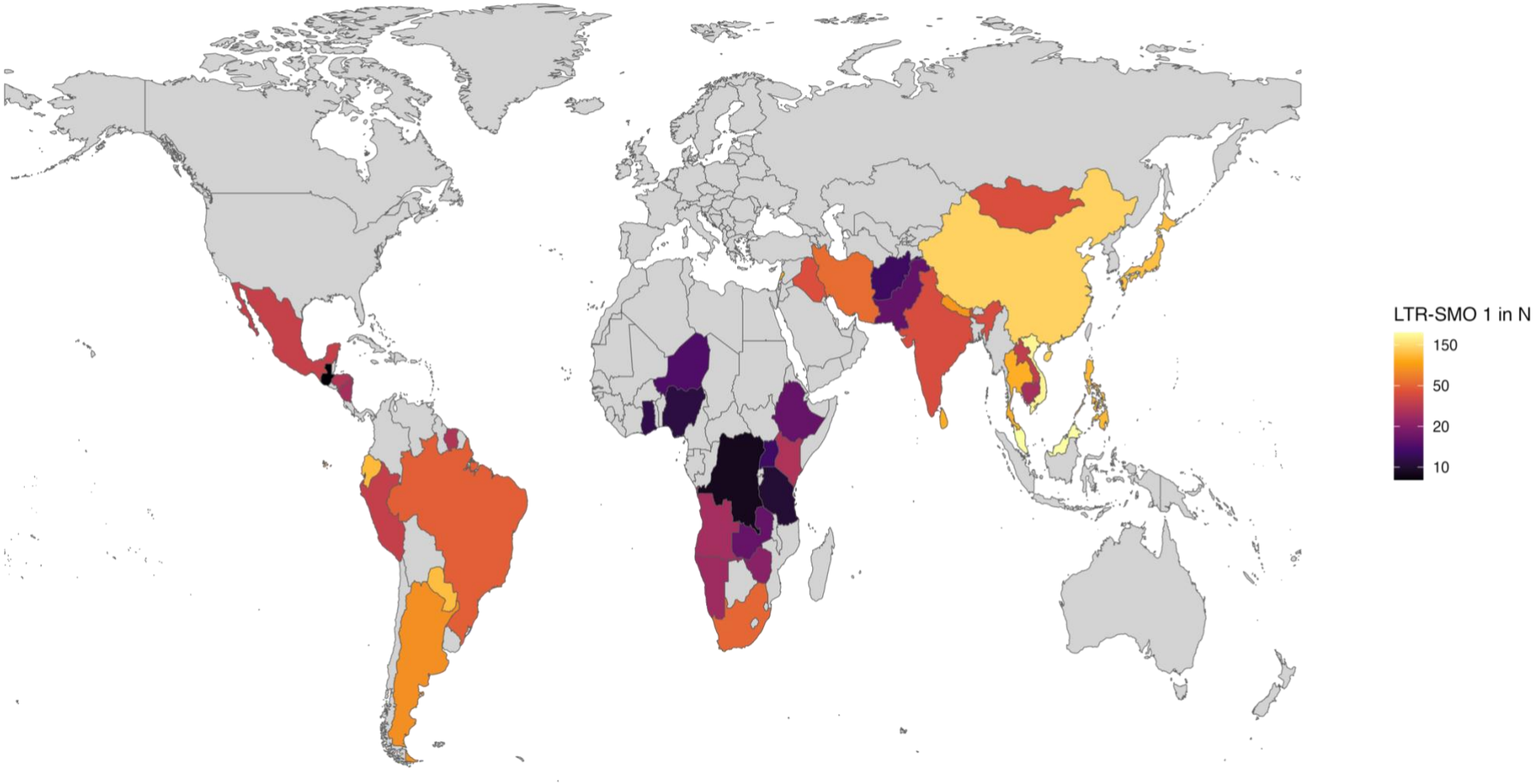
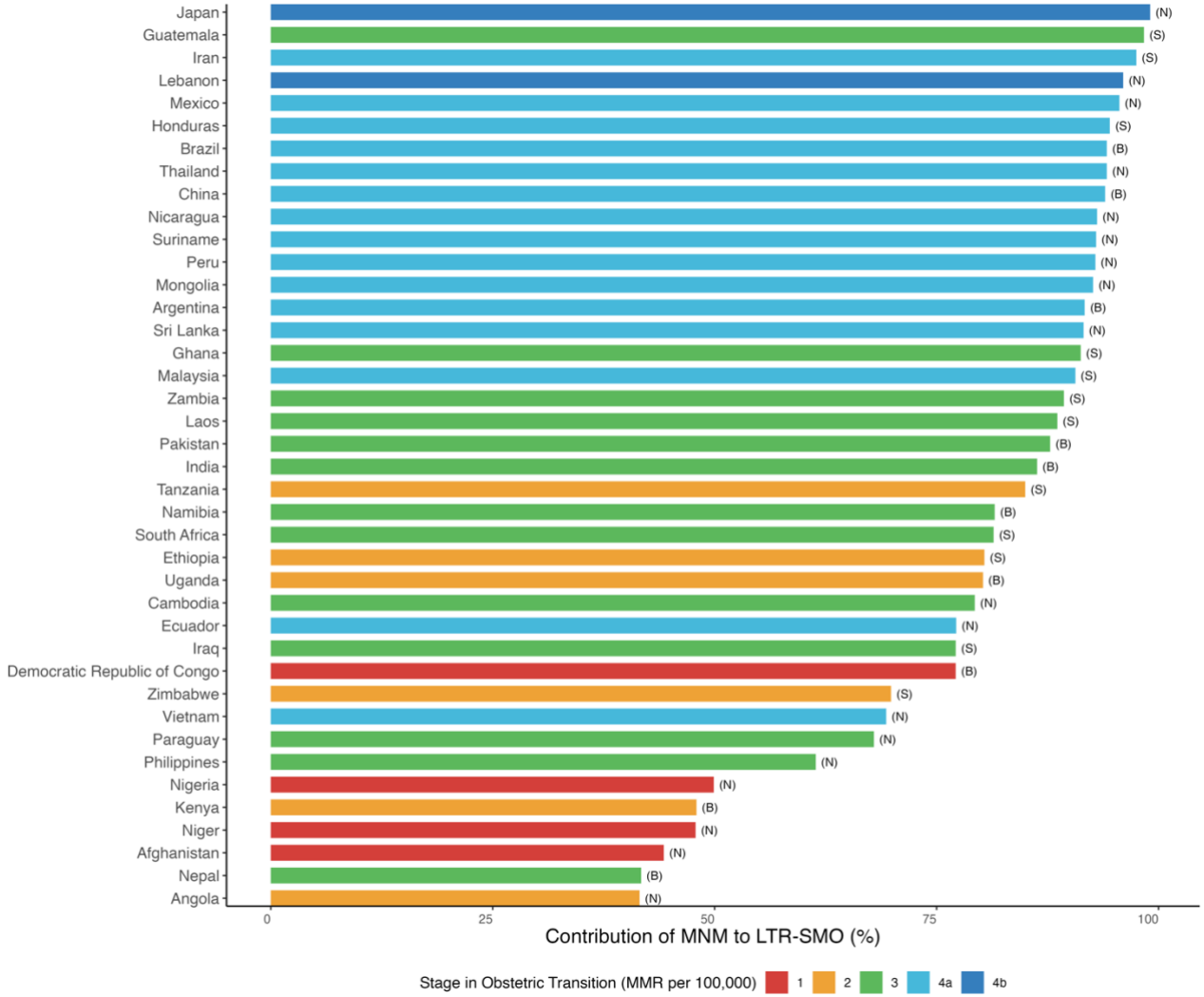


Figure 7.3 Contribution of near miss morbidity to Lifetime Risk of Severe Maternal Outcome (LTR-SMO) by obstetric transition



Notes: (N) = national only; (S) = subnational only; (B) = both. Stage 1 = very high maternal mortality, MMR ≥ 500; Stage 2 = high maternal mortality, MMR 300-499; Stage 3 = intermediate maternal mortality, MMR 100-299; Stage 4 = low maternal mortality, 4a = MMR 20-100; Stage 4b <20 per 100,000 live births

Sensitivity analysis

We calculated the LTR-MNM for estimates of the MNM without applying the denominator adjustment for facility-based studies. This adjustment makes a much greater difference in low resource contexts where the institutional delivery rate is low (see Table S11, Appendix pp.27-28). This downward adjustment of the level of obstetric risk therefore results in a lower estimate of the LTR-MNM than would if this adjustment was not applied (Table S12, Appendix p.29).

Discussion

To our knowledge, we present the first cross-country estimates of the LTR-MNM – a new indicator that calculates the cumulative burden of severe maternal morbidity across the female reproductive life course. This measure addresses calls for more comparable measures of maternal morbidity. Unlike existing global comparisons of MNM prevalence, the LTR-MNM accounts for women's repeated exposure to the risk of severe maternal morbidity with each pregnancy, and her survival throughout the reproductive ages 15-49. Capturing changes in the level of obstetric risk, while accounting for prevailing fertility and mortality levels, means this is a better indicator of the burden of maternal morbidity in population.

Our results indicate that a 15-year-old girl in Guatemala has a 1 in 6 chance of experiencing a maternal near miss during her reproductive lifetime, and this is largely driven by a high (adjusted) MNM ratio estimate. A 15-year-old in the Democratic Republic of the Congo has a 1 in 8 chance, due to a moderately high MNM ratio and high fertility levels. Finally, with a very low (adjusted) MNM ratio, and low fertility, we estimate that a 15-year-old girl in Vietnam has a 1 in 269 chance of experiencing a near miss in her reproductive lifetime. This substantial inter- and intra-regional heterogeneity in the LTR-MNM highlights persistent inequities in maternal health outcomes. Global variation in the level of obstetric risk associated with an individual pregnancy (i.e. the MNM ratio) may reflect both low access to- and poor quality of- ante-, intra-, and post-partum care, and signify a health system's capacity to identify and treat complications before they progress to become life-threatening.[2,3] But the LTR-MNM also reveals how these inequities in obstetric risk are cumulative

across the female reproductive life course. High fertility in many sub-Saharan African countries [28], and repeated exposure to near miss with each subsequent pregnancy, contributes to the high and extremely high LTR-MNM. The LTR-MNM therefore presents a more accurate picture of the scale of global inequity in near miss morbidity than would be implied by differences in the MNM ratio alone.[11]

We also provide the first cross-country estimates of the LTR-SMO – the risk that a 15-year-old girl would experience either a maternal near miss complication or die from maternal cause during her reproductive lifetime. This is an important tool for advocacy because most maternal near miss complications and almost all maternal deaths are preventable. The LTR-SMO provides a more comprehensive depiction of the cross-country inequities in reproductive outcomes and the work required to end preventable forms of maternal morbidity and mortality.[11,29]

The relative contribution of LTR-MNM to the LTR-SMO may be indicative of a country's position in the obstetric transition – the secular shift from high to low maternal mortality, and direct to indirect causes of maternal death [7,8]. As a country progresses through the obstetric transition, the capacity of the health care system to manage severe complications and save women's lives should improve with expansions in access to and the quality of emergency obstetric care. It may be expected, therefore, that the contribution of LTR-MNM to the LTR-SMO would be higher for countries which are further progressed through the obstetric transition. Our results largely support this. Exceptions (e.g., Guatemala and Tanzania) indicate that the relative contribution of LTR-MNM to the LTR-SMO is higher than might be expected given their levels of maternal mortality.

An unavoidable conclusion of our efforts to generate comparable estimates of the LTR-MNM is the urgent need for improved standardisation in the measurement of MNM globally.[2,4,19] To measure the same severity of maternal morbidity, we restricted estimation of the LTR-MNM to countries with national, regional, or multi-facility data on the MNM ratio measured using (modified) WHO criteria of organ dysfunction. Many disease- and/or management-based criteria of severe maternal morbidity capture part of the morbidity spectrum closer to so-called 'potentially life-threatening conditions', that

may or may not develop into life-threatening maternal near miss events. Studies using these broader criteria – predominantly from high income countries – were excluded to avoid substantial heterogeneity in MNM measurement biasing our LTR-MNM results. This reaffirms the need for increased global compliance to the WHO criteria to improve comparability of MNM data.[4]

The lack of standard MNM criteria implemented across all income settings means that we are left with an incomplete picture of global inequities in the LTR-MNM, with Europe and North America unrepresented. These are the countries where almost all severe maternal outcomes are near miss events, and not maternal deaths, and hence where estimation of the LTR-MNM is imperative. Unlike most existing criteria used in high-income countries, the WHO near miss criteria do not use ICD codes, although ICD codes are routinely used in public health surveillance in most high income countries.[19] This likely contributes to the low uptake of the WHO criteria across high-income settings.[19] The application of ICD codes to the WHO clinical and laboratory criteria may facilitate measurement in countries' routine administrative records or Health Management Information Systems. In turn, this may help to incentivise compliance with the WHO criteria and improve the consistency of MNM measurement across income settings.

Finally, our systematic search for MNM data highlights a lack of nationally representative MNM data in many countries. Ultimately, the development of surveillance systems to institutionalise routine collection of MNM are essential to improve the availability of national-level MNM data and its global comparability.[4,30] Continuous monitoring frameworks developed in Latin America and the Caribbean propose prospective and retrospective identification of MNM cases in health facilities based on WHO criteria, before aggregation and review at local, regional, and national Maternal and Perinatal Morbidity and Mortality Surveillance and Response (MPMMSR) committees.[4,30] However, as electronic health records are a pre-requisite for the successful implementation of these initiatives, this underscores the need for health system digitisation to improve national MNM surveillance in many LMICs, especially in sub-Saharan Africa.

Strengths and limitations

Although this study has multiple strengths – including its novelty, advancement of population-level indicators of maternal morbidity, and our attempts to standardise heterogeneous MNM measurement – it also has limitations.

First, the LTR-MNM is a population-average measure that does not account for heterogeneity of risk within a population (by parity, age, previous morbidity, etc.). Second, the use of WHO and modified WHO criteria may miss true MNM cases, meaning our LTR-MNM estimates may be conservative. Third, our estimates may not be nationally representative, especially for countries where the adjusted MNM ratio estimate is based only on regional or multi-facility data. This reiterates the need for more nationally representative MNM data. Fourth, differences in study design and MNM measurement are substantial, and for countries with multiple studies, the random effects model might not solve all heterogeneity problems. Our approach to standardise study design differences (facility vs. population-level MNM ratio estimates) also has a considerable effect on the estimated level of obstetric risk in some African populations. This emphasises the need for more standardised, population-level data on severe maternal morbidity, especially in LMICs. Finally, some input data may have included MNM cases among women and girls outside of the age range used to calculate the LTR-MNM (i.e., below age 15 or above age 49), although the overall effect on the LTR-MNM is likely to be small.

Conclusion

Our findings expose substantial global and regional disparities in the cumulative burden of maternal near miss morbidity across the female reproductive life span. The LTR-MNM and LTR-SMO are valuable indicators to emphasise the magnitude of maternal morbidity and mortality, and the need for the global community to redouble its efforts to improve maternal outcomes.

Declarations

Ethics approval

Ethics approval was not required to calculate the LTR-MNM as we used population-level data available in the public domain (published data on the MNM ratio and twin birth rate, and open-access fertility and mortality data from the United Nations World Population Prospects).

Data availability

The full list of included MNM estimates are available in the supplementary material. Data on the twin birth rate are available from Monden et al (2021) Supplementary Table 2.

World Health Organization data on the institutional delivery rates are available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/institutional-births-(-)

WHO and UN Joint Agency estimates of the maternal mortality ratio are available at: https://www.who.int/publications/i/item/9789240068759

All fertility and mortality data used in this article are available for download from the United Nations World Population Prospects Download Centre: https://population.un.org/wpp/Download/Standard/CSV/.

All code is available at: https://osf.io/n3uwx/?view_only=649efa0029ab4285b3f7a3e0143c5f95

Author contributions

U.G. conceived the idea, developed the search strategy, ran the database searches, extracted the maternal near miss data, performed the computations, developed the code, and drafted the initial manuscript. J.R.P., J.M.A., A.P., G.R. and V.F. supported the refinement of the study design and the interpretation of results. A.P. developed the code and built the code repository. J.R.P., J.M.A., A.P., G.R. and V.F. revised the article. U.G and A.P accessed and verified the data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Conflict of Interest

None declared.

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Chapter 8 Discussion

Stagnating progress to reduce maternal mortality, persistent and substantial inequities in maternal outcomes, and a rapidly changing epidemiological profile of maternal health challenge the global maternal health agenda in 2024. Against this backdrop, the overall aim of this thesis was to contribute to advances in the conceptualisation and measurement of maternal morbidity and mortality. In Chapter 1, I outlined five specific objectives of this thesis. These objectives intended to confront the 'measurement trap' described in Chapter 2: the lack of information and comparative neglect from the global maternal health agenda concerning (1) adverse maternal outcomes beyond 42 days postpartum, and (2) the burden of maternal morbidity throughout the reproductive lifespan.

This chapter is divided into four sections. First, I synthesise how each research objective was met and the key findings from each of the five papers included in this thesis. Second, I summarise the cross-cutting limitations of this research. Third, I summarise the key implications of each paper for measurement; for health services and clinical practice; for guidelines and multilateral support; and for further research. Finally, moving towards a life cycle approach to maternal health, I discuss two cross-cutting implications of my work: the importance of reconceptualising the postpartum period, and the need to reconceptualise the cumulative risk of severe maternal outcomes across the female reproductive life cycle.

8.1 Synthesis of findings

8.1.1 Objective 1

To determine the duration of an elevated risk of death following childbirth and delivery up to one year postpartum in sub-Saharan Africa

Objective 1 was achieved in Chapter 3 (Paper 1) titled: "*Women's risk of death beyond 42 days postpartum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa*" (178). Pooling population-level HDSS data from 30 sites across 12 countries, I estimated the duration of an elevated risk of death to assess the validity of the 42-day postpartum

threshold. This is the first multi-country study that estimates the risk of death in the extended postpartum period in sub-Saharan Africa. Relative to a baseline risk period of 12-17 months postpartum, the adjusted rate ratio of death from 43 days to four months postpartum was 1.20 – corresponding to a 20% increased risk of death. Extending the 42-day postpartum threshold up to four months postpartum would increase the postpartum pregnancy-related mortality ratio by 40%. These deaths would be excluded from definitions of maternal and pregnancy-related mortality that include deaths only up to 42 days postpartum, and hence excluded from the MMR and PRMR. This finding strengthens the case for a review of the 42-day threshold used in these definitions to capture the full duration of an elevated risk of death. It emphasises the need for an internationally agreed indicator called 'late pregnancy-related mortality' to monitor deaths from 43 days to one year postpartum, when cause of death data are not available. Finally, it also reaffirms calls for the schedule and content of postpartum care packages to be revised to reflect this elevated risk up to four months postpartum.

Paper 1 analysed postpartum mortality in sub-Saharan Africa. This work prompted the following research question to understand causes of death in the extended postpartum period:

1. What causes are women dying from beyond 42 days postpartum in sub-Saharan Africa? (Explored in Paper 2)

Paper 1 identified an elevated risk of death up to four months postpartum across the pooled sample. Prior research suggests that women who experience severe obstetric complications are a subgroup at a higher risk of mortality in the extended postpartum. Some of these women may have experienced chronic or unresolved maternal morbidity beyond 42 days postpartum. To better understand women's experiences in the extended postpartum, including access to- and utilisation of- postpartum care, Paper 1 therefore also prompted the following research question:

2. How can we understand women's recovery trajectories beyond 42 days after severe maternal morbidity in a high maternal mortality context? (Explored in Paper 3)

8.1.2 Objective 2

To determine the causes and circumstances of death during pregnancy and up to one year postpartum in sub-Saharan Africa.

Objective 2 was achieved in Chapter 4 (Paper 2) titled: "*Pregnancy-related mortality up to 1 year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries"* (179). This is the first multi-country study of pregnancy-related deaths up to one year postpartum in sub-Saharan Africa. Although Paper 1 identified an elevated risk of pregnancy-related death up to 4 months postpartum, in Paper 2 I analysed the cause of death up to one year as a more conservative cut off, until the duration of risk is analysed in more populations, using more data sources. Pooled verbal autopsy data from 10 HDSS highlighted the predominance of deaths from infectious and non-communicable diseases in the extended postpartum period, with direct obstetric causes significantly less likely than for deaths occurring during pregnancy and within 42 days. HIV and TB were the dominant causes beyond 42 days, and there was no significant change over time (2000-2009 vs. 2010-2019).

Cross-country heterogeneity in the cause distribution was substantial. In Southern Africa, a significantly higher proportion of late pregnancy-related deaths were attributed to HIV and TB, whereas in West Africa, infectious diseases were the leading contributors. This variation highlights the urgent need for cause of death data from more countries in sub-Saharan Africa. As the VA algorithms use whether the death occurred within 42 days of pregnancy termination as an input into the probability base, further research is required to understand the effect of this weighting on assignment of cause of death in the extended postpartum.

Circumstances of Mortality Categories (COMCATs) revealed that health system failures – knowledge failures (lack of recognition of the severity of disease or doubts about whether medical care was needed) and access to care (difficulty in receiving care and adhering to treatment) – were important in the circumstances of late pregnancy-related deaths. Access barriers reiterate the importance of

UHC to improve access to care, including from non-obstetric providers, for new onset or chronic morbidity in the extended postpartum.

These barriers to care faced by women who died during the extended postpartum period may also impact many more women who experience severe obstetric complications or chronic morbidity after childbirth. To better understand women's experiences of recovery, clinical care, and familial support beyond 42 days after severe maternal morbidity, this study also prompted the following additional research question:

3. How can we understand women's recovery trajectories beyond 42 days after severe maternal morbidity in a high maternal morbidity context (Kenya)? (Explored in Paper 3).

8.1.3 Objective 3

To develop a theory of longer-term postpartum recovery following severe maternal morbidity in Kilifi, Kenya

Objective 3 was achieved in Chapter 5 (Paper 3) titled: "*Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: A Grounded Theory of recovery trajectories beyond 42 days*" (180). Paper 3 developed a testable theory of women's recovery trajectories in the extended postpartum period after severe maternal morbidity, grounded in women's experiences in Kilifi, Kenya. Based on in-depth interviews with 20 women who were between 6 and 36 months postpartum, I hypothesised that women's recovery after severe maternal morbidity encompasses three interconnected phases characterised by 'loss', 'transition', and 'adaptation' to a new normal. This recovery process is multi-dimensional, potentially cyclical (in the case of repeat pregnancy) and extends far beyond the standard 42-day postpartum period. Women's complex needs following severe maternal morbidity require a re-conceptualisation of postpartum recovery as extending far beyond the standard 42-day postpartum period to inform effective management of chronic morbidity in the extended postpartum. Women's accounts expose major deficiencies in the provision of postpartum and mental healthcare in Kilifi, Kenya. With many women struggling to return to the hospital, improved postpartum care

provision at the primary healthcare level, with reach extended through community health workers, is essential. For some women, particularly those who experienced severe maternal morbidity and/or perinatal death, the results highlight that postpartum care may be required for many months or weeks postpartum. This emphasises the importance of UHC for postpartum health.

For several women in the sample, the experience of morbidity influenced their future fertility decisions. In some cases, moreover, women's experience of maternal morbidity was recurrent, as they had experienced complications in previous and/or subsequent pregnancies. My Grounded Theory therefore highlighted the need to adopt a life cycle approach to understand women's experiences of maternal morbidity and the impact this may have on future reproductive health (fertility preferences, repeat pregnancy, and recurrent episodes of morbidity). Without longitudinal data this is challenging. Therefore, working with the constraints of cross-sectional data most readily available, this study also relates to the following research question:

4. How does the risk of near miss morbidity accumulate over women's reproductive lives due to repeat pregnancy? (Explored in Paper 4).

8.1.4 Objective 4

To develop a new indicator to quantify the cumulative risk of experiencing a maternal near miss complication

Objective 4 was achieved in Chapter 6 (Paper 4) titled: "*The Lifetime Risk of Maternal Near Miss: a novel indicator of maternal health*" (181). Paper 4 proposed a new indicator of maternal morbidity – the lifetime risk of maternal near miss (LTR-MNM) – to estimate the burden of near miss morbidity across women's reproductive lifetimes. Unlike existing measures of MNM prevalence, the LTR-MNM is a period cumulative measure which accounts for three dynamics that determine women's cumulative risk: the level of obstetric risk (i.e., the MNM ratio), the number of times a woman is exposed to pregnancy (i.e., population average fertility-levels), and reproductive age survival (i.e.,

mortality levels). Taking Namibia as a demonstration, the LTR-MNM was 1 in 38, and the lifetime risk of severe maternal outcome (maternal death or MNM, LTR-SMO) was 1 in 30.

This is a novel contribution to global measurement of severe maternal outcomes. The LTR-MNM can reorient how we quantify the burden of life-threatening maternal morbidity in a population. Likewise, the LTR-SMO is a valuable metric to emphasise the combined burden of maternal death and near miss morbidity on women's lives. The intuitive appeal of the concept of lifetime risk means these new indicators could be used to highlight reproductive injustice and leverage increased commitment to ending preventable maternal mortality and morbidity.

Following the demonstration for Namibia only, this study prompted the following research question:

5. How can we understand cross-country variation in the cumulative burden of maternal near miss morbidity on women's reproductive lives? (Explored in Paper 5).

8.1.5 Objective 5

To develop the first comparable, cross-country estimates of the lifetime risk of maternal near miss

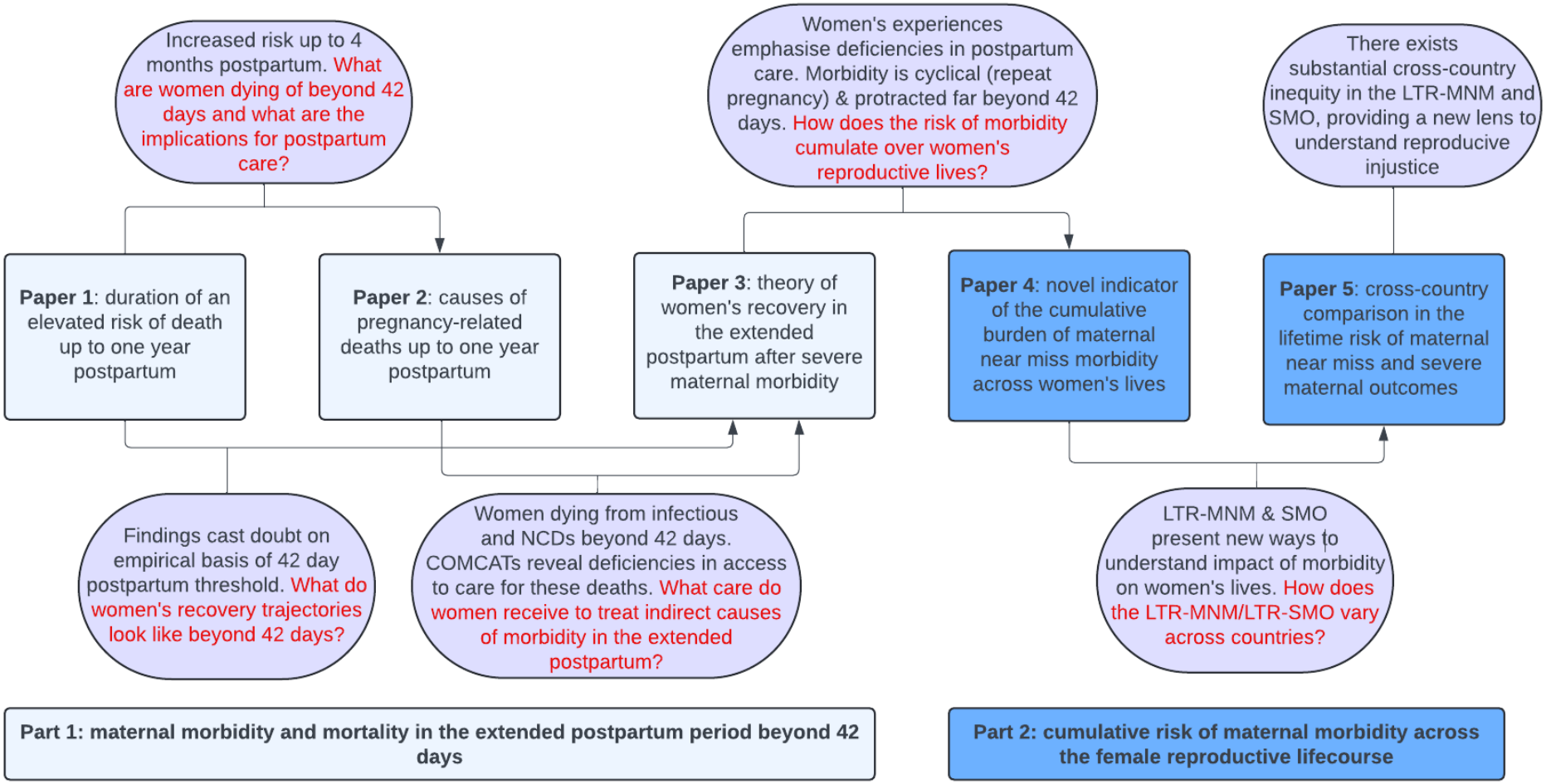
Objective 5 was achieved in Chapter 7 (Paper 5) titled: "*The lifetime risk of maternal near miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis*." I estimated the LTR-MNM for 40 countries across six SDG regions, with multi-facility, subnational, or national data on the MNM ratio. The results reveal substantial cross-country heterogeneity in the LTR-MNM – ranging from a 1 in 6 lifetime risk in Guatemala to 1 in 269 in Vietnam. The LTR-MNM is an important metric to highlight how inequities in obstetric risk are cumulative across women's reproductive lives. High fertility, especially in many sub-Saharan African countries, results in repeated exposure to the risk of near miss morbidity with each pregnancy and contributes to high lifetime risk.

For all 40 countries, I also calculated the LTR-SMO of maternal death or near miss. In 11 countries, a 15-year-old girl has a 1 in 20 risk or higher of either dying from a maternal cause or experiencing a MNM complication in her reproductive lifetime; eight of these countries are in sub-Saharan Africa. The contribution of morbidity to LTR-SMO differs depending on countries' stage in the obstetric transition: countries at an earlier stage with high maternal mortality have a lower contribution of morbidity because a relatively larger proportion of severe maternal outcomes are deaths in these settings. The contribution of morbidity to the LTR-SMO ranges from 42% in Angola to over 99% in Japan. As health systems should focus on reducing preventable maternal mortality and morbidity, the LTR-SMO is an important tool to accentuate reproductive injustice and strengthen advocacy for increased commitment to EPMM.

A key implication of this work is the need for improved standardisation in the measurement of MNM. The analysis was limited to studies using WHO organ-dysfunction criteria or modified WHO criteria for low-income settings. Most studies in high-income countries used broader disease- or management-based criteria, resulting in an incomplete picture of global inequities in the LTR-MNM and LTR-SMO, with Europe and North America unrepresented. The WHO may need to revisit the MNM criteria to facilitate adherence across income levels. Assigning ICD codes to the WHO criteria could enhance their integration into countries' routine administrative records and HMIS. Additionally, the predominance of facility-level estimates also reiterates the need for better population-level maternal morbidity prevalence data.

Figure 8.1 (below) summarises the research questions and findings in this thesis.

Figure 8.1 Schematic of thesis findings and iterative exploration of research questions



8.2 Limitations

Specific limitations of each paper are described at the end of each of the five papers, in Chapters 3-7. In addition to the study specific limitations, I also identify three cross-cutting, broader limitations that emerge from this thesis which affected my research. Within the framing of the measurement trap, these relate primarily to the need for better data sources to analyse maternal outcomes beyond 42 days and the burden of maternal morbidity:

1. Generalisability and representativeness
2. Reliance on facility-based morbidity data
3. Misclassification bias:
    a. Pregnancy status
    b. Cause of death

Each are discussed in turn.

8.2.1 Generalisability and representativeness

Whether findings from a particular setting and using specific methods can plausibly be applied more widely (generalisability) and whether the contextual characteristics of the population under study approximate those of other areas (representativeness) (182) are both important considerations for the papers presented in this thesis. Outdated data, limited geographic coverage, and reliance on subnational data all impact the generalisability and representativeness of my findings.

Outdated data

The burden of maternal deaths is greatest where accurate data for planning and action are not readily available. For deaths occurring beyond 42 days, data are even scarcer, particularly in sub-Saharan Africa. HDSS and VA data are among the main sources of information that help address this deficit, but much of the data are now outdated. Paper 1 included data from 1991 onwards, whereas Paper 2 included data from 2000 onwards. Some of these data are now considerably

outdated, especially considering changes in the HIV epidemic (183). I found that the contribution of HIV and TB did not decline significantly over time (2000-2009 vs. 2010-2019), despite expansions in access to ART over this period (184,185). However, this may reflect either true persistence or a lack of power to detect change. Much of the data in Paper 2 precedes the WHO's 2012 shift in policy towards Option B+, which recommends lifelong ART for pregnant and postpartum women, regardless of gestational age, clinical stage and CD4 cell count (186). Implementation of Option B+ in most priority African countries began between 2013 and 2014 (187). Many countries have also now adopted a 'universal test and treat' (UTT) policy for the whole population (188,189) – which will affect women who are beyond 42 days postpartum and/or who are no longer breastfeeding. The reduction of risk these programmes should confer emphasises the need for more up-to-date data to understand the causes of death in the extended postpartum.

For maternal morbidity, I restricted the MNM prevalence data included in Paper 5 to studies with reference periods from 2010 onwards. However, for some countries included in the analyses, the obstetric risk (MNM ratio), fertility and mortality levels may have changed considerably since then. As is also the case with maternal mortality monitoring, this reiterates how global estimates can be affected by the lag between reference periods and reporting, may be based on sparse empirical data, and may not accurately reflect current conditions (36).

Geographic coverage

Although my work on the risks and causes of death in the extended postpartum goes some way to addressing the evidence gap on these outcomes in sub-Saharan Africa, much of the region is unrepresented. Paper 1 included INDEPTH Network HDSS data from 13 countries; Paper 2 included verbal autopsy data from some ALPHA Network sites and other HDSS from six countries. Countries without surveillance systems also typically lack other data sources (described in section 2.4) to analyse these outcomes beyond 42 days.

The near miss data used in this thesis were similarly limited in terms of geographic coverage. The Grounded Theory of postpartum recovery developed in Paper 3 was based on the experiences of 20 women from Kilifi, Kenya, and should be validated in other contexts, in Kenya and elsewhere. Paper 5 derived cross-country estimates of LTR-MNM and LTR-SMO for 40 countries, but many entire regions (e.g., North America and Europe) were unrepresented in the estimates due to ineligibility of MNM data.

Subnational data

All the data used in this thesis on maternal mortality (Papers 1 and 2) was subnational. HDSS data cover a district-level population and are not designed to be generalisable to the national level (129). Although there are no best-practice guidelines for improving the representativeness or generalisability of HDSS data (182), triangulation with national administrative, census, or survey data, and/or facility-based data may be one approach. However, I did not explore triangulation of sources of maternal mortality data in this PhD and this limited my ability to make national-level inferences.

Similarly, much of the MNM prevalence data used in Paper 5 derived from multi-facility or subnational data that were not nationally representative. Although there are valid reasons to prefer subnational studies despite their lack of national-level representativeness (e.g., due to the type of facilities included, the measurement of MNM cases, and estimation of live births at the population-level), my estimates of lifetime risk may not accurately represent national trends. Since national-level data are often prohibitively expensive to collect and may not always be logistically feasible, methodological innovations to derive nationally representative estimates from subnational data (e.g., advances in small area estimation that can be aggregated (190)) could be an impactful avenue of future research in maternal morbidity and mortality measurement. This was beyond the scope of my PhD.

Conversely, although much of the input data for Paper 5 was subnational, I did not compute disaggregated subnational estimates of the LTR-MNM. To do so would require subnational fertility

and mortality data, which are not readily available (e.g., World Population Prospects data are at the national level). Monitoring regional inequities in maternal outcomes is useful to identify areas of particular deprivation and target health programmes, which are usually administered at the subnational/district level (37,190,191). Future work to generate subnational estimates of the LTR-MNM and LTR-SMO would be an important contribution to highlight inequity within countries and identify areas for prioritisation.

8.2.2 Lack of population-level data on maternal morbidity

Despite growing recognition that maternal morbidity must be a focus of international maternal health policy, reliable, population-level data on maternal morbidity is lacking. In Paper 3, I relied exclusively on facility-level data to recruit women, and the most of the raw MNM prevalence data used in Paper 5 was also facility-based (MNM cases need to be facility-based due to the criteria used in their identification, but live birth estimates can be population-based). I utilised the available facility-level data despite the inherent select biases in contexts where access to affordable health services is limited. In Paper 5, I attempted to address the problem of facility-based live birth estimates – often overlooked in meta-analyses of the MNM ratio – but my approximation was imperfect. Specifically, where data derive from tertiary facilities only, adjusting the denominator (live births) by the institutional delivery rate still results in an underestimation, as many women deliver in primary and secondary facilities.

Additionally, I focused primarily on severe complications because these are more clearly defined. Although I identified some non-life-threatening types of morbidity among women in the sample for Paper 3 (both with and without severe maternal morbidity), these conditions were not identified systematically. These limitations underscore the need for more population-level data on maternal morbidity.

8.2.3 Misclassification bias

For a death to be considered pregnancy-related, accurate assignment of a woman's pregnancy status is required. Accurate classification of the cause of death is required to identify which pregnancy-related deaths are maternal (i.e., not incidental to pregnancy) (77).

a. Pregnancy status

First, all the papers in this thesis depended on accurately identifying women's pregnancy status – whether for the identification of pregnancy-related deaths (Papers 1 and 2), severe maternal morbidity (Paper 3), or maternal near miss (Papers 4 and 5). Misreporting of pregnancy status is a significant source of misclassification in estimates of maternal mortality and morbidity (77,107).

Pregnancy identification within HDSS may face several limitations. First, respondents themselves might not be aware of their pregnancy status. Consequently, the accuracy of pregnancy records in HDSS will depend on the frequency of data collection rounds. Second, many HDSS use proxy respondents (192,193), who may also be unaware of the pregnancy status of each woman of reproductive age in the household. Reporting on pregnancy status is sensitive, and when a pregnancy is deemed appropriate to disclose varies between contexts. Women may choose not to disclose their pregnancy to other household members or HDSS enumerators to avoid gossip – especially in cases of socially stigmatised pregnancies (e.g., among adolescent girls, unmarried women), unwanted pregnancies, or to avoid shame associated with pregnancy loss (75,76). While a field worker might probe if a respondent was visibly pregnant, they are likely to miss many, if not most, first trimester and second trimester pregnancies if they are not disclosed by the respondent or proxy.

Identifying pregnancy status based on recorded birth outcomes also poses challenges. Many HDSS sites register pregnancies only after delivery (live or stillborn) (192). Although most sites collect data on stillbirths, these are likely to be substantially underreported (192), particularly if stigma or taboos

inhibit disclosure to enumerators (75,76). Furthermore, fewer sites collect information on early pregnancy losses, such as miscarriages or abortions (193). Some sites gather pregnancy information exclusively for married women, and only 20% of HDSS supplement pregnancy surveillance with linkage to antenatal clinics (194).

Jointly, these features of pregnancy surveillance within HDSS data mean some pregnancy-related deaths in Paper 1 and Paper 2 may have been misclassified as non-pregnancy-related. In Paper 1, my analysis was restricted to postpartum mortality after delivery (of a livebirth or stillbirth) because pregnancy status was not available in the consolidated INDEPTH Network data. In Paper 2, four sites included data on early pregnancy losses, and I also included deaths where no delivery was recorded but a proxy respondent indicated that the woman was pregnant or recently pregnant at the time of death. However, this approach does not fully address the misclassification issues, and deaths after early pregnancy termination (e.g., ectopic pregnancy and unsafe abortion) may still be underrepresented.

Misclassification of pregnancy status was less of a concern for Paper 3 because the PRECISE study tested women of reproductive age for pregnancy. However, with an average gestation of 20 weeks at enrolment, women who had miscarriages or abortions earlier in pregnancy were unlikely to be included in the PRECISE cohort (the sampling frame for Paper 3). Some women may have experienced severe maternal morbidity following these outcomes, and their postpartum recovery trajectories may have differed from women with a live birth or stillbirth, but they were not included in my analyses.

Finally, in Papers 4 and 5, misclassification of pregnancy status may have led to the omission of some MNM cases from the raw input data. This could downwardly bias the MNM ratio and underestimate the LTR-MNM. Like maternal deaths, this may be a particular issue for socially stigmatised pregnancies and related complications (e.g., from unsafe abortion), where women may avoid seeking treatment at a facility or where the cause of complications might not be accurately

recorded in medical records. Misclassification is likely to vary depending on input data, with different protocols used across studies. I was unable to assess the magnitude of this limitation in my analyses.

b. Cause of death assignment

Verbal autopsy data are an essential source on information on causes of death in the extended postpartum in contexts where medical certification of the cause of death is inadequate. However, in addition to the more general VA misclassification biases for maternal mortality outlined in Chapter 2, automated algorithms may be an imperfect way to assess differences in the causes of death beyond 42 days specifically. This is because whether the death occurred within 42 days is an input in the probability base, meaning InterVA5 and InSilicoVA may be more likely to attribute a direct obstetric cause to deaths occurring within the 42-day postpartum period, and less likely for deaths occurring afterwards. While this could significantly impact cause attribution, investigating this potential bias was beyond the scope of my PhD. Given the WHO's recommendation to integrate VA within CRVS systems to address deficits in medical certification of causes of death in many low resource countries (115,135–137,139), this represents an avenue of research with potentially significant implications for understanding late pregnancy-related mortality.

My experiences attending VA interviews in person during my ESRC-funded International Institutional Visit to the MRC The Gambia after paper 2 was published prompted further reflections on the utility and limitations of VA data. Many respondents provided few affirmative responses (i.e., low endorsement rates) to questions on symptoms and provided very little detail in the narratives, particularly for neonatal and infant deaths. This raised concerns about whether respondents can reliably recall the sequence of events and symptoms of the deceased, especially in cases of acute illness with non-specific symptoms. The trauma of witnessing a death may either help, hinder, or distort a respondent's recall of events (196). Not all deaths are traumatic, but unexpected deaths among pregnant and recently pregnant women could be, whose death may be perceived as less 'natural' than those of older adults (197). Deaths may also be traumatic to witness but have few

obvious signs and symptoms. Investigating how the recall of (late) maternal and pregnancy-related deaths varies depending on the cause of death was beyond the scope of this PhD.

Relatedly, recall time between death and VA interview may potentially affect the assignment of the cause of death. In one study, longer recall time increased the odds of assignment of HIV/AIDS but reduced the odds for infectious diseases (198)). Choosing a recall period that minimises participant harm, however, is also an important consideration (197,199). I did not examine the effect of recall time in my analyses, but this could have introduced bias if VA interviews for deaths occurring within 42 days were conducted more quickly than for those occurring in the extended postpartum (107).

Finally, in Paper 2, I extracted the single most likely cause of death attributed by InterVA5 (and InSilicoVA for sensitivity) for each pregnancy-related death. This approach was the most straightforward and made it easier to communicate findings when deaths were disaggregated by timing of death. However, this represents only one possible approach to analysing VA data. The results might have differed if I had extracted all probabilities assigned to each cause for each death and aggregated the probabilities across individuals.

8.3 Study specific implications

From each of the five papers presented this thesis (Chapters 3-7), I identified implications for measurement, health services and clinical practice, policy guidance, and future research. These implications are described in Table 8.1.

Table 8.1 Paper specific implications

Implications for measurement	Implications for health services and clinical practice	Implications for health policy guidance	Implications for research
Paper 1: Women's risk of death beyond 42 days postpartum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa			
• When more supportive evidence exists across countries, this will justify a review of the 42-day threshold used to identify maternal and pregnancy-related deaths in ICD-11. • Need an internationally agreed definition of 'late pregnancy-related deaths'. These deaths otherwise fall through the cracks of national and international surveillance. • Household surveys that use the sisterhood method, such as the DHS, should extend measurement of pregnancy-related mortality up to one year postpartum (with a separate sub-question for disaggregated statistics by timing) for a source of comparable, population-based data. • Need to improve HMIS linkage of women's pregnancy/delivery status within one year and admission to other wards to identify potential late maternal deaths.	• Risk of death remains elevated until roughly four months postpartum. This means there is a need to revisit the schedule and content of postpartum care beyond 42 days. The six-week visit could be used to identify women at higher risk of chronic morbidity and a higher risk of death in the extended postpartum period who should be prioritised for further care and monitoring.	• Need to revisit the schedule and content of postpartum care, with a fifth contact scheduled beyond 42 days. • There is a need for greater WHO support for all countries to monitor and report late maternal mortality in CRVS systems. This includes efforts to improve adherence to ICD-11 coding procedures to improve standardisation and reduce ad hoc coding that prevent these data from being used. • WHO should support the strengthening of MPDSR and CEMD in low-resource countries to identify late maternal deaths that occur outside of obstetric wards or in the community. Deaths outside of the facility will require VA to identify potential causes if no attending physician was present to certify the cause of death.	• Need to research the causes of pregnancy-related mortality beyond 42 days, especially in other high burden settings, to contribute to the evidence base on the duration of an elevated risk of death across populations. This should include more up-to-date data.
Paper 2: Pregnancy-related mortality up to one year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries			

• Need for better vital registration of deaths and medical certification of the cause of death in the extended postpartum period in high burden contexts. Improved medical certification is a by-product of greater access to health services and more deaths occurring in facilities. • In settings reliant on VA data for cause of death information, there is a need for improved linkage of VA with clinical records to triangulate data. This is essential to differentiate which pregnancy-related deaths from indirect causes are indirect maternal deaths and which are coincidental to the pregnancy (i.e., non-maternal). This is not possible from VA data alone. • Need to validate VA algorithms against gold standard medical certification for late pregnancy-related deaths occurring beyond 42 days postpartum.	• Health systems are more geared towards reducing deaths from direct obstetric causes, and less so from indirect causes that are the dominant causes of late maternal deaths. Indirect causes will also become more important as countries continue to progress through the obstetric transition. There is a need for improved integration of obstetric and non-obstetric care providers in the postpartum period, to treat infectious diseases and NCDs. This may also require improved training of providers to identify and manage chronic indirect causes of maternal morbidity. • There is a need to improve access to care in the extended postpartum period through a fifth postpartum visit, prioritising women at high-risk of morbidity and mortality if providing universal services in the extended postpartum is not financially feasible. This is also a consideration for UHC: Otherwise, in many health systems, out-of-pocket costs may prevent women from accessing care for chronic conditions or maternal morbidity that presents later than 42 days.	• Need for guidance on the integration of obstetric and non-obstetric care for women with delayed onset or unresolved, chronic pregnancy-related morbidity in the extended postpartum period. • Need for guidance on improving the provision of and access to care beyond 42 days postpartum, including the schedule of postpartum care (fifth contact) and UHC.	• Need for population-based estimates of the prevalence of morbidity in the extended postpartum. • Need for further epidemiology and pathophysiology research on women's postpartum immune response and potential susceptibility to a deterioration of HIV and TB infections beyond 42 days postpartum. This is important to disentangle why there are so many deaths from infectious diseases in the extended postpartum. Research should focus on risks and potential causal mechanisms if increased risk exists. This includes co-infection and co-morbidity of infectious and NCDs in the postpartum period. • Need to update the evidence for the proportion of all HIV-related deaths to pregnant and recently pregnant women that are assumed to be HIV-related indirect maternal deaths. The WHO currently uses an estimate of 0.3 – meaning 30% of all HIV-related deaths among pregnant and recently pregnant women are assumed to be indirect maternal deaths; the remaining 70% are assumed to be coincidental to the pregnancy. This includes efforts

	• Postpartum care programmes in contexts with a high prevalence of HIV and TB require more emphasis on treatment adherence during pregnancy and the postpartum. Complication readiness programmes should also include postpartum monitoring of women living with HIV, which should extend beyond 42 days. Those involved in HIV and TB service provision must also be made aware of potential risks of non-adherence and disease progression in the extended postpartum period.		to estimate the proportion of late maternal deaths that are HIV-related indirect late maternal deaths. There is currently no WHO estimate for the proportion of HIV-related deaths among postpartum women beyond 42 days which are late maternal deaths. • Whether a death occurred within 42 days of pregnancy is an input in the probability base for InterVA5 and InSilicoVA. Need further research to ascertain the effect of the 42-day threshold on VA assignment of direct obstetric vs. indirect causes of death beyond 42 days.
Paper 3: Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: A Grounded Theory of recovery trajectories beyond 42 days			
• Need to reconceptualise the postpartum period as extending far beyond 42 days for women to feel 'recovered' beyond a strictly clinical assessment.	• Need for improved communication between providers and women about the type of morbidity they experienced, treatment received, and aftercare required (including follow-up beyond 42 days). When appropriate, for example where women are incapacitated and when accompanied by members of their social network, improved communication between providers and those accompanying her is required. • Need for improved provision of postpartum care at the PHC	• Need for guidelines on the integration of maternal health care – routine postpartum care – with non-obstetric care for chronic/untreated conditions in the extended postpartum, with an emphasis on mental health support. Guidelines on integration of perinatal mental health with exiting MCH services exist, but this does not include an explicit focus on the extended postpartum when routine postpartum care contacts have finished (200).	• Need to validate the Grounded Theory 'loss', 'transition', and 'adaptation' among other populations. • Need further research to identify which high-risk women are the most likely to need care for the longest duration to inform sub-population prioritisation for further follow-up in the extended postpartum, particularly in low-resource contexts. • Need for population-based prevalence estimates of delayed onset or chronic pregnancy-

	level, and in some settings, with CHWs to extend access and utilisation for women unable to return to the facility. • Need to improve the provision of care and coverage of services beyond 42 days, especially for women with severe maternal morbidity or who experienced perinatal death. Some women may need referral to specialist services, and some may require care for months or even years. This emphasises the need for UHC. • With several women experiencing recurrent episodes of maternal morbidity, this emphasises the need for services to incorporate the continuum of care to include a focus on optimising pre-pregnancy and interconception health to reduce risks in subsequent pregnancies. This includes health worker training on the future risks associated with certain interventions and birth complications that increase the risk of medium-to-long term complications (e.g., mental health conditions, incontinence, cardiomyopathy, fistula, venous thromboembolism, HIV seroconversion) and risks in subsequent pregnancies (e.g., uterine rupture, placenta previa	09/10/2024 10:32:00	related morbidity in the extended postpartum period. • Need for further research to develop a standardised package of postpartum care beyond 42 days that can be adapted to different contexts and health systems.

	or accreta, placental abruption, secondary infertility (18)).		
Paper 4: The lifetime risk of maternal near miss: a novel indicator of maternal health			
• Need better population-level data on the MNM ratio where the denominator accounts for births occurring outside of facilities. • Need to re-examine denominators of measures of maternal risk. Women are at risk of MNM (or maternal death) with each pregnancy they have, not each live birth. Pregnancies can end in livebirth, stillbirth, miscarriage, or abortion. However, there may a trade-off between fixing the incongruence between the numerator and denominator of maternal ratios, and the difficulties of pregnancy surveillance and misclassification. Measurement should explore the use of total pregnancies or total births, relative to live births, as the denominator of maternal ratios (MMR, PRMR, MNMR, SMOR etc.)	• The cumulative risk of MNM increases multiplicatively with to fertility levels. This emphasises the need to ensure access to contraception and safe abortion services for all women who wish to use these.		• Need better data on the parity-specific and age-specific risk of MNM to account for heterogeneity in the risk of maternal near miss. LTR-MNM is a population-average measure which does not account for potential heterogeneity of risk. • Need better data on women's risk of experiencing recurrent near miss complications i.e., future risk if she experienced a MNM in a previous pregnancy to inform interconception care.
Paper 5: The lifetime risk of maternal near miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis			
<u>As above for paper 4</u>, but also: • Need comparable MNM ratio estimates that adhere to WHO organ dysfunction MNM criteria,	<u>As above for paper 4</u>	<u>As above for paper 4, but also:</u> • Need to understand barriers to adoption of the WHO standard MNM criteria in high- and low-	<u>As above for paper 4, but also:</u> • Need methodological research to inform the aggregation of subnational (regional and multi-

to include high-income countries in the measurement of LTR-MNM. • Need national surveillance systems to institutionalise the routine monitoring of MNM through MPDSR, such as the continuous monitoring frameworks in Latin America. In turn, these systems require greater health system digitisation to facilitate national aggregation.		income countries. Including ICD-11 codes for clinical/laboratory criteria may help improve compliance. Difficulties with application may require WHO to revisit the criteria with the objective of improving uptake and comparability of MNM data so it is feasible to use MNM (or dependent metrics) for global monitoring. • Need to advocate for maternal morbidity metrics such as the MNM ratio or LTR-MNM to be considered among indicators of progress for the post-SDG era. The decision to put maternal morbidity at the forefront of the maternal health agenda is a WHO/ UN policy decision. Improved comparability of data is likely a pre-requisite to adoption of MNM metrics in global targets, however.	facility) MNM data to derive nationally representative estimates of MNM prevalence where national surveys are not available.

8.4 Cross-cutting implications of my PhD research

The overarching implication of my work is for the need to move towards a life cycle approach to improve maternal health. The need for such an approach has been articulated previously, for example in Filippi et al.'s conceptual framework of maternal morbidity (19) and in Firoz et al.'s related framework for interventions to address maternal morbidity (20). The life cycle approach is a longer-term perspective which integrates reproductive episodes of women's lives (pregnancy, labour, postpartum, and extended postpartum periods) within women's lifetimes, including pre-menarche, pre-pregnancy, peri-menopausal, menopausal, and post-menopausal stages. Adopting this conceptualisation can help to facilitate closer integration of maternal health policy, practice, and measurement with NCD and infectious disease agendas. This approach acknowledges that maternal outcomes are not limited to the nine months of pregnancy, but intrinsically linked to women's health over the life course, including pre-conception health (19). Conversely, women's future post-reproductive health is also intrinsically linked to her health earlier in the reproductive life course (19,20). For example, conditions such as pre-eclampsia are associated with an increased future risk of hypertension, stroke, and cardiovascular disease (201), while gestational diabetes mellitus is linked to a higher risk of type 2 diabetes later in life (202,203).

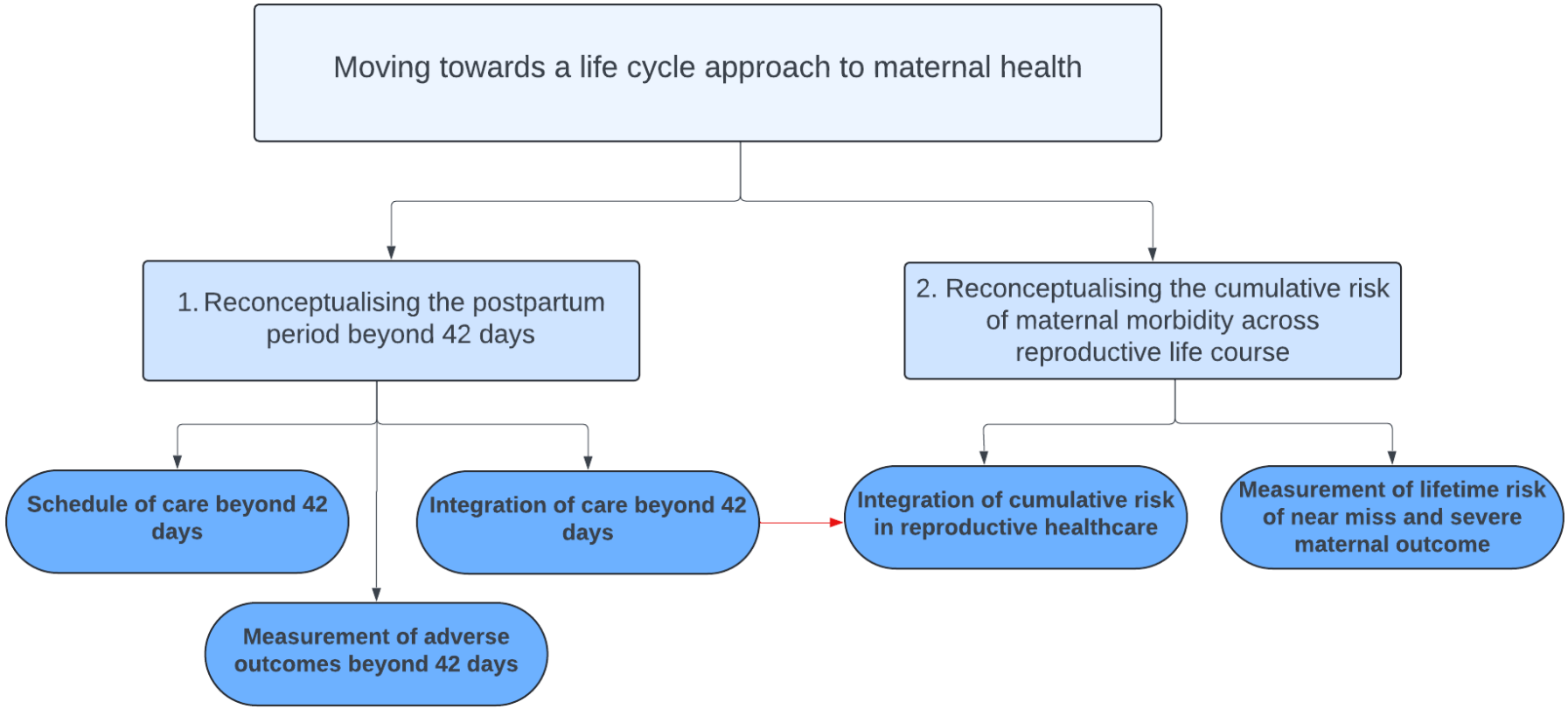
In many LMICs, maternal health services often represent the only contact women of reproductive age have with health services. Thus, pregnancy and the postpartum period become key windows of opportunity to improve women's overall health (19,20,204). My research highlights two specific areas where moving towards a reproductive life cycle approach can help to reorient the maternal health agenda to improve outcomes:

1. To reconceptualise the postpartum period beyond the standard 42-day definition, with implications for the:
    a. Schedule of care beyond 42 days
    b. Integration of postpartum care beyond 42 days
    c. Measurement of maternal morbidity and mortality beyond 42 days

2. To reconceptualise the cumulative risk of maternal morbidity across the reproductive life course, including:
    a. Integration of cumulative risk in models of reproductive healthcare
    b. Measurement of the lifetime risk of near miss morbidity and severe maternal outcome

These cross-cutting implications, and the interconnections between them, are shown in Figure 8.2:

Figure 8.2 Cross-cutting implications of PhD research



8.4.1 Reconceptualising the postpartum period and reimagining postpartum care

Postpartum care remains the most undervalued component of the maternal care continuum (25,205,206). It consistently has the lowest coverage rates (161), and postpartum care coverage is not an indicator used to assess UHC (207). This is despite the majority of maternal deaths occurring in the postpartum period (59) and this proportion is increasing globally (59,117,208). The postpartum period – also named 'the fourth trimester' (209,210) – is a critical time to support the transition to parenthood and promote healthy behaviours for women and the care of her baby (25).

Postpartum services have been criticised for their tendency to focus predominantly on the baby, and to some extent, neglect women's needs beyond their new role as mothers (211). However, postpartum care is essential for identifying and managing acute and chronic maternal morbidity and for reducing lifelong risks associated with pregnancy-related physical, mental, and sexual health problems (25,207,212). Women whose pregnancy does not end in a live birth (miscarriage, stillbirth, abortion) may also require access to appropriate services. The quality-of-care women receive during the postpartum period can affect their health trajectories for the rest of their lives. This underscores the importance of postpartum care as a key opportunity to improve women's health (204).

A joint implication of my work is the need to revisit the postpartum period, including a re-evaluation of its importance for women's wellbeing and long-term health outcomes. The convention of defining the postpartum period as the first 42 days following childbirth, termination, or miscarriage, is entrenched with far-reaching implications for the maternal health agenda. However, there is growing recognition that the current conceptualisation of the postpartum period is not adequately oriented to the timing and diversity of postpartum challenges women face (18,19,64). The 2023 Lancet series suggests a paradigm shift is underway. This series voiced new evidence-based narratives from leading maternal health experts on the need to take a longer-term lens to women's postpartum

health, prioritise morbidity beyond 42 days, and re-evaluate how recovery trajectories are conceptualised (9,18,21).

A reconceptualisation of the postpartum period could take several forms, and some changes may be easier to implement than others. Below I discuss three areas of reconceptualisation to the postpartum period: a. The recommended schedule of care; b. Integration of care; and c. Measurement of maternal morbidity and mortality, beyond 42 days postpartum.

a. Schedule of postpartum care beyond 42 days

The standard definition of the postpartum period up to 42 days following childbirth, termination, or miscarriage determines the upper boundary of the WHO's recommended schedule of postpartum contacts. The 42-day upper limit for recommended postpartum contacts is vitally important because it determines the outer limit for when unresolved chronic postpartum physical, mental, or sexual health problems can be identified through routine postpartum care. Beyond this time point, treatment and management of postpartum morbidity not previously identified or that manifests later requires women to self-elect to seek care. This creates an additional barrier to women accessing appropriate care for ongoing morbidity beyond 42 days postpartum. It also narrows clinical prioritisation to the prevention and treatment of maternal morbidity and mortality which occurs within this 42-day timeframe (19,213).

Only recently has recognition grown that this timeframe is not fit for purpose (18,69). A comprehensive review by WHO is needed to ensure international guidelines for the schedule of postpartum care are evidence-based and able to meet women's needs in the postpartum period and beyond. Undoubtedly, a shift in the WHO's recommended schedule of postpartum care beyond 42 days is insufficient in isolation to change the provision of postpartum care. However, it is necessary to establish best practices and improve awareness of maternal outcomes beyond 42 days postpartum at regional and national levels. Updates to this guidance should be informed by further

research to determine how long routine care should be provided to women (and their babies) and whether this should be provided universally to all women or to subpopulations who are at greater risk of adverse outcomes beyond 42 days postpartum. These considerations are discussed below.

Postpartum contact beyond 42 days

A fifth, delayed postpartum contact could provide a key routine outlet to identify unresolved or delayed-onset morbidity and optimise interpregnancy health in the following ways: screening (e.g., for conditions that may not present or be identified until after 42 days, such as postpartum depression, fistula, and HIV/TB in high-prevalence contexts), monitoring and treatment of chronic conditions (e.g., hypertension, peripartum cardiomyopathy, and HIV/TB), and to offer women additional support with contraception (69). The optimal schedule for a fifth visit requires rigorous feasibility, acceptability, and cost-effectiveness assessments. Epidemiological research is also needed to assess the impact of contact timing on maternal outcomes in the extended postpartum period. However, a six month postpartum visit might be an intuitive place to start for a fifth postpartum contact (69,214) as this revisits the WHO's 1998 guidance (218), is the minimum recommended birth interval (216,217), coincides with the recommended schedule for multiple routine immunisations for children (218), and encompasses the period of an elevated risk of death I identified in Paper 1 (4 months) (178).

Existing challenges in the coverage and utilisation of postpartum care in LMICs

The existing coverage and uptake of the WHO's four recommended postpartum contacts up to 42 days is poor in many LMICs (206). A 2019 study of DHS data across 33 countries in sub-Saharan Africa found one-third of women did not receive a single clinical consultation between delivery and discharge from the health facility (219). However, the survey year ranged from 2006 to 2015, and with a five year recall period, some of this data are now considerably outdated (223). A 2015 systematic review and meta-analysis found that postpartum care within 2 days of birth remains highly inequitable across LMICs (based on DHS data from 2005 to 2010) and use of postpartum services varies by socioeconomic status (data from 2007 to 2012) (220). Based on data from 2003-2019 and

2002-2013, respectively (221,222), barriers to the uptake of postpartum care include access constraints (health insurance, transportation), the perceived and actual quality of services, and social norms (221), in addition to a lack of awareness of postpartum care, low health literacy, and lack of autonomy (222). For adolescents, barriers to utilisation may further include a lack of knowledge around the benefits of postpartum care and stigma from healthcare providers (based on data from 2007 to 2018) (205). Although much of the data is now outdated, many of these findings suggest that greater attention should be paid to the quality and content ('effective coverage') of postpartum care to encourage women to return to facilities (206).

Health financing constraints, poor coverage, and low uptake of existing postpartum care services suggest extending care beyond current standards would be challenging for many health systems (69). Despite these challenges, the current difficulties in the routine provision of postpartum care in LMICs should not prevent us from redefining the gold standard based on updated evidence. In 2016, the WHO re-defined the recommended ANC model from basic ANC with four visits (i.e., the 'goal oriented' model) to eight recommended ANC contacts (223), even though many countries in sub-Saharan Africa had not yet achieved coverage of at least four ANC visits (ANC4+) (224). It is important that the upper limit of the WHO's recommended postpartum contacts is informed by evidence on improving maternal outcomes in the extended postpartum, rather than being constrained by the feasibility and implementation challenges of certain health systems.

Universal or targeted fifth postpartum contact

There is a need to define a standard package of routine care at a fifth postpartum contact that can be adapted across contexts (64,225). In low resource settings, an initial step towards universal provision of this additional contact could involve targeting women identified as being at a higher risk of chronic mental or physical morbidity during in the extended postpartum period. Based on the findings from Paper 3, a non-exhaustive list of high-risk groups may include: women who have had a traumatic childbirth (assessed using a PTSD screening tool, e.g., Trauma Screening Tool (TSQ) for primary care (64,225,226)), those who screen highly for symptoms of depression or anxiety,

women with chronic conditions, those who had a PLTC (severe haemorrhage, eclampsia, severe preeclampsia, sepsis, uterine rupture), women who experienced a stillbirth or neonatal death, and those who had an emergency caesarean or hysterectomy. The fourth (six week) postpartum visit provides an opportunity to systematically identify these subpopulations and triage them as high priority for a fifth follow-up contact.

Mode of contact

In low resource settings, it may not be appropriate or feasible for a fifth postpartum contact to be a traditional in-person clinic visit, particularly where transport costs are high (227). A variety of alternative contact types are available, including home visits, telephone consultations, self-administered questionnaires, or a combination (227). Participatory action research is needed to determine the best way to deliver care beyond 42 days (64). Based on the findings of Paper 3 in Kilifi, Kenya, in this context specifically, strengthening provision at the PHC level, supported by CHWs to extend its reach, could improve uptake. The WHO 2022 postnatal care guidance web annex also highlights the efficacy of postpartum care home visits after uncomplicated births by trained CHWs, compared to routine outpatient postpartum care, as a priority research question to improve maternal outcomes (62). However, implementation research to assess the feasibility, cost-effectiveness, and uptake of a fifth postpartum visit needs to be context specific, based on the extension of PHC services and role of CHWs, health system financing, mobile phone coverage, and the availability of electronic health records (227).

For low-risk women, group-based postpartum care, facilitated by PHC doctors, nurses, midwives, or CHWs, may offer cost-effective opportunities to provide care beyond 42 days in low-resource settings. There is some evidence supporting the efficacy of women's participatory groups and the benefits of peer-to-peer support for antenatal care (228,229), healthy behaviours during or after home deliveries (230), and the reduction of maternal, neonatal and stillbirth mortality (231). However, there has been less research focused on the efficacy of group-based models for postpartum care (64). Co-designed prototypes developed with pregnant and postpartum women and health care

workers in Malawi suggest that sessions should correspond with child vaccination schedules to provide multiple opportunities for assessments and screening (232). Additionally, meeting the same provider repeatedly throughout the postpartum and extended postpartum periods could improve women's assessments of the quality of care (232).

CHW-led models of at-home care may also present an opportunity to provide care in the extended postpartum while relieving pressure on facility-based services in low-resource settings. An example of this approach was the Community-Level Interventions for Pre-eclampsia (CLIP) trials. CLIP was an mHealth supported task-sharing intervention, where trained CHWs supported by digital devices provided at home assessment, basic treatment, and triage for pregnancy hypertension up to six weeks postpartum (233). For women identified during the six-week postpartum visit as requiring further follow-up, an CHW mHealth supported platform was used to triage women for a fifth postpartum visit.

b. Integration of postpartum care beyond 42 days

The provision of clinical care for chronic or delayed onset pregnancy-related morbidity beyond 42 days requires improved integration of services in the extended postpartum period. This includes strengthening the integration of postpartum care with primary care, maternal and child health care (MCH), as well as with non-obstetric specialisms. These are key cornerstones of integrated care, defined by the WHO as "*health services that are managed and delivered so that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease-management, rehabilitation and palliative care services, coordinated across the different levels and sites of care within and beyond the health sector, and according to their needs throughout the life course*" (234).

The level of care women require beyond 42 days depends on the type and severity of morbidity. For most women, the final postpartum contact is the key transition point from maternity services to primary healthcare services. Without coordinated transitions between these levels of care, women

are at risk of falling through the cracks of service provision (20). Efficient transition mechanisms can help ensure that women with chronic or delayed onset pregnancy-related morbidity beyond 42 days can still access essential services. This is crucial for many forms of morbidity which are not potentially life-threatening, but still negatively impact women's wellbeing (19).

Some women who experience ongoing morbidity beyond 42 days, however, may require specialist care, necessitating referrals from routine postpartum services to specialist providers in the extended postpartum period. For instance, referral may be needed for specialist mental health services (for moderate to severe postpartum depression, suicidal ideation, or PTSD); urogynaecology (for urinary incontinence, pelvic floor dysfunction) and cardiology (for peripartum cardiomyopathy). Effective postpartum referral processes require maternity care providers receive adequate training on referral criteria (200), but even more fundamentally, that specialist services to refer women to are available (214). In many LMICs, the availability of specialist care doctors are severely constrained (235). Two examples of integrated postpartum care beyond 42 days – perinatal mental health and HIV – are discussed below.

Integration of perinatal mental health care beyond 42 days postpartum

For perinatal mental health, the WHO Mental Health Gap Action recommends a 'stepped care approach' that integrates mental health care within existing maternal and child health (MCH) services to deliver care in non-specialist settings (200). This approach is as follows:

1. Screening: All women are screened for perinatal mental health conditions within existing MCH services. The specific services are not specified in the WHO guidance, but could include child immunisation, family planning, or lactation support.
2. Initial interventions: Women identified as needing mental health support receive basic psychosocial interventions within MCH settings. These interventions are provided by general healthcare practitioners, CHWs, nurses, or midwives, who have been trained by mental health specialists. Psychosocial interventions offered within MCH include behavioural

activation, relaxation training, cognitive behavioural therapy (CBT), group interpersonal therapy (IPT), or parenting skills training, depending on the condition (200,236).

3. Referral to specialists: Women whose symptoms do not improve after receiving primary care, or whose symptoms are moderate to severe, are referred to specialist mental health services for further support.

The effective integration of perinatal mental health care within MCH, particularly for steps one and two of the stepped approach, relies heavily on task sharing. In this model, PHC providers are trained and supervised by mental health specialists to screen for mental health symptoms and deliver psychosocial interventions in primary and community care (237). Task sharing may help mitigate access barriers that arise due to shortages of specialist mental health providers (200,237). In most countries in sub-Saharan Africa, the availability of psychiatrists is particularly overstretched, ranging from 0.007 per 100,000 population (Chad, 2016), to 1.52 (South Africa, 2016), excluding small islands (238).

Integrating perinatal mental health care into MCH services may contribute to the prevention, identification, and management of perinatal health problems beyond 42 days. By leveraging women's attendance at child immunisation clinics up to one year postpartum (232), integration would present an opportunity to provide ongoing support for those experiencing mental health challenges in the extended postpartum, after the final routine postpartum contact. However, more evidence is needed from LMICs on the feasibility and sustainability of integrated models of perinatal mental health care (237). It is important to consider the systemic effects on healthcare planning and increased workloads. High workloads and time constraints have repeatedly been identified as barriers to the delivery of mental health services by MCH providers (239). Appropriate training and supervision by specialists at the primary-tertiary interface is also vital to the success of the stepped care model (237).

Integration of HIV care beyond 42 days postpartum

Paper 2 highlights the substantial contribution of HIV and TB to pregnancy-related mortality beyond 42 days postpartum, particularly in Southern Africa. For women to have died from HIV in the extended postpartum, despite health system contact during ante-, intra-, and post-partum care, this suggests there may be multiple missed opportunities to improve initiation and retention in HIV services (207,240,241).

Furthermore, while many more women may now be initiated on ART due to policy shifts such as Option B+ (lifelong ART for all pregnant and postpartum women living with HIV) (186), for ART to be fully effective, a high degree of adherence is required (186). Existing evidence suggests that adherence tends to decrease during the postpartum period compared to during pregnancy (242–245), and compared to non-pregnant periods for women who had already initiated ART before pregnancy (246).

Several factors contribute to this reduced adherence postpartum. At the individual level, there may be a poor understanding of HIV, ART, and the prevention of vertical transmission (mother to child), including the misconception that the risk of vertical transmission has abated in the postpartum (242,243); difficulty managing the practical demands of ART adherence (242,243); and physical and mental health challenges, including postpartum depression, substance abuse, and the demands of caring for a new baby (243). Interpersonal factors include serostatus disclosure to a spouse and the level of spousal involvement in treatment (242), while structural barriers relate to healthcare access and health worker attitudes (242).

Missed opportunities to improve the retention of women living with HIV in HIV services, and poor adherence to ART in the postpartum period, indicates a need for improved integration of HIV care with existing MCH services at the primary care level (240). In 2006, the WHO recommended the integration of routine HIV services within MCH services to reduce fragmentation of services and promote postpartum retention (247). Integration of HIV services within MCH refers to the co-location

and sharing of services and resources for HIV testing, prevention, and treatment (247,248). Over half of treatment sites in 40 LMICs are now fully integrated, with the highest levels of integration in East Africa (248). Evidence from South Africa suggests that integrating HIV care within MCH-focused ART services leads to higher retention rates and increased viral suppression by one year postpartum, compared to standard adult ART clinics (240). Similar to perinatal mental healthcare, with many women returning to MCH clinics beyond 42 days for childhood immunisation, linkage of services at a single visit may help improve retention in HIV services (249,250).

Strategies to enhance integration of care beyond 42 days: continuity of care

There are four components of continuity of care: longitudinal continuity (care from the same provider over time), relational continuity (the quality of the relationship between patient and provider), sequential coordination (collaboration between different facilities or levels of care), and parallel coordination (collaboration within the same facilities or levels of care) (251). For example, midwifery-led continuity of care – where the same midwife or team of midwives provide care throughout the ante-, intra-, and post-partum periods – is associated with fewer adverse pregnancy outcomes, including episiotomy and instrumental delivery, according to a Cochrane review (252). This model of care primarily addresses both longitudinal and relational continuity but also has the potential to improve sequential and parallel coordination. In one mixed methods facility-based study in Kenya, women who experienced a MNM were less likely to visit the same facility repeatedly during antenatal care (indicating lower longitudinal and relational continuity) due to concerns about the quality of care and interpersonal relationships. Providers were less likely to follow-up high risk women in the first trimester (poor parallel coordination), and near miss survivors were also more likely to perceive poor coordination between facilities involved in their care (sequential coordination) (253). During the extended postpartum period, enhancing sequential and parallel coordination becomes particularly vital.

When referrals necessitate a change in provider, maintaining continuity of care benefits from the availability of women's electronic medical records or handheld referral records women keep with them when electronic records are not available. Appropriate identification and management of pregnancy-related morbidity beyond 42 days from non-obstetric providers also depend on linked medical records that details the woman's pregnancy history. In many LMICs, electronic medical records and the integration of obstetric and non-obstetric referrals within HMIS systems are often lacking (254). Especially for referrals between facilities, this impedes the identification of women's postpartum status and the accurate assessment of delayed onset or chronic pregnancy-related morbidity. Improving electronic record linkage is needed for information continuity – such that comprehensive information is shared between providers at all levels and follows the patient through the health system (255). Thus, investment in and integration of electronic medical records are essential components of continuity of postpartum care beyond 42 days.

Strategies to enhance integration of care beyond 42 days: Universal Health Coverage

UHC, as defined by WHO, means, "*that all people have access to the full range of quality health services they need, when and where they need them, without financial hardship. It covers the full continuum of essential health services*" (256). UHC encompasses two interrelated components of health system performance: service coverage and financial protection, aimed at improving equity (257). For some women with complex needs following pregnancy and childbirth, care may be required far beyond 42 days postpartum. Maternal multimorbidity also requires moving beyond fragmented disease-based services to centre the person and consider their morbidities holistically (258,259). These considerations align with the importance of strengthening PHC and UHC (258,260).

Achieving UHC for maternity care, including postpartum care, is a priority recommendation in the EPMM strategies (8,38,260). However, to effectively manage chronic morbidity in the extended postpartum, UHC initiatives must extend beyond 42 days. Women requiring care beyond this point may not be able to access care through existing initiatives that follow the WHO's recommended

schedule of postpartum care up to 42 days postpartum only. Integrating postpartum care up to a fifth contact at 6 months or beyond in UHC initiatives would reflect growing recognition that continued financing is essential to prevent maternal morbidity and mortality beyond 42 days. A notable example of this is the USA's extension of Medicaid coverage up to 12 months postpartum (261). While a recent systematic review found no evidence that health insurance coverage increases the uptake of postpartum care (262), the type and timing of access were unspecified. It is plausible that removing financial barriers may be most impactful for women with health problems, who may be more likely to use postpartum care compared to women attending routine check-ups. Nonetheless, in addition to financing, other barriers to uptake beyond 42 days need to be addressed simultaneously. This includes whether postpartum services are appropriately designed to respond to women's needs as they arise (25,263).

c. Measurement of maternal morbidity and mortality beyond 42 days

Accurate measurement of maternal outcomes beyond 42 days is critical for political mobilisation and the commitment of resources to end all forms of preventable maternal morbidity and mortality. Robust epidemiological, population-level data on the prevalence of adverse maternal outcomes beyond 42 days is essential to increase recognition of the scale of preventable long-term maternal morbidity and late maternal mortality.

Mortality beyond 42 days postpartum

First, when more supportive evidence becomes available across more geographies, the limits used for measurement of maternal and pregnancy-related mortality should reflect the duration of an elevated risk of death, as suggested in Paper 1 (254). Extending the upper postpartum limit would temporarily affect the comparability of estimates of the MMR over time. However, maintaining the upper limit as 42 days despite evidence showing that women remain at a heightened risk of death far beyond this threshold artificially keeps the MMR lower than it should be. An upward revision of

the threshold would also signal the need for health systems and healthcare providers to reassess the potential for delayed and chronic adverse maternal outcomes in the extended postpartum period.

Second, there is a need to intensify global measurement of maternal outcomes beyond 42 days postpartum, even if the 42-day threshold itself is not changed in the definitions of maternal, late maternal, and pregnancy-related mortality. It would be relatively straightforward for the WHO and Joint UN Agencies to establish a definition for what I have termed 'late pregnancy-related deaths' to estimate maternal survival in the extended postpartum where cause of death information is lacking. This approach would serve as an interim strategy until countries' CRVS systems are equipped to measure late maternal deaths. Without an internationally agreed-upon indicator for deaths that occur beyond 42 days postpartum from any cause, these deaths will continue to fall through the cracks: excluded from both the measurement of pregnancy-related mortality up to 42 days and late maternal mortality. An internationally recognised indicator may also incentivise measurement where information on timing in relation to pregnancy is available, even if the underlying cause of death is unknown.

For example, a low hanging fruit for improved measurement of mortality beyond 42 days would be for estimation in population-based surveys using the sisterhood method. In the DHS, respondents are currently asked if they have any sisters aged 12 and above, and if any of these sisters died during pregnancy, childbirth, or within two months following the end of pregnancy (249). This could be modified to also separately measure 'late pregnancy-related mortality' by adding an additional sub-question on whether a female sibling died between two months and one year postpartum. Additionally, the DHS pseudo maternal mortality rates and ratios (which exclude accidental causes and deaths from violence) could also be extended with a sub-question covering the period from 43 days up to one year postpartum. These modifications would provide population-level estimates of mortality beyond 42 days across LMICs.

Third, particularly in LMICs, improved measurement of late maternal deaths beyond 42 days postpartum will likely require additional technical support from the WHO. This includes assisting countries to monitor and report the numbers, timing, and causes of late maternal deaths in their CRVS systems through country consultation processes. The WHO's estimates of maternal causes of death do not currently disaggregate global estimates for late maternal deaths because insufficient data exists (4), and cross-country comparisons are hindered by ad hoc coding practices that do not uniformly adhere to ICD-11 (117,264). More research is required to identify barriers to consistent recording of late maternal deaths in CRVS systems, aligned with ICD-11 and ICD-MM coding principles. While the WHO's national guidance is a valuable resource to aid reporting, there may be additional ways the WHO can support consistent coding of late maternal mortality to improve comparability (3,77).

Prevalence of morbidity beyond 42 days postpartum

For morbidity surveillance beyond 42 days, population-level estimates of maternal morbidity in the extended postpartum are urgently needed, particularly in LMICs (18,19,259,265,266). This includes a need for standardised, comprehensive, measurement of maternal multimorbidity in the extended postpartum (259). Current epidemiological evidence predominantly derives from facility-based studies, but the group of women who can seek care for persistent or late onset morbidity or disability are not representative of all women (71). The magnitude of this bias may be substantial in contexts where few women access postpartum care and where out-of-pocket costs are high. Population-level data on the burden of different forms of postpartum morbidity are important for programme prioritisation, intervention design, and for assessing the need (and cost-effectiveness) of additional postpartum contacts (18). This may require special studies, where women are identified in the community and seen by a provider. The lack of accurate prevalence estimates also contributes to the absence of high-quality guidelines for some conditions affecting women in the extended postpartum period, particularly in LMICs (18,227).

Epidemiology of women's vulnerability beyond 42 days

The WHO currently recommend systematic screening of postpartum women in areas with an estimated TB prevalence of 0.1% or higher, and HIV postpartum 'catch up' testing is recommended in areas with an estimated prevalence of 5% or higher (25). However, alongside better estimates of postpartum infectious disease prevalence, more research is needed to understand the pathophysiology and epidemiology of infectious diseases in the extended postpartum period (267). To assess this, comprehensive longitudinal studies of women from early pregnancy through the extended postpartum period are required (19,166).

From the description of causes I present in Paper 2, it is a puzzle how women, who were likely already HIV positive before pregnancy but well enough to conceive (268), died in the extended postpartum from HIV-related causes. Since women with very progressed HIV disease are less likely to conceive (268), it is unclear how their health deteriorated sufficiently throughout pregnancy and the postpartum to result in death. There is no evidence that pregnancy accelerates HIV disease progression where ART are available, but there is weak evidence of progression in the absence of ART (268). However, analysis of HDSS data revealed that women living with HIV have an eight times higher risk of dying in pregnancy and up to 42 days postpartum relative to women without HIV (185). There does, therefore, seem to be an excess mortality risk conferred by HIV up to 42 days postpartum. Consistent with the higher contribution of HIV to pregnancy-related deaths beyond 42 days identified in Paper 2, it is plausible that excess mortality will continue to increase further from pregnancy. Prior research indicates that women living with HIV who are neither pregnant nor postpartum have much higher relative risks of mortality than their pregnant or postpartum counterparts (i.e., 'healthy pregnant woman' selection effect) (185).

Moreover, the postpartum period is accompanied by its own unique changes in the immune system, including early postpartum immune upregulation called 'immune reconstitution': the reversal of inflammatory responses in the postpartum period after temporary immunosuppression during pregnancy (269–272). Further research is needed to understand the trajectory of immune reconstitution on latent infection in the postpartum and extended postpartum period.

8.4.2 Reconceptualising the cumulative risk of maternal morbidity across the reproductive life course

Women's accounts in Paper 3 emphasised that the lived experienced of maternal morbidity and postpartum recovery are not only outcomes of individual pregnancies, but rather, are shaped by the trajectories of previous pregnancies and prior physical, mental, or sexual health challenges. Prior complications or unresolved conditions from a previous pregnancy can also increase the likelihood of severe maternal morbidity in future pregnancies (20,170–172). As further demonstrated in Papers 4 and 5, maternal risks accumulate with each pregnancy across the life course. Reconceptualising maternal morbidity within a cumulative risk framework helps to foreground these dynamics and its impact across women's lives.

Below I discuss two potential areas of this reconceptualisation of cumulative risk: a. integration of cumulative risk approaches in reproductive healthcare; b. measurement of cumulative risk of near miss and severe maternal outcomes.

a. Integration of cumulative risk in models of reproductive healthcare

One approach to recognising women's cumulative risk of adverse maternal health outcomes may be achieved by considering post-pregnancy care – both in the extended postpartum period and beyond – as 'interconception care' (214,273). As a subset of pre-conception care, this refers to healthcare and ancillary services provided to women between pregnancies, to assess their level of risk, promote health, and offer clinical and psychosocial interventions before the next pregnancy (214). Interconception care explicitly recognises that women's risk of adverse outcomes recurs with each subsequent pregnancy, and that care between pregnancies is essential to mitigate these risks. This approach provides an opportunity to also manage chronic morbidity or lifestyle factors that may put women at a higher risk of complications in the next pregnancy, such as hypertension, diabetes, weight management, or smoking cessation (214). Practically, since providers (and women

themselves) do not know if a new pregnancy will occur, most post-pregnancy care provided to reproductive age women should be considered as potential 'interconception' care (273).

Beyond a fifth, delayed postpartum visit, Lu et al (2006) recommend annual 'interconception' or 'internatal' care contacts, starting at one year postpartum, to optimise women's health between pregnancies (214). They propose a recommended schedule of interpregnancy care, as relying on women to self-elect for services between pregnancies exacerbates inequities in access to reproductive health care (214). For all women, they suggest a holistic package of services, including risk assessments (for violence, mental health, STIs, nutrition), health promotion (breastfeeding, sleep, exercise, exposures including smoking/alcohol, family planning), clinical interventions (weight monitoring, blood pressure monitoring, cervical screening and pelvic examination), and psychosocial interventions (214). This model was proposed for the United States, however, and universal provision of these services is likely to be infeasible in low resource settings and where routine services are already overstretched.

It may be most beneficial, and more feasible, to prioritise providing interconception care to women with prior severe maternal or foetal outcomes, many of which are associated with a high risk of recurrence (170–172). Enhanced interconception care is proposed for high-risk women (chronic hypertension or gestational hypertension in a previous pregnancy, pregestational or gestational diabetes mellitus, overweight or obese, or with a prior pre-term birth) to reduce the risks of recurrence and future adverse outcomes (214). This relies on the adoption of a 'vulnerability approach' to identify the 'threats' and 'barriers', to women's reproductive health that may increase her risk of morbidity recurrence (9). In turn, leveraging women's return to health services during this window could also help improve the continuity of care and transfer between primary and specialist providers (273).

b. Measurement of the lifetime risk of near miss and severe maternal outcome

As the obstetric transition progresses and maternal mortality declines (21), there have been global calls for more comparable, population-level estimates of maternal morbidity (7,18). The LTR-MNM and LTR-SMO extend the concept of lifetime risk from its previous exclusive focus on maternal mortality (the lifetime risk of maternal death (LTR-MD)) to include maternal near miss morbidity. In doing so, these metrics provide a new lens through which to consider the cumulative burden of near miss morbidity and severe maternal outcomes on women's lives (274). They also reveal the magnitude of inequities in reproductive outcomes between countries that result from obstetric risk, fertility, and survival differences between populations. Finally, as these metrics make explicit the multiplicative effect of risk with each repeat pregnancy, they also underscore the importance of ensuring access to contraception and safe abortion services for all women who wish to use them, a key EPMM strategy (8).

The LTR-MNM and LTR-SMO are population average, period measures of a synthetic cohort, using cross-sectional data that is most readily available. While these measures may oversimplify an individual's cumulative risk by overlooking parity-specific risks and the impact of prior morbidity on the likelihood of severe morbidity in future pregnancies (170–172), they nonetheless represent a significant advancement in maternal morbidity metrics.

By foregrounding the cumulative risk across a woman's reproductive lifespan, the LTR-MNM and LTR-SMO could help to reposition maternal morbidity at the centre of the development agenda. With progress to reduce mortality stalling, reframing the impact of maternal morbidity on women's lives may help to renew commitment and intensify action towards the goals of EPMM (8,38). MNM are generally quite well understood, and data are much more readily available than other, less severe forms of maternal morbidity. Additionally, the LTR-MD may arguably be the most widely used indicator by non-technical audiences from the WHO and UN Joint Agency maternal mortality reports. This may be because the lifetime risk – expressed as a 1 in N chance – is intuitive and the risk level

is easier to comprehend than the MMR per 100,000 live births. The same may be true of the LTR-MNM compared to the MNM ratio.

No measures of maternal morbidity are currently included in the SDG indicators (12). To adopt the MNM ratio (or the LTR-MNM) as an SDG indicator, improved compliance with the WHO's organ-dysfunction criteria for identifying MNM cases is essential to ensure comparability and benchmark progress (22,91,275). For consistent monitoring across both LMICs and high-income countries, the WHO may need to simplify the criteria to make them more accessible for non-specialists to implement. Updating the WHO's standard MNM tool to include ICD codes for clinical and laboratory criteria could also facilitate integration with countries' routine administrative and HMIS, reducing the opportunity cost of adoption (91). This update could increase uptake in high-income countries with fully functioning HMIS, as well as LMICs, where most prevalence data currently come from ad hoc, facility-based surveys that are not representative at the population-level. Given growing investment to strengthen HMIS (276–278), and increasing institutional delivery (279), integrating the WHO tool into HMIS could enhance MNM surveillance in LMICs. This integration may also reduce reliance on highly skilled specialists to identify MNM from women's records.

8.5 Conclusion

This thesis contributes to growing calls for an ambitious expansion of the maternal health agenda, to move beyond its focus on maternal survival up to 42 days postpartum. A broader call to action is necessary to prioritise research, monitoring, policy, and programmes that address maternal outcomes in the extended postpartum period, and the impacts of maternal morbidity on women's wellbeing across the reproductive life course.

The research presented in this thesis has tackled critical questions relating to: (i) the duration of risk, causes of death, and recovery trajectories beyond 42 days postpartum; and (ii) the measurement of, and cross-country inequity in, the cumulative risk of maternal near miss morbidity throughout the

reproductive life course. Taken together, the findings of this research collective reaffirm the need to prioritise a life cycle approach to maternal health in the post-SDG era. To facilitate this shift, two key areas of reconceptualisation are required:

First, there is an urgent need to redefine the postpartum period beyond 42 days:

1. **Re-envisioning models of postpartum care**: Rigorous feasibility, cost-effectiveness, and implementation research across different contexts is essential to inform the schedule and content of postpartum care beyond 42 days. Particularly in LMICs, where coverage of routine postpartum care is often poor, it is critical to determine the optimal provision of a fifth postpartum contact, including whether this should be universally provided or targeted towards high-risk groups.
2. **Improving measurement of maternal mortality and morbidity beyond 42 days**: Stronger indicators of 'late pregnancy-related deaths' and accurate population-level estimates of the burden of morbidity and mortality in the extended postpartum period are essential to inform programming and improve outcomes.
3. **Strengthening the integration of care:** Improved provision of care beyond the standard 42-day postpartum period will necessitate improved integration of obstetric and non-obstetric care providers. This will require strengthening UHC and improving the continuity of care.

Second, it is necessary to reconceptualise the cumulative burden of maternal ill-health across the reproductive life course:

1. **Incorporating cumulative risk models into reproductive healthcare:** Recognising the cyclical nature of maternal health, including recurrent maternal morbidity, underscores the need to view reproductive episodes as key opportunities to optimise women's health and prevent complications from recurring. This approach should encompass 'interconception care', especially for high-risk groups, during the extended postpartum period and beyond.
2. **Promoting the measurement of the cumulative risk of maternal morbidity**: This is essential to reveal the true magnitude of inequity in reproductive outcomes. The adoption of

the lifetime risk of near miss by the WHO would help to reorient the maternal health agenda towards a stronger commitment to tackling maternal morbidity in the post-SDG era.

With only five years remaining of the SDGs, these for avenues for future research, monitoring, policy and programming can galvanise momentum and shape the post-SDG era maternal health agenda.

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Appendix A Ethical approval documents

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Observational / Interventions Research Ethics Committee

Ms Ursula Gazeley

LSHTM

13 December 2021

Dear Ursula

Submission Title: Maternal mortality in Sub-Saharan Africa: An Assessment of Health and Demographic Surveillance Site Data

LSHTM Ethics Ref: 26603

Thank you for responding to the Observational Committee Chair'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 is as follows:

Document Type	File Name	Date	Version
Other	Research_Ethics_certificate_Gazeley	20/10/2021	1
Protocol / Proposal	Protocol Maternal Mortality Gazeley	20/10/2021	1
Investigator CV	CV Ursula Gazeley 10_2021	20/10/2021	1
Local Approval	LEO 26603 Maternal mortality in subSaharan Africa	18/11/2021	1
Covering Letter	LEO 26603 covering letter	18/11/2021	1

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 the 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.

Further information is available at: www.lshtm.ac.uk/ethics.

Yours sincerely,

Professor Jimmy Whitworth
Chair

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Observational / Interventions Research Ethics Committee

Ms Ursula Gazeley

LSHTM

1 June 2023

Dear Ms Ursula Gazeley

Study Title: Maternal mortality in Sub-Saharan Africa: An Assessment of Health and Demographic Surveillance Site Data

LSHTM Ethics Ref: 26603 - 2

Thank you for your application for the above amendment to the existing ethically approved study and submitting revised documentation The amendment application has been considered by the Observational Committee via Chair's Action.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above amendment to 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 for the amendment having been received, where relevant.

Approved documents

The final list of documents reviewed and approved is as follows:

Document Type	File Name	Date	Version
Other	Protocol Maternal Mortality Gazeley_v3_tracked_22052023	22/05/2023	3
Other	approval data_Kersa_Agincourt_Kisesa_Kilifi	22/05/2023	1
Local Approval	approval data_Kersa_Agincourt_Kisesa_Kilifi	22/05/2023	1
Local Approval	TAZAMA Data Sharing Agreement_SignedUG + MU	22/05/2023	1

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 the 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.

Further information is available at: www.lshtm.ac.uk/ethics.

Yours sincerely,

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Observational / Interventions Research Ethics Committee

Ms Ursula Gazeley
LSHTM

1 September 2022

Dear Ursula,

Study Title: Understanding women's long-term recovery from severe maternal morbidity in Kenya

LSHTM Ethics Ref: 27267

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
Investigator CV	CV Ursula Gazeley 02_2022	28/02/2022	v1
Other	Research_Ethics_certificate_Gazeley	28/02/2022	v1
Advertisements	Recruitment process	16/03/2022	1
Local Approval	Conditional RAF approval to access PRECISE data to identify study participants	16/03/2022	1
Protocol / Proposal	Protocol qualitative study PRECISE UG 300322	30/03/2022	2
Protocol / Proposal	Protocol qualitative study PRECISE UG v2 2706222	27/06/2022	2
Information Sheet	Informed Consent Form Male Partners	27/06/2022	1
Information Sheet	Informed Consent Form Women	27/06/2022	2
Information Sheet	Participant Information Leaflet Male Partners	27/06/2022	1
Information Sheet	Participant Information Leaflet Women v2 2706222	27/06/2022	2
Covering Letter	Cover Letter 060722 UGazeley	06/07/2022	1

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,

Professor David Leon and Professor Clare Gilbert
Co-Chairs

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

THE AGA KHAN UNIVERSITY

Re: Understanding women's recovery beyond six-weeks postpartum after severe maternal morbidity in Kilifi, Kenya

The Aga Khan University, Nairobi Institutional Scientific Ethics Review Committee (ISERC), is in receipt of your protocol. The ISERC has reviewed andapprovedthis project *{as per attached official stamped protocol and attachments - version Ref:* 2022/ISERC-113(v2*)*. You are authorized to conduct this study from **December 15, 2022**. This approval is valid until **December 14, 2023** and is subject to compliance with the following requirements;

1. The conduct of the study shall be governed at all times by all applicable national and international laws, rules and regulations. ISERC guidelines and Aga Khan University Hospital policies shall also apply, and you should notify the committee of any changes that may affect your research project (amendments, deviations and violations)
2. Researchers desiring to initiate research activities during COVID-19 pandemic must comply with the COVID-19 SOPs for Research as well as submit to the Research Office a Request Form to Initiate, Reinstate or Continue Research During COVID-19 Pandemic.
3. **Prior** to human subjects enrolment you must obtain a research license from the National Commission for Science, Technology and Innovation(NACOSTI), *where applicable*, site approvals from the targeted external site(s) and file the copies with the RO.
4. *As applicable*, **prior** to export of biological specimens/data, ensure a Material Transfer Agreement (MTA)/Data Transfer Agreement (DTA), is in place as well as seek shipment authority/permit from the relevant government ministry. Copies of these approvals, should be submitted to the RO for records purpose.
5. All Serious Adverse Events and the interventions undertaken must be reported to the ISERC as soon as they occur but not later than 48 hours. The SAE shall also be reported through the AKUHN quality monitoring mechanism(s) at Client Relations Department of the Chief of Staff's Office.
6. All consent forms must be filed in the study binder and where applicable, patient hospital record.
7. Further, you must provide an interim Progress Report Form**60 days before expiration** of the validity of this approval and request extension if additional time is required for study completion; as well as submit the completed Self-Assessment Tool -Monitoring Ethical Compliance in Research. You must advise the ISERC when this study is complete or discontinued and a final report submitted to the Research Office for record purposes.
8. The Aga Khan University Hospital management should be notified of manuscripts emanating from this work.

If you have any questions, please contact Research Office at AKUKenya.ResearchOffice@aku.edu or 020-366 2148/1136.

With best wishes,

Dr. Christopher Opio,
Chair – Institutional Scientific and Ethics Review Committee (ISERC)
Aga Khan University, (Kenya)

Copy: Co-Investigators

Appendix B Supplementary material for Chapter 3

Women's risk of death beyond 42 days postpartum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa

B1. Risk of death 42-122 days postpartum over time, by five-year childbirth cohort

Descriptive statistics indicate that there was a decline in postpartum pregnancy-related mortality from about 4/1000 to 2/1000 from the 1991-95 cohort and the 2016-20 cohort. This could indicate either declining risk, heterogeneity in the sample, or both.

We analysed the ratio of childbirths to deaths within the interval 42-122 days for each cohort in the HDSS sample. The 95% confidence intervals were calculated using bootstrapping of 1000 resamples. There is evidence of a statistically significant lower risk of death for the 2006-10 cohort onwards, which may reflect changing mortality conditions as indicated by the multivariable regression results but may also be affected by heterogeneity in the sample.

Table B1. Risk of death 42-122 days over time, by five-year childbirth cohort

Childbirth cohort	Total childbirths	Died 42-122 days	Ratio per 1000	95% CI lower	95% CI upper
1991-95	20284	17	0.84	0.50	1.24
1996-00	47543	38	0.81 0·80	0.55	1.06
2001-05	81801	71	0.87	0.69	1.08
2006-10	182733	100	0.55	0.46	0.65
2011-15	271458	115	0.42	0.35	0.51
2016-20	43285	17	0.39	0.24	0.63

B2. Comparison of unadjusted and adjusted death distributions

The distribution of deaths by days since childbirth was adjusted to correct for the overestimation of days until death when calculated using calendar days, (e.g., a woman who survived less than 24 hours but who died on the next calendar day would be misattributed to day 1), splitting deaths between the calendar day of occurrence and the day before. This shifts the density of deaths towards earlier postpartum intervals.

The univariable and multivariable analyses are run on the adjusted distribution.

Table B2 Comparison of unadjusted and adjusted death distributions

Interval	Death Distribution	Person-years	Crude Death Rate (M_x) (per 1000 person-years)
Unadjusted			
0 to 1 day	283	3548·2	79·8
2 to 6 days	136	8858·5	15·4
7 to 13 days	105	12379·1	8·5
14 to 41 days	229	49243·4	4·7
42-122 days	360	139665·9	2·6
4 to 11 months	859	388164·4	2·2
[12 to 18 months]	574	262877·7	2·2
Adjusted			
0 to 1 day	306	3541·0	86·6
2 to 6 days	118	8840·6	13·4
7 to 13 days	101	12354·2	8·2
14 to 41 days	223	49144·5	4·5
42-122 days	363	139386·8	2·6
4 to 11 months	856	388903·1	2·2
[12 to 18 months]	574	263591·7	2·2

B3. Hazard of death by time since delivery

We used the hazard of death by time since delivery to choose the risk interval cut points for the Piecewise Constant Hazard model. The figures below (**Figure B1** & **Figure B2**) show the death rates, smoothed using a non-parametric p-spline, for the first 42-days and the first year postpartum. The hazard is exponentially decreasing, and has reached a relatively low level by 42-days postpartum.

Figure B1 Death rate by time since delivery (up to 42-days)

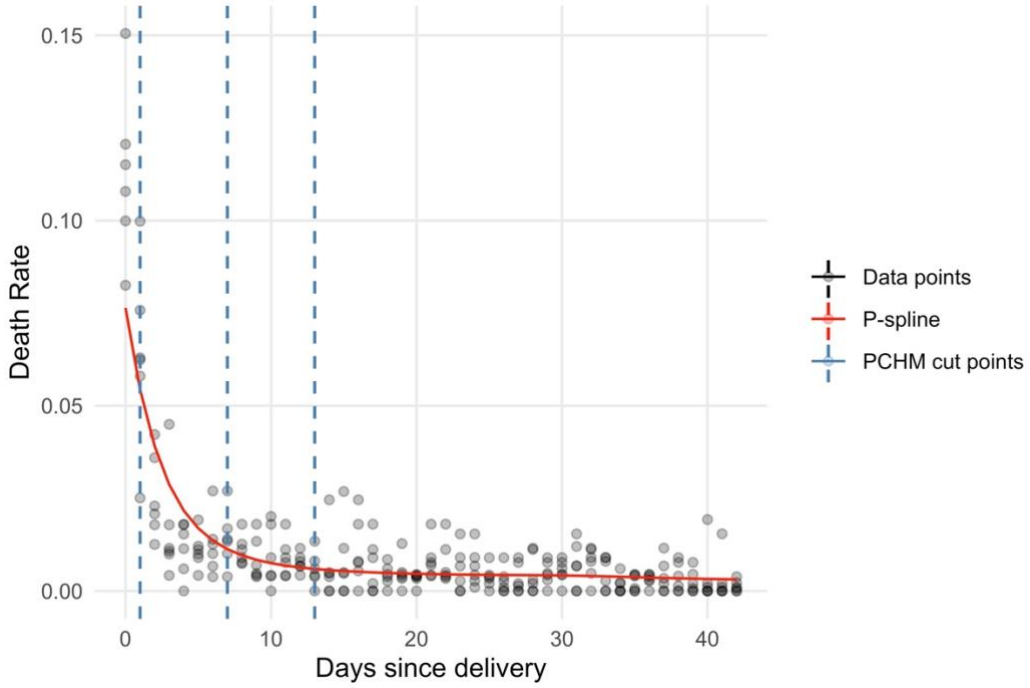
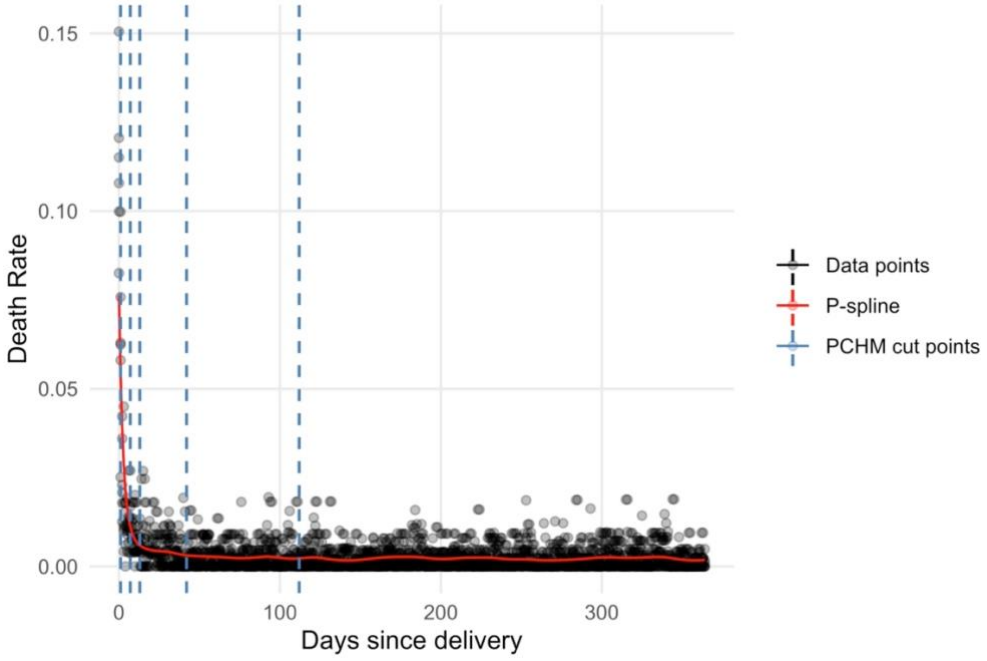


Figure B2 Death rate by time since delivery (up to one year)



B4. Calculation of the postpartum Pregnancy-Related Mortality Ratio (PRMR)

The PRMR would conventionally be calculated as the number of pregnancy-related deaths divided by the number of live births, multiplied by 100 000. We are unable to restrict the denominator to live births, but we approximate this as the number of postpartum pregnancy-related deaths divided by the number of births, multiplied by 100 000.

We summed the total deaths occurring within 42 days (748), the total deaths within four-months (1111) and divided these by the total number of births: 647 104. This yields 116 per 100,000 and 174 per 100,000, respectively. To calculate the percentage increase, we then took the natural logarithm of the two, to adjust for the sensitivity of the denominator in the fraction: $ln\left(\frac{174}{116}\right)$ = 40%.

We also calculated the percentage increase in the PRMR implied by a four-month postpartum threshold by estimating a life table with the adjusted death distribution. This yields the same result:

Table B3 Life Table using adjusted death distribution

x	n(days)	n(years)	d	nLx	nMx	lx	dx
0	2	0.00548	306	3541.0	0.0864	100000.0	47.3
2	5	0.0137	118	8840.6	0.0134	99952.6	18.3
7	7	0.0192	101	12354.2	0.00818	99934.4	15.3
14	28	0.0767	223	49144.5	0.00454	99918.7	34.8
42	81	0.222	363	139386.8	0.00260	99883.9	57.7
123	242	0.663	856	388903.1	0.00220	99826.2	145.6
365	182.875	0.501	573	263591.7	0.00217	99680.7	108.5
547.875						99572.2	

$$PRMR\ (0-41days) = \sum_{x=0}^{x=14} dx$$

$$= 116$$

$$PRMR\ (0-122\ days) = \sum_{x=0}^{x=42} dx$$

$$= 174$$

$$\% \text{ increase in the postpartum PRMR} = ln\left(\frac{174}{116}\right)$$

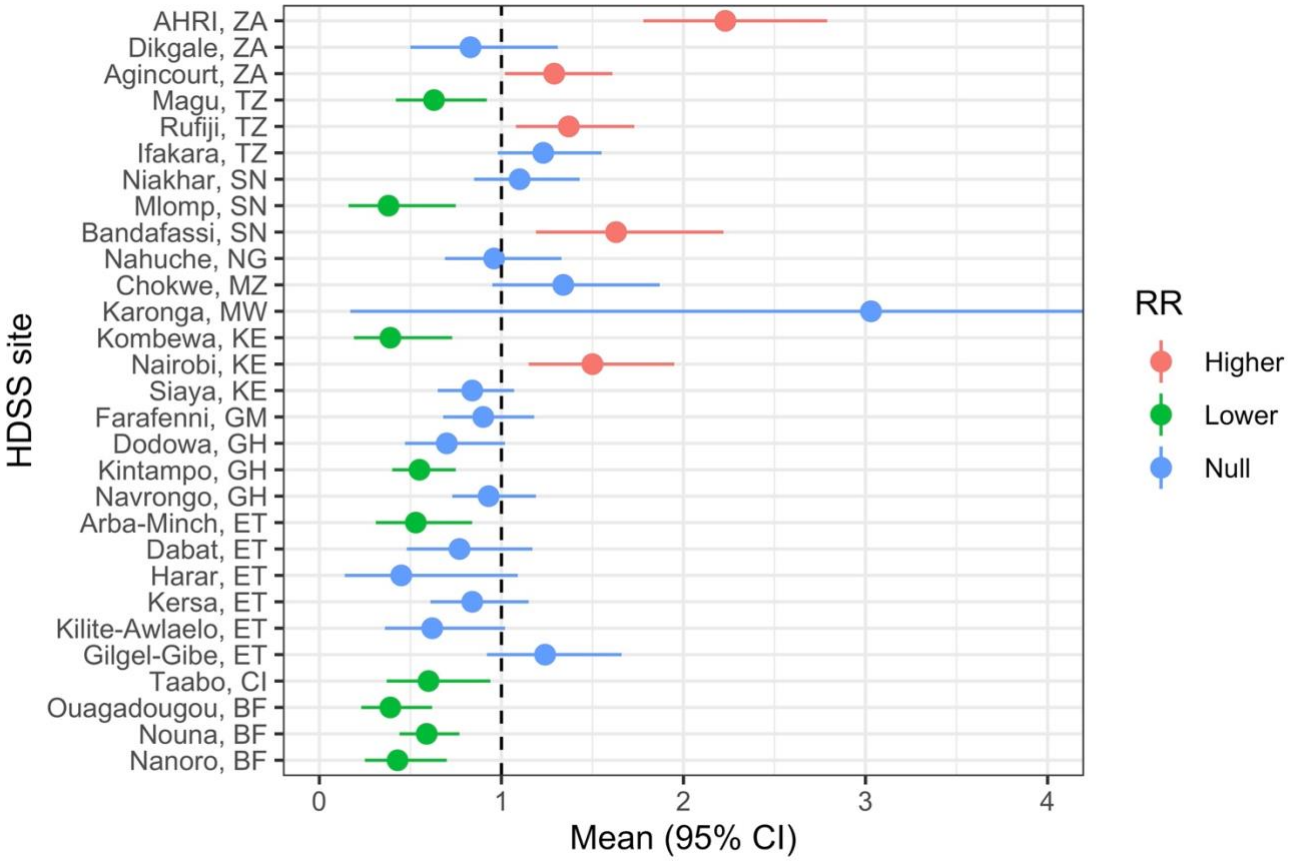
$$= 40\%$$

B5. Main model HDSS site heterogeneity: aggregate-level fixed effects

The main model used aggregate-level fixed effects to control for heterogeneity between HDSS site. Since the model weights the death counts by the person-years exposure for each dummy variable, the effect sizes are independent of population size. The reference category was Basse (The Gambia), since Basse HDSS had the most deliveries. Wald test of joint significance confirmed that aggregate-level fixed effects for HDSS site were significant.

Figure B3 shows the risk ratios for each HDSS site. In total, nine sites had a lower risk of death, relative to Basse. Only five sites had an increased risk of death, in four countries – South Africa, Tanzania, Kenya and Senegal.

Figure B3 Risk ratio of death by HDSS site: aggregate-level fixed effects



ZA = South Africa, TZ = Tanzania, SN = Senegal, NG = Nigeria, MZ = Mozambique, MW = Malawi, KE = Kenya, GM = The Gambia, GH = Ghana, ET = Ethiopia, CI = Cote d'Ivoire, BF = Burkina Faso
Upper CI for Karonga, Malawi (13.58) not displayed.

B6. Sensitivity Tests

i. Choice of postpartum risk interval beyond 42 days

Given the lack of consistency between studies in the choice of the risk period beyond 42 days, we incrementally increased the risk period by an additional week to test the sensitivity of the effect size to the choice of the interval.

Table B4 shows the coefficient estimates for the risk intervals in the multivariable model, in two week increments from up to 8 weeks to up to four months. The shorter the risk interval beyond 42 days, the higher the risk of death, relative to the baseline period 12-18 months postpartum (except for 42 days to 12 weeks). This trend of a decrease in the risk of death as the interval lengthens strengthens the case that the risk of death is not constant at pre-pregnancy levels by 42 days.

Table B4 Sensitivity of the multivariable results to the length of the risk interval from 43 days onwards, interval coefficients only

	42 days to 8 weeks		**42 days to 10 weeks**		**42 days to 12 weeks**		**42 days to 14 weeks**		**42 days to 4 months (final model)**	
Variable	Rate Ratio	P-value	Rate Ratio	P-value	Rate Ratio	P-value	Rate Ratio	P-value	Rate Ratio	P-value
Interval										
0-1 day	38·80	<0·0001	38·76	<0·0001	38·79	<0·0001	38·81	<0·0001	38·82	<0·0001
2-6 days	4·97	<0·0001	4·97	<0·0001	4·97	<0·0001	4·97	<0·0001	4·97	<0·0001
7-13 days	3·35	<0·0001	3·35	<0·0001	3·35	<0·0001	3·35	<0·0001	3·35	<0·0001
14-41 days	2·06	<0·0001	2·06	<0·0001	2·06	<0·0001	2·06	<0·0001	2·01	<0·0001
42 days to X[1] weeks	1·31	0·041	1·29	0·012	1·21	0·031	1·27	0·0041	1·20	0·016
X[1]-365 days	1·06	0·33	1·05	0·40	1·06	0·36	1·03	0·64	1·02	0·76
12-17 months (reference)	1·0		1·0		1·0		1·0		1·0	

[1] X increases incrementally from 8 weeks in the left-most column to 4 months in the final model.

ii. Choice of baseline period

The choice of the baseline period used to proxy women's background risk of death differs between studies, with little consistency. While our main results depend on an assumed baseline period of 12-17 months postpartum, we re-ran our multivariable model with two alternate choices of baseline period: 12-23 months, and 12-35 months postpartum. The results of these models are presented in Table B5.

The risk for the period 42-122 days postpartum remains elevated in both models, although the effect size decreases slightly as the baseline period lengthens. Relative to a baseline of 12-23 months, the risk is 17% higher between 42-122 days; relative to a baseline of 12-35 months, the risk is 15% higher. In both models, the effects are significant at 95% confidence.

Table B5 Sensitivity of the multivariable results to the baseline risk period

	Multivariable with baseline 12-24 months			Multivariable with baseline 12-36 months		
Variable	Rate Ratio	95% CI	P-value	Rate Ratio	95% CI	P-value
Interval						
0-1 day	37·94	32·85 – 43·70	<0·0001	37·27	32·47 – 42·63	<0·0001
2-6 days	4·88	3·89 – 6·04	<0·0001	4·79	3·84 – 5·90	<0·0001
7-13 days	3·25	2·58 – 4·04	<0·0001	3·19	2·54– 3·95	<0·0001
14-41 days	2·00	1·71 – 2·34	<0·0001	1·96	1·68 – 2·28	<0·0001
42-122 days	1·17	1·02 – 1·33	0·022	1·15	1·01 – 1·30	0·033
4-11 months	0·99	0·89 – 1·10	0·83	0·97	0·88 – 1·07	0·53
Baseline (reference)	1·0			1·0		
Parity (within HDSS)						
1	1·28	1·16 – 1·40	<0·0001	1·24	1·14 – 1·35	<0·0001
2-3 (reference)	1·0			1·0		
4-6	0·89	0·75 – 1·05	0·18	0·85	0·73 – 0·98	0·035
7+	0·72	0·49 – 1·04	0·072	0·78	0·57 – 1·08	0·13
Age group						
<15	0·92	0·55 – 1·43	0·74	0·82	0·51 – 1·24	0·39
15-24	0·64	0·58 – 0·71	<0·0001	0·65	0·59 – 0·71	<0·0001
25-34 (reference)	1·0			1·0		
35+	1·33	1·20 – 1·48	<0·0001	1·31	1·19 – 1·44	<0·0001
Cohort						
1991-1995	0·94	0·75 – 1·19	0·61	0·94	0·76 – 1·16	0·56
1996-2000 (ref)	1·0			1·0		
2001-2005	0·98	0·84 – 1·15	0·80	0·96	0·83 – 1·10	0·56
2006-2010	0·82	0·70 – 0·96	0·012	0·79	0·68 – 0·91	0·00078
2011-2015	0·70	0·60 – 0·82	<0·0001	0·66	0·57 – 0·77	<0·0001
2016-2020	0·63	0·48 – 0·82	<0·0001	0·58	0·45 – 0·75	<0·0001

B7. Date Heaping

Figure B4 and Figure B5 show the frequency of dates recorded for delivery date (child DOB) and for date of death (for women who have delivered in the past 18 months), respectively. Both dates are badly affected by heaping. For the date of delivery, across all months, the 15th of the month is significantly more common than any other date, followed by the 1st of the month. This suggests that in some sites, imputing the mid-point of the month when the precise date is unknown is standard practice, while for other sites, the first day of the month is used. For the date of maternal death, the 16th of the month is the most common, followed by the 15th. This again suggests that date imputation to the middle of the month is common. As the delivery event is most likely to be recorded as the 15th, if the mother dies the following calendar day, this explains why the 16th of the month is so frequently recorded for the maternal date of death.

June is the most frequently recorded month for delivery date, while March is the most common for the maternal date of death. While this is suggestive of date imputation, the effect of heaping is difficult to disentangle from genuine seasonality in deliveries and deaths.

Figure B4 HDSS Data Date Heaping: Delivery Date

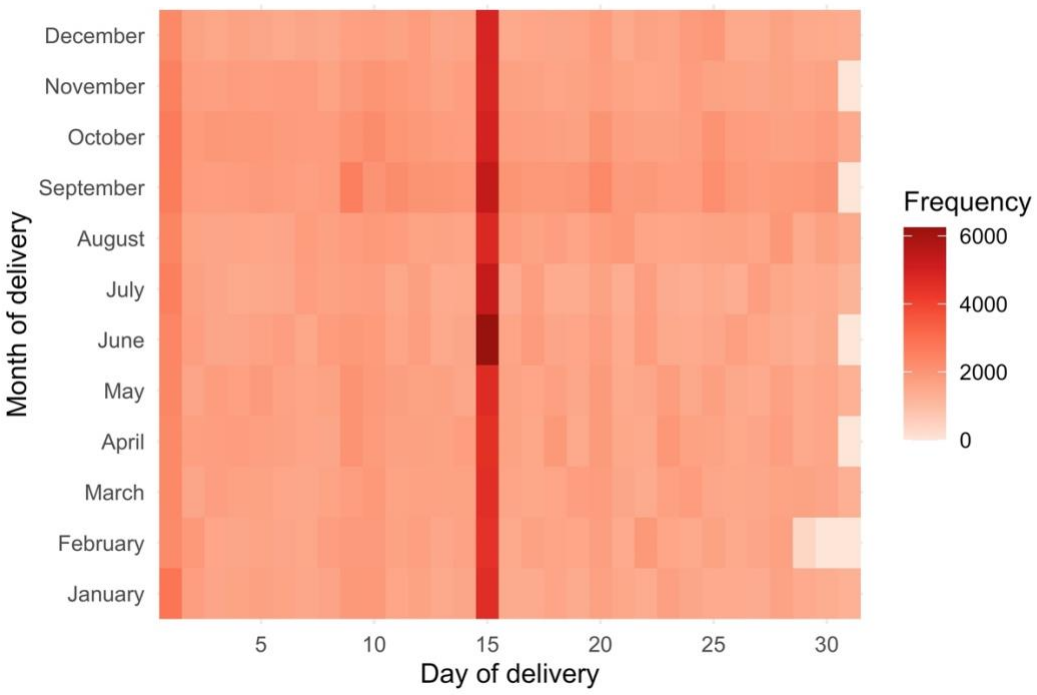
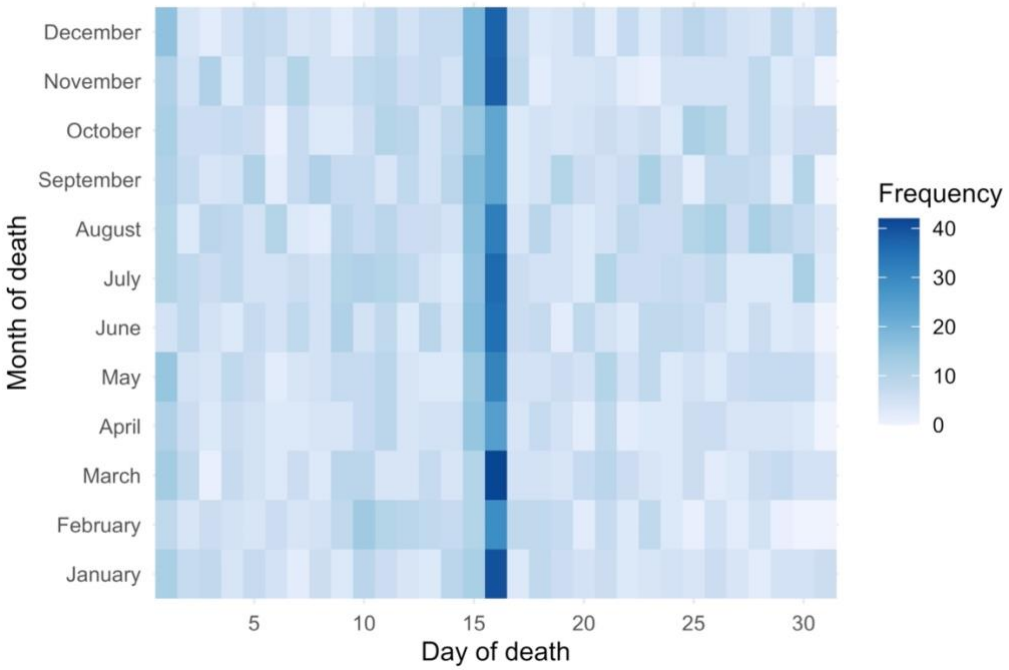


Figure B5 HDSS Data Date Heaping: Date of Maternal Death



Appendix C Supplementary material for Chapter 4

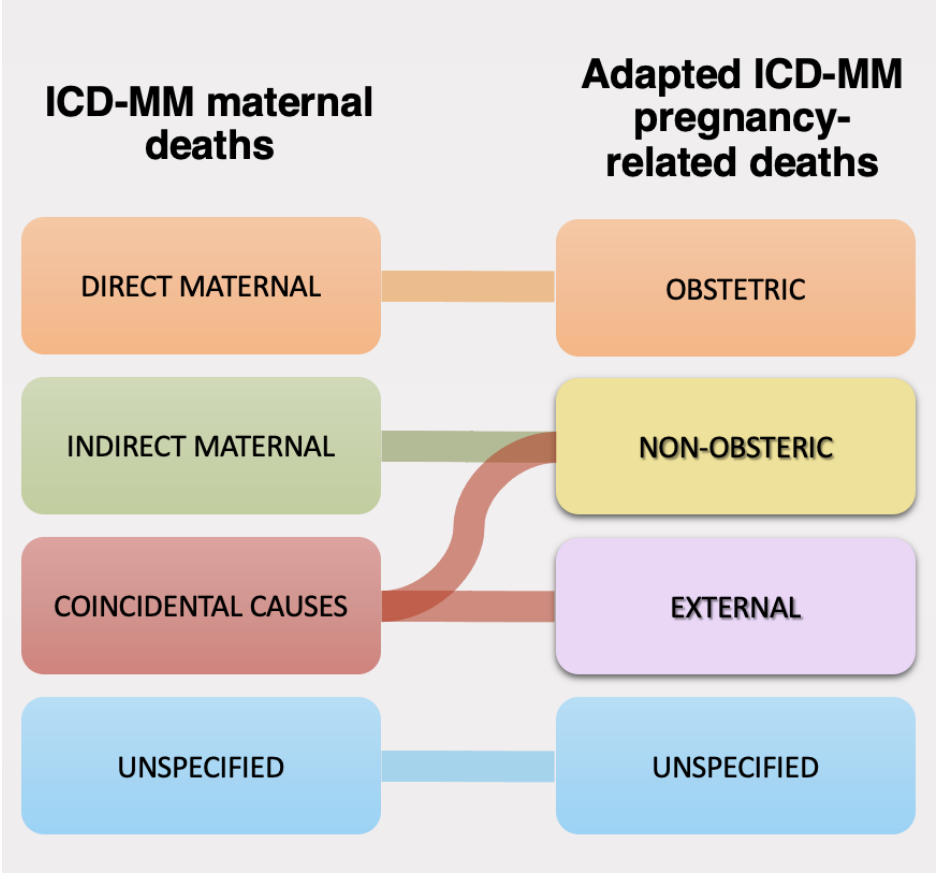
Pregnancy-related mortality up to one year postpartum in sub-Saharan Africa: an analysis of verbal autopsy data from six countries

C1. Adapted ICD-MM categories applied to pregnancy-related mortality

We grouped deaths according to the four types and nine adapted International Classification of Diseases-Maternal Mortality (ICD-MM) categories as follows: *Obstetric* (1. Pregnancy with abortive outcome, 2. Hypertensive disorders, 3. Obstetric haemorrhage, 4. Pregnancy-related infection, 5. Other obstetric complications, 6. Unanticipated complications of management); *Non-obstetric* (7a. HIV and tuberculosis, 7b. Other infectious diseases, 7c. Cardiovascular diseases, 7d. Other NCDs); *Unspecified* (8. Undetermined); and *External* (9. Accidental). Exact replication of the ICD-MM categories was not possible because we analysed pregnancy-related deaths (i.e. defined only by time of death), and not maternal mortality. From VA data alone, it is not possible to differentiate which non-obstetric pregnancy-related deaths were indirect maternal and which were coincidental; this would require a clinical COD expert reviewing a patients' medical records to ascertain whether the underlying condition (e.g., HIV, carcinoma, or cardiovascular disease) was "aggravated by pregnancy" – as is required for the death to be considered maternal. Without further record linkage and data source triangulation this was not possible, and hence we modified the ICD-MM categories to apply to pregnancy-related mortality (see Figure S1 below).

Obstetric and *Unspecified* groups replicate the ICD-MM categories; *Non-obstetric* includes all non-obstetric causes without an attribution whether the death was indirect maternal or coincidental to the pregnancy; *External* includes deaths from accidents and violent injuries only.

Figure C1 Mapping of adapted ICD-MM categories



C2. Obstetric deaths beyond 42 days postpartum

Most direct obstetric deaths occur very shortly after delivery or pregnancy termination. In total, we identified 63 deaths that HDSS and verbal autopsy data suggest occurred beyond 42 days postpartum and from a direct obstetric cause. Figure C2 shows the timing of these deaths by days postpartum.

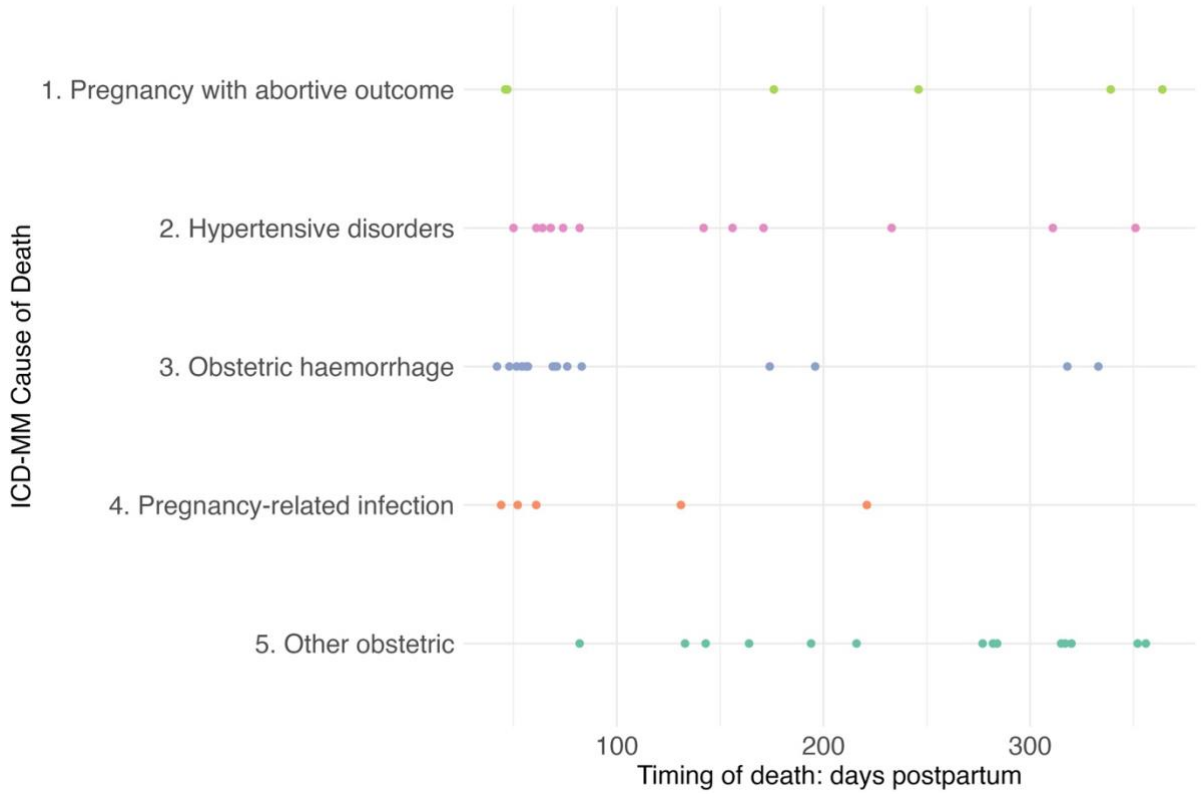
There are several potential explanations for these causes occurring so late postpartum:

1. Delayed effects of the obstetric complication. A woman's death may have been prevented for the standard postpartum period but she may die later on after prolonged illness.
2. The obstetric death may relate to a repeat pregnancy, not the index pregnancy recorded in the HDSS data or the verbal autopsy data. If this is the case, these are deaths during pregnancy and within 42 days, and not late pregnancy-related deaths.
3. Incorrect date of death, date of delivery, or cause of death.

Though only speculative, the concentration of deaths shortly after 42 days from obstetric haemorrhage, hypertensive disorders, and pregnancy-related infection, may suggest explanation 1, with some women may die from prolonged illness.

For all obstetric causes, deaths occurring very late on may suggest explanation 2, with enough time elapsed for a woman to have become pregnant again, e.g. pregnancy with abortive outcome at day 300 postpartum may relate to pregnancy n+1.

Figure C2 Late obstetric deaths by postpartum day of death



C3. Multinomial predicted proportions for the main results, InterVA5

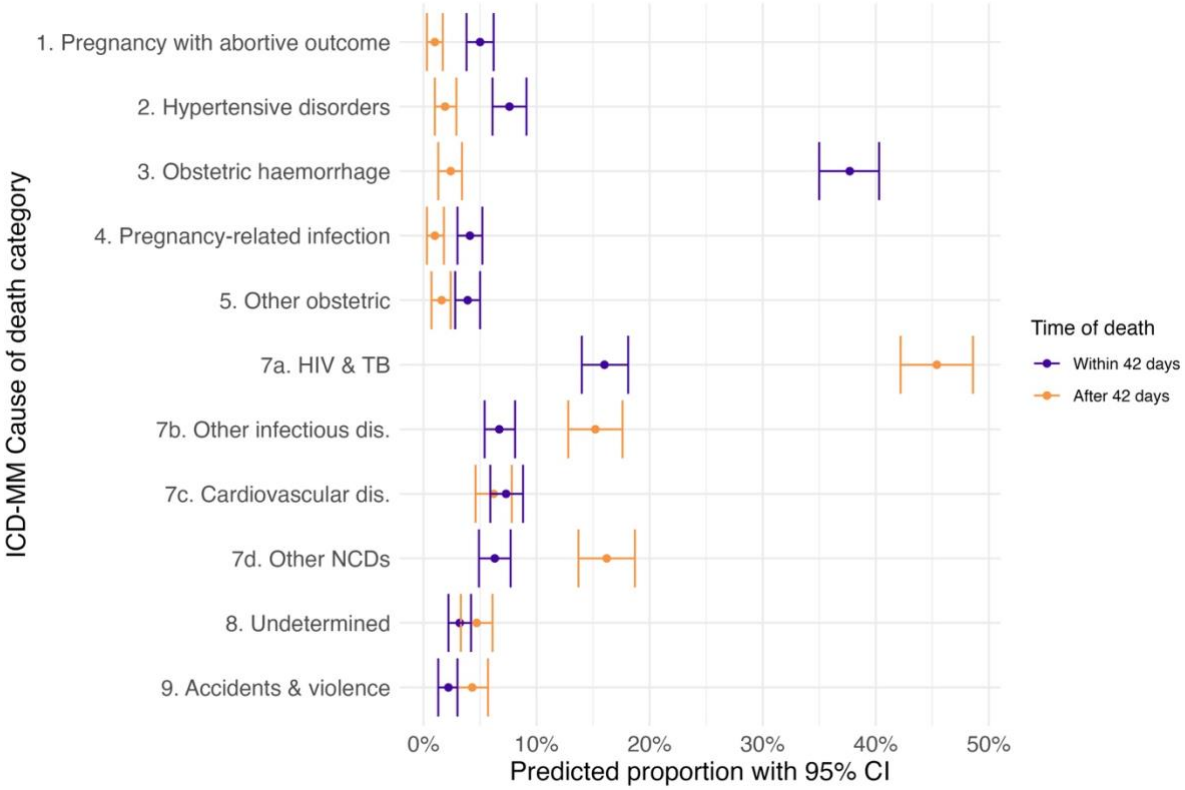
Table C1 presents the full predicted margins results for the multinomial regression for the proportion of deaths in each ICD-MM category by timing for InterVA5. These results are shown graphically in Figure C3 below.

Table C1 Predicted proportion results by ICD-MM category and timing, InterVA5

Adapted ICD-MM Category[a]	Timing	Margin	SE[b]	p-value	Lower CI	Upper CI
1. Pregnancy with abortive outcome	After 42 days	0.010	0.004	0.005	0.003	0.017
	Within 42 days	0.050	0.006	0.000	0.038	0.062
2. Hypertensive disorders	After 42 days	0.019	0.005	0.000	0.010	0.029
	Within 42 days	0.076	0.008	0.000	0.061	0.091
3. Obstetric haemorrhage	After 42 days	0.024	0.005	0.000	0.013	0.034
	Within 42 days	0.377	0.014	0.000	0.350	0.403
4. Pregnancy-related infection	After 42 days	0.010	0.004	0.004	0.003	0.018
	Within 42 days	0.041	0.006	0.000	0.030	0.052
5. Other direct obstetric	After 42 days	0.016	0.004	0.000	0.007	0.024
	Within 42 days	0.039	0.006	0.000	0.028	0.050
7a. HIV & TB	After 42 days	0.454	0.016	0.000	0.422	0.486
	Within 42 days	0.160	0.011	0.000	0.140	0.181
7b. Other infectious diseases	After 42 days	0.152	0.012	0.000	0.128	0.176
	Within 42 days	0.067	0.007	0.000	0.054	0.081
7c. Cardiovascular diseases.	After 42 days	0.062	0.008	0.000	0.046	0.078
	Within 42 days	0.073	0.008	0.000	0.059	0.088
7d. Other NCDs	After 42 days	0.162	0.013	0.000	0.137	0.187
	Within 42 days	0.063	0.007	0.000	0.049	0.077
8. Undetermined	After 42 days	0.047	0.007	0.000	0.033	0.061
	Within 42 days	0.032	0.005	0.000	0.022	0.042
9. Accidents & violence	After 42 days	0.043	0.007	0.000	0.030	0.057
	Within 42 days	0.022	0.004	0.000	0.013	0.030

[a] There were no deaths in the data attributed to category 6. Unanticipated complications of management, so not shown.
[b] Standard error

Figure C3 Predicted proportion results by ICD-MM category and timing, InterVA5



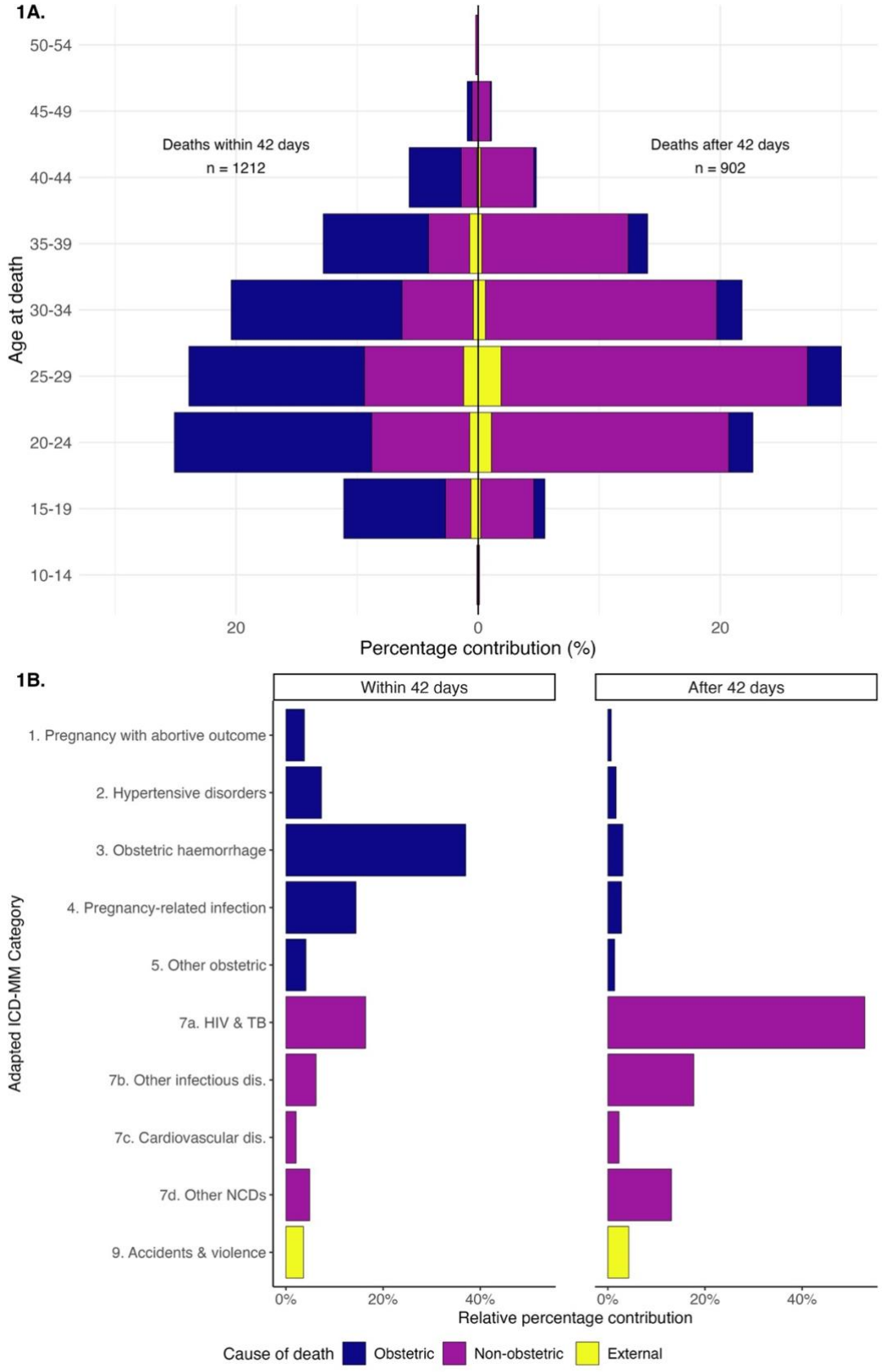
C4. Replication of the main results with InSilicoVA

Figure C4 panel A shows the proportion of deaths for three categories of pregnancy-related death: obstetric, non-obstetric, and external. Unlike InterVA5, InSilicoVA does not assign “undetermined” cause, and hence the fourth category is not represented in Figure C4. However, consistent with the InterVA5 results, across all age groups, obstetric deaths are dominant for deaths occurring within 42 days, while non-obstetric deaths are dominant for deaths occurring beyond 42 days postpartum. External deaths from accidental causes comprise a small proportion of the deaths.

Figure C4 panel B shows the breakdown of these three cause groupings by the ICD-MM categories. Category 7 – non-obstetric deaths – are disaggregated by subgroup: a) HIV and tuberculosis, b) other infectious diseases, c) cardiovascular diseases, d) other non-communicable diseases (NCDs). Consistent with the InterVA5 results, for deaths occurring within 42 days, obstetric haemorrhage is the dominant cause of obstetric deaths, and HIV and tuberculosis are the dominant causes of non-obstetric deaths. For late pregnancy-related deaths occurring beyond 42 days but within one year, HIV and TB are the leading causes, followed by other infectious diseases, and other NCDs.

ICD-MM category 6 for unanticipated complications of management is missing because there were no deaths in this category in this pooled sample.

Figure C4 Cause of pregnancy-related deaths up to one year postpartum by timing, age, and type of cause, InSilicoVA



Note: There were no deaths attributed to ICD-MM category 6. Unanticipated complications of management so this category is not shown. InSilicoVA does not have a category for 8. Unspecified, so not shown.

C5. Concordance between algorithm- and physician-assigned cause of death

The percent concordance for each HDSS and algorithm is shown in Table C2. Concordance was assessed as agreement in the string (allowing for spelling differences) in the underlying cause of death, adapted ICD-MM category, and broad type. Physician-assigned cause of death data were only available for three HDSS: Kisumu and Nairobi (Kenya), and Karonga (Malawi). For all ten HDSS, we calculated the concordance between InterVA5 and InSilicoVA. Concordance of either algorithm with physician-assigned underlying cause of death was low, but slightly higher for InterVA5. Across all HDSS, concordance between the algorithms is much higher than concordance with physician-assigned causes. Concordance of InterVA5 with physician-coded VA slightly outperforms InSilicoVA. Since hospital-based deaths are the reference standard, it is not clear which method determined the true underlying cause of death.

Table C2 Agreement between physician-assigned and algorithm-assigned cause of death

HDSS	Category	InterVA5 vs. Physician review	InSilicoVA vs. Physician review	InterVA5 vs. InSilicoVA
Agincourt, South Africa	Underlying cause	-	-	69%
	Adapted ICD-MM category	-	-	72%
	Type	-	-	87%
Basse, The Gambia	Underlying cause	-	-	64%
	Adapted ICD-MM category	-	-	67%
	Type	-	-	85%
Farafenni, The Gambia	Underlying cause	-	-	68%
	Adapted ICD-MM category	-	-	70%
	Type	-	-	81%
Karonga, Malawi	Underlying cause	32%	- 25%	61%
	Adapted ICD-MM category	44%	- 34%	73%
	Type	83%	- 82%	91%
Kersa, Ethiopia	Underlying cause	-	-	73%
	Adapted ICD-MM category	-	-	76%
	Type	-	-	92%
Kilifi, Kenya	Underlying cause	43%	-	79%
	Adapted ICD-MM category	55%	-	79%
	Type	83%	-	91%
Kisumu, Kenya	Underlying cause	43%	-	51%
	Adapted ICD-MM category	55%	-	58%
	Type	83%	-	87%
Magu, Tanzania	Underlying cause	-	-	47%
	Adapted ICD-MM category	-	-	64%
	Type	-	-	88%
Nairobi, Kenya	Underlying cause	27%	26%	68%

	Adapted ICD-MM category	36%	33%	79%
	Type	68%	65%	81%
uMkhanyakude, South Africa	Underlying cause	-	-	78%
	Adapted ICD-MM category	-	-	84%
	Type	-	-	92%
Total	Underlying cause	34%	26%	65%
	Adapted ICD-MM category	45%	34%	71%
	Type	78%	74%	89%
Missing values are present as not all HDSS had physician-coded VA data. For Kisumu, physician-coded COD was only available for deaths with an InterVA5 VA result.				

C6. Multinomial predicted proportions for the additional predictors, InterVA5

Time period (2000-2009 and 2010-2019)

Table C3 and Figure C5 show the predicted proportions from multinomial regression for InterVA5 for deaths within 42 days postpartum; Table S4 and Figure S6 show the predicted proportions for deaths from 43 days to one year postpartum. Margins were stratified by the timing of death because of differences in the cause-specific mortality fractions by timing for each decade. Using the mean of the whole sample to analyse the margins for decade may therefore obscure changes to the causes of death depending on when the death occurs. There were no significant changes in the causes of death over this time period.

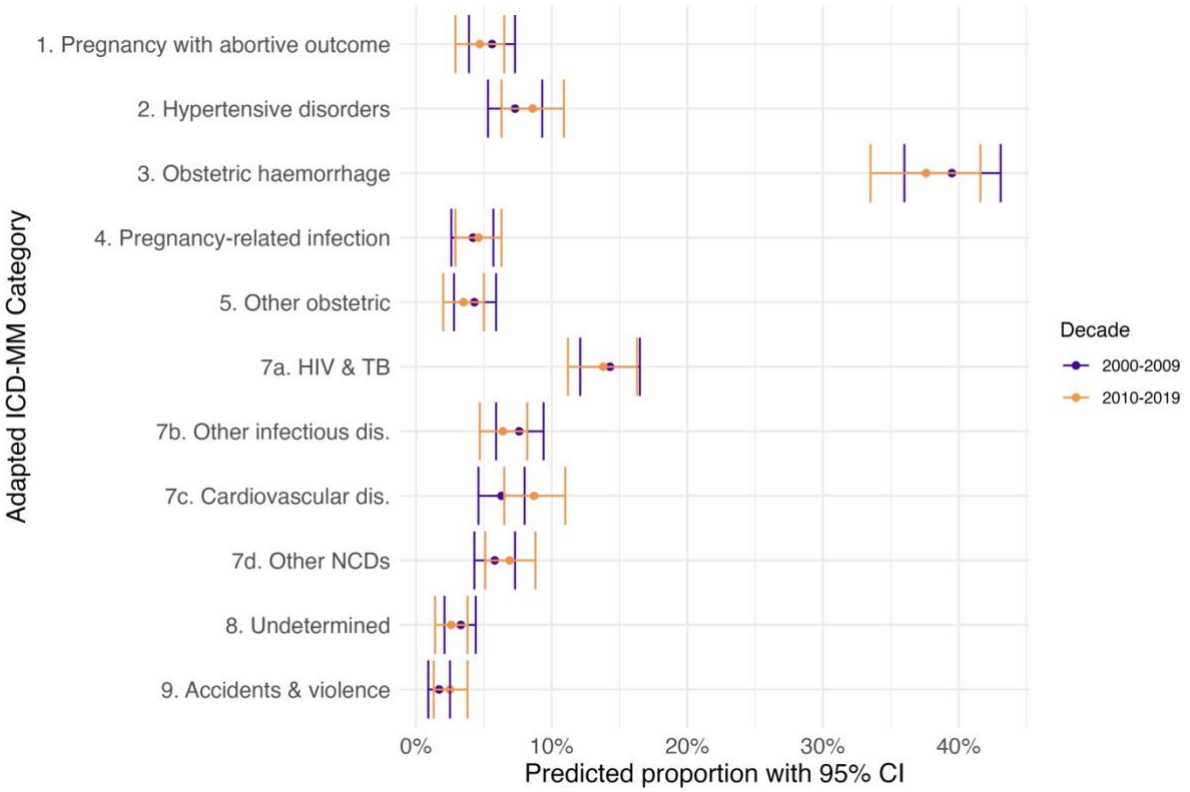
Deaths within 42 days postpartum

Table C3 Predicted margins results by ICD-MM category and decade, InterVA5, deaths within 42 days

ICD-MM Category[a]	Decade	Margin	SE[b]	p-value	Lower CI	Upper CI
1. Pregnancy with abortive outcome	2000-2009	0.056	0.009	0.000	0.039	0.073
	2010-2019	0.047	0.009	0.000	0.029	0.065
2. Hypertensive disorders	2000-2009	0.073	0.010	0.000	0.053	0.093
	2010-2019	0.086	0.012	0.000	0.063	0.109
3. Obstetric haemorrhage	2000-2009	0.395	0.018	0.000	0.360	0.431
	2010-2019	0.376	0.021	0.000	0.335	0.416
4. Pregnancy-related infection	2000-2009	0.042	0.008	0.000	0.026	0.057
	2010-2019	0.046	0.009	0.000	0.029	0.063
5. Other direct obstetric	2000-2009	0.043	0.008	0.000	0.028	0.059
	2010-2019	0.035	0.008	0.000	0.020	0.050
7a. HIV & TB	2000-2009	0.143	0.011	0.000	0.121	0.165
	2010-2019	0.138	0.013	0.000	0.112	0.163
7b. Other infectious diseases	2000-2009	0.076	0.009	0.000	0.059	0.094
	2010-2019	0.064	0.009	0.000	0.047	0.082
7c. Cardiovascular diseases.	2000-2009	0.063	0.008	0.000	0.046	0.080
	2010-2019	0.087	0.011	0.000	0.065	0.110
7d. Other NCDs	2000-2009	0.058	0.008	0.000	0.043	0.073
	2010-2019	0.069	0.010	0.000	0.051	0.088
8. Undetermined	2000-2009	0.033	0.006	0.000	0.021	0.044
	2010-2019	0.026	0.006	0.000	0.014	0.038
9. Accidents & violence	2000-2009	0.017	0.004	0.000	0.009	0.025
	2010-2019	0.025	0.006	0.000	0.013	0.038

[a] There were no deaths in the data attributed to category 6. Unanticipated complications of management, so not shown.
[b] Standard error

Figure C5 Multinomial regression predicted proportions for deaths within 42 days postpartum by decade, InterVA5



Note: InterVA attributed no deaths to category 6. Unanticipated complications of management, so not shown.

Deaths after 42 days postpartum (43-365 days)

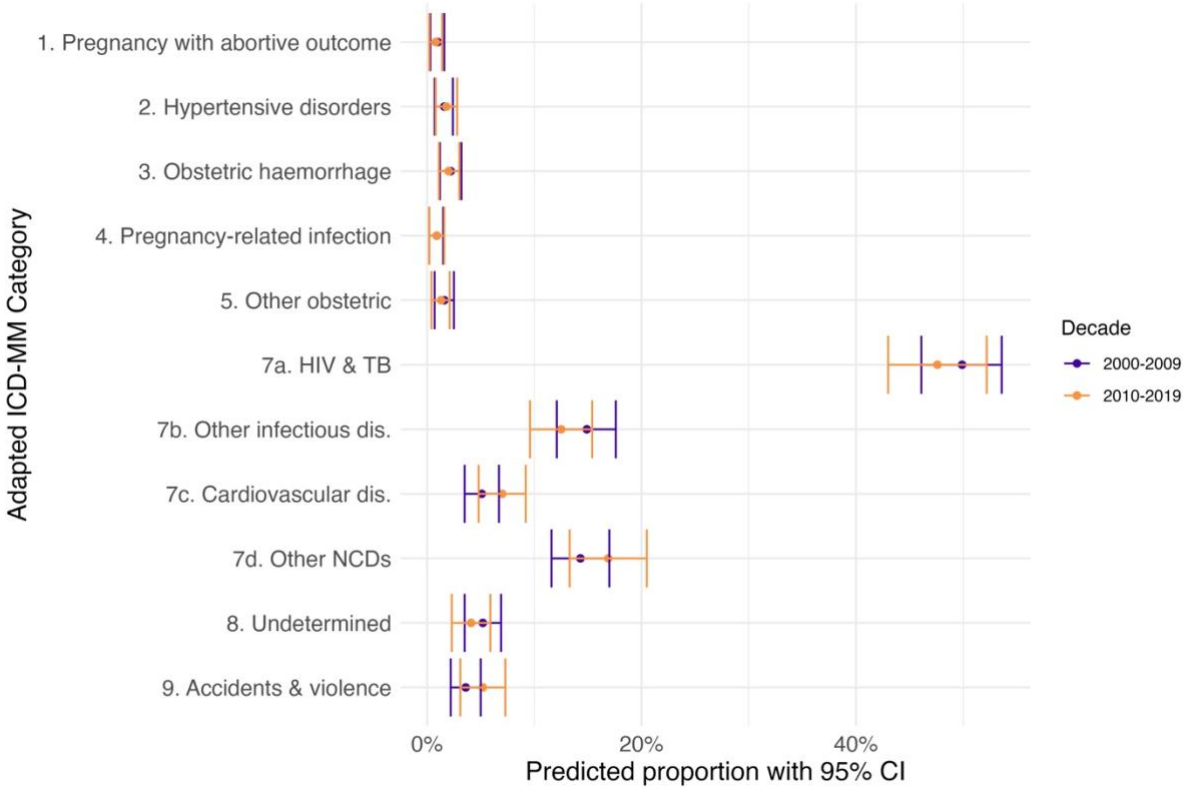
Table C4 Predicted margins by ICD-MM category and decade, InterVA5, deaths after 42 days

ICD-MM Category[a]	Decade	Margin	SE[b]	p-value	Lower CI	Upper CI
1. Pregnancy with abortive outcome	1998-2008	0.010	0.003	0.006	0.003	0.016
	2009-2019	0.008	0.003	0.011	0.002	0.014
2. Hypertensive disorders	1998-2008	0.016	0.004	0.000	0.007	0.024
	2009-2019	0.018	0.005	0.000	0.008	0.028
3. Obstetric haemorrhage	1998-2008	0.022	0.005	0.000	0.012	0.032
	2009-2019	0.020	0.005	0.000	0.011	0.030
4. Pregnancy-related infection	1998-2008	0.009	0.003	0.008	0.002	0.015
	2009-2019	0.009	0.004	0.009	0.002	0.016
5. Other direct obstetric	1998-2008	0.016	0.005	0.001	0.007	0.025
	2009-2019	0.013	0.004	0.002	0.004	0.021
7a. HIV & TB	1998-2008	0.499	0.019	0.000	0.461	0.536
	2009-2019	0.476	0.023	0.000	0.430	0.522
7b. Other infectious diseases	1998-2008	0.149	0.014	0.000	0.121	0.176
	2009-2019	0.125	0.015	0.000	0.096	0.154
7c. Cardiovascular diseases.	1998-2008	0.051	0.008	0.000	0.035	0.067
	2009-2019	0.070	0.011	0.000	0.048	0.092
7d. Other NCDs	1998-2008	0.143	0.014	0.000	0.116	0.170
	2009-2019	0.169	0.018	0.000	0.133	0.205
8. Undetermined	1998-2008	0.052	0.009	0.000	0.035	0.069
	2009-2019	0.041	0.009	0.000	0.023	0.059

9. Accidents & violence	1998-2008	0.036	0.007	0.000	0.022	0.050
	2009-2019	0.052	0.011	0.000	0.031	0.073

[a] There were no deaths in the data attributed to category 6. Unanticipated complications of management, so not shown.
[b] Standard error

Figure C6 Multinomial regression predicted proportions for deaths after 42 days postpartum by decade, InterVA5



Note: InterVA attributed no deaths to category 6. Unanticipated complications of management, so not shown.

Health and Demographic Surveillance Systems

Table C5 and Figure C7 show the predicted proportions from multinomial regression for InterVA for each HDSS. These margins were not stratified by the timing of the death, within or beyond 42 days postpartum, because splitting the data across ten HDSS and two timing categories results in too few deaths in each combination. After accounting for timing and decade, there remain significant differences between at least two HDSS in the predicted proportions of the 11-cause categories for deaths from pregnancy with abortive outcome, hypertensive disorders, obstetric haemorrhage, other direct obstetric, HIV and tuberculosis, other infectious diseases, cardiovascular diseases, and accidental deaths.

For example, the predicted probability of deaths from obstetric haemorrhage is significantly higher in Karonga, Malawi, than in Basse, The Gambia; the predicted proportion of deaths from hypertensive disorders are significantly higher in Basse, The Gambia, than in Kisumu, Kenya or Agincourt, South Africa; the predicted proportions of deaths from HIV and tuberculosis is much greater, and deaths from other infectious diseases much lower, in uMkhanyakude, South Africa, than in other HDSS; and finally, the predicted proportion of deaths from cardiovascular disease is significantly higher in Nairobi, Kenya, than in uMkhanyakude, South Africa.

Table C5 Predicted margins results by ICD-MM category and HDSS, InterVA5

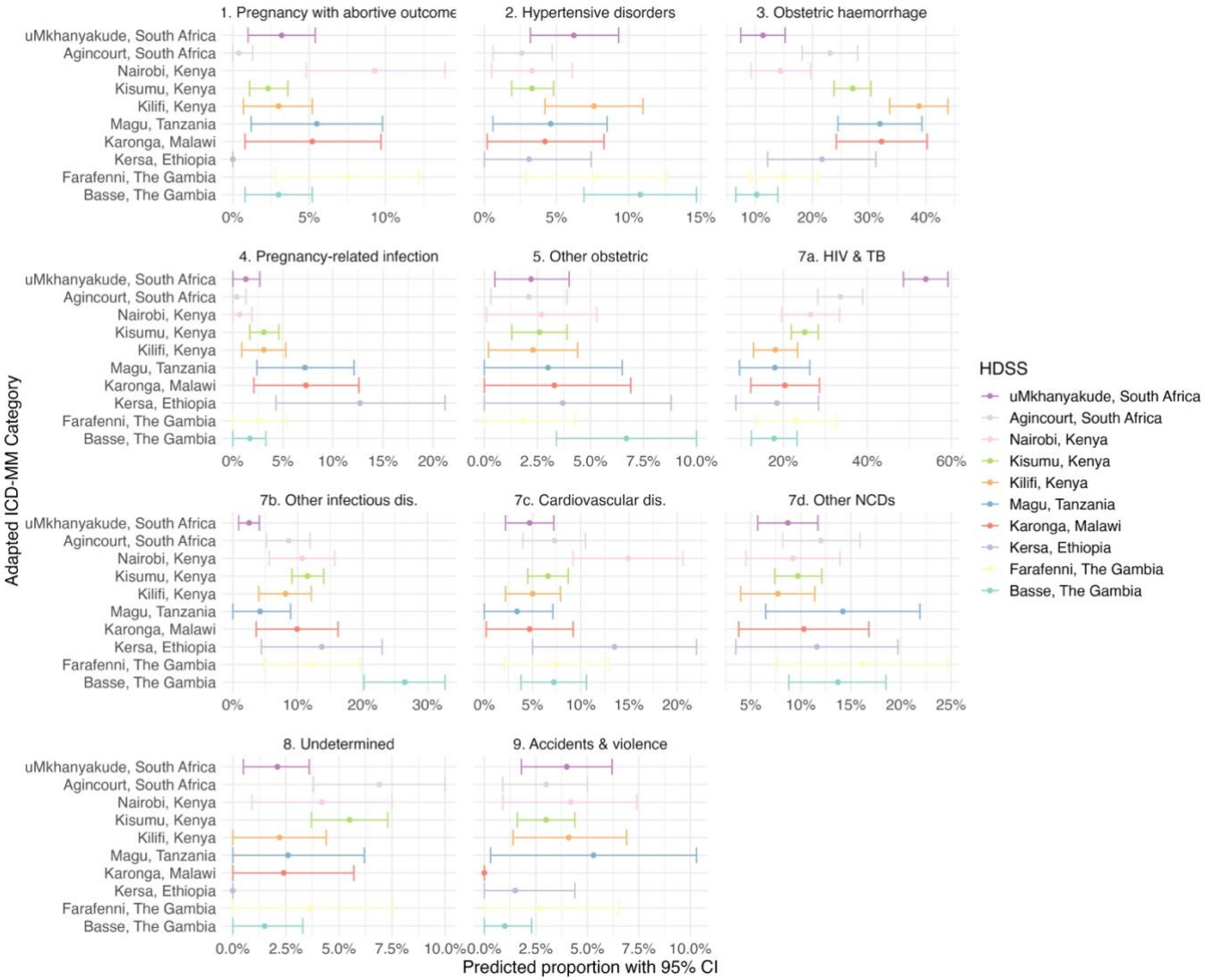
HDSS	Adapted ICD-MM Category[a]	Margin	SE[b]	p-value	Lower CI	Upper CI
Agincourt, South Africa	1. Pregnancy with abortive outcome	0.004	0.004	0.316	-0.004	0.013
	2. Hypertensive disorders	0.026	0.011	0.013	0.006	0.047
	3. Obstetric haemorrhage	0.231	0.025	0.000	0.182	0.280
	4. Pregnancy-related infection	0.004	0.004	0.316	-0.004	0.013
	5. Other direct obstetric	0.021	0.009	0.024	0.003	0.039
	7a. HIV & TB	0.336	0.027	0.000	0.282	0.389
	7b. Other infectious diseases	0.086	0.017	0.000	0.052	0.119
	7c. Cardiovascular diseases.	0.073	0.016	0.000	0.040	0.105
	7d. Other NCDs	0.120	0.020	0.000	0.082	0.159
	8. Undetermined	0.069	0.016	0.000	0.038	0.100
	9. Accidents & violence	0.030	0.010	0.004	0.009	0.050
Basse, The Gambia	1. Pregnancy with abortive outcome	0.030	0.011	0.007	0.008	0.052
	2. Hypertensive disorders	0.108	0.020	0.000	0.069	0.147
	3. Obstetric haemorrhage	0.102	0.019	0.000	0.065	0.139
	4. Pregnancy-related infection	0.017	0.008	0.044	0.000	0.033
	5. Other direct obstetric	0.067	0.017	0.000	0.034	0.100
	7a. HIV & TB	0.178	0.028	0.000	0.124	0.233
	7b. Other infectious diseases	0.265	0.032	0.000	0.202	0.327
	7c. Cardiovascular diseases.	0.072	0.017	0.000	0.038	0.106
	7d. Other NCDs	0.137	0.025	0.000	0.088	0.185
	8. Undetermined	0.015	0.009	0.082	-0.002	0.033
	9. Accidents & violence	0.010	0.007	0.156	-0.004	0.023
Farafenni, The Gambia	1. Pregnancy with abortive outcome	0.075	0.024	0.002	0.028	0.122
	2. Hypertensive disorders	0.078	0.025	0.002	0.029	0.126
	3. Obstetric haemorrhage	0.150	0.030	0.000	0.091	0.209
	4. Pregnancy-related infection	0.025	0.014	0.079	-0.003	0.054
	5. Other direct obstetric	0.018	0.013	0.154	-0.007	0.043
	7a. HIV & TB	0.231	0.049	0.000	0.136	0.326
	7b. Other infectious diseases	0.122	0.038	0.001	0.048	0.196
	7c. Cardiovascular diseases.	0.075	0.028	0.006	0.021	0.129
	7d. Other NCDs	0.162	0.043	0.000	0.077	0.247
	8. Undetermined	0.036	0.020	0.080	-0.004	0.076
	9. Accidents & violence	0.027	0.019	0.153	-0.010	0.065
Karonga, Malawi	1. Pregnancy with abortive outcome	0.052	0.023	0.021	0.008	0.097
	2. Hypertensive disorders	0.042	0.021	0.041	0.002	0.083
	3. Obstetric haemorrhage	0.322	0.041	0.000	0.242	0.402
	4. Pregnancy-related infection	0.073	0.027	0.006	0.021	0.126
	5. Other direct obstetric	0.033	0.019	0.078	-0.004	0.069
	7a. HIV & TB	0.204	0.041	0.000	0.123	0.286
	7b. Other infectious diseases	0.099	0.032	0.002	0.036	0.162
	7c. Cardiovascular diseases.	0.047	0.023	0.040	0.002	0.092
	7d. Other NCDs	0.103	0.033	0.002	0.038	0.168
	8. Undetermined	0.024	0.017	0.151	-0.009	0.057
	9. Accidents & violence	0.000	0.000	0.999	0.000	0.000
Kersa, Ethiopia	1. Pregnancy with abortive outcome	0.000	0.000	0.999	0.000	0.000
	2. Hypertensive disorders	0.031	0.022	0.153	-0.011	0.074
	3. Obstetric haemorrhage	0.217	0.049	0.000	0.121	0.312
	4. Pregnancy-related infection	0.127	0.043	0.003	0.043	0.212

	5. Other direct obstetric	0.037	0.026	0.155	-0.014	0.088
	7a. HIV & TB	0.185	0.050	0.000	0.087	0.284
	7b. Other infectious diseases	0.137	0.047	0.004	0.044	0.230
	7c. Cardiovascular diseases.	0.135	0.043	0.002	0.050	0.220
	7d. Other NCDs	0.116	0.041	0.005	0.035	0.197
	8. Undetermined	0.000	0.000	0.999	0.000	0.000
	9. Accidents & violence	0.015	0.015	0.317	-0.014	0.044
Kilifi, Kenya	1. Pregnancy with abortive outcome	0.030	0.011	0.010	0.007	0.052
	2. Hypertensive disorders	0.076	0.017	0.000	0.042	0.110
	3. Obstetric haemorrhage	0.388	0.026	0.000	0.336	0.439
	4. Pregnancy-related infection	0.031	0.011	0.006	0.009	0.053
	5. Other direct obstetric	0.023	0.011	0.029	0.002	0.044
	7a. HIV & TB	0.181	0.027	0.000	0.129	0.234
	7b. Other infectious diseases	0.081	0.020	0.000	0.040	0.121
	7c. Cardiovascular diseases.	0.050	0.015	0.001	0.022	0.079
	7d. Other NCDs	0.077	0.019	0.000	0.040	0.114
	8. Undetermined	0.022	0.011	0.046	0.000	0.044
	9. Accidents & violence	0.041	0.014	0.003	0.014	0.069
Kisumu, Kenya	1. Pregnancy with abortive outcome	0.023	0.006	0.000	0.011	0.036
	2. Hypertensive disorders	0.033	0.008	0.000	0.019	0.048
	3. Obstetric haemorrhage	0.271	0.017	0.000	0.238	0.303
	4. Pregnancy-related infection	0.031	0.007	0.000	0.017	0.046
	5. Other direct obstetric	0.026	0.007	0.000	0.013	0.039
	7a. HIV & TB	0.251	0.016	0.000	0.219	0.283
	7b. Other infectious diseases	0.115	0.013	0.000	0.091	0.140
	7c. Cardiovascular diseases.	0.066	0.010	0.000	0.045	0.087
	7d. Other NCDs	0.097	0.012	0.000	0.074	0.121
	8. Undetermined	0.055	0.009	0.000	0.037	0.073
	9. Accidents & violence	0.030	0.007	0.000	0.016	0.044
Magu, Tanzania	1. Pregnancy with abortive outcome	0.055	0.022	0.012	0.012	0.098
	2. Hypertensive disorders	0.046	0.020	0.022	0.006	0.085
	3. Obstetric haemorrhage	0.319	0.038	0.000	0.245	0.393
	4. Pregnancy-related infection	0.072	0.025	0.003	0.024	0.121
	5. Other direct obstetric	0.030	0.017	0.080	-0.004	0.065
	7a. HIV & TB	0.180	0.043	0.000	0.096	0.263
	7b. Other infectious diseases	0.042	0.024	0.073	-0.004	0.089
	7c. Cardiovascular diseases.	0.034	0.019	0.079	-0.004	0.071
	7d. Other NCDs	0.142	0.039	0.000	0.065	0.219
	8. Undetermined	0.026	0.018	0.151	-0.010	0.062
	9. Accidents & violence	0.053	0.026	0.038	0.003	0.103
Nairobi, Kenya	1. Pregnancy with abortive outcome	0.093	0.023	0.000	0.048	0.139
	2. Hypertensive disorders	0.033	0.014	0.022	0.005	0.061
	3. Obstetric haemorrhage	0.144	0.027	0.000	0.092	0.197
	4. Pregnancy-related infection	0.007	0.007	0.315	-0.006	0.019
	5. Other direct obstetric	0.027	0.013	0.042	0.001	0.053
	7a. HIV & TB	0.265	0.035	0.000	0.196	0.334
	7b. Other infectious diseases	0.107	0.026	0.000	0.056	0.157
	7c. Cardiovascular diseases.	0.149	0.029	0.000	0.092	0.206
	7d. Other NCDs	0.092	0.024	0.000	0.045	0.139
	8. Undetermined	0.042	0.017	0.012	0.009	0.075
	9. Accidents & violence	0.042	0.017	0.012	0.009	0.074
uMkhanyakunde, South Africa	1. Pregnancy with abortive outcome	0.032	0.011	0.004	0.010	0.054
	2. Hypertensive disorders	0.062	0.015	0.000	0.032	0.093
	3. Obstetric haemorrhage	0.113	0.020	0.000	0.074	0.152
	4. Pregnancy-related infection	0.013	0.007	0.082	-0.002	0.027

	5. Other direct obstetric	0.022	0.009	0.014	0.005	0.040
	7a. HIV & TB	0.539	0.027	0.000	0.486	0.592
	7b. Other infectious diseases	0.025	0.008	0.003	0.009	0.041
	7c. Cardiovascular diseases.	0.047	0.013	0.000	0.022	0.072
	7d. Other NCDs	0.087	0.015	0.000	0.057	0.117
	8. Undetermined	0.021	0.008	0.008	0.005	0.036
	9. Accidents & violence	0.040	0.011	0.000	0.018	0.062

[a] InterVA5 attributed no deaths to category 6. Unanticipated complications of management, so not shown.

Figure C7 Multinomial regression predicted proportions for deaths after 42 days postpartum by HDSS, InterVA5

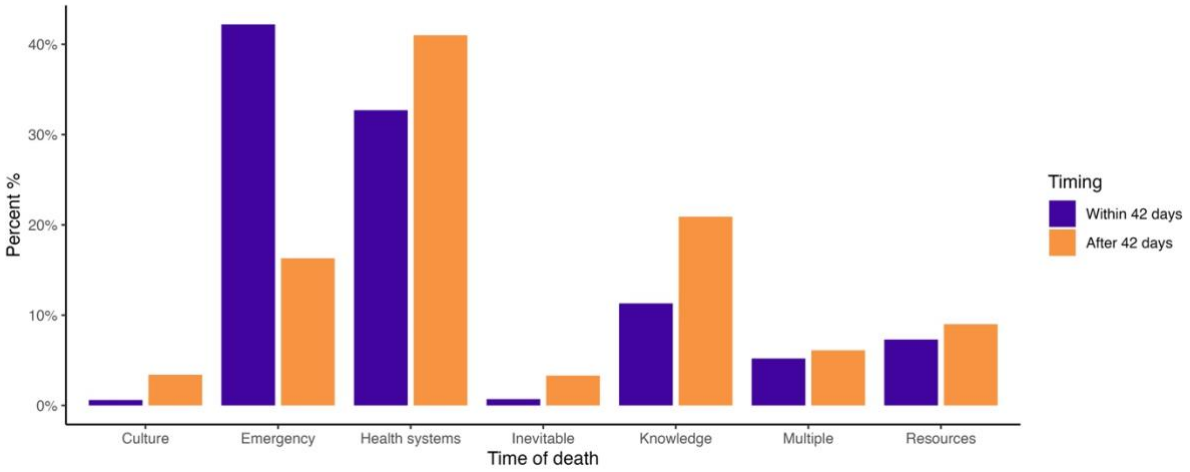


Note: InterVA5 attributed no deaths to category 6. Unanticipated complications of management, so not shown.

C7. Circumstances of Mortality Categories (COMCATs)

The circumstances of deaths within 42 days differ from those which occurred from 43-365 days postpartum. Figure C8 shows that for deaths occurring after (vs. within) 42 days postpartum, fewer were emergencies and more related to either problems receiving care in health systems, or to knowledge, recognition, or awareness of serious disease.

Figure C8 COMCATs by time of death, InterVA5



C8. Verbal autopsy coverage by HDSS

Coverage of verbal autopsy interviews is not complete for all deaths in all HDSS (Table C6). We calculated the coverage of VA data as the proportion of all deaths, regardless of age and sex, in the HDSS where there was an available VA record. Residency records of deaths in the HDSS and verbal autopsy records were restricted to cover the same time interval.

Coverage estimates are NA for Kilifi and Kersa HDSS because we only had verbal autopsy data for deaths to pregnant or recently pregnant women in those two sites.

Table C6 Coverage of VA data by HDSS

HDSS	Coverage (%)	Years of deaths in the sample
Agincourt, South Africa	84	2000-2017
Basse, The Gambia	33	2006-2019
Farafenni, The Gambia	26	2000-2019
Kersa, Ethiopia	NA	NA
Kilifi, Kenya	NA	NA
Kisumu, Kenya	57	2003-2013
Magu, Tanzania	42	2000-2017
Nairobi, Kenya	100	2002-2016
Karonga, Malawi	100	2002-2017
uMkhanyakude, South Africa	100	2000-2017

In all eight HDSS with available data, some verbal autopsy records have no corresponding match in a death record. In Nairobi, Karonga, and uMkhanyakude, this means coverage exceeds 100%. This may occur for two reasons:

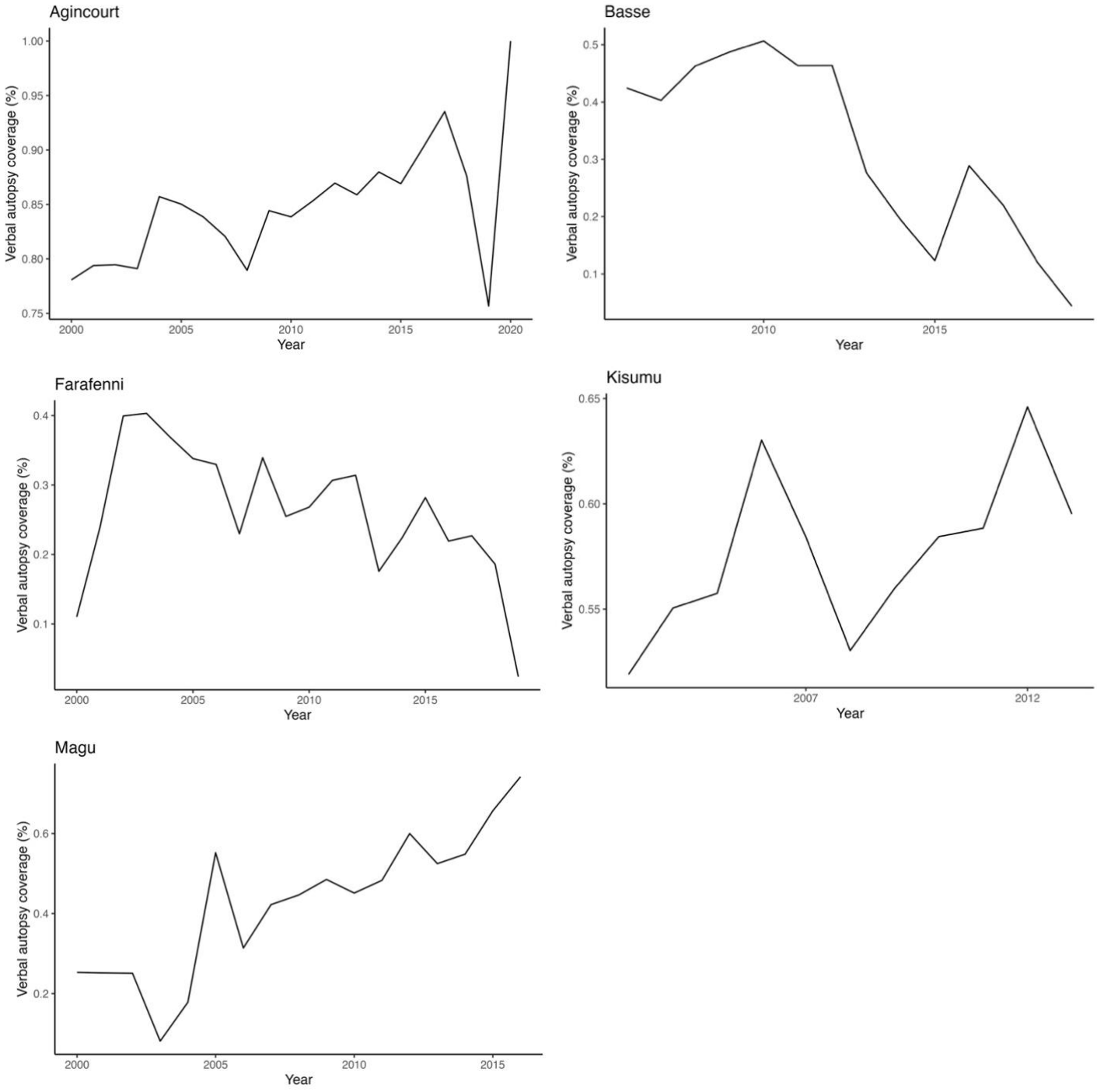
1. Some verbal autopsy interviews are conducted for non-residents of the site
2. Changes to the individual unique ID numbers prevents record merges.

Incompleteness in Agincourt, Basse, Farafenni, Kisesa, Kisumu and Magu may occur if:

1. Not all deaths in the HDSS are followed-up with a verbal autopsy interview
2. Changes in individual unique ID numbers prevent merges of death and VA records

Figures C9 shows the changes in coverage of verbal autopsy records for deaths in the HDSS by year. Coverage varies significantly over time in all three HDSS. In the HDSS in The Gambia, coverage has steadily declined – in Basse from 2010, and in Farafenni from 2003. In Agincourt and Magu, coverage has increased over time.

Figure C9 Verbal autopsy coverage for deaths by year



Appendix D Supplementary material for Chapter 5

Postpartum recovery after severe maternal morbidity in Kilifi, Kenya: A Grounded Theory of recovery trajectories beyond 42 days

D1. Members of the PRECISE Network

Table D1 Members of the PRECISE Network

In-country teams	Members
THE GAMBIA: Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara	Umberto D'Alessandro, Anna Roca, Hawanatu Jah, Andrew Prentice, Melisa Martinez-Alvarez, Brahima Diallo, Abdul Sesay, Sambou Suso, Baboucarr Njie, Fatima Touray, Yahaya Idris, Fatoumata Kongira, Modou F.S. Ndure, Lawrence Gibba, Abdoulie Bah and Yorro Bah.
KENYA: Aga Khan University, Nairobi	Marleen Temmerman, Angela Koech, Patricia Okiro, Consolata Juma, Geoffrey Omuse, Grace Mwashigadi, Joseph Mutunga, Isaac Mwaniki, Moses Mukhanya and Onesmus Wanje, Marvin Ochieng and Emily Mwadime.
MOZAMBIQUE : Centro de Investigação em Saúde de Manhiça, Manhiça	Esperança Sevene, Corssino Tchavana, Salesio Macuacua, Anifa Vala, Helena Boene, Lazaro Quimice, Sonia Maculuve, Eusebio Macete, Inacio Mandomando, Carla Carrilho
Central co-ordinating team	
Department of Women and Children's Health, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London	Peter von Dadelszen, Laura A. Magee, Rachel Craik, Hiten Mistry, Marie-Laure Volvert, Thomas Mendy
Donna Russell Consulting	Donna Russell
Co-Investigator team	
Midlands State University, Zimbabwe	Prestige Tatenda Makanga, Liberty Makacha and Reason Mlambo
Kings College London	Lucilla Poston, Jane Sandall, Rachel Tribe, Andrew Shennan, Sophie Moore, Tatiana Salisbury and Lucy Chappell
University of Oxford	Aris Papageorghiou, Alison Noble, Rachel Craik
London School of Hygiene and Tropical Medicine	Hannah Blencowe, Veronique Filippi, Joy Lawn, Matt Silver, Joseph Waiswa and Ursula Gazeley
St George's, University of London	Judith Cartwright, Guy Whitley, Sanjeev Krishna
University of British Columbia	Marianne Vidler, Jing (Larry) Li, Jeff Bone, Mai-Lei (Maggie) Woo Kinshella, Domena Tu, Ash Sandhu, Kelly Pickerill
Imperial College London	Ben Barratt

D2. COnsolidated criteria for REporting Qualitative research (COREQ)

Table D2 COREQ Checklist

Topic	Item No	Guide Questions/Description	Reported on page no.
Domain 1: Research team and reflexivity			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	11
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	11
Occupation	3	What was their occupation at the time of the study?	11
Gender	4	Was the researcher male or female?	33
Experience and training	5	What experience or training did the researcher have?	11
Relationship established	6	Was a relationship established prior to study commencement?	11
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	11
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	12, 34
Domain 2: Study design			
Methodological orientationand Theory	9	What methodological orientation was stated to underpin the study? e.g.grounded theory, discourse analysis, ethnography, phenomenology, content analysis	6
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	2
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	11
Sample size	12	How many participants were in the study?	7
Non-participation	13	How many people refused to participate or dropped out? Reasons?	11
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	12
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	11
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10

Interview guide	1 7	Were questions, prompts, guides provided by the authors? Was it pilot tested?	11
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	11
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	12
Field notes	20	Were field notes made during and/or after the inter view or focus group?	13
Duration	21	What was the duration of the inter views or focus group?	11
Data saturation	22	Was data saturation discussed?	11, 34
Transcripts returned	23	Were transcripts returned to participants for comment or correction?	36
Domain 3: analysis and findings			
Number of data coders	24	How many data coders coded the data?	12
Description of the coding tree		Did authors provide a description of the coding tree?	12
Derivation of themes		Were themes identified in advance or derived from the data?	12
Software		What software, if applicable, was used to manage the data?	12
Participant checking		Did participants provide feedback on the findings?	36
Quotations presented		Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	14-28
Data and findings consistent		Was there consistency between the data presented and the findings?	14-36
Clarity of major themes		Were major themes clearly presented in the findings?	14
Clarity of minor themes		Is there a description of diverse cases or discussion of minor themes?	14

D3. Criteria used to identify maternal morbidity categories

Table D3 presents the criteria used to define potentially life-threatening conditions (PLTCs), were defined according to adapted WHO criteria[1,2] with variables included in the PRECISE study.

Table D4 presents the WHO criteria, modified criteria for low resource settings (Haydom criteria and Tura criteria for sub-Saharan Africa), and the adapted criteria we used in the qualitative study to identify maternal near miss events within PRECISE facilities

Table D3 Definition of potentially life-threatening conditions

PLTC Criteria	WHO definition	Authors' adaptation for PRECISE facilities
1. Severe maternal complications		
Severe postpartum haemorrhage	Genital bleeding after delivery, with at least one of the following: perceived abnormal bleeding (1000 ml or more) or any bleeding with hypotension or blood transfusion.	PPH with at least one of: use of NASG, any transfusion, systolic blood pressure below 90 mmHg or diastolic blood pressure below 40 mmHg
Severe pre-eclampsia	Persistent systolic blood pressure of 160 mmHg or more or a diastolic blood pres- sure of 110 mmHg; proteinuria of 5 g or more in 24 hours; oliguria of <400 ml in 24 hours; or HELLP syndrome or pulmonary oedema. Excludes eclampsia.	. Any recorded severe hypertension with systolic blood pressure of 160 mmHg or more or a diastolic blood pres- sure of 110 mmHg; Proteinuria of 3 g or more in 24 hours; or HELLP syndrome or pulmonary oedema. Excludes eclampsia
Eclampsia	Generalized fits in a patient without previous history of epilepsy. Includes coma in pre-eclampsia.	No change
Sepsis or severe systemic infection	Presence of fever (body temperature >38°C), a confirmed or suspected infection (e.g. chorioamnionitis, septic abortion, endometritis, pneumonia), and at least one of the following: heart rate >90, respiratory rate >20, leukopenia (white blood cells <4000), leukocytosis (white blood cells >12 000).	No change
Ruptured uterus	Rupture of uterus during labour confirmed by laparotomy.	No change
Severe complications of abortion	No guideline provided	N/A not measured
2. Critical interventions or intensive care unit use		
Admission to intensive care unit		Measured in the PRECISE Network but there are no ICU/high dependency unit available Rabai or Mariakani facilities.
Interventional radiology		Not measured
Laparotomy	Laparotomy (includes hysterectomy, excludes caesarean section)	No change
Use of blood products		No change

Table D4 Definition of maternal near miss events

WHO criteria[1]	Haydom criteria[2]	Tura criteria[3]	Authors' adaptation for PRECISE facilities
1. Clinical criteria			
Acute cyanosis	Acute cyanosis	Acute cyanosis	Acute cyanosis
Gasping	Gasping	Gasping	Gasping
Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min
Shock	Shock	Shock	Shock[a]
Oliguria non-responsive to fluids or diuretics	Oliguria non-responsive to fluids or diuretics	Oliguria non-responsive to fluids or diuretics	Oliguria[b]
Failure to form clots	Failure to form clots	Failure to form clots	Failure to form clots
Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr
Cardiac arrest	Cardiac arrest	Cardiac arrest	Cardiac arrest
Stroke	Stroke	Stroke	Stroke
Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis
Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia
	Eclampsia	Eclampsia	Eclampsia
	Uterine rupture	Uterine rupture	Uterine rupture
	Sepsis or severe systemic infection	Sepsis or severe systemic infection	Sepsis or severe systemic infection
		Pulmonary oedema	Pulmonary oedema
		Sepsis or severe systemic infection	Sepsis or severe systemic infection
		Severe abortion complications	
		Severe malaria	Severe malaria
		Severe pre-eclampsia with ICU admission	Severe pre-eclampsia[c]
2. Laboratory-based criteria			
Oxygen saturation <90% for > 60min	Oxygen saturation <90% for > 60min	Oxygen saturation <90% for > 60min	Oxygen saturation <90%[d]
PaO2/FiO2 <200 mmHg			
Creatinine ≥ 300 μmol/l or ≥3.5 mg/dl		Creatinine ≥ 300 μmol/l or ≥3.5 mg/dl	Creatinine ≥ 300 μmol/l or ≥3.5 mg/dl[e]
Bilirubin > 100 μmol/l or > 6.0 mg/dl			
pH <7.1			
Lactate ≥5 mEq/ml			
Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)
Los of consciousness and ketoacids in urine		Loss of consciousness and ketoacids in urine	
3. Management-based criteria			
Use of continuous vasoactive drugs		Use of continuous vasoactive drugs	

Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage
Transfusion of ≥ 5 units of blood	Transfusion of ≥ 1 units of blood	Transfusion of ≥ 2 units of blood	Transfusion of ≥ 1 units of blood
Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia
Dialysis for acute renal failure			
Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation
		Laparotomy other than caesarean section	Laparotomy other than caesarean section
	Admission to intensive care unit		Admission to intensive care unit[f]

[a] Shock defined as any case meeting either of the following criteria:
(i) systolic BP < 90 mmHg with heart rate >120 with IV fluids;
(ii) (iii) systolic BP < 90 mmHg or diastolic < 40 mmHg with heart rate >90 or respiratory rate > 20 or oliguria <30ml/4hr.
[b] Use of diuretics not specified
[c] ICU admission for severe pre-eclampsia not specified because most PRECISE facilities do not have ICU or high dependency units.
[d] Duration of oxygen saturation below 90% not specified
[e] Creatinine measurement not universally available.
[f] Measured in the PRECISE Network but there are no ICU/high dependency unit available Rabai or Mariakani facilities.

References

[1] Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol. 2009 Jun 1;23(3):287–96.
[2] Nelissen E, Mduma E, Broerse J, Ersdal H, Evjen-Olsen B, van Roosmalen J, et al. Applicability of the WHO Maternal Near Miss Criteria in a Low-Resource Setting. Young RC, editor. PLoS ONE. 2013 Apr 16;8(4):e61248
[3] Tura AK, Stekelenburg J, Scherjon SA, Zwart J, van den Akker T, van Roosmalen J, et al. Adaptation of the WHO maternal near miss tool for use in sub-Saharan Africa: an International Delphi study. BMC Pregnancy Childbirth. 2017;17(1):445

D4. English interview guide for women with severe morbidity

Interview introductory greetings

[Interviewer to introduce themselves, and briefly remind the participant of the purpose of the study, estimatedduration, and remind the participant of informed consent procedures]

[For women who experienced a stillbirth or neonatal death only:]
Our sincere condolences to you and your family for the loss of your baby.

How are you, and [if applicable] how is your baby?"

Recollection of pregnancy and delivery

[Interviewer to clarify whether the woman has had another pregnancy since the pregnancy where she experienced a complication. Clarify that the questions you will ask refer to the pregnancy with complications]

In your own words, could you tell me about your last pregnancy and how you felt?
Potential probes if not mentioned in conversation:

- Can you tell me about when you found out you were pregnant and how you felt? Was the pregnancyplanned?
- How did you feel during your pregnancy?
- How did you feel during delivery?
- Did you have any problems during pregnancy?
- When did you first learn that there was a problem?
- Did the doctors explain to you what the problem was? Did you understand what was happening at thetime?
- What treatment did you receive?
- How long did you spend in the hospital before being discharged?

Looking back now at your experience of pregnancy and delivery, how do you feel when you think aboutthat time?

- How have your feelings about what happened changed over time?

Aftermath and Recovery from Maternal Morbidity

Now I'd like to ask you about how you have been since the pregnancy/delivery. *Would you like to take abreak, or are you okay to continue?*

A. Events following pregnancy/delivery

In your own time, and in your own words, can you tell me what happened once you came home fromthe hospital after the pregnancy had ended/ after the birth of your child?
Potential probes:

- What happened soon after you got home?
- How did you feel to be home?

B. Postpartum care and support

Can you tell me about the care you received from health service providers since the birth [since the lossof your baby] and in the weeks and months that have followed?
Potential probes:

- This could be care you received from health services, Community Health Workers (CHW), or anyother provider of postpartum care.
- For how long after the birth did you receive this care? Did you feel this was long enough?
- What could the health workers have done better to support you and your partner during the postpartum period?
- Are there any other services you wish had been offered to you that weren't?

Now can you tell me about the support you have received since the birth [and since the loss of yourbaby] and in the weeks and months that have followed?
Potential probes:

- Who supported you? This could be support from your partner, other family members, friends, amember of the community, traditional birth attendants, neighbours, or a member of your church/mosque.
- Support could be in the form of help with housework and household responsibilities, financialsupport, or social and emotional support.
- What support did you receive from your husband? What about from your mother? And mother-in-law?
- For how long after the birth did you receive this support? Was this long enough? How did the supportyou were offered change over time?
- Are there any types of help or support you wish had been offered to you that wasn't?
- Have you felt people around you have understood what you went through?

Can you tell me about how your life has changed since your last pregnancy and with your new baby/ following the loss of your baby?

Physical recovery: How have you felt physically since the delivery / since the loss of your baby?
Potential probes:

- You gave birth in [INSERT MONTH/YEAR]. Could you tell me about your physical recovery in theweeks and months that followed? What does it mean to you to feel physically recovered from the pregnancy and birth? How long did it take for you to feel physically recovered?
- How has how you have felt physically changed over time?
- If you feel like you have not yet physically recovered, in what way? How does this make you feel?

Emotional recovery: How have you felt emotionally since the delivery / since the loss of your baby?

- Could you tell me about your emotional recovery in the weeks and months that followed?
- In the weeks and months that have followed the delivery, what emotions have you felt? Have you felthappy? Sad? Worried? Anxious? In control? Are there any other emotions you felt?
- How has how you have felt emotionally changed over time?
- If you feel like you have not yet emotionally recovered, in what way? How does this make you feel?
- Has the complication affected your self-esteem, identity, and body image, and if so, how?

Social recovery: How have you felt emotionally since the delivery / since the loss of your baby?

- Could you tell me about the social impact the complication has had on you in the weeks and monthsthat followed?
- Could you tell me about how the complication has affected your relationship with your partner?
- How has it affected your sex life? When did you feel ready to have sex again?
- How about any other members of your family?

Economic recovery: How have you been financially since the delivery / since the loss of your baby?

- Could you tell me about the economic impact the complication has had on you in the weeks andmonths that followed?

Plans for the future

What are your hopes and plans for the future?

- *[If she mentions only hopes, then probe plans. If she only mentions plans, probe hopes.]*
- Potential Probes:
- How has your experience at pregnancy/delivery and the complication changed your hopes or plans forthe future?
- Have you been pregnant again? How does the thought of a future pregnancy make you feel?
- Have your feelings towards a future pregnancy changed since your experience, and if so, how?
- How has the complication has affected your partner's hopes and plans for the future? In what way?

Final remarks

- What advice would you have for other women who have experienced something similar to you?
- Do you have anything to add about your experience which perhaps I haven't asked you about?
- Do you have any questions for me?

I would like to thank you very much for your time on behalf of Aga Khan University, PRECISE Study team.Thank you for sharing your story with us. We understand that today may have brought up difficult feelings and memories for you. If you would like to receive counselling support, please let me know and I will link you to the facility counsellor. [IF APPLICABLE]: Please accept my deepest condolences again for the death of your baby.

D5. Supportive quotations for super categories and themes

Table D5 Supportive quotations

Theme	Super category	Participant	Quotation	Interpretation
Loss	**1a. Of understanding**	**Woman 13**	*"I went back because I was in a lot of pain even walking. I was walking slowly and when I walk I just feel pain. I failed to understand whether it is giving birth or what is it? Because even if it is injection… what is the biggest problem here?"*	Poor understanding of the PLTC or MNM event and their expected recovery trajectory contributed to women's ongoing mental and physical pain
		Woman 12	*They didn't explain the reason [for the operation] because myself I was awake but didn't understand much, could not even remember the pin number of my phone".*	Some women saw their loss of cognitive functioning during the event as the reason why health care workers did not sufficiently explain what was happening.
		Woman 9	*[So did the doctors explain the problem? What did they say the problem was?]* *"Because that time I came, I was semi-conscious, and was brought here directly. I was just hearing the doctor saying let's take her for scanning and she will be taken to the maternity ward. That time I was with my friend and we went to the ward so I didn't know if my friend was told."*	
		Woman 5	*[Now they just told you had a problem, but did they explain to you what the problem was?] "They just said during the time of delivery it's when I started convulsing"/* *[Ooh, did they tell you the cause of the convulsions?] "No".*	Health care worker explanation was often inadequate.
		Woman 12	*Some of these things you see can surprise you, is it discrimination or what?" [What made you feel you were being treated unfairly?] Now see, you see these husbands of ours. I can't even blame my husband's people being that I'm his wife. Even if there's no transport vehicles, is the distance to Mariakani too long? You can do whatever it takes to get there? He didn't come" & "He took like a whole month… He called but that couldn't tell the importance of a partner. If I was a man and my wife was pregnant, and my wife was going through a hard time and struggling then I wouldn't stay far away. He is a big*	The absence of her partner during pregnancy, the morbidity event and/or during the postpartum period contributed to impacted women emotionally and contributed to their poor understanding of the morbidity they experienced.

			problem. I gave birth at 10 and stayed unconscious til two in the afternoon. He didn't even worry about the wellbeing of his wife. It's not good, I felt bad about it".	
		Woman 2	*"They didn't explain. What they told me was that my temperature was high. Upon giving birth, they never explained what had transpired I was just discharged and I went home and haven't been called."*	Poor understanding about the event also affected women whose morbidity coincided with neonatal death or stillbirth, and their understanding of the cause of death. Health care workers did not sufficiently explain what occurred and why the baby died.
	1b. Of functioning	**Woman 6**	*"Just after delivery the problem became sleeping a lot. Sleeping a lot that I couldn't understand myself, even if someone talks to me I won't hear."*	Loss of functioning contributed to a feeling of disconnection from women's sense of self.
		Woman 20	*"I have tried to tell my husband but he has never undergone experiences women go through so when you tell him he thinks that you are exhausted by house chores and the stress of laying that is why you are tired, but he won't understand the pain you feel"*	Some women felt there was a lack of empathy and understanding from their partner about the severe morbidity she experienced and their loss of functioning in the postpartum period.
		Woman 15	*"The support that I wish for and I am now still wishing for was that of my partner that I have never had. I want even today what we call love [[F; mmhm]] I don't have that thing, so I feel so lonely though my brother helps me".* *"I don't know what happened because we used to love each other madly but it reached a time where he didn't call me, and he wasn't doing anything I needed. I would tell him I want to buy maybe medicine that doctor has prescribed medicine to boost blood, fruits or something, he said 'okay I will send you', but in one week I would not get the money or the medicine".*	Some women expressed sadness at the lack of support from her partner in the postpartum period.

		Woman 11	*“She [her mother-in-law] used to prepare hot water for me, bathe me, cook for me, bathe my baby. And she helped me to take the medicine I was given at the hospital”.*	Personal care was usually provided by either women’s mother or mother-in-law.
		Woman 8	***“****My husband used to help me in bathing myself, he used to carry water to the bathroom and help bathe me”*	Care from the husband with bathing was a rare exception.
		Woman 4	*"My sister helped with like cooking, washing clothes, and my husband let's say on the side of holding me he was supportive. There were no problems, he was very supportive,"*	Some women reported that their husbands provided adequate emotional support.
		Woman 10	*“My mother is deceased, my mother died that day I gave birth to this child and my mother in law lives far away from here, so it was me, my husband and my childen"*	In exceptional cases where personal care derived predominantly from the husband, women’s mother or mother-in-law were not alive or close by to provide support.
		Woman 3	*"There was a time where there was no happiness in the household, I don't know why. There was a time where they started competing for the chores, do it, do it. They did not want [to do the chores]"*	Women’s loss of functioning led to conflict within some households, with disputes about who would assume responsibility for chores.
		Woman 14	*"Eeeh he used to get angry, his work was just to get angry… It's that, not meeting up with other people outside."*	In some relationships, women’s loss of functioning also led to conflict. This woman’s husband was angry at her postpartum social isolation.
		Woman 18	*"They used to go walking and I couldn't. I was indoors 24/7 just in with the baby."*	Loss of physical functioning and an inability to participate in activities led to social isolation in the postpartum period.

	1c. Of autonomy	**Woman 8**	*"I went back home when I was seven months [postpartum]. So my husband told me to go to my mother in law's since he used to go to work."*	A reliance on women's mother-in-law for household support was sometimes against women's wishes
		Woman 16	*"Sometimes I think and say, "why did I even get pregnant". Back then did you treat me like this or it's now that I have become a mother you are treating me this way. So I think a lot and that is why this thought of going back to school comes to me. I got pregnant because I did not have any certificate, I am just a housewife, and that is why you are treating me this way. Wait until I go back to school. The day I have my certificate you will respect me."*	Disruption to women's education, and loss of autonomy to decide their own career path, affected adolescent mothers, with or without severe morbidity.
		Woman 16	*"Once I got pregnant, I had to stop [working]. I was used to getting money and that was my money. I used to decide what to do, now if you go there you sit to be given money, and then it is budgeted. Now there were things I could not accomplish, like I used to send my mum some money."*	Pregnancy and postpartum recovery initiated a loss of financial autonomy and greater reliance on her husband for financial needs.
Transition	**2a. In identity**	**Woman 19**	*"[After delivery, how did you feel when you saw the baby?] I was happy now being a mother (laughter)"*	Some nulliparous women expressed happiness at their transition to motherhood.
		Woman 14	*"You see at home where I have been married to when they heard I lost the first pregnancy they started to say, "that is not a wife she is just playing she is playing with your mind" so when I got this one even if it really hurt me but when I got it even them themselves told me "now come home we know now that you are a wife."*	Pregnancy initiated complex transitions in women's identity as a wife. Without producing a healthy live baby, community members perceived women to be unqualified as a wife.
	2b. In relationships	**Woman 4**	*"My husband was patient enough. It's me who said now is enough is enough, but he was okay. He was caring, he is not among the ones who says "oooh we have stayed [without sex] for long" cause I think we had finished a month and some weeks"*	Husbands who were patient and understanding of their wives' decision not to have sex after the PLTC or MNM event were rare. This woman's partner was an outlier in partner's responses to delayed sexual activity.
		Woman 16	*"For me after seven months, six months actually, I was not having sex again with him for experiencing pain and I was suffering a lot. I stayed like that until the baby was six or*	Some women delayed the resumption of sexual activity for many months in the

			seven months and then I resumed sex, and normally it would be painful… He told me when I visit a clinic I explain myself since it was not normal. Normally during sex one should not experinece pain. I have never enjoyed, I just hear people say having sex is pleasant. For me it is just painful."	postpartum due to chronic pain.
		Woman 14	*"Something that surprised me is pain, I did not know where the pain is coming from, another pain eee now that happiness wasn't happiness again… The first time he told me I am pretending. There is no enjoyment."*	One partner displayed coercive behaviour to try to resume sex with allegations his wife was pretending that sex was causing her pain.
		Woman 12	*"Eee I want to take a break… because I have passed through a lot… For about five years. [Why?] Let's say it's also healthy. For example, I gave birth with all problems. If after one year I got pregnant, I would have given birth again and at three years my baby would have had a younger sibling, and then the same cycle every year again, wouldn't it be harmful? That's the reason I decided to take a break".*	Motivated by a need to regain strength after the complication, many women expressed a desire to space or postpone future childbearing.
		Woman 8	*"My hope is even when I become pregnant again, I should never go through what I went through [before]".*	The PLTC or MNM event women experienced often affected women's attitudes towards a future pregnancy.
		Woman 10	*"Yes they [future fertility plans] have changed… Mmmhh I thought I would carry this and the other, mmmh but I said let me stop at that, that's enough"*	
		Woman 15	*"It's only just pain because even the one who told me I killed my child I decided to leave him I didn't keep it in my mind I left him to speak like a crazy person… My partner said I killed the baby."*	Two husbands blamed their wife for the perinatal death, contributing to a breakdown of the relationship.
Adaptation	**Postpartum care**	**Woman 10**	*"Aaaah there's no care [in the postpartum]. Mmmm because when you get discharged you are removed."*	For many women, hospital discharge was described as the point at which their medical care ended.
	3a. Physical	**Woman 7**	*"From six months onwards, I felt good. I could carry a ten litre jerrican of water. It was good progress."*	Women's ability to carry water again was a common barometer of having physically recovered from the severe maternal morbidity.
		Woman 18	*"I was good in two weeks, I could even carry water… 20 litres. I myself I could do everything [by two weeks], it was just that they didn't want me to… They were saying I*	

			hadn't fully recovered when for me I was feeling totally healed. They said if I do the chores then later on I'd have pain."	
		Woman 10	*"Mmmh after three months I was fine. Mmmm I used to carry water"*	
		Woman 1	*“My body was fine because after three months I was told to rest for three months, not to do hard work, not to lift heavy things, when I obeyed the conditions, my scar healed.”*	Women’s recovery in their ability to carry water and other heavy objects was associated with delivery caesarean section, though some women with vaginal births also expressed recovery in these terms.
	3b. Psychological	**Woman 13**	*"You see that difficult situation in the six months, at the start when that situation was reducing, I continued to feel happiness in my body."*	Progress with physical recovery in the postpartum period contributed to women’s emotional wellbeing.
		Woman 18	*"I had gone through all the challenges and now my baby is healthy, it was good, and I felt excited”.*	The health of her baby brought women happiness in the postpartum period.
		Woman 13	*"I got my child in full health, but I am going through a trying time from a problem I don't understand."*	For women whose baby survived, concern for the child’s health often outweighed concerns about their own recovery.
		Woman 14	*“The one who did for me scanning told me "if the child has reached eight months and hasn't turned it might die in the stomach at the time of giving birth" so it was time to give birth and I said maybe it has died, but the moment I saw him and the moment I reached home I felt happiness because the devil was ashamed what they were talking about is different and they changed their words"*	Women’s emotional recovery was mediated by the health of her child. For this participant, the survival of her child against the warnings of health care workers that she might lose the pregnancy brought happiness.
		Woman 10	*"It has affected because when I go to church and witness other babies walking, those who we gave birth with I see their children walking and others sitting and others are*	Poor health of her child affected women’s emotional recovery from the complication.

			standing, then I look at my child and ask God what I did wrong?"	
		Woman 1	*"I cried for my son for a whole year."*	Bereavement caused ongoing pain.
	3c. Economic	**Woman 12**	*"I was able to buy medicine because my partner was looking out for money. He would send me, "buy half the dose and finish the rest the next day". That was the situation. We could not afford full doses, I would buy doses for two or three days, until I got well".*	At times, treatment for chronic conditions following the pregnancy complication in the extended postpartum period was unaffordable, and women were forced to delay or limit their treatment.
		Woman 17	*My life has changed because initially I could step out and go and do any kind of job or say let me today go to work because someone has called me saying "come there is something" and I do. But now it's like my life has become a litter harder, because now who will hire you and the baby? No one. You just do a little bit of laundry, I clean dishes, I do some cleaning, and be given the little I will be given, that's all."*	Among many women who experienced morbidity, women highlighted the effect of (single) motherhood and exit from the labour market on her economic recovery, more than the complication *per se.*

D6. Reflexivity statement

Table D6 includes the reflexivity statement required by BMJ Global Health.

Table D6 Reflexivity statement

Area	Question	Answer
Study conceptualisation	How does this study address local research and policy priorities?	No existing research has studied women's recovery after severe morbidity in Kilifi, Kenya. As local context is so important to women's experience of morbidity and recovery, this research was designed to address a critical evidence gap: the complex needs of women recovering from severe maternal morbidity in Kilifi County, so that services can be planned. Postnatal care was raised at the Kilifi County Scientific Symposium, where our work (presented by MCO) won the award for the best poster presentation. This recognition from policy makers and healthcare workers working in Kilifi County is an indication of the importance of this topic locally.
	How were local researchers involved in study design?	The initial idea for the study was suggested by the lead author (UG) who is doing a PhD at LSHTM in the form of a concept note and discussed with leads in Kenya who suggested changes to the sampling strategy, participant recruitment, and interview tool (AK, MT). An introductory session before data collection began was held with all Kenyan team members to refine the study design. This provided an opportunity for members of the research team to suggest further changes to the study design. Substantive changes were made to the interview tool and participant recruitment plans.
Research management	How has funding been used to support the local research team(s)?	This qualitative study was supported by the UKRI Economic and Social Research Council as the funders of UG's PhD studentship (ES/P000592/1), as well as a doctoral travelling scholarship awarded to UG from LSHTM. This funding was used to support the local research team with regards to recruitment, reimbursement for time and travel, training (including qualitative analysis group training), and costs of consultants (transcription and translation). The PRECISE Network was funded by UKRI GCRF Award (MR/P027938/1) and a NIHR–Wellcome Partnership for Global Health Research Collaborative Award (217123/Z/19/Z). This has provided the salaries for all Kenyan named co-authors. The UKRI award is a capacity-building grant designed to develop scientific research capacity in Africa.
	How are research staff who conducted data	All research staff who conducted the qualitative data collection are co-authors of this paper (MCO,

Area	Question	Answer
Data acquisition and analysis	collection acknowledged?	NB, AMK, MB, and GMa). Kenyan research staff who were involved in the logistics of sample recruitment and data collection organisation are also co-authors (OW, AK, GMw). Other members of the PRECISE Network who conducted the PRECISE data collection, which was used as a sampling frame to identify women with severe morbidity for this qualitative study, are also authors in the PRECISE Network. (The full author list is available in Table S1.)
	How have members of the research partnership been provided with access to study data?	All the study data is held at Aga Khan University, Kenya, with copies shared to LSHTM. Three members of the research team who conducted the analysis (UG, OW and MCO) had access to the full transcripts. All Kenyan members of the research team were involved in a full-day qualitative analysis workshop, where one transcript analysed together.
	How were data used to develop analytical skills within the partnership?	This study contributed to the analytical capacity-building within the partnership. The Kenyan research team had a qualitative method training session led by the first author (UG). This training session was designed to build team members' experience with the qualitative data after it has been collected – including transcription processes, data coding, analysis, interpretation, and results write-up. Further training on qualitative data interpretation and results write-up was provided during virtual hands-on sessions by UG to two Kenyan early career researchers (MCO, OW). UG also provided mentorship on proposal writing and conference submission to MCO.
Data interpretation	How have research partners collaborated in interpreting study data?	All named co-authors provided critical interpretation of the results upon review of the manuscript. Interpretation discussions were held between the three authors involved in data analysis (UG, MCO, OW) and with UG's supervisory team (VF, LAM, PvD). Where differences in interpretation emerged, the interpretation of Kenyan members of the research team was prioritised, given their greater contextual exposure and understanding.
Drafting and revising for intellectual content	How were research partners supported to develop writing skills?	UG (an early career researcher) drafted the manuscript. The manuscript was revised critically for intellectual content by Kenyan early career researchers. For some members of the research team, editing this article was one of their first exposures to scientific journal article writing. The research findings were also presented by a Kenyan early career researcher (MCO) at the Kilifi County 2nd Scientific Symposium poster session,

Area	Question	Answer
		which helped to develop her science communication skills to summarise the research findings for a poster presentation.
	How will research products be shared to address local needs?	Our findings highlighted areas for improvement in postpartum physical and mental health care in Kilifi County. These results will be included in future PRECISE Network dissemination which includes healthcare workers and local community members. In addition, these policy recommendations were presented at the Kilifi County 2nd Scientific Symposium. This was a county-level meeting: most of the guests were healthcare workers, healthcare managers, policy makers from Kilifi County Department of Health, and several NGOs and research institutions working in Kilifi County.
Authorship	How is the leadership, contribution, and ownership of this work by LMIC researchers recognised within the authorship?	9 of the 14 co-authors in the research team are affiliated with the Aga Khan University in Kenya (MCO, OW, AK, GMw, NB, MK, AMK, GMa, MT). Eight of these authors are Kenyan nationals. Three Kenyan early career researchers, who are second, third and fourth authors on the paper, respectively (MO, OW, AK), played substantial roles in the logistics, participant recruitment, data collection, analysis, interpretation and manuscript revision.
	How have early career researchers across the partnership been included within the authorship team?	Nine co-authors in the research team, including the first author, are ECRs (UG, MCO, OW, GMw, NB, MK, AMK, GMa, and AK).
	How has gender balance been addressed within the authorship?	10 of the 14 co-authors in the research team are female, including the first (UG) and senior author (VF).
Training	How has the project contributed to training of LMIC researchers?	This project has contributed to the qualitative methods training, scientific journal writing skills, and conference presentation skills of Kenyan researchers (see above).
Infrastructure	How has the project contributed to improvements in local infrastructure?	Some of the funds from this qualitative project will contribute to minor repairs of the PRECISE study offices. Further, the PRECISE Network, within which this sub-study is embedded, has contributed to substantial improvements in local infrastructure. New study office buildings were commissioned, and new laboratory equipment was purchased. More detail about the PRECISE Network can be found here.
Governance	What safeguarding procedures were used to protect local study participants and researchers?	The research team used distress protocols to identify participants who experienced negative emotional responses to participation in the study. Participants who raised concerns over their mental or physical health during the interview were provided with referral information for follow-up care. We have formally engaged a psychologist to assist in providing mental health support to both

Area	Question	Answer
		participants and staff. Participants of this study (especially those who lost a child) have received individual and/or group counselling. This is ongoing. To safeguard the wellbeing of the research team, we held daily debriefs to offload after potentially triggering interviews. We also had two debrief sessions during data collection with a trained psychologist to offload and process after emotionally difficult interviews.

Appendix E Supplementary material for Chapter 6

Lifetime risk of maternal near miss morbidity: A novel indicator of maternal health

E1. Calculation of the lifetime risk of maternal near miss for potential age distributions of the maternal near miss ratio

As shown in Table E1, calculation of the lifetime risk of maternal near miss (LTR-MNM) with age-disaggregated data depends on the age pattern of the maternal near miss ratio (MNMRatio). The LTR-MNM varies from 0.0252 (1 in 40) to 0.0282 (1 in 35). When we assume the MNMRatio is constant across the reproductive ages 15-49, the LTR-MNM is 0.0262 (1 in 38); this estimate falls within the range of the age-disaggregated estimates. Hence, the LTR-MNM using an estimate of the MNMRatio for all ages combined is a reasonable approximation when age-disaggregated data are not available.

Decreasing, Constant, and N-shaped are unlikely based on what we know about the age pattern of maternal mortality. Maternal near miss are expected to be so close to death that we would expect the age pattern to behave similarly.

Table E1: The lifetime risk of maternal near miss, Namibia 2019 calculation for each simulated maternal near miss age distribution

	Age group	MNM Cases	Livebirths	MNMRatio	fx	Lx	survivor	LTR-MNM
J-shape	15-19	68	7,939	8.57	0.07	474,932	4.98	0.0029
	20-24	82	18,050	4.57	0.15	470,667	4.94	0.0035
	25-29	107	18,241	5.86	0.16	464,275	4.87	0.0045
	30-34	143	12,772	11.19	0.14	455,467	4.78	0.0075
	35-39	91	7,492	12.19	0.10	443,928	4.66	0.0059
	40-44	44	2,895	15.06	0.05	429,401	4.51	0.0031
	45-49	11	612	17.57	0.01	411,688	4.32	0.0008
Total	—	546	68,001	—	—	—	—	0.0282
Increasing	15-19	34	7,939	4.25	0.07	474,932	4.98	0.0014
	20-24	98	18,050	5.45	0.15	470,667	4.94	0.0042
	25-29	145	18,241	7.97	0.16	464,275	4.87	0.0061
	30-34	133	12,772	10.41	0.14	455,467	4.78	0.0070
	35-39	85	7,492	11.34	0.10	443,928	4.66	0.0055
	40-44	41	2,895	14.01	0.05	429,401	4.51	0.0029
	45-49	10	612	16.35	0.01	411,688	4.32	0.0008
Total	—	546	68,001	—	—	—	—	0.0278
Decreasing	15-19	89	7,939	11.15	0.07	474,932	4.98	0.0037
	20-24	172	18,050	9.56	0.15	470,667	4.94	0.0073
	25-29	141	18,241	7.73	0.16	464,275	4.87	0.0059
	30-34	91	12,772	7.10	0.14	455,467	4.78	0.0048
	35-39	41	7,492	5.44	0.10	443,928	4.66	0.0026
	40-44	11	2,895	3.72	0.05	429,401	4.51	0.0008
	45-49	2	612	2.90	0.01	411,688	4.32	0.0001
Total	—	546	68,001	—	—	—	—	0.0252
Constant	15-19	64	7,939	8.03	0.07	474,932	4.98	0.0027
	20-24	145	18,050	8.03	0.15	470,667	4.94	0.0061
	25-29	146	18,241	8.03	0.16	464,275	4.87	0.0061
	30-34	103	12,772	8.03	0.14	455,467	4.78	0.0054
	35-39	60	7,492	8.03	0.10	443,928	4.66	0.0039
	40-44	23	2,895	8.03	0.05	429,401	4.51	0.0017
	45-49	5	612	8.03	0.01	411,688	4.32	0.0004
Total	—	546	68,001	—	—	—	—	0.0262
N-shape	15-19	27	7,939	3.37	0.07	474,932	4.98	0.0011
	20-24	78	18,050	4.33	0.15	470,667	4.94	0.0033
	25-29	164	18,241	9.00	0.16	464,275	4.87	0.0068
	30-34	166	12,772	12.98	0.14	455,467	4.78	0.0087
	35-39	83	7,492	11.13	0.10	443,928	4.66	0.0054
	40-44	24	2,895	8.26	0.05	429,401	4.51	0.0017
	45-49	4	612	6.33	0.01	411,688	4.32	0.0003
Total	—	546	68,001	—	—	—	—	0.0274
U-shape	15-19	109	7,939	13.78	0.07	474,932	4.98	0.0046
	20-24	185	18,050	10.23	0.15	470,667	4.94	0.0078
	25-29	98	18,241	5.36	0.16	464,275	4.87	0.0041
	30-34	53	12,772	4.18	0.14	455,467	4.78	0.0028
	35-39	59	7,492	7.84	0.10	443,928	4.66	0.0038
	40-44	32	2,895	11.15	0.05	429,401	4.51	0.0023
	45-49	10	612	16.07	0.01	411,688	4.32	0.0008
Total	—	546	68,001	—	—	—	—	0.0261

Columns from left to right: Age group denotes five year age group from 15 to 49 years; MNM cases denotes simulated distribution of maternal near miss cases across the five year age group; livebirths denotes the number of live births in five year age group from World Population Prospects (adjusted by stillbirth rate of 17.68 per 1000); MNMRatio denotes the corresponding maternal near miss ratio for simulated distribution of maternal near miss cases; fx denotes fertility rates by five year age group; Lx are the person-years lived in five year age group; survivor denotes the person years divided by number of survivors at age 15 ($\boldsymbol{l_{15}}$ = 95283); LTR-MNM is the lifetime risk of maternal near miss for a given age distribution of near miss cases, for a fixed prevalence of maternal near miss morbidity (8.03 per 1000 live births).

E2. Bias in the maternal near miss ratio and maternal near miss rate

Where available, the MNMRatio used to estimate the LTR-MNM should be both nationally representative and population-based. As women with a maternal near miss would likely have died without receiving care at the facility, a facility-based estimate of MNM cases should closely approximate the true number of cases in a community. Facility-based estimates of the numerator of the MNMRatio are therefore likely to be representative of MNM in the population. However, the facility-based estimates of the number of live births may be an underestimate of the true number of live births in the community, especially when the prevalence of institutional delivery is low and there are significant numbers of home births. If the denominator is an underestimate, this would result in an upwardly biased estimate of the MNMRatio.

If the MNMRatio is biased, this also results in a biased maternal near miss rate (MNMRate). The following Equations 1-7 show how an unbiased estimate of the MNMRate can be derived from the biased estimate and the number of births occurring within (vs. outside) a facility. This adjusted MNMRate (and hence MNMRatio) can then be used in calculations of the LTR-MNM.

Starting with the relation between the MNMRate and the MNMRatio:

$$(1) \qquad MNMRate_{biased} = MNMRatio_{biased} \cdot {}_nf_x$$

This becomes:

$$(2) \qquad MNMRate_{biased} = \frac{All\ MNM}{Births\ in\ facility} \cdot \frac{All\ births}{All\ exposures}$$

Rearranging the terms gives:

$$(3) \qquad MNMRate_{biased} = \frac{All\ MNM}{All\ exposures} \cdot \frac{All\ births}{Births\ in\ facility}$$

Hence, an unbiased estimate of the MNMRate can be derived as follows:

$$(4) \qquad \frac{All\ MNM}{All\ exposures} = MNMRate_{biased} \cdot \frac{Births\ in\ facility}{All\ births}$$

$$(5) \qquad MNMRate_{true} = MNMRate_{biased} \cdot institutional\ delivery\ rate$$

where the institutional delivery rate is the number births in facilities divided by the total number of births. This accounts for the births occurring at home.

This adjustment is more accurate when facility-based estimates encompass all levels of care (primary, secondary, and tertiary). If estimates of live births derive from tertiary facilities only (e.g., referral or teaching hospitals), then adjusting by the institutional delivery rate will still yield an underestimate of the number of births, since women can give birth in many other types of facility. Therefore, caution is advised when interpreting the LTR-MNM in cases where institutional delivery is low and live birth estimates derive solely from tertiary facilities.

E3. International Journal of Epidemiology Blog

Why we need a new measure of maternal health: the "lifetime risk of maternal near miss"

Ursula Gazeley

According to the most recent data from the World Health Organization, the lifetime risk of maternal death for a girl in Chad is a staggering 1 in 15, compared with 1 in 43,000 in Norway. This means that a girl in Chad has an almost 3000 times greater risk of dying from a maternal cause during her reproductive lifetime than a girl in Norway. The lifetime risk of maternal death is a useful measure to help us understand this global inequality in maternal mortality.

Maternal death is a tragic outcome of pregnancy. Although it is now rare in most parts of the world, progress is slowing. Additionally, many more women experience severe pregnancy complications that bring them dangerously close to death — so close that they are very likely to need emergency hospital care to save their lives. Such events are known as "maternal near misses" and are identified based on organ dysfunction (e.g. cardiovascular, respiratory, renal, haematological, hepatic or neurological) or complication-specific criteria, such as eclampsia, septicaemia or the need for hysterectomy or blood transfusion following obstetric haemorrhage.

Maternal near miss is an important maternal health outcome that reflects a health care system's ability to provide emergency obstetric care and save a woman's life when complications arise. Moreover, experiencing such severe complications can have long-term consequences for a woman's physical, psychological, sexual, social and economic wellbeing.

There have been many calls to improve metrics on maternal morbidity, but relatively little progress in achieving this. In our recent study, published in the *IJE*, we introduce a new measure called the "lifetime risk of maternal near miss" to estimate the burden of maternal near miss morbidity across women's reproductive lifetimes. This measure is analogous to the lifetime risk of maternal death, applied to life-threatening morbidity.

Existing indicators of maternal near miss prevalence — both the maternal near miss ratio and maternal near miss rate — only account for the level of obstetric risk associated with a given pregnancy. Neither measure accounts for the risks associated with fertility levels (women are at risk of experiencing a near miss during each pregnancy they have), nor women's chances of surviving the reproductive ages of 15–49 years (to experience a near miss, a woman must not have died from a maternal cause or anything else). The lifetime risk of maternal near miss addresses these deficits and captures the dynamics associated with obstetric risk, fertility levels and women's reproductive age survival.

In our study, we demonstrated use of this measure in Namibia. Our estimates indicate that a 15-year-old girl in Namibia faces a 1 in 38 lifetime risk of experiencing a maternal near miss, compared with a 1 in 142 lifetime risk of maternal death. When these risks are combined, the girl has a 1 in 30 chance of either dying from a maternal cause or experiencing a near-miss complication during her reproductive years.

This combined lifetime risk of maternal death or near miss is an important tool for advocacy — to highlight the impact of maternal health on women's lives and the need for the global community to redouble its efforts to end preventable maternal mortality and morbidity. Estimation is needed across high- and low-income settings to draw attention to global inequities in adverse pregnancy outcomes.

To measure a country's lifetime risk of maternal near miss, the ideal scenario is to use nationally representative data on the maternal near miss ratio (the number of maternal near misses per 1000 live births). The number of maternal near misses can only come from health care facilities. In countries where many women give birth at home, the number of live births should come from population-based estimates, so that births at home are also counted.

Across all world regions, births in health care facilities are lowest in sub-Saharan Africa. We will therefore overestimate the lifetime risk of maternal near miss if we rely on (unadjusted) facility-based estimates of births in these settings. In our study, we chose to apply this indicator to Namibia because, although it is a high-burden setting, high-quality national population-based maternal near miss surveillance data were available.

To start measuring the lifetime risk of maternal near miss globally, more countries need to routinely measure and report how many maternal near misses occur at the national level, as they do for maternal deaths. Several high-income countries already report this regularly (e.g. the Scottish Confidential Audit of Severe Maternal Morbidity and the Irish National Audit of Severe Maternal Morbidity). Aside from the maternal near miss ratio, all other data required to estimate the lifetime risk of maternal near miss are available via open access from World Population Prospects.

Read more:

Gazeley U, Polizzi A, Romero-Prieto JE, et al. Lifetime risk of maternal near miss morbidity: a novel indicator of maternal health. *Int J Epidemiol* 2023; 18 December. doi: 10.1093/ije/dyad169

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Appendix F Supplementary material for Chapter 7

The Lifetime Risk of Maternal Near Miss morbidity in Asia, Africa, the Middle East, and Latin America: a cross-country systematic analysis

F1. Search strategy

Table F1 includes the search terms used to identify eligible records in Embase, Global Health, and MEDLINE reporting multi-facility, regional, or national-level estimates of the prevalence of maternal near miss. This search was supplemented by also searching the included records of several recent meta-analyses on the prevalence of maternal near miss.

Table F1 Search terms for eligible maternal near miss prevalence studies

Item number	Search term	Records retrieved
Search date: 15th July 2024		
1	(prevalence or incidence or ratio or burden or surveillance).ti,ab.	9113064
2	("population-based" or "region" or "regional" or "national").ti,ab.	5572209
3	("maternal near miss maternal near-miss" or "severe acute maternal morbidity" or "SAMM" or "severe maternal morbidity" or "life-threatening complication" or "life-threatening maternal morbidity" or "life-threatening condition" or "life threatening complication" or "life threatening maternal morbidity" or "life threatening condition").ti,ab.	43526
4	1 and 2 and 3	1426
5	limit 4 to yr="2010 -Current"	1312
6	Limit 5 to English language	1285
7	Remove duplicates from 6	787 Embase: 729 Global Health: 28 MEDLINE: 30

F2. Maternal near miss prevalence studies included in analysis

Table F2 includes all studies included in to estimate a single population-level maternal near miss ratio (MNM ratio) per country with available multi-facility, regional, or national-level data. Studies were included only if (i) they used the World Health Organization (WHO) organ dysfunction criteria, or a modified version of the WHO criteria for low-income contexts; (ii) the reference period was from 2010 onwards. Where studies estimated the prevalence according to multiple WHO/modified organ dysfunction criteria, each estimate is included as a separate row of the meta-analyses.

Where more than one study was available for a given country, a random effects meta-analysis was used to estimate a pooled (adjusted) MNM ratio, see Tables F5 and F6 for more detail.

Table F2 Maternal near miss prevalence studies included in analysis

Country	Reference	Study period	Study design	Location detail	MNM criteria	MNM cases	Denominator	Denominator type	MNM ratio[1]
Central and Southern Asia									
Afghanistan	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	421	25,227	livebirths	16.7
India	Bakshi et al. (2016)[2]	2015	Regional	2 primary, 1 community, and 1 tertiary facility	WHO	51	688	livebirths	74.1
India	Goldenberg et al. (2017)[3]	2014-2016	Regional	Surveillance area Belagavi - 18 primary health centers, 3 tertiary hospitals and 8 secondary hospitals Belagavi	Global Network	615	21,548	livebirths	28.5
India	Goldenberg et al. (2017)[3]	2014-2016	Regional	Surveillance area Nagpur - 20 primary health centers, 10 tertiary hospitals and 129 secondary hospitals, Nagpur	Global Network	79	17,541	livebirths	4.5
India	Kulkarni et al. (2016)[4]	2012-2014	Regional	2 tertiary centres	Modified WHO - include severe anaemia	525	14,508	livebirths	36.2
India	Mansuri et al. (2019)[5]	2015-2016	Regional	Four hospitals Ahmedabad	WHO	247	21,491	livebirths	11.5
India	Roopa et al. (2013)[6]	2011-2012	Regional	1 tertiary and 6 PHC	WHO	131	7,330	livebirths	17.9
India	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	174	30,094	livebirths	5.8
Iran	Ghazivakili et al. (2016)[7]	2012	Regional	All 13 public and private hospitals Alborz	WHO	192	38,663	livebirths	5.0
Iran	Hashemi et al. (2020)[8]	2016	Regional	Five hospitals in Ahvaz	WHO	81	3,002	livebirths	26.9
Iran	Mohammadi et al. (2016)[9]	2012-2014	Regional	1 secondary and 2 tertiary facilitiies	Modified WHO (transfusion of ≥4 units of blood and platelet count to ≤75 000 platelets/mL)	82	12,965	livebirths	6.3
Iran	Naderi et al. (2015)[10]	2013	Regional	Eight hospitals in Southeast Iran	WHO	501	19,908	livebirths	25.2
Nepal	Rana et al. (2013)[11]	2012	Regional	9 facilities Kathmandu valley	WHO	157	41,676	livebirths	3.8

Country	Reference	Study period	Study design	Location detail	MNM criteria	MNM cases	Denominator	Denominator type	MNM ratio[1]
Nepal	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	65	10,999	livebirths	5.9
Pakistan	Goldenberg et al. (2017)[3]	2014-2016	Regional	Surveillance area - 47 primary health clinics, 25 secondary care facilities and 3 referral hospitals, Thatta district	Global Network	1,830	21,604	livebirths	84.7
Pakistan	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	94	12,729	livebirths	7.4
Sri Lanka	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	73	17,988	livebirths	4.1
Eastern and South-Eastern Asia									
Cambodia	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	59	4,635	livebirths	12.7
China	Ng et al. (2023)[12]	2019	Regional	Three tertiary centres in Hong Kong	WHO	61	11,075	livebirths	5.5
China	Ma et al. (2020)[13]	2012-2017	Regional	18 hospitals in Zhejiang province	WHO	3,208	543,109	livebirths	5.9
China	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	34	13,242	livebirths	2.6
China	Xiong et al. (2020)[14]	2012-2018	Regional	17 hospitals in Hunan province	WHO	1,751	511,793	livebirths	3.4
China	Yi Mu et al. (2019)[15]	2012-2017	National	National hospital surveillance	WHO	37,060	9,051,638	pregnant women	4.1
China	Zhou et al. (2024)[16]	2012-2022	Regional	National hospital surveillance, Hunan province	WHO	2461	731185	livebirths	3.4
Japan	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	21	3,527	livebirths	6.0
Laos	Luexay et al. (2014)[17]	2010	Regional	11 districts in Sayaboury province	Global Network	11	1,122	livebirths	9.8
Malaysia	Norhayati et al. (2016)[18]	2014	Regional	2 facilities in Kelantan	WHO	47	21,579	livebirths	2.2
Mongolia	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	61	7,303	livebirths	8.3
Philippines	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	29	10,609	livebirths	2.7
Thailand	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	51	8,894	livebirths	5.7
Vietnam	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	33	15,411	livebirths	2.1

Country	Reference	Study period	Study design	Location detail	MNM criteria	MNM cases	Denominator	Denominator type	MNM ratio[1]
Latin America and the Caribbean									
Argentina	De Mucio et al. (2016)[19]	2013-2014	Regional	3 hospitals with >3000 deliveries a year	WHO	2	762	livebirths	2.6
Argentina	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	51	9,729	livebirths	5.2
Brazil	Dias et al. (2014)[20]	2011-2012	National	Birth in Brazil study	WHO	23,737	2,325,394 (weighted)	livebirths	10.2
Brazil	Menezes et al. (2015)[21]	2011-2012	Regional	2 hospitals in Aracaju	WHO	77	16,243	livebirths	4.7
Brazil	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	17	7,019	livebirths	2.4
Ecuador	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	30	10,108	livebirths	3.0
Guatemala	Goldenberg et al. (2017)[3]	2014-2016	Regional	Surveillance area - 1 referral hospital, 30 health centers, and 42 health posts, Chimaltenango region	Global Network	1,221	19,712	livebirths	61.9
Honduras	De Mucio et al. (2016)[19]	2013	Regional	2 hospitals with >3000 annual deliveries	WHO	10	613	livebirths	16.3
Mexico	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	153	13,167	livebirths	11.6
Nicaragua	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	119	6,426	livebirths	18.5
Paraguay	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	8	3,595	livebirths	2.2
Peru	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	169	15,021	livebirths	11.2
Suriname	Verschueren et al. (2020)[22]	2017-2018	National	Country-wide surveillance	WHO	71	9,114	livebirths	7.8
Suriname	Verschueren et al. (2020)[22]	2017-2018	National	Country-wide surveillance	Namibian criteria	118	9,114	livebirths	12.9
Suriname	Verschueren et al. (2020)[22]	2017-2018	National	Country-wide surveillance	SSA criteria	242	9,114	livebirths	26.6
Northern Africa and Western Asia									
Iraq	Jabir et al. (2013)[23]	2010	Regional	6 hospitals in Baghdad	WHO	129	25,472	livebirths	5.0
Lebanon	Souza et al. (2013)[1]	2010-11	National	WHO Multicountry survey	WHO	18	4,008	livebirths	4.5
Sub-Saharan Africa									

Country	Reference	Study period	Study design	Location detail	MNM criteria	MNM cases	Denominator	Denominator type	MNM ratio[1]
Angola	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	57	9,966	livebirths	5.7
Democratic Republic of Congo	Goldenberg et al. (2017) [3]	2014-2016	Regional	Surveillance area	Global Network	521	13,637	livebirths	38.2
Democratic Republic of Congo	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	88	8,395	livebirths	10.5
Ethiopia	Beyene et al. (2022)[24]	2018	Regional	Three hospitals in southern Ethiopia	WHO	90	2,880	livebirths	31.2
Ethiopia	Gebremariam et al. (2022)[25]	2012-2017	Regional	Three hospitals in North Shewa Zone, Central Ethiopia	WHO	36	905	deliveries	40.0
Ethiopia	Kamangira et al. (2024)[26]	2024	Regional	Four public hospitals in Borena zone	WHO	55	1421	livebirths	38.7
Ethiopia	Kusheta et al. (2023)[27]	2019	Regional	All public hospitals in Hadiya zone, southern Ethiopia	sub-Saharan Africa criteria	70	2,724	livebirths	25.7
Ethiopia	Tenaw et al. (2021)[28]	2019-2020	Regional	Two major private hospitals in Harar and Dire Dawa	sub-Saharan Africa criteria	108	1,173	livebirths	92.1
Ethiopia	Tura et al. (2018)[29]	2016-2017	Regional	Two hospitals in Eastern Ethiopia	sub-Saharan Africa criteria	594	7,404	livebirths	80.2
Ethiopia	Tura et al. (2018)[29]	2016-2017	Regional	Two hospitals in Eastern Ethiopia	WHO	128	7,404	livebirths	17.3
Ethiopia	Wakgar et al. (2019)[30]	2014-2016	Regional	Hawassa University and Yirgalem hospital	WHO	501	15,059	admissions	33.3
Ethiopia	Worke et al. (2019)[31]	2018	Regional	Three out of five referral hospitals in Amhara chosen randomly	Modified WHO	152	572	deliveries	265.7
Ethiopia	Yemane et al. (2020)[32]	2017	Regional	Three randomly selected public hospitals in south western Ethiopia	WHO	210	5,530	livebirths	38.0
Ghana	Oppong et al. (2019)[33]	2015	Regional	Three tertiary hospitals in Southern Ghana	Modified WHO	288	8,433	livebirths	34.1
Kenya	Goldenberg et al. (2017) [3]	2014-2016	Regional	Surveillance area	Global Network	433	13,724	livebirths	31.6
Kenya	Owolabi et al. (2020)[34]	2018	National	Nationally representative cross-sectional survey of 54 facilities.	WHO	5,116	708,459 (weighted)	livebirths	7.2
Kenya	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	77	19,658	livebirths	3.9

Country	Reference	Study period	Study design	Location detail	MNM criteria	MNM cases	Denominator	Denominator type	MNM ratio[1]
Namibia	Heemelaar et al. (2019)[35]	2018	Regional	Four representative hospitals	WHO	61	5,772	livebirths	10.6
Namibia	Heemelaar et al. (2019) [35]	2018	Regional	Four representative hospitals	Modified WHO	184	5,772	livebirths	31.9
Namibia	Heemelaar et al. (2020)[36]	2018-2019	National	Country-wide surveillance	Modified WHO	298	37,106	livebirths	8.0
Niger	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	196	10,714	livebirths	18.3
Nigeria	Oladapo et al. (2016)[37]	2012-2013	National	Nigeria Maternal Near Miss and Death Survey of 42 tertiary facilities	WHO	1,451	91,724	livebirths	15.8
Nigeria	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	298	11,775	livebirths	25.3
Nigeria	Tukur et al. (2022)[38]	2019-2020	National	Nationwide network of Nigerian referral hospitals	WHO but unclear	5,678	69,055	livebirths	82.2
South Africa	Heitkamp et al. (2022)[39]	2014-2015	Regional	Metro east cape town	WHO	268	31,163	livebirths	8.6
South Africa	Iwuh et al et al. (2018)[40]	2014	Regional	Metro west cape town	WHO	112	19,222	livebirths	5.8
South Africa	Soma-pillay et al. (2017)[41]	2013-2014	Regional	Tshwane SA	WHO	117	26,614	deliveries	4.4
Tanzania	Litorp et al. (2014)[42]	2012	Regional	Two hospitals, dar es Salaam	WHO	467	13,121	livebirths	35.6
Uganda	Nakimuli et al. (2016)[43]	2013-2014	Regional	Two referral hospitals	WHO	695	25,840	livebirths	26.9
Uganda	Souza et al. (2013) [1]	2010-11	National	WHO Multicountry survey	WHO	120	10,467	livebirths	11.5
Zambia	Goldenberg et al. (2017) [3]	2014-2016	Regional	Surveillance area	Global Network	167	12,827	livebirths	13.0
Zimbabwe	Chikadaya et al. (2018)	2016	Regional	Two referral hospitals for all of Harare	WHO	110	11,871	livebirths	9.3

[1]Maternal near miss cases per 1000 live births implied by reported cases and denominator. This estimate is not used in our calculations unless it is a population-level estimate. Rather, for facility-based data, we use the adjusted denominator that accounts for births occurring outside of facilities in our estimates of a population-level adjusted MNM ratio.

F3. National and sub-national data

To derive estimates of the LTR-MNM by country, we required data on the MNM ratio. Since our objective was to derive population-level estimates, and as the fertility and mortality data used to calculate the LTR-MNM are at the national level, we included only multi-facility/regional ("subnational" for shorthand), or more nationally representative ("national") data on the MNM ratio, excluding prevalence estimates derived from a single facility only.

There is not always a sharp dichotomy between "national" and "subnational" studies. We have used this shorthand to group data types, but in reality, there is more of a continuum between data that are more nationally-representative and less nationally representative. For example, only two studies were national surveillance study and included all facilities in the country (Namibia, Heemelaar et al, 2020; Suriname, Verschueren et al, 2020). Other national data derived from samples that aimed towards national representation (e.g. Nigeria Near Miss and Death survey, Oladapo 2016, WHO Multicountry Survey, Souza 2013), with multi-stage random sampling to select facilities across multiple regions/provinces. How truly nationally representative these data are varies and this is influenced by other study characteristics, e.g., whether they only selected tertiary hospitals above a certain annual delivery volume which means the selected facilities do not represent all types of facilities in the country (e.g. WHO Multicountry Survey).

The available data varies across countries as shown in Figure F1. For each country included in the analysis, Table F3 below shows the number of eligible studies, and whether only national data, only subnational data, or a combination of both data types were available. For countries with only sub-national data available, this highlights the current paucity of nationally representative MNM data and the need for increased sub-national aggregation and national-level surveillance.

For 10 countries where a combination of both national and subnational data were available, the national data had the largest sample in six countries, while subnational data had the largest sample in four countries (the Democratic Republic of Congo, Nepal, Pakistan, and Uganda).

Figure F2 Distribution of MNM data by type

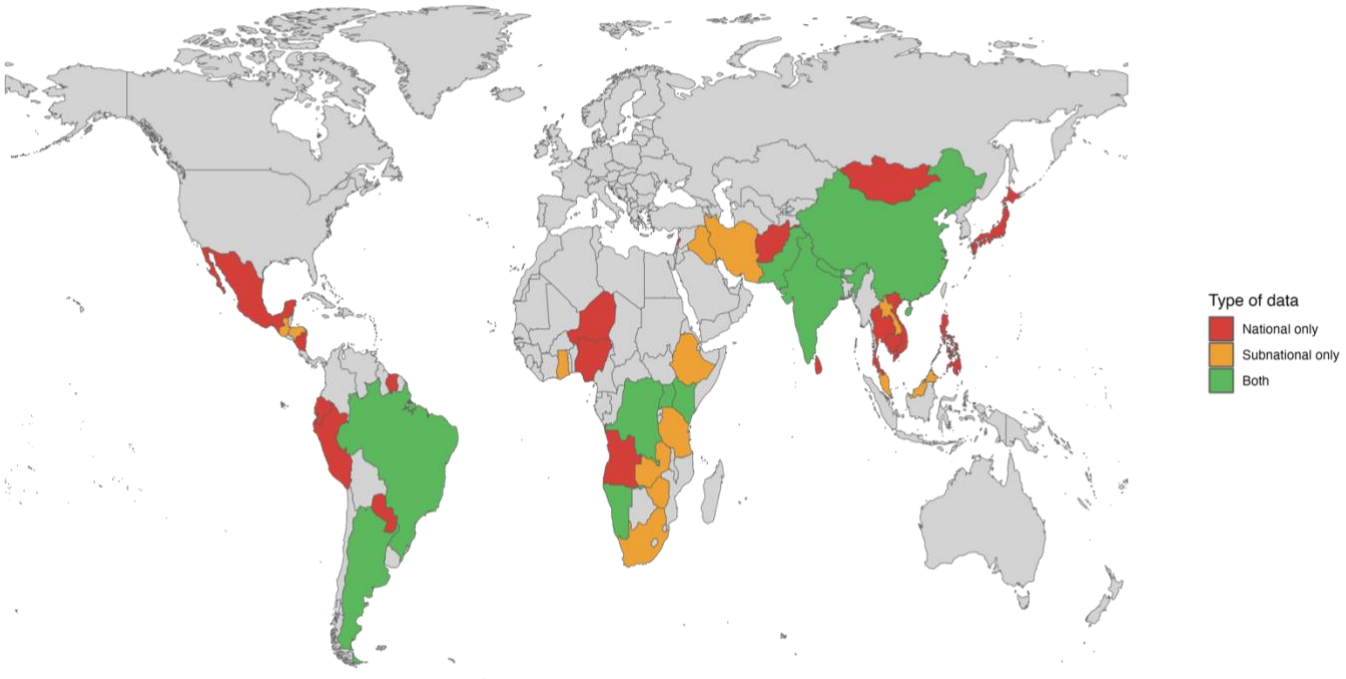

Table F3 Type of MNM data available by country

Country	Type of data	Number of studies
Central and Southern Asia		
Afghanistan	National only	1
India	Both	7
Iran	Subnational only	4
Nepal	Both	2
Pakistan	Both	2
Sri Lanka	National only	1
Eastern and South-Eastern Asia		
Cambodia	National only	1
China	Both	6
Japan	National only	1
Laos	Subnational only	1
Malaysia	Subnational only	1
Mongolia	National only	1
Philippines	National only	1
Thailand	National only	1
Vietnam	National only	1
Latin America and the Caribbean		
Argentina	Both	2
Brazil	Both	3
Ecuador	National only	1
Guatemala	Subnational only	1
Honduras	Subnational only	1
Mexico	National only	1
Nicaragua	National only	1
Paraguay	National only	1
Peru	National only	1
Suriname	National only	3
Northern Africa and Western Asia		
Iraq	Subnational only	1
Lebanon	National only	1
Sub-Saharan Africa		
Angola	National only	1
Democratic Republic of Congo	Both	2
Ethiopia	Subnational only	10
Ghana	Subnational only	1
Kenya	Both	3
Namibia	Both	3
Niger	National only	1
Nigeria	National only	3
South Africa	Subnational only	3
Tanzania	Subnational only	1
Uganda	Both	2
Zambia	Subnational only	1
Zimbabwe	Subnational only	1

F4. WHO and modified WHO criteria for organ dysfunction

The WHO definition categorises MNM according to organ system dysfunction (i.e., cardiovascular, respiratory, renal, haematologic/coagulation, hepatic, neurologic, and uterine). These are grouped according to clinical, laboratory, and management-based markers of organ dysfunction. Table F4 shows three modified versions of the WHO organ dysfunction criteria included as input data to estimate the population-level MNM ratio for each country in our LTR-MNM analyses. For the full list of criteria used in the input MNM data, please refer to Table F2. Studies using their own modification are labelled as "modified WHO".

Table F4 WHO organ dysfunction criteria for maternal near miss and modifications

WHO criteria[1]	Haydom criteria[2]	Tura criteria for sub-Saharan Africa[3]	Global Network criteria[4]
a. Clinical criteria			
Acute cyanosis	Acute cyanosis	Acute cyanosis	Acute cyanosis
Gasping	Gasping	Gasping	Gasping
Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min	Respiratory rate > 40 or <6/min
Shock	Shock	Shock	Shock
Oliguria non-responsive to fluids or diuretics	Oliguria non-responsive to fluids or diuretics	Oliguria non-responsive to fluids or diuretics	Oliguria
Failure to form clots	Failure to form clots	Failure to form clots	Failure to form clots
Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr	Loss of consciousness lasting more than 12hr
Cardiac arrest	Cardiac arrest	Cardiac arrest	Cardiac arrest
Stroke	Stroke	Stroke	Stroke
Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis	Uncontrollable fit/total paralysis
Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia
	Eclampsia	Eclampsia	
	Uterine rupture	Uterine rupture	
	Sepsis or severe systemic infection	Sepsis or severe systemic infection	
		Pulmonary oedema	
		Sepsis or severe systemic infection	
		Severe abortion complications	
		Severe malaria	
		Severe pre-eclampsia with ICU admission	
b. Laboratory-based criteria			
Oxygen saturation <90% for > 60min	Oxygen saturation <90% for > 60min	Oxygen saturation <90% for > 60min	
PaO2/FiO2 <200 mmHg			
Creatinine ≥ 300 μmol/l or ≥3.5 mg/dl		Creatinine ≥ 300 μmol/l or ≥3.5 mg/dl	
Bilirubin > 100 μmol/l or > 6.0 mg/dl			
pH <7.1			
Lactate ≥5 mEq/ml			
Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)	
Los of consciousness and ketoacids in urine		Loss of consciousness and ketoacids in urine	
c. Management-based criteria			

Use of continuous vasoactive drugs		Use of continuous vasoactive drugs	
Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage	
Transfusion of ≥ 5 units of blood	Transfusion of ≥ 1 units of blood	Transfusion of ≥ 2 units of blood	Transfusion of any volume of blood
Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia	Intubation and ventilation for ≥60min not related to anaesthesia
Dialysis for acute renal failure			Dialysis for acute renal failure
Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation
		Laparotomy other than caesarean section	
	Admission to intensive care unit		
			Surgical procedure to stop bleeding

[1] Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol. 2009 Jun 1;23(3):287–96.
[2] Nelissen E, Mduma E, Broerse J, Ersdal H, Evjen-Olsen B, van Roosmalen J, et al. Applicability of the WHO Maternal Near Miss Criteria in a Low-Resource Setting. Young RC, editor. PLoS ONE. 2013 Apr 16;8(4):e61248
[3] Tura AK, Stekelenburg J, Scherjon SA, Zwart J, van den Akker T, van Roosmalen J, et al. Adaptation of the WHO maternal near miss tool for use in sub-Saharan Africa: an International Delphi study. BMC Pregnancy Childbirth. 2017;17(1):445
[4] Goldenberg RL, Saleem S, Ali S, Moore JL, Lokangako A, Tshefu A, et al. Maternal near miss in low-resource areas. Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. 2017 Sep;138(3):347–55.

F5. Maternal near miss ratio estimates

To derive estimates of the LTR-MNM by country, we first required a single, population-level estimate of the MNM ratio for each country. The full results can be found in Table F5 below.

To estimate the MNM ratio for each country, for each study, facility-based estimates of live births were first adjusted by the institutional delivery rate to account for births occurring outside of facilities. See Tables F11 and F12 for the sensitivity of the adjusted MNM ratio and LTR-MNM to this denominator adjustment.

For 26 out of 40 countries, only a single MNM ratio estimate was available, and hence this was used as the input to the LTR-MNM. For the remaining 14 countries with multiple multi-facility, regional, or national studies, we used a random-effects only meta-analysis model to derive a pooled MNM ratio estimate (R package 'metafor'). See column "meta-analysis pooled MNM ratio estimated" in Table F5.

Table F5 Meta-analysis results for estimation of the maternal near miss ratio

Country	Year[a]	No. of MNM estimates[b]	Meta-analysis pooled ratio estimated[c]	Adjusted MNM ratio[d] (95% CI)
Central and Southern Asia				
Afghanistan	2010	1	0	7.1 (6.5, 7.9)
India	2014	7	1	8.5 (3.4, 21.4)
Iran	2014	4	1	8.2 (2.8, 23.7)
Nepal	2012	2	1	2.1 (1.8, 2.4)
Pakistan	2013	2	1	14.8 (0.7, 336.2)
Sri Lanka	2010	1	0	4.0 (3.2, 5.1)
Eastern and South-Eastern Asia				
Cambodia	2010	1	0	10.6 (8.2, 13.7)
China	2015	6	1	4.1 (2.5, 6.6)
Japan	2010	1	0	5.9 (3.9, 9.1)
Laos	2020	1	0	9.8 (5.4, 17.6)
Malaysia	2014	1	0	2.2 (1.6, 2.9)
Mongolia	2010	1	0	8.2 (6.4, 10.6)
Philippines	2010	1	0	1.7 (1.2, 2.4)
Thailand	2010	1	0	5.7 (4.3, 7.5)
Vietnam	2010	1	0	2.0 (1.4, 2.8)
Latin America and the Caribbean				
Argentina	2012	2	1	5.0 (3.8, 6.5)
Brazil	2011	3	1	10.0 (2.6, 38.9)
Ecuador	2010	1	0	2.6 (1.8, 3.7)
Guatemala	2016	1	0	61.9 (58.7, 65.4)
Honduras	2014	1	0	11.8 (6.3, 21.8)
Mexico	2010	1	0	11.1 (9.5, 13.0)
Nicaragua	2010	1	0	13.2 (11.0, 15.7)
Paraguay	2010	1	0	2.1 (1.1, 4.2)
Peru	2010	1	0	10.0 (8.6, 11.6)
Suriname	2018	3	1	12.9 (6.4, 25.9)
Northern Africa and Western Asia				
Iraq	2010	1	0	3.9 (3.3, 4.6)
Lebanon	2010	1	0	4.3 (2.7, 6.9)
Sub-Saharan Africa				
Angola	2010	1	0	2.6 (2.0, 3.4)
Democratic Republic of Congo	2013	2	1	19.7 (4.4, 88.4)
Ethiopia	2018	10	1	12.8 (5.3, 30.5)
Ghana	2016	1	0	26.9 (24.0, 30.1)
Kenya	2015	3	1	4.5 (0.3, 56.1)
Namibia	2018	3	1	9.6 (3.5, 26.6)
Niger	2010	1	0	5.5 (4.7, 6.3)
Nigeria	2014	3	1	11.3 (3.4, 37.2)
South Africa	2014	3	1	6.2 (4.2, 9.2)
Tanzania	2012	1	0	22.3 (20.4, 24.4)
Uganda	2012	2	1	13.6 (4.4, 41.9)
Zambia	2016	1	0	13.0 (11.2, 15.1)
Zimbabwe	2016	1	0	9.3 (7.7, 11.2)

Country	Year[a]	No. of MNM estimates[b]	Meta-analysis pooled ratio estimated[c]	Adjusted MNM ratio[d] (95% CI)

[a] Year is the average of the reference period midpoints across the studies for that country.

[b] Data type is classified as “national” if the input data aimed towards national representation of the MNM ratio by using multistage/random sampling to select facilities from multiple regions, provinces, or states in the country, and “subnational” if facilities were selected from one region or without random sampling.

[c] The number of MNM estimates corresponds to the number of separate studies and separate estimates within a single study (e.g., if two different MNM criteria were applied, both estimates were extracted).

[d] The denominator of facility-based studies has been adjusted by the institutional delivery rate. The adjusted denominator is used to re-calculate the MNM ratio and is used as the denominator in the meta-analysis for countries with more than one study available.

F6. Sensitivity of meta-analysis results to weights

The meta-analysis model estimated a pooled MNM ratio estimate for 14 countries where more than one multi-facility, regional, or national study was available. Since we used the cases and adjusted denominator to estimate a pooled proportion (the MNM ratio), we required a weighting schedule that was independent of the prevalence estimate. Inverse variance weighting was therefore inappropriate, since low prevalence studies of the same sample size would be weighted more highly. Using weights proportional to sample size is therefore standard procedure.

Nonetheless, in Table F6, we present the MNM ratio estimates according to three weighting procedures: (i) proportional to sample size, N; (ii) the square root of N; and (iii) the logarithm of N. The two monotonic transformations mean the weight is related to sample size, but not linearly – i.e., there is some discounting of sample size.

For most countries, except Ethiopia, the difference between the three weighting procedures is insubstantial. We therefore used weights proportional to sample size in the final model as this is more standard.

Table F6 Sensitivity of pooled MNM ratio estimates to weights

	Weights used in meta-analysis model		
Country	**N[1]**	**sqrt(N)[2]**	**log(N)[3]**
Argentina	4.96	4.48	3.90
Brazil	10.01	8.91	5.50
China	4.06	4.04	3.97
Democratic Republic of Congo	19.74	18.79	18.08
Ethiopia	12.78	15.58	18.73
India	8.51	10.11	12.37
Iran	8.15	9.43	10.97
Kenya	4.45	4.83	6.37
Namibia	9.63	11.02	12.38
Nepal	2.06	2.04	2.01
Nigeria	11.31	11.84	11.90
Pakistan	14.82	16.04	17.09
South Africa	6.19	6.11	6.05
Suriname	12.90	12.90	12.90
Uganda	13.57	12.47	11.60

[1] Where N is the population-adjusted denominator for each study

[2] Square root of the population-adjusted denominator

[3] Logarithm of the population-adjusted denominator

F7. Heterogeneity in meta-analysis results

For 14 countries with more than one eligible study on the MNM ratio, we conducted a meta-analysis to estimate the pooled, population-level MNM ratio. We used a random effects model to partially account for the heterogeneity between studies that influences the estimate of the MNM ratio: study design (population-level vs. facility-level), WHO or modified organ dysfunction criteria to identify MNM cases, denominator).

However, the random effects meta-analysis is unable to fully solve the problem of heterogeneity. With between two and nine available studies for each country, heterogeneity between studies is substantial in most cases, except for two countries where overlapping confidence intervals in MNM ratio estimates mean the I-squared estimate is very low – Argentina and Nepal (see I-squared estimate in Table F7 below). Very high heterogeneity is a common finding among meta-analyses of MNM prevalence. This emphasises the need for more standardised, population-level data on the prevalence of MNM.

Table F7 Heterogeneity in random effects meta-analysis model

Reference	MNM cases	Population-adjusted denominator	Adjusted MNM estimate	Pooled RE MNM ratio	I squared
Argentina					
De Mucio et al. (2016)	2	765	2.6	5.0 (3.8, 6.5)	0.0
Souza et al. (2013)	51	9,788	5.2		
Brazil					
Dias et al. (2014)	23,737	2,348,883	10.1	10.0 (2.6, 38.8)	97.9
Menezes et al. (2015)	77	16,407	4.7		
Souza et al. (2013)	17	7,097	2.4		
China					
Carmen et al. (2023)	61	11,086	5.5	4.1 (2.5, 6.6)	99.6
Ma et al. (2020)	3,208	545,290	5.9		
Souza et al. (2013)	34	13,540	2.5		
Xiong et al. (2020)	1,751	513,333	3.4		
Yi Mu et al. (2019)	37,060	9,104,685	4.1		
Zhou et al. (2024)	2,461	731,917	3.4		
Democratic Republic of Congo					
Goldenberg et al. (2017)	521	13,637	38.2	19.7 (4.4, 88.4)	99.4
Souza et al. (2013)	88	10,507	8.4		
Ethiopia					
Beyene et al. (2022)	90	6,063	14.8	12.8 (5.3, 30.5)	99.3
Gebremariam et al. (2022)	36	3,411	10.6		
Kamangira et al. (2024)	55	2,992	18.4		
Kusheta et al. (2023)	70	5,735	12.2		
Tenaw et al. (2021)	108	2,469	43.7		
Tura et al. (2018)	594	15,587	38.1		
Tura et al. (2018)	128	15,587	8.2		
Wakgar et al. (2019)	501	56,802	8.8		
Worke et al. (2019)	152	1,193	127.4		
Yemane et al. (2020)	210	11,642	18.0		
India					
Bakshi et al. (2015)	51	872	58.5	8.5 (3.4, 21.5)	99.6
Goldenberg et al. (2017)	615	21,548	28.5		
Goldenberg et al. (2017)	79	17,541	4.5		
Kulkarni et al. (2016)	525	18,388	28.6		
Mansuri et al. (2019)	247	27,238	9.1		
Roopa et al. (2013)	131	11,006	11.9		
Souza et al. (2013)	174	49,742	3.5		
Iran					
Ghazivakili et al. (2016)	192	40,570	4.7	8.2 (2.8, 23.7)	99.3
Hashemi et al. (2020)	81	3,150	25.6		
Mohammadi et al. (2016)	82	13,604	6.0		
Naderi et al. (2015)	501	20,890	24.0		
Kenya					
Goldenberg et al. (2017)	433	13,724	31.6	4.4 (0.4, 56.2)	99.9
Owolabi et al. (2020)	5,116	1,157,613	4.4		
Souza et al. (2013)	77	32,121	2.4		
Namibia					
Heemelaar et al. (2019)	61	6,604	9.2	9.6 (3.5, 26.6)	98.6
Heemelaar et al. (2019)	184	6,604	27.9		
Heemelaar et al. (2020)	298	37,106	8.0		

Reference	MNM cases	Population-adjusted denominator	Adjusted MNM estimate	Pooled RE MNM ratio	I squared
Nepal					
Rana et al. (2013)	157	72,606	2.2	2.1 (1.8, 2.4)	0.0
Souza et al. (2013)	65	34,807	1.9		
Nigeria					
Oladapo et al. (2016)	1,451	256,212	5.7	11.3 (3.4, 37.2)	99.9
Souza et al. (2013)	298	32,891	9.1		
Tukur et al. (2022)	5,678	175,266	32.4		
Pakistan					
Goldenberg et al. (2017)	1,830	21,604	84.7	14.8 (0.7, 336.2)	99.9
Souza et al. (2013)	94	26,409	3.6		
South Africa					
Heitkamp et al. (2022)	268	31,163	8.6	6.2 (4.2, 9.1)	94.2
Iwuh et al et al. (2018)	112	19,222	5.8		
Soma-pillay et al. (2017)	117	26,589	4.4		
Suriname					
Verschueren et al. (2020)	71	9,811	7.2	12.9 (6.4, 25.9)	97.9
Verschueren et al. (2020)	118	9,811	12.0		
Verschueren et al. (2020)	242	9,811	24.7		
Uganda					
Nakimuli et al. (2016)	695	35,204	19.7	13.6 (4.4, 41.9)	99.2
Souza et al. (2013)	120	18,235	6.6		

Meta-regression to identify sources of heterogeneity

Meta-regression combining data from all countries was used to explore sources of heterogeneity in the estimates of MNM prevalence. Five potential sources of heterogeneity, specified *a priori*, were examined: (i) years included in the reference period; (ii) country; (iii) MNM criteria; (iv) whether the study was population-based or facility-based; and (v) whether the study was national or sub-national.

Univariable meta-regression

Univariable results for each moderator are presented in models 1-5 in Table S8 (below). Out of the five potential moderators, only the MNM criteria used was a statistically significant source of heterogeneity in the univariable analyses (reject the null in the test of moderators at 95%). Relative to modified versions for low resource settings, the MNM prevalence was negatively associated with use of the full WHO criteria. This is unsurprising, given prior research has found that the WHO criteria has low sensitivity but high specificity.

Table F8 Univariable meta-regression results

Model	Moderator	Coefficient	P-value	I^2	R^2	Tau^2
Model 1	**Years of observation in reference period**					
	intercept	-4.54	0.000	99.58	31.13	0.64
	2010	-1.67	0.055			
	2011	0.82	0.298			
	2012	-0.89	0.127			
	2013	0.19	0.753			
	2014	-0.18	0.759			
	2015	-0.02	0.970			
	2016	0.42	0.513			
	2017	-0.44	0.653			
	2018	-0.69	0.313			
	2019	0.16	0.848			
	2020	0.43	0.653			
Model 2	**Country**					
	intrcpt	-4.94	0.000	99.77	16.18	0.78
	Angola	-1.01	0.422			
	Argentina	-0.37	0.763			
	Brazil	0.34	0.786			
	Cambodia	0.39	0.754			
	China	-0.57	0.624			
	Democratic Republic of Congo	1.02	0.349			
	Ecuador	-1.02	0.420			
	Ethiopia	0.58	0.559			
	Ghana	1.33	0.289			
	Guatemala	2.16	0.084			
	Honduras	0.50	0.699			
	India	0.18	0.857			
	Iran	0.13	0.899			
	Iraq	-0.61	0.626			
	Japan	-0.18	0.885			
	Kenya	-0.47	0.699			
	Laos	0.32	0.805			
	Lebanon	-0.50	0.695			
	Malaysia	-1.19	0.345			
	Mexico	0.44	0.724			
	Mongolia	0.14	0.910			
	Namibia	0.30	0.788			
	Nepal	-1.24	0.261			
	Nicaragua	0.61	0.626			
	Niger	-0.27	0.829			
	Nigeria	0.46	0.666			
	Pakistan	0.73	0.501			
	Paraguay	-1.21	0.350			
	Peru	0.33	0.790			

Model	Moderator	Coefficient	P-value	I^2	R^2	Tau^2
	Philippines	-1.45	0.249			
	South Africa	-0.14	0.889			
	Sri Lanka	-0.57	0.649			
	Suriname	0.59	0.562			
	Tanzania	1.14	0.362			
	Thailand	-0.22	0.859			
	Uganda	0.64	0.559			
	Vietnam	-1.28	0.308			
	Zambia	0.60	0.631			
	Zimbabwe	0.26	0.835			
Model 3	**MNM criteria**					
	intrcpt	-3.88	0.000	99.84	28.81	0.66
	WHO criteria	-1.44	0.008			
Model 4	**Population based**					
	intrcpt	-5.31	0.000	99.88	4.71	0.88
	Population-based	1.04	0.102			
Model 5	**Area**					
	intrcpt	-5.30	0.000	99.85	17.41	0.77
	Subnational	0.03	0.964			

Multivariable meta-regression

A multivariable meta-regression model was initially constructed by including the country variable. This approach was taken because the relationship between country and MNM prevalence might be influenced by other sources of heterogeneity. Additional variables were then added to the model one by one, starting with the variable that had the strongest association with MNM prevalence in a univariable analysis. A variable stayed in the multivariable model if it was independently associated with MNM prevalence with a significance level of $p <= 0.1$.

Only the type of MNM criteria (WHO or modified WHO) remained significant in the model with country. The comparison between the univariable model for type of MNM criteria, and the multivariable model with both country and type of MNM criteria, is presented in Table S9. The test of moderators rejected the null test of moderators at 90% for M1 ($p = 0.0571$), and 95% for M2 ($p = 0.0073$).

The reduction in the coefficient in the model with country suggests there the type of criteria used is also associated with the country, i.e. country confounds the relationship between the criteria and MNM prevalence. Once country is controlled for, the direct effect of the MNM criteria on prevalence is weaker, but the coefficient is still significant.

In M2 the type of data (national/subnational) was not statistically significant. This was also the case even when country was dropped from the model, i.e., only criteria and type of data were included. Consistent with the univariable results, these results confirm that whether the input data were national or subnational was not a significant source of heterogeneity in the MNM ratio. For this reason, we pool both national and subnational data together in the meta-analysis for the MNM ratio.

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Table F9 Select multivariable meta-regression results

Variable		**M0: Univariable model, criteria only**		**M1: Multivariable, criteria and country[1]**		**M2: Multivariable, criteria, country, type of data (national/subnational)**	
		Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
MNM criteria	[Modified]	-	-	-	-	-	-
	WHO	-1.4354	0.0079	-1.0951	0.0025	-1.0763	0.0161
Type of data	[National]	-	-	-	-	-	-
	Regional	-	-	-	-	0.0395	0.9606
Model fit details		tau^2: 0.6603 (SE = 0.1084) tau: 0.8126 I^2: 99.84% H^2: 612.68 R^2: 28.81%		tau^2: 0.6478 (SE = 0.1495) tau: 0.8049 I^2: 99.73% H^2: 366.02 R^2: 30.16%		tau^2: 0.5526 (SE = 0.1296) tau: 0.7434 I^2: 99.53% H^2: 212.79 R^2: 40.42%	

[1] Multivariable results for country not presented. No country coefficient was significant at 90%.

F8. Uncertainty

We estimated uncertainty in the LTR-MNM that derives from underlying uncertainty in the estimate of the MNM ratio only. This is to understand the contribution of uncertainty in the prevalence of MNM to the resulting estimates of the LTR-MNM and does not account for additional potential uncertainty that derives from the fertility and mortality estimates. World Population Prospects do not publish the uncertainty in their lifetable estimates.

Table F10 presents the MNM ratio and LTR-MNM with their corresponding 95% confidence intervals in parentheses. For countries where there is a large degree of variability in the MNM ratio estimates across studies, this corresponds to substantial uncertainty in the pooled MNM ratio estimate, and hence also in the LTR-MNM estimate. This emphasises the heterogeneity in MNM study design and measurement.

Table F10 Uncertainty in the estimates of the lifetime risk of maternal near miss

Country	Year midpoint	No. of studies in MNM ratio meta-analysis	MNM ratio (95% CI)	LTR-MNM 1 in N (95% CI)
Central and Southern Asia				
Afghanistan	2010	1	7.1 (6.5, 7.9)	24 (26, 22)
India	2014	7	8.5 (3.4, 21.4)	52 (130, 20)
Iran	2014	4	8.2 (2.8, 23.7)	61 (176, 21)
Nepal	2012	2	2.1 (1.8, 2.4)	207 (235, 181)
Pakistan	2013	2	14.8 (0.7, 336.2)	17 (381, 1)
Sri Lanka	2010	1	4.0 (3.2, 5.1)	114 (143, 91)
Eastern and South-Eastern Asia				
Cambodia	2010	1	10.6 (8.2, 13.7)	35 (45, 27)
China	201	6	4.1 (2.5, 6.6)	149 (240, 92)
Japan	2010	1	5.9 (3.9, 9.1)	122 (186, 79)
Laos	2020	1	9.8 (5.4, 17.6)	41 (73, 23)
Malaysia	2014	1	2.2 (1.6, 2.9)	222 (295, 167)
Mongolia	2010	1	8.2 (6.4, 10.6)	49 (63, 38)
Philippines	2010	1	1.7 (1.2, 2.4)	186 (267, 129)
Thailand	2010	1	5.7 (4.3, 7.5)	112 (147, 85)
Vietnam	2010	1	2.0 (1.4, 2.8)	269 (378, 192)
Latin America and the Caribbean				
Argentina	2012	2	5.0 (3.8, 6.5)	87 (114, 66)
Brazil	2011	3	10.0 (2.6, 38.9)	56 (217, 14)
Ecuador	2010	1	2.6 (1.8, 3.7)	150 (213, 105)
Guatemala	2016	1	61.9 (58.7, 65.4)	6 (6, 5)
Honduras	2014	1	11.8 (6.3, 21.8)	33 (60, 18)
Mexico	2010	1	11.1 (9.5, 13.0)	39 (45, 33)
Nicaragua	2010	1	13.2 (11.0, 15.7)	30 (35, 25)
Paraguay	2010	1	2.1 (1.1, 4.2)	174 (350, 87)
Peru	2010	1	10.0 (8.6, 11.6)	39 (46, 34)
Suriname	2018	3	12.9 (6.4, 25.9)	32 (65, 16)
Northern Africa and Western Asia				
Iraq	2010	1	3.9 (3.3, 4.6)	59 (70, 50)
Lebanon	2010	1	4.3 (2.7, 6.9)	109 (173, 69)
Sub-Saharan Africa				
Angola	2010	1	2.6 (2.0, 3.4)	65 (85, 50)
Democratic Republic of Congo	2013	2	19.7 (4.4, 88.4)	8 (37, 2)
Ethiopia	2018	10	12.8 (5.3, 30.5)	19 (45, 8)
Ghana	2016	1	26.9 (24.0, 30.1)	10 (11, 9)
Kenya	2015	3	4.5 (0.3, 56.1)	62 (784, 5)
Namibia	2018	3	9.6 (3.5, 26.6)	31 (86, 11)
Niger	2010	1	5.5 (4.7, 6.3)	26 (30, 22)
Nigeria	2014	3	11.3 (3.4, 37.2)	17 (56, 5)
South Africa	2014	3	6.2 (4.2, 9.2)	69 (102, 47)
Tanzania	2012	1	22.3 (20.4, 24.4)	9 (10, 8)
Uganda	2012	2	13.6 (4.4, 41.9)	13 (41, 4)
Zambia	2016	1	13.0 (11.2, 15.1)	17 (20, 15)
Zimbabwe	2016	1	9.3 (7.7, 11.2)	30 (36, 25)

F9. Lifetime risk of maternal near miss vs. death

Figure F2 plots the lifetime risk of maternal near miss against the lifetime risk of maternal death, on a log-log scale. A log-log scale was chosen due to the data spans several orders of magnitude between the lowest observed LTR-MNM or LTR-MD and the highest values. There is a positive association between these two indicators: the higher the LTR-MNM (smaller number), the higher the LTR-MD (smaller number). Some exceptions exist, indicating morbidity underperformers for their LTR-MD (e.g. Guatemala).

Figure F2 Lifetime risk of maternal near miss versus lifetime risk of maternal death

F10. Sensitivity of lifetime risk to population adjustment

Most MNM ratio estimates derive from facilities. Since MNM typically require emergency intervention in a facility, facility-level estimates of MNM cases are likely accurate. However, in countries with low institutional delivery rates, facility-based estimates of live births in the MNM ratio denominator risk under-estimating live births in a population. This potential bias is even greater if the MNM ratio derives only from tertiary referral facilities. To avoid over-estimating the MNM ratio and the LTR-MNM, we adjusted facility-based estimates of live births using open access data on the institutional delivery rate from the closest available year to studies' reference period to derive a population-level estimate of total live births (facility live births multiplied by the inverse of the institutional delivery rate).

Table F11 presents a comparison of the estimated MNM ratio when the adjustment for facility-based live birth estimates is applied, and when it is not applied.

Table F12 presents a comparison the resulting LTR-MNM using these unadjusted vs. adjusted MNM ratio estimates. We also show the percentage difference in the resulting LTR-MNM estimate with and without facility-based denominator adjustment. The effect of our adjustment is large and heterogeneous by region. It has a much greater effect in regions such as sub-Saharan Africa where institutional delivery rates are low and population-based surveillance data are scarce.

This results in a reduction of the estimated level of obstetric risk for many studies conducted in low resource settings, and consequently, results in a lower estimate of the LTR-MNM than would be the case if this adjustment was not applied.

However, despite the substantial effect of our adjustment, this is preferable to using the unadjusted MNM ratio in our meta-analyses and LTR-MNM calculation. For countries with low institutional delivery rate, the number of births recorded in a tertiary facility is not representative of the number of births in the population, and therefore results in an overestimation of the MNM ratio and hence also the LTR-MNM. Since we only adjust for the institutional delivery rate, and not according to the level of facility (primary, secondary, tertiary), this is an imperfect adjustment, but preferable to no adjustment at all.

Table F11 Sensitivity of the MNM ratio estimates to denominator adjustment

ISO	Country	Year midpoint	No. of studies	Unadjusted MNM ratio	Population-level adjusted MNM ratio[1]
Central and Southern Asia					
AFG	Afghanistan	2010	1	16.69	7.14
IND	India	2014	7	11.87	8.51
IRN	Iran	2014	4	8.55	8.15
NPL	Nepal	2012	2	4.14	2.06
PAK	Pakistan	2013	2	34.28	14.82
LKA	Sri Lanka	2010	1	4.06	4.04
Eastern and South-Eastern Asia					
KHM	Cambodia	2010	1	12.73	10.59
CHN	China	2015	6	4.07	4.06
JPN	Japan	2010	1	5.95	5.94
LAO	Laos	2020	1	9.80	9.80
MYS	Malaysia	2014	1	2.18	2.18
MNG	Mongolia	2010	1	8.35	8.23
PHL	Philippines	2010	1	2.73	1.67
THA	Thailand	2010	1	5.73	5.71
VNM	Vietnam	2010	1	2.14	1.98
Latin America and the Caribbean					
ARG	Argentina	2012	2	4.99	4.96
BRA	Brazil	2011	3	10.11	10.01
ECU	Ecuador	2010	1	2.97	2.58
GTM	Guatemala	2016	1	61.94	61.94
HND	Honduras	2014	1	16.31	11.75
MEX	Mexico	2010	1	11.62	11.11
NIC	Nicaragua	2010	1	18.52	13.15
PRY	Paraguay	2010	1	2.23	2.13
PER	Peru	2010	1	11.25	9.97
SUR	Suriname	2018	3	13.89	12.90
Northern Africa and Western Asia					
IRQ	Iraq	2010	1	5.06	3.88
LBN	Lebanon	2010	1	4.49	4.34
Sub-Saharan Africa					
AGO	Angola	2010	1	5.72	2.61
COD	Democratic Republic of Congo	2013	2	23.34	19.74
ETH	Ethiopia	2018	10	36.75	12.78
GHA	Ghana	2016	1	34.15	26.88
KEN	Kenya	2015	3	7.30	4.45
NAM	Namibia	2018	3	9.77	9.63
NER	Niger	2010	1	18.29	5.45
NGA	Nigeria	2014	3	31.59	11.31
ZAF	South Africa	2014	3	6.19	6.19
TZA	Tanzania	2012	1	35.59	22.28
UGA	Uganda	2012	2	21.03	13.57
ZMB	Zambia	2016	1	13.02	13.02
ZWE	Zimbabwe	2016	1	9.27	9.27

[1] This is the estimated population-level MNM ratio, after the denominators of facility-based input data have been adjusted to account for births occurring outside of health facilities.

Table F12 Sensitivity of lifetime risk of maternal near miss to denominator adjustment of facility-based studies

Country	Year midpoint	LTR-MNM Denom. Adjusted	LTR-MNM Denom. Unadjusted	Difference in LTR-MNM (%)
Central and Southern Asia				
Afghanistan	2010	24	10	57.2
India	2014	52	37	28.3
Iran	2014	61	58	4.7
Nepal	2012	206	103	50.2
Pakistan	2013	17	7	56.8
Sri Lanka	2010	114	113	0.5
Eastern and South-Eastern Asia				
Cambodia	2010	35	29	16.8
China	2015	148	148	0.2
Japan	2010	122	122	0.2
Laos	2020	41	41	0.0
Malaysia	2014	222	222	0.0
Mongolia	2010	49	48	1.4
Philippines	2010	186	114	38.8
Thailand	2010	112	112	0.3
Vietnam	2010	269	249	7.5
Latin America and the Caribbean				
Argentina	2012	87	86	0.6
Brazil	2011	56	55	1.0
Ecuador	2010	150	130	13.1
Guatemala	2016	6	6	0.0
Honduras	2014	33	24	28.0
Mexico	2010	39	37	4.4
Nicaragua	2010	30	21	29.0
Paraguay	2010	174	166	4.5
Peru	2010	40	35	11.4
Suriname	2018	32	30	7.1
Northern Africa and Western Asia				
Iraq	2010	59	46	23.3
Lebanon	2010	109	105	3.3
Sub-Saharan Africa				
Angola	2010	65	30	54.4
Democratic Republic of Congo	2013	8	7	15.4
Ethiopia	2018	19	6	65.2
Ghana	2016	10	8	21.3
Kenya	2015	62	38	39.0
Namibia	2018	31	31	1.4
Niger	2010	26	8	70.2
Nigeria	2014	17	6	64.2
South Africa	2014	69	69	0.0
Tanzania	2012	9	6	37.4
Uganda	2012	13	9	35.5
Zambia	2016	17	17	0.0
Zimbabwe	2016	30	30	0.0

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