Cause of and Factors Contributing to Stillbirth in sub-Saharan Africa

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy

By

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Liverpool School of Tropical Medicine

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Dedication

To Dad, who would have been so proud.

To Mum, whose love never withers.

To Meena, for her support.

To Abdul, Imam, Sultan and Sadeeq, for being great gifts.

To mothers who had stillbirth, I hope you somehow find solace.

To all mothers everywhere, for supporting human survival.

Acknowledgements

I'll spend the rest of my life singing the praises of many people for their contributions to this work. No words can adequately express my profound gratitude to my supervisor, Professor Nynke van den Broek, for being the greatest supervisor ever, a source of inspiration, a mentor and a leader. Ma'am, thank you for seeing something in me and believing in it when even I couldn't see it. For that, I remain forever indebted to you.

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I'll remain forever thankful to my family for tolerating my seemingly endless absence while I spent many weekends and "holidays" in the library.

Finally, to all who have helped me in this journey, mentioned or unmentioned, I remain profoundly grateful to you now and forever. To my Creator, I'm most grateful for surrounding me with all these smart, kind and generous people.

Na gode kwarai da gaske!

Dr Mamuda Aminu

(October 2017)

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Frequently Used Acronyms

ANOVA	Analysis of variance
CI	Confidence interval
EmOC	Emergency obstetric care
HCPs	Healthcare providers
HIC	High-income country (ies)
ICD-PM	International Classification of Diseases for Perinatal Mortality
LMIC	Low- and middle-income country (ies)
LSTM	Liverpool School of Tropical Medicine
MiH	"Making it Happen"
MNH	Maternal and newborn health
PNDR	Perinatal death review
ReCoDe	Classification according to **Re**levant **Co**ndition at **De**ath
SBR	Stillbirth rate
SD	Standard deviation
SDGs	Sustainable Development Goals
SNDR	Stillbirth and neonatal death review
SSA	Sub-Saharan Africa
WHO	World Health Organization

Declaration

This thesis is the result of my work. The material contained in the thesis has not been presented nor it is currently being presented, either wholly or as part of any other degree or qualification.

Specifically, I did the following:

- Chapter 1 (Introduction): I wrote the structure of the thesis, conceptualise the study, and drafted the study objectives and its research questions. I then drafted the chapter.
- Chapter 2A (Systematic review I): I designed the review and created its protocol, conducted the literature search, screened titles and abstracts of all articles, downloaded articles that met criteria, conducted full review of the articles, extracted data into a summary table, analysed the data and drafted the review.
- Chapter 2B (Systematic review II): I designed the review and created its protocol, conducted the literature search, screened titles and abstracts of all documents, downloaded publications that met criteria, conducted full review of the publications, extracted data into a summary table, analysed the data and drafted the review.
- Chapter 3 (Methodology): I designed the study and led its conduct. I created the data collection tool and piloted it; I designed the computer algorithm, coordinated its review by experts and I tested it. I wrote ethics application to LSTM as well as to ethics committees in all the four countries in the study. I trained healthcare providers who took part in case reviews; I coordinated and took part in the identification, data extraction and review of stillbirth cases with the healthcare providers; I organised the review of cases by the expert panel. I did most of data entry into the computer and cleaned the data. I then drafted the methodology chapter.
- Chapter 4 (Results): I conducted all analyses, created all tables and graphs and drafted the chapter.
- Chapter 5 (Results): I conducted all analyses, created all tables and graphs and drafted the chapter.
- Chapter 6 (Results): I applied the classification systems and conducted all analyses. I created all tables and graphs and drafted the chapter.
- Chapter 7 (Results): I applied the criteria used to assess care and categorised cases in relation to outcome. I conducted all analyses; I created all tables and graphs and drafted the chapter.
- Chapter 8 (Discussion): I created all tables and graphs and drafted the chapter.

Abstract

Cause of and Factors Contributing to Stillbirth in sub-Saharan Africa

Mamuda Aminu

Background

Every year, an estimated 2.6 million stillbirths occur worldwide, with up to 98% occurring in low- and middle-income countries (LMIC). Most stillbirths are preventable. To develop strategies and take effective actions to end preventable stillbirths, a good understanding of the cause of death and its contributing factors is necessary. There is, however, a paucity of data from most LMIC settings. This study aimed to determine the cause of stillbirth in LMIC using three methods of assessment, and to assess quality of care delivered to mothers who had stillbirth.

Methods

The study involved 1,563 stillbirths which occurred in 12 selected secondary and tertiary hospitals in Kenya, Malawi, Sierra Leone and Zimbabwe. The cause of death was determined by: (1) consensus of healthcare providers (HCPs) through stillbirth review; (2) expert review of cases and; (3) computer algorithms. Cause of death was classified using the classification according to Relevant Condition at Death (ReCoDe) and the International Classification of Diseases for Perinatal Mortality (ICD-PM). Quality of antenatal and intrapartum care and health system factors were reviewed using a set of criteria.

Results

A total of 1,329 cases were reviewed, of which 1,267 (95.3%) stillbirths met the inclusion criteria. By country, the stillbirth rate ranged from 20.3 (Malawi) to 118.1 (Sierra Leone) per 1,000 births. The distribution of the major causes of stillbirth differed by method of assessment: asphyxia (18.5% – 37.4%), placental disorders (8.4% – 15.1%), hypertensive disorders in the mother (5.1% – 13.6%), infection (4.3% – 9.0%), cord problems (3.3% – 6.5%), and ruptured uterus due to obstructed labour (2.6% – 6.1%). Information was insufficient to assign cause of stillbirth in 17.9% - 26.0% of cases. Significant

agreement was observed between cause of stillbirth assigned by the expert panel and by HCP (k=0.69; p<0.0005) but there was a weaker agreement between expert panel and when using computer algorithms (k=0.34; p<0.0005).

Using ReCoDe, intrapartum events (mainly intrapartum asphyxia) contributed to most of the deaths, followed by maternal diseases (mainly hypertensive disorders and infection), placental and fetal conditions. With application of ICD-PM, 42.0% were antepartum, 50.7% were intrapartum and 7.3% could not be categorised. The major categories accounting for the death were: intrapartum hypoxia and fetal growth restriction. Major contributing maternal conditions in ICD-PM were: M1 (placental, cord and membranes) and M3 (other complications of labour and delivery).

Poor quality of care during antenatal care was identified in 97.8% of cases, and only 30.7% of cases of Caesarean section were conducted within one hour of decision. For 414 (37.9%) stillbirths, the outcome could have been different with better care.

Conclusion

Stillbirth rate was high, with high variations between countries. HCPs should be encouraged to conduct reviews and act upon findings to improve quality of care. Data requirements of computer algorithms need to be balanced between ability to find a cause and the availability of information. The new ICD-PM could work in LMIC, but there is the need for more guidance on how to handle cases of stillbirths whose time of death cannot be determined.

CHAPTER 1: INTRODUCTION

1.1 Background

Annually, an estimated 2.6 million stillbirths occur worldwide (Lawn et al, 2016), making it the fifth leading global cause of death when compared with leading global causes of death in all age categories, outranking diarrhoea, HIV/AIDS, tuberculosis, road traffic accidents and any form of cancer (Froen et al, 2011). Every stillbirth is a tragedy and a potential life lost. There are, in addition, many psycho-social consequences for parents including anxiety, long-term depression, post-traumatic stress disorder and stigmatisation (Froen et al, 2011). Sadly, women who have experienced a stillbirth are more likely to experience this again in subsequent pregnancies than those who have not (Kupka et al, 2009; Ouyang et al, 2013; Stringer et al, 2011; Watson-Jones et al, 2007; Yatich et al, 2010).

The vast majority (98%) of stillbirths occur in low- and middle-income countries (LMIC), and more than half (55%) of these happen in rural sub-Saharan Africa (Lawn et al, 2011). While some developed countries report a stillbirth rate (SBR) of 3 per 1,000 births (McClure et al, 2011; Stanton et al, 2006), a ten-fold increase is noted in some settings in sub-Saharan Africa and Southeast Asia with reported stillbirth rates of 30 per 1,000 births and over (McClure et al, 2011; Lawn et al, 2011; McClure et al, 2007).

Data suggests that most of these deaths could be prevented (Lawn et al, 2011; Stanton et al, 2006). Pattinson et al, in a systematic review of perinatal audit in low- and middle-income countries, showed that if audit is conducted at health facility level by healthcare providers, this has the potential to improve the quality of care (Pattinson et al, 2009). When they meta-analysed seven before-and-after studies, they observed a reduction in perinatal mortality of 30% (95% confidence interval: 21%–38%) after introduction of perinatal audit.

In order to do so, it is crucial that we understand the causes of and factors which have led to a stillbirth and develop interventions with a focus on high risk groups (George et al, 2011). However, for many cases of stillbirths the cause of death is currently never established (McClure et al, 2006; Edmond

et al, 2008a; Baqui et al, 2011). Causes of death are very often not recorded accurately or not recorded at all; training of healthcare providers is required to improve understanding of causes of stillbirth and factors contributing to it (Cockerill et al, 2012).

Available systems for classifying the underlying cause of stillbirth differ in their approach and even when applied there is a high proportion of unclassified stillbirths (Gardosi et al, 2005; Flenady et al, 2009).

1.2 Recognition of Stillbirth as a Public Health Problem

Millions of stillbirths throughout the developing world are not counted. Stillbirth is currently not recognised in the Global Burden of Disease; it is neither counted as missed lives in disability-adjusted life-years nor fully identified as an individual death by the International Classification of Diseases (Froen et al, 2011), until when a separate classification system was launched in 2016 by the WHO for use in perinatal mortality (WHO, 2016b). Furthermore, it is reported that stillbirths are not included as part of routine national data in 90 countries worldwide (Froen et al, 2011).

This lack of recognition and paucity of data on stillbirth has continued to make assessment of the true rates of stillbirth difficult in many developing country settings (McClure et al, 2006), placing the problem at the back banner of public health problems.

1.3 Variations in Stillbirth Definition

The World Health Organization (WHO) defines stillbirth as the birth of a baby at ≥ 22 weeks of gestation or with birth weight of ≥ 500g or body length of ≥ 25cm who died before or during labour and birth. For international comparisons, the WHO defines stillbirth as a baby born dead at ≥ 28 weeks of gestation, or birth weight of ≥ 1000 g, or a body length of ≥ 35cm (WHO, 2004).

However, the definition of stillbirth varies from country to country. In high-income countries, the definition tends to be at lower level of baby's maturity. For example, in the UK, the definition of stillbirth is from 24 weeks of gestation (Stanton et al, 2006) while in Canada and some states in the USA, it is as low as 20 weeks (Ray, 2012). In low- and middle-income countries,

however, definitions of stillbirth are typically at a higher level of maturity. For example, it is from 28 weeks in Nigeria (Olusanya & Solanke, 2009), South Africa (Ntuli et al, 2012) and Nepal (Shrestha et al, 2010).

Definitions also vary within countries. In India, for example, while Bhattacharya & Pal used 28 weeks of gestation as a benchmark for stillbirth (Bhattacharyya, 2012), another study in the country used 24 weeks (Aggarwal et al, 2011).

1.4 Overview & Trends of Global Stillbirth Rates

Stillbirth rates (SBR) vary from one country to another and variation also exists within different regions of the same countries.

In 2006, Stanton et al estimated the rates and numbers of stillbirths for 190 countries for the year 2000 (Stanton et al, 2006). They reported that the resultant stillbirth rates ranged from five per 1,000 in high-income countries to 32 per 1,000 in south Asia and sub-Saharan Africa. The estimated number of global stillbirths was 3.2 million (uncertainty range 2.5-4.1 million). In light of the data limitations and the conservative approach taken, the real numbers might be higher than reported (Stanton et al, 2006).

Similarly, in 2011, Lawn et al estimated the SBR for various countries based on data collected in 2008 (Lawn et al, 2011). They reported a worldwide total of 2,646,800 stillbirths, resulting in an average global SBR of 19.1 per 1,000 births.

In 2008, although there were more stillbirths in South Asia (1,083,000; uncertainty range: 835,900 – 1,671,000), resulting in a SBR of 26.7 per 1,000 births, sub-Saharan Africa had the highest SBR of 29.0 per 1,000 births (943,900 stillbirths; uncertainty range: 701,800 – 1,388,800). Southeast Asia and Oceania had a lower mean SBR at 14.2 per 1,000 births, while North Africa and the Middle East had an average SBR of 12.9 per 1,000 births. The average SBR for Latin America and the Caribbean was lower at 9.4 per 1,000 births while East Asia had a mean rate of 9.0 per 1,000 births. High-income countries had the lowest mean SBR at 3.1 per 1,000 births (Lawn et al, 2011).

Lawn et al also reported that the top 10 countries with the highest burden of stillbirth were India, Nigeria, Pakistan, China and Bangladesh. The rest were

Congo (DRC), Ethiopia, Indonesia, Tanzania and Afghanistan (Lawn et al, 2011).

In a systematic analysis of national, regional, and worldwide estimates of stillbirth rates, Cousens et al estimated number of stillbirths and develop a time series from 1995 for 193 countries (Cousens et al, 2011). They reported that the estimated number of global stillbirths was 2.64 million (uncertainty range 2.14 million to 3.82 million) in 2009 compared with 3.03 million (uncertainty range 2.37 million to 4.19 million) in 1995. They also reported a decline in global stillbirths by 14.5%, from 22.1 stillbirths per 1000 births in 1995 to 18.9 stillbirths per 1000 births in 2009. In 2009, 76.2% of stillbirths occurred in south Asia and sub-Saharan Africa.

In 2016, Lawn et al reported that, in 2015, the estimated number of global stillbirths remained 2.6 million, half of which occurred during the intrapartum period (Lawn et al, 2016). They identified some of the major factors contributing to the slow progress in the reduction of global stillbirth to include: multiple countries affected by conflict, especially in Africa; lack of an agreed classification system for stillbirth, as well as poor record and registration of stillbirths.

Trends

There is paucity of studies which investigated stillbirth over a long enough period to observe trends of global stillbirth. However, in their paper discussing global data on stillbirth, Lawn et al reported that there has been a very slow decline in global SBR with average worldwide annual rate of reduction of 2.0% between 2000 and 2015 (Lawn et al, 2016). This is much lower than the average reduction observed for neonatal mortality (3.1%), under-five mortality (4.5%) and maternal mortality (3.0%) in the same period.

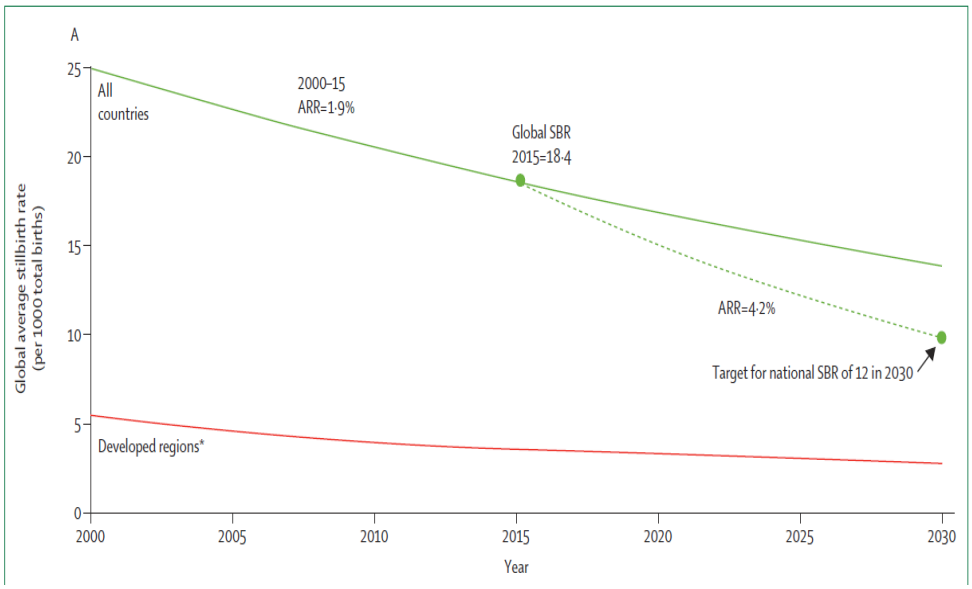
While the slowest reduction in stillbirth rates was observed in sub-Saharan Africa where almost no change was observed, by contrast, the stillbirth rate was halved in East Asia largely because of the significant reduction in stillbirth in China. Significant progress has also been reported from Latin America and Eurasia (Lawn et al, 2016 & 2011).

If current trends of global stillbirth rates remain the same, it is projected that the worldwide stillbirth rate in 2020 will be about 16.7 per 1000 total births (Lawn et al, 2011), and it is unlike that every country will reach the Every Newborn Action Plan (ENAP; WHO, 2014) stillbirth target of 12 or less per 1000 births by 2030 (Figure 1.1; Lawn et al, 2016). Without targeted interventions focused on high-burden countries, the total number of lives lost due to stillbirth worldwide will be about 2 million per year by 2020, with potentially 90% in sub-Saharan Africa and South Asia (Lawn et al, 2011).

High-income countries and upper middle-income countries have already achieved the ENAP target of 12 stillbirths or less per 1000 births (Lawn et al, 2016). The long-term trend indicates that the most significant reduction in stillbirth occurred between the years 1950 and 1975 when stillbirths were reduced by two-thirds. This is mainly attributed to improvement in prevention and treatment of infection and improved obstetric care (Lawn et al, 2011).

Therefore, the poor progress in reducing stillbirth and indeed maternal and neonatal deaths in low- and middle-income countries has severally been attributed to lack of action rather than lack of knowledge.

Figure 1.1: Estimated trends of global stillbirth rates, with predictions to 2030.



Source: Lawn et al (2016)

1.5 Rationale for & Importance of This Study

Rationale for the study

To be effective, interventions to reduce global stillbirth require up-to-date information about cause of and factors contributing to stillbirth. However, there is a scarcity of such data from perinatal death reviews in LMIC, particularly sub-Saharan Africa. Moreover, with continuous advancements in science and technology and improvements in socioeconomic conditions across the world, the distribution of causes of stillbirth also changes. Thus, stakeholders rely on limited and often outdated information to plan and execute programmes aimed at reducing stillbirths.

A systematic review summarising data on cause of, and factors associated with, stillbirth in LMIC, which included 142 papers, found that most stillbirth studies in LMIC were narrowly focused on a few causes of death (Aminu et al, 2014). Most of the studies were also of low quality. Hence, the need for a more comprehensive and up-to-date study of cause of death and its contributing factors.

Furthermore, unlike maternal death reviews, the sheer numbers of stillbirths make reviews overwhelming, especially in settings with severe shortages in human resources. The audit process can also be subject to human bias. To address these problems, computer algorithms have been used to study causes of stillbirths in a community based study (McClure et al, 2017). The use of these algorithms eliminates human influence on information analysis and helps to reduce bias; it makes the review process more transparent, faster and easier even in settings with staff shortages. However, there is limited information on how algorithms perform in facility-based perinatal death reviews. A study comparing cause of stillbirth assigned by healthcare workers, experts and computer algorithms will add to the existing scanty evidence and provide a much-needed insight into the performance of computer algorithms.

Presently, there is a variety of classification systems used to assign cause of perinatal death (Aminu et al, 2017). Most of these classification systems show poor comparability (Lawn et al, 2011) and consistently report about two-thirds of stillbirths as “unexplained” or “cause unknown” (Gardosi et al,

2005). Some of the systems cannot be used for classification of cause of death in case of stillbirth as they were not designed for this and others are considered difficult to apply and have been reported to have high inter-observer variability (Flenady et al, 2009).

In 2016, the WHO introduced a new classification framework, the International Classification of Diseases for Perinatal mortality (ICD-PM), which was developed using data from the United Kingdom and South Africa. The new system uses a layered approach to classify cause of perinatal mortality, and it is hoped that this will reduce the proportion of deaths categorised as having unknown cause. Nevertheless, the classification framework is yet to be tested in other sub-Saharan African countries, where most stillbirths occur. Thus, the need to apply the ICD-PM and assess its performance and feasibility in low-resource settings.

Importance of the study

This study, therefore, aimed to provide deeper knowledge of the causes of stillbirth in sub-Saharan Africa, providing up-to-date data upon which programmes could rely to focus interventions targeting reduction of stillbirth in LMIC. It is hoped that the application of the ICD-PM to the cause of stillbirth in several LMIC provides a valuable insight into how the new classification system works and highlights where it could be improved.

The wide difference between the proportion of stillbirth that occurs during the intrapartum period in LMIC (46%) and high-income countries (14%) (Lawn et al, 2011), despite improvements in the availability of maternal and newborn care in low-resource settings during the last decades, suggests a potential role of quality of care improvement in prevention. This study highlights vital priority areas for overall improvement in quality of maternal and newborn care, a key strategy for reduction of stillbirth in LMIC (Goldenberg et al, 2016).

Because prevention of stillbirth is closely linked with prevention of maternal and neonatal deaths (Froen et al, 2011), it is hoped that the data presented will support formulation of feasible solutions for prevention of maternal and neonatal mortalities; thus, contribute to the achievement of the Sustainable Development Goals (SDGs).

1.6 Aim, Objectives & Research Questions

The primary aim of this PhD study was to gain a deeper understanding of causes of and factors contributing to stillbirth in sub-Saharan African countries.

The specific objectives were:

1) **To explore current literature on causes of, factors associated with, and classification systems used for stillbirth in LMIC. The research questions were:**
    a) What are the major causes of stillbirth in LMIC from existing literature?
    b) Which factors are associated with stillbirth in LMIC?
    c) What classification systems for stillbirth exist; what are their advantages and limitations for use in LMIC, and; which are commonly used in LMIC?
2) **To assess cause of stillbirth in LMIC and compare findings as identified by healthcare providers conducting stillbirth review at health facility level, an independent expert panel and computer algorithms. The research questions were:**
    a) What is the stillbirth rate by health facility?
    b) What are the characteristics of mothers and babies?
    c) What characteristics of mothers and babies are similar or different across settings?
    d) What proportion of the stillbirths are antepartum and intrapartum?
    e) What are the major causes of stillbirth by method of assessment?
    f) Are their differences in the distribution of causes of stillbirth between countries?
    g) What is the distribution of cause based on time of death (antepartum / intrapartum death)?
    h) What are the advantages and disadvantages of each method of cause assessment?
3) **To classify causes of stillbirth using two classification systems: The International Classification of Diseases for Perinatal Mortality (ICD-**

PM) and the classification of stillbirth according to Relevant Condition at Death (ReCoDe). The research questions were:

a) Which category of causes accounts for most stillbirths?
b) What are the similarities and/or differences in the classification of causes of stillbirth by different methods of assessment?

4) **To assess standard of care provided to women who had stillbirth. The research questions were:**
   a) What is the coverage and quality of care provided to mothers and babies?
   b) What proportion of stillbirths could have been saved with better care (using a set of criteria)?
   c) What proportion of cases meet a pre-set standard of care?
5) **To formulate recommendations for improvement of quality of maternal and newborn health services. The research questions were:**
   a) What recommendations could be made for improvement in the following areas:
      i. Stillbirth audit process?
      ii. Classification of stillbirth?
      iii. Quality of maternal and newborn health services?
      iv. Further research?

1.7 Thesis Structure

This thesis is structured by chapters as follows.

Chapter 1 (Introduction)

Chapter 1 introduces the topic of the research and highlights the problem, the research gap, and justifies why the study was undertaken. It then states the study aim and objectives, as well as the research questions related to each objective.

Chapter 2 (Literature Review)

Chapter 2 is divided into two parts. The first part, Chapter 2A, presents a systematic review of existing literature on factors associated with and cause

of stillbirth in low- and middle-income countries. It also reports the pattern of use of existing classification systems in developing countries.

Chapter 2B is another (separate) systematic review which summarises available classification frameworks for stillbirth, and highlights their advantages and limitations for use in LMIC.

Chapter 3 (Methodology)

The methodology of the primary thesis study is provided in Chapter 3. It explains the research design, and describes the study sites. It also describes how the sample size was determined and how data collection tools were developed, tested and piloted. In addition, the chapter gives details of the data collection, processing and analysis, and concludes with notes on how data quality was assured and considerations for ethics.

Chapters 4, 5, 6 and 7 (Results)

These chapters present the results of the primary study, structured as per the objectives of the study, as follows:

- Chapter 4 presents demographics and participants' characteristics;
- Chapter 5 reports the causes of stillbirth;
- Chapter 6 presents classification of the cause of stillbirth, and;
- Chapter 7 reports on the standard of care provided to mothers and their babies.

Results are presented in a narrative format and complemented with tables, graphs and diagrams. Where supplementary information is necessary, this is presented in the appendices.

Chapter 8 (Discussion and Recommendations)

In chapter 8, the results of the study are discussed. It begins with a summary of the major findings and then provides a contextual meaning of the results and compares the findings of this study with those from previous studies. The chapter also highlights the strengths and weaknesses of the study and comments on the generalizability of the results. It concludes by making key recommendations to improve perinatal health, which fulfils the last objective of the study.

CHAPTER 2A: LITERATURE REVIEW I

2A.1 Introduction

This chapter presents the first of the two systematic reviews of literature conducted in this PhD programme. The systematic review in this chapter was conducted to explore current, available evidence on identification of causes of, and factors associated with, stillbirth in low- and middle-income countries. In addition, classification systems used in these settings were sought to be identified.

The methods section of this chapter describes how the systematic review was conducted. In the results section, findings of the systematic review are presented in a narrative synthesis and complemented with diagrams, graphs and tables. The discussion explains what the results mean; the major findings are briefly introduced and compared with results of previous studies; explanation is provided on key similarities and differences before conclusions are drawn. This chapter ends with a summary.

2A.2 Methods (For Systematic Review)

2A.2.1 Databases searched

The following electronic databases were searched. They were selected based on their relevance to the topic as well as their wide geographical coverage.

- MEDLINE
- CINAHL Plus
- Global Health and
- LILACS

2A.2.2 Search terms

The following search terms were used:

- “stillb*” AND
- causes OR risk OR audit OR review OR “perinatal audit” OR “perinatal review”

2A.2.3 Search strategy

The databases were searched for studies conducted between January 2000 and March 2017 (inclusive) in low- and middle-income countries. The year 2000 was selected as the starting point to cover the period when many developing countries became more proactive in addressing the burden of maternal and perinatal mortality and morbidity through the implementation of programmes, initially to achieve MDGs numbers 4 and 5, and later the SDGs.

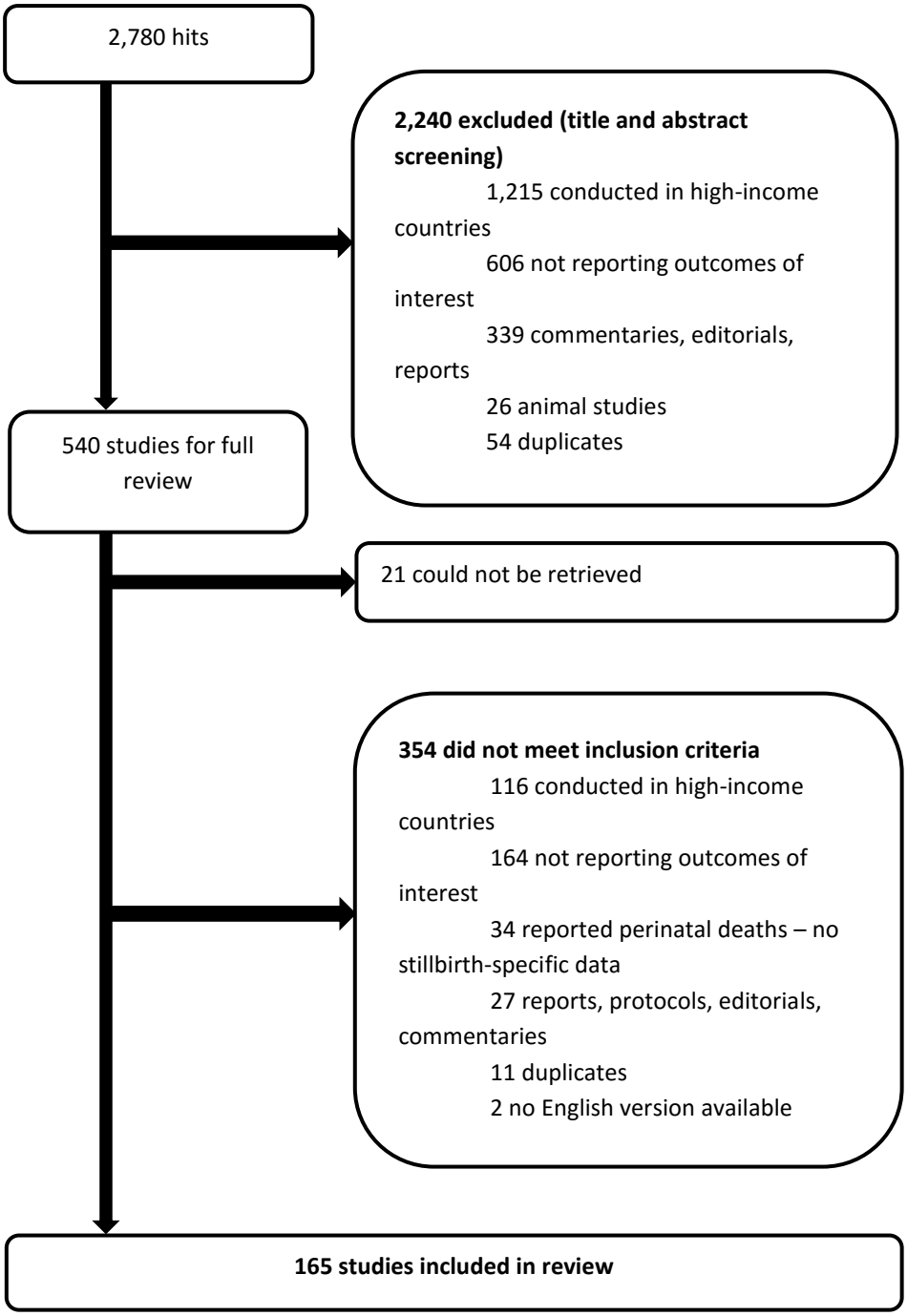
2A.2.4 Inclusion / exclusion criteria

Studies were included if they reported at least one of the known causes of, or risk factors associated with, stillbirth (irrespective of definition) and were conducted in a LMIC, as defined by the World Bank (World Bank, 2017). Studies conducted in high-income countries (HIC) and publications that did not contain data on cause of / risk factors associated with stillbirths, such as commentaries and editorials, were excluded. Studies published in languages other than English (and did not have an English abstract) were also excluded (Figure 2A.1).

2A.2.5 Data extraction

Using the inclusion / exclusion criteria, two reviewers (the principal investigator and a second reviewer) independently screened all titles and abstracts. Lists of papers to be included / excluded were compared. A third reviewer was consulted on the seven papers that the two reviewers could not reach consensus on their inclusion / exclusion. All included studies were then summarised and outcomes of interest were captured in a summary table with a pre-agreed format (Appendix 1: Summary table for included studies).

Figure 2A.1: PRISMA diagram for article selection process



2A.2.6 Quality assessment

Studies were assessed for quality using the GRADE system (Grade Working Group, 2004). This system was used because of its objective approach to grading studies. Studies were assigned scores based on their design, as indicated in Table 2A.1. The studies were then assessed for the seriousness of their limitations, consistency, directness, precision and probability of reporting bias. A study could be upgraded or downgraded from their initial score depending on the result of their assessment on each of the parameters. While clinical trials could only be downgraded, cross-sectional studies could only be upgraded.

Table 2A.1: Initial scores assigned based on study designs (GRADE system)

Study Design	Initial Score
Randomised controlled trials	4
Cohort studies	3
Case-control studies	2
Cross-sectional studies	1

Depending on their final scores, evidence presented by the studies was categorised as:

- **High**: If the final score was 4
- **Moderate**: If the final score was 3
- **Low**: If the final score was 2
- **Very low**: If the final score was 1

The methodologies and results of studies belonging to the same outcome category were compared to look for similarities and differences. The results were discussed with appropriate emphasis given to studies that were more methodologically robust.

2A.2.7 Data analysis & synthesis

Descriptive statistical analysis was conducted using SPSS® (version 22, NY, USA), and a narrative synthesis method was used summarise findings. A

distinction was made between "factors associated with" (or "risk factors for") and "causes of" stillbirth. When this was not clear in the publication, we defined a (risk) factor associated with stillbirth as "a maternal/paternal characteristic associated but without an obvious causal relationship with the stillbirth", while cause was defined as "any condition with a plausible mechanism likely to lead to the death of the fetus" (McClure et al, 2009). Studies were considered as population-based if they were conducted at community level with or without involvement of a health facility for a clear catchment population.

The studies were grouped into three outcome categories: those providing information on cause(s) of stillbirths, those with information on factors associated with stillbirth, and those providing information on both causes and associated factors. Where a classification system had been used, this was also recorded. For summarising findings in this review, the ReCoDe classification system was used. This system classifies causes of stillbirth according to relevant condition at death, and it is one of the few classification systems specifically developed for stillbirth alone (Gardosi et al, 2005).

2A.3 Results of Literature Review

2A.3.1 Characteristics of studies included

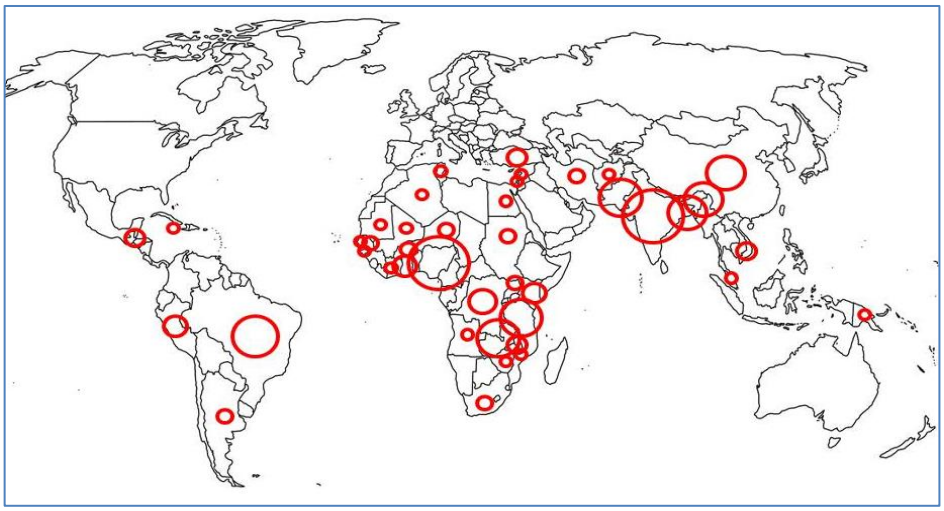
A total of 165 studies were included (Figure 2A.1); 132 reported the number of stillbirths studied, which totalled 63,920 cases. Some papers (21/540; 3.9%) could not be retrieved for review, most of which were published in Southeast Asia. The included studies were conducted in 49 countries across six continents (Figure 2A.2). Asia (70/165) and sub-Saharan Africa (59/165) contributed most of the studies. The rest came from Latin America (16/165), multiple regions (10/165), Europe (3/165), Middle East (3/165), North Africa (2/165), the Caribbean (1/165), and the Pacific (1/165).

Most studies were descriptive. Of the 165 studies, the majority (57.0%) were cross-sectional, and mostly (76.4%) of very low or low quality (Table 2A.2).

In terms of outcomes, 43 (26.1%) studies reported on cause of stillbirth, 78 (47.3%) reported on risk factors associated with stillbirth and 44 (26.7%)

reported on both cause and risk factors. However, it was observed that some of studies reported cause as risk factors and vice versa.

Figure 2A.2: Distribution of included papers



** Size of circles indicates number of papers from the region.*

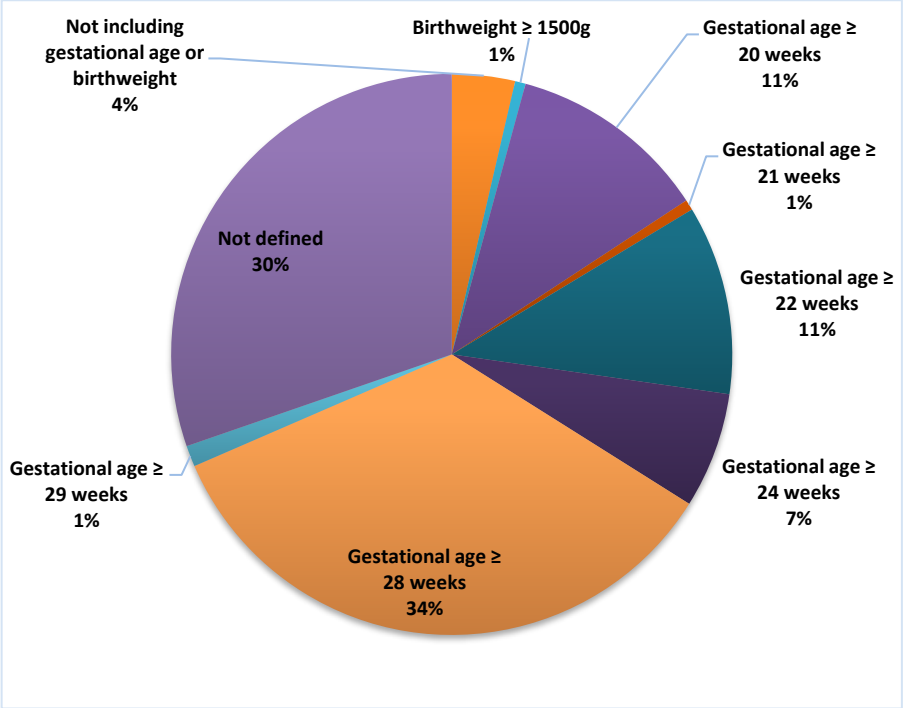
Table 2A.2: Study designs and methodological quality (GRADE)

Study Design	Methodological Quality (GRADE)				
	Very low	Low	Moderate	High	Total n=165 (%)
Cross-sectional	56	33	5	0	**94 (57.0)**
Case-control	2	28	2	0	**32 (19.4)**
Cohort	1	2	24	0	**27 (16.4)**
Clinical trial	0	0	0	6	**6 (3.6)**
Review	1	0	0	0	**1 (0.6)**
Systematic review	0	1	2	0	**3 (1.8)**
Secondary analysis	0	2	0	0	**2 (1.2)**
Total n=165 (%)	**60 (36.4)**	**66 (40.0)**	**33 (20.0)**	**6 (3.6)**	**165 (100.0)**

2A.3.2 Definition of stillbirth

The definition of stillbirth used in the studies varied by country and often by studies within the same country. The gestational age ranged from 20 weeks or more to 29 weeks or more (Figure 2A.3). Only 57 (34%) studies used the WHO definition for international comparison (28 weeks of gestation or more), while 18 (11%) studies used the WHO standard definition (22 weeks or more). About one-third (33%) of all studies did not include the definition of stillbirth used. Some used narrative definitions, such as "neonate born dead" (Liu et al, 2013) "absent cardiac activity" (Mwanyumba et al, 2003), without specifying gestational age, birth weight or birth length.

Figure 2A.3: Variations in definitions of stillbirth used



2A.3.3 Stillbirth rates

A total of 36 (out of 44) population-based studies reported stillbirth rates (SBR), which ranged from 5.1 per 1,000 births in a study of 350 stillbirths in a relatively healthy population in India (Mukhopadhyay et al, 2010) to 61 per 1,000 births among 76 mothers in consanguineous marriages in Iran (Aboualsoltani et al, 2009).

Of the 108 facility-based studies included, 87 reported the SBR. This ranged from 2.7 per 1,000 births in a study of 29,303 ethnically Chinese women with a singleton pregnancy and at least 24 weeks (Leung et al, 2008) to 170 per 1,000 births in a tertiary hospital in Nigeria (Ugwa & Ashimi, 2015). Much higher rates have been reported in unhealthy populations of mothers in India (Lionel et al, 2008; Bangal et al, 2012; Sarkar et al, 2012), Tanzania (Watson-Jones, 2002; Muganyizi & Kidanto, 2013; Macheku et al, 2015) and Nigeria (Ashimi et al, 2014).

2A.3.4 Factors associated with stillbirth

The most commonly reported factors associated with stillbirth were (Figure 2A.4): maternal factors (McClure et al, 2011; Zhang et al, 2009; Ali & Adam, 2011; Assaf et al, 2008; Engmann et al, 2012a; Gilbert et al, 2010; Ukaegbe et al, 2011), gestational age at birth, parity (McClure et al, 2011; Assaf et al, 2008; Ukaegbe et al, 2011; Ntuli et al, 2012), history of previous stillbirth (Ukaegbe et al, 2011; Lee et al, 2011; Stringer et al, 2011; Flenady et al, 2011), poor antenatal care (Graner et al, 2009; Gilbert, 2010; Nouaili et al, 2010; Olusanya et al, 2009; Del Rosario et al, 2004), socioeconomic status (Graner et al, 2009; Engmann et al, 2012a; Cripe et al, 2007; Lee et al, 2011), environmental pollution (Pope et al, 2010; Hu et al, 2012; Graner et al, 2009). In addition, a number of more recent studies have reported obstetric complications as risk factors for stillbirth (Endale et al, 2016; Perveen & Somroo, 2016; Tshibumbu & Blitz, 2016; Neogi et al, 2016; Litorp et al, 2015; Singh et al, 2014; Dassah et al, 2014). One study in Bangladesh reported an association between obesity and stillbirth (Khan et al, 2017).

Maternal factors

Four studies graded as moderate to high quality reported an increased risk of stillbirth in older mothers (Gilbert et al, 2010; Lee et al, 2011; Nahar et al, 2013; Stringer et al, 2011). In a study assessing risk factors for antepartum stillbirths in rural Nepal, Lee et al (2011) reported a relative risk of stillbirth of 2.0 among mothers aged 35 or older (95% CI: 1.51 – 2.63). Mothers who were 30 years or older were observed to have an increased risk of stillbirth in a study in Zambia (OR: 1.79; 95% CI: 1.46 – 2.20) (Stringer et al, 2011). On the other hand, low quality evidence suggests that teenage mothers are at

higher risk of stillbirth than older mothers (Engmann et al, 2012; Olusanya & Solanke, 2009). For teenage mothers, OR of 1.49 (CI: 1.12–1.99) has been reported from Ghana (Engmann et al, 2012).

Multiple very low to low quality studies suggests that nulliparity (Engmann et al, 2012; Lee et al, 2011; McClure et al, 2007) and multi-parity (McClure et al, 2007; Mutihir & Eka, 2011; Olusanya et al, 2009; Ukaegbe et al, 2011; Ashish et al, 2015) are associated with increased risk of stillbirth. However, the reported increase in risk is consistently low, and often contradictory. For example, while Olusanya et al. reported an odds ratio of 1.92 (95% CI: 1.16 – 3.20) for multi-parous women in Nigeria (Olusanya et al, 2009), Bhattacharyya & Pal reported an odds ratio of 0.13 (95% CI: 0.10 – 0.16) for multi-parity (Bhattacharyya & Pal, 2012).

Figure 2A.4: Major factors associated with stillbirth (SB) in low- and middle-income countries

Obstetric factors

Obstetric complications, such as breech presentation and prelabour rupture of membranes (PROM), have been reported to increase the risk of stillbirth. In a case-controlled study in India, Neogi et al reported that the presence of obstetric complications increased the risk of stillbirth (OR 3.3; 95% CI 2.1, 5.3) (Neogi et al, 2016). In neighbouring Pakistan, a prospective cohort study on the association between sideropaenic anaemia among women and adverse

perinatal outcome reported an increased risk of stillbirth among anaemic women, with a relative risk of 1.75 (95% CI: 1.26 – 2.44; p=0.055) (Perveen & Somroo, 2016).

Endale et al reported an increased risk of adverse fetal outcomes when the duration of PROM exceeded 12 hours (OR: 12.0; 95% CI: 2.8–51.7), when there was meconium stained liquor (aOR: 9.9; 99% CI: 3.3–33.7), or when the birthweight was less than 2500g (aOR: 7.8; 95% CI: 1.2–51.2) (Endale et al, 2016). However, they did not report specific outcomes for stillbirth.

On the other hand, in a cross-sectional study in Tanzania, Litorp et al observed a decreased risk of stillbirth (OR 0.42; 95% CI 0.29–0.62; p<0.001) among multiparous mothers who had undergone a previous Caesarean section (Litorp et al, 2015).

Access to care

Many studies reported an association between poor antenatal attendance and stillbirth. In a multi-national study, McClure et al. reported that mothers who did not attend antenatal care were almost twice more likely to experience a stillbirth than mothers who attended (RR: 1.6; 95% CI: 1.4 – 1.9) (McClure et al, 2011). Similar results have been reported from Nigeria (Olusanya & Solanke, 2009; Olusanya et al, 2009), Malawi (Kalanda et al, 2006), Jamaica (Del Rosario et al, 2004) and Nepal (Ashish et al, 2015).

Mothers who live in rural areas were also reported to have an increased risk of stillbirth (Bhattacharyya & Pal, 2012; Cripe et al, 2007; Feresu et al, 2004). However, these studies did not correct for access to care.

Socioeconomic factors and education

In a study assessing risk factors for stillbirth in rural Nepal, higher socioeconomic status, measured by proxies such as land ownership, lowered the risk of stillbirth (ARR: 0.85; 95% CI: 0.74–0.98) (Lee et al, 2011). Low socioeconomic status has been reported to increase the risk of stillbirth in multiple studies (Engmann et al, 2012a; Cripe et al, 2007; Graner et al, 2009; Bell et al, 2008; Katz et al, 2008). In a systematic review, low socioeconomic status has been reported to have a population attributable fraction of higher than 50% (Di Mario et al, 2007).

Poor maternal education is another demographic factor frequently reported to increase the risk of stillbirth (Cripe et al, 2007; Omokhodion et al, 2010; Olugbuji et al, 2012; Mutihir & Eka, 2011; McClure et al, 2011; Ashish et al, 2015). In a multi-country study of 4,301 births in multiple LMIC, McClure et al. reported that women with no education were at increased risk of stillbirth (RR: 1.4, CI: 1.2, 1.5) (McClure et al, 2011). Other studies have similarly reported an association between poor maternal education and stillbirth (Assaf et al, 2008; Engmann et al, 2012a; Nankabirwa et al, 2011; Williams et al, 2008; Sehgal et al, 2014).

Emerging factors

Some factors that were rarely reported before are beginning to emerge from various studies. A secondary analysis of data from India has shown an increased risk of stillbirth among women who used biomass for cooking (OR: 1.26; 95% CI: 1.12, 1.43) (Sehgal, 2014). This strengthens the earlier report by Pope et al that indoor air pollution increases the risk of stillbirth (OR=1.51; 95% CI: 1.23 - 1.85) (Pope et al, 2010). Environmental pollution has been associated with stillbirth in a growing number of studies (Hu et al, 2012; Graner et al, 2009).

In another secondary analysis of data from the Demographic and Health Survey in Bangladesh, Khan et al observed higher risk of stillbirths (ARR, 3.20; 95% CI: 0.77-13.55) among overweight and obese women in Bangladesh (Khan et al, 2017).

2A.3.5 Cause of stillbirth

Generally, studies tended to focus on a few categories of causes of stillbirth, namely: maternal, fetal and placental, with only a few reporting causes in other categories (Figure 2A.5).

Maternal conditions

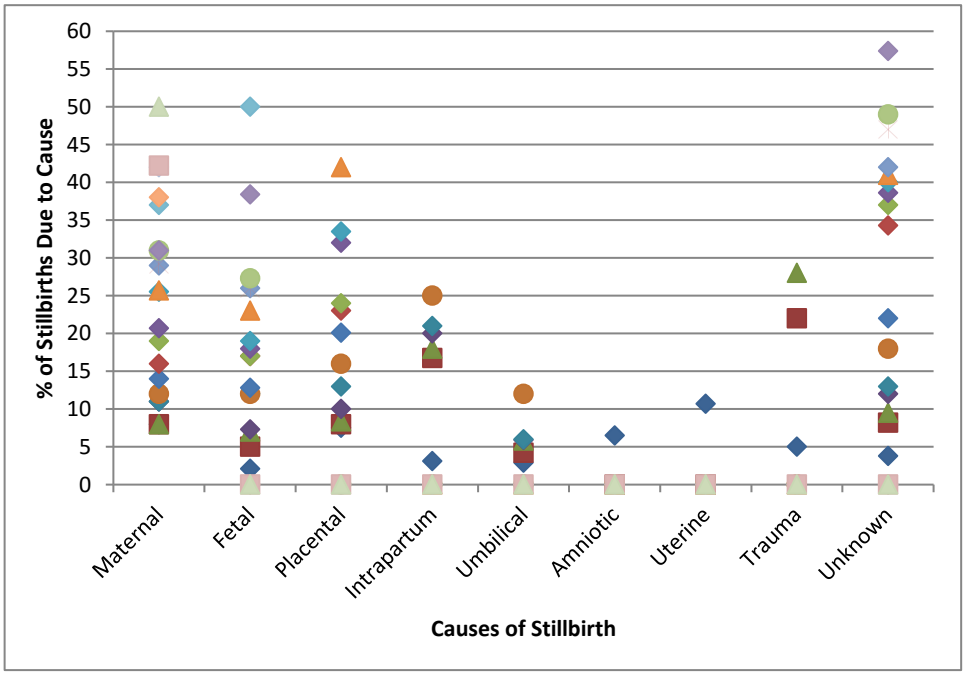
For maternal conditions causing stillbirth, hypertensive disorders were frequently reported by researchers (Table 2A.3) (McClure et al, 2017; Awoleke & Adanikin, 2016; Ugwa & Ashimi, 2015; Lori et al, 2014; Khanam et al, 2017). In a clinical trial involving 6,285 mothers in Bangladesh which reported patterns of antepartum complications and the risk of perinatal deaths, pregnancy-induced hypertension was found to be a significant risk

for stillbirth (IRR: 1.8; 95% CI: 1.3–2.5) (Khanam et al, 2017). The reported proportion of stillbirths due to hypertensive disorders ranged from 5% in a study of 143 stillbirths in Liberia (Lori et al, 2014) to 18% in a large prospective observational study of 2,847 stillbirths in six LMIC (McClure et al, 2017).

Three studies from India, Liberia and Tanzania reported sickle cell disease as a cause of stillbirth in their settings (Lori et al, 2014; Muganyizi & Kidanto, 2013; Desai et al, 2017). While Desai et al reported an increased risk of stillbirth among mothers with sickle cell disease in an Indian hospital (OR: 3.45; 95% CI: 1.92–6.21), Lori et al reported that sickle cell disease accounted for less than 1% of stillbirths in a hospital in Liberia (Lori et al, 2014).

Some studies have also reported infections as maternal causes of stillbirth (Awoleke & Adanikin, 2016; Ugwa & Ashimi, 2015) (Table 2A.3).

Figure 2A.5: Studies reporting causes of stillbirth by category (ReCoDe; Gardosi et al, 2005).



* Symbols represent studies in the analysis

Fetal causes

Fetal causes of stillbirth, such as congenital anomalies, infections and intrauterine growth restriction, have been reported frequently (Table 2A.3).

Fetal causes account for 6.7% to 30.0% of stillbirths in LMIC (Musafili et al, 2017; Hinderaker et al, 2003).

In the multi-national study by McClure et al, computer algorithms were used to assess cause of stillbirth. They reported infections and congenital anomalies incompatible with life to account for 20.8% and 8.4% of stillbirths, respectively (McClure et al, 2017). However, in a small hospital-based study of intrauterine death using autopsy data in India, congenital anomalies were the most prevalent cause of death, accounting for 28.6% of the 14 stillbirths included in the study (Uroos et al, 2014).

Table 2A.3: Reported causes of stillbirth in LMIC based on frequency of reporting

Attributed cause of stillbirth	% cause range	No. of studies reporting causes	Total no. of stillbirths reported on	No. of stillbirths per study
Mother's disease e.g. diabetes, infections	8.0 – 50.0	44	12,516*	3 – 2,847
Fetal e.g. congenital anomalies, infections	2.1 – 33.3	26	8,229	12 – 2,847
Placental e.g. placenta abruptio, praevia	7.5 – 48.6	29	11,158*	12 – 5,257
Intrapartum e.g. asphyxia, birth trauma	3.1 – 55.0	9	11,408*	24 – 5,257
Umbilical prolapse, loop, knot	2.9 – 13.0	9	2,518	17 – 761
Trauma e.g. external, iatrogenic	0.7 – 2.0	3	200*	31 – 169
Amniotic e.g. chorioamnionitis, oligohydramnios	1.0 – 14.2	11	1,600*	14 – 917
Uterine e.g. rupture, anomalies	9.5 – 11.7	11	9,433	40 – 7,497
Unclassified / unknown / unexplained	3.3 – 62.7	24	7,255	11 – 2,847

* Not all studies reported number of stillbirths.

Placental conditions

Placental causes of stillbirth, mainly placenta abruptio and placenta praevia, continue to be some of the most frequently investigated causes of stillbirth (Stringer et al, 2011; Litorp et al, 2015; Ashish et al, 2015; Kaistha et al, 2016;

Nan et al, 2015; Hwang et al, 2011, Al Mamun et al, 2006). In the clinical trial by Khanam et al, antepartum haemorrhage was found to increase the risk of stillbirth almost four-fold (IRR = 3.7; 95% CI: 2.3–5.9) (Khanam et al, 2017).

The percentage of stillbirths attributable to placental causes ranges between 8.0% and 17.7% (Lori et al, 2014; Ugwa & Ashimi et al, 2015).

Intrapartum causes and trauma

There seems to be an increasing recognition of intrapartum causes of stillbirth. Asphyxia remains the most common cause of intrapartum stillbirth, accounting for 46.6% of 2,847 stillbirths in the population-based, multi-country study by McClure et al (McClure et al, 2017). Other studies have reported intrapartum events leading to asphyxia (prolonged obstructed labour) to account for between 14% and 24% of stillbirths (Lori et al, 2014; Ugwa & Ashimi, 2015).

Only one study reported trauma as cause of stillbirth. In an Indian hospital, birth trauma accounted for 3.1% of stillbirths (Bhattacharyya & Pal, 2012).

Umbilical causes

Some studies reported on umbilical conditions, such as cord prolapse, as causes of stillbirth (Khanam et al, 2017; Musafili et al, 2017; Engmann et al, 2012b; Turnbull et al, 2011; Bell et al, 2008). In a study of 917 stillbirths in Nigeria, cord accidents were reported to significantly increase the risk of stillbirth (OR 29.63; 95% CI: 14.23–61.71) (Olusanya & Solanke, 2009). The proportion of stillbirths attributed to cord problems ranged from 2.9% (Kuti et al, 2003) to 13% (Musafili et al, 2017).

Unknown cause

Generally, studies reported cause of death as unknown when there was not enough information to substantiate the assignment of any condition as the underlying cause of death or when the cause could not be identified despite clinical information being available.

Only 13 studies reported on the proportion of stillbirths with unknown cause, and this varied significantly between studies. While a hospital-based study of 761 stillbirths in Nigeria found only 3.3% as unknown (Ugwa & Ashimi et al, 2015), a similar study of 153 stillbirths in East Timor reported up to 62.7% as

unknown (Wilkins et al, 2015). However, the median proportion for stillbirth with unknown cause was 18% across all studies in which this information was provided. None of the studies were conducted using verbal autopsy data.

2A.3.6 Classification systems for stillbirth used in developing countries

Of the 70 studies that could have used a classification system to assign cause of death, only 14 (20%) used a classification system; 35 (50%) categorised cause of death using physical appearance (Fresh/Macerated) or time of death (Antepartum/Intrapartum), and; 21 (30%) did not report using any classification system (Table 2A.4).

Of the 35 studies that categorised cause by physical appearance or time of death, the reported proportion of fresh/intrapartum stillbirths ranged from 4.3% in a hospital-based case-control study of 25 stillbirths in Brazil (Andrade et al, 2009) to 88.2% in another hospital-based study of 116 stillbirths in The Gambia (Cham et al, 2009), with a median of 53% (IQR: 26.6). In addition, Wilkins et al reported one-third (31.4%) of stillbirths as having unknown time of death (Wilkins et al, 2015).

Seven studies reported the time of death (antepartum/intrapartum), but it was not clear how this was deduced (Wilkins et al, 2015; Kaistha et al, 2016; Awoleke & Adanikin, 2016; Baqui et al, 2011; Bhattacharyya & Pal, 2012; Edmond et al, 2008a and 2008b; Guidotti et al, 2009; Kuti et al, 2003).

Table 2A.4: Classification systems used in studies from LMIC to categorise cause of death.

Classification system used	Frequency	%
Aberdeen	2	3.3%
"Baird-Pattinson classification"	1	1.6%
CODAC	1	1.6%
NICE & CHERG	1	1.6%
Global Network Stillbirth Classification System	1	1.6%
ICD-10 and CODAC	1	1.6%
Nordic-Baltic	1	1.6%
PSANZ-PDC	1	1.6%
Wigglesworth	4	6.6%
Physical appearance / time of death	31	50.8%
Not Documented	17	27.9%
Total	**61**	**100.0%**

ICD: International Classification of Diseases; PSANZ-CPG/PDC: Perinatal Society of Australia and New Zealand Clinical Practice Guide/Perinatal Death Classification; NICE: Neonatal and Intrauterine Death Classification according to Etiology; CHERG: Child Health Epidemiology Reference Group; CODAC: Causes of death and associated conditions

2A.4 Discussion

This systematic review was conducted to summarise recent evidence on cause of, and factors associated with, stillbirth in LMIC. It is hoped that these findings provide information for practitioners and managers involved in efforts to reduce the global burden of stillbirths whether at the facility or at national and international levels.

Main findings

Data reporting on cause of stillbirth and factors associated with stillbirth occurring in low-resource settings, where 98% of stillbirths occur (Lawn et al, 2011 & 2016), is relatively scarce. The quality of studies from LMIC remains low.

There is no consistent definition of stillbirth across countries with only about half (48%) of all included studies using any of the WHO definitions (22 or 28 weeks of gestation or more). With a paucity of population-based studies from LMIC, information about stillbirth rates also remains scarce. The limited surveillance information available highlights that stillbirth rates continue to

be unacceptably high and well above the new international targets of 12 per 1,000 births by the year 2030 (WHO, 2014).

Reported factors associated with stillbirth in LMIC are: maternal age, gestational age, parity, history of previous stillbirth, poor access to quality antenatal and emergency obstetric care, socioeconomic factors and environmental pollution. However, researchers are now also increasingly focusing on obstetric complications, such as abnormal presentation and premature rupture of membranes. Data on risk factors thought to be common in high-income countries, such as obesity, are also beginning to emerge from LMIC.

The most commonly reported causes of stillbirth are maternal disease, fetal conditions and placental conditions. However, an increase has been noted in the reporting of intrapartum causes of stillbirth. The variation in the proportion of stillbirths with unknown cause is wide. A high proportion of stillbirths are reported to occur in the intrapartum period.

Only a few studies systematically use a classification system to categorise the identified cause of stillbirth. Most studies are simply using physical appearance or time of death.

Strengths and limitations of this systematic review

Overall, the quality of evidence was low as most studies were hospital-based and cross-sectional by design. However, with the inclusion of a large body of evidence, it is hoped that the evidence presented will be more generalisable.

Other systematic reviews exploring the cause of or factors associated with stillbirth have been published. However, these have not been updated in this rapidly developing field (McClure et al, 2006; Mario et al, 2007; Pope et al, 2010), or were recently conducted but most data pertains to HIC settings (Conner et al, 2016; Ptacek, 2014). Some focused on a single cause of stillbirth without providing an overview of causes and/or the relevant proportion of stillbirths due to that particular cause of death (Lai et al, 2013; Nan et al, 2015).

As there is still no consistent use of the international definition and inclusion criteria for stillbirths, data from the different studies cannot simply be

included in a meta-analysis. Similarly, as different classification systems are used, data on cause of death cannot automatically be combined.

Interpretation of findings

Many of the factors contributing to stillbirth in LMIC are modifiable. While some factors, such as poor antenatal care and service delivery delays, require improvement in quality of maternal and newborn health services, others (such as education and poverty) will require coordinated action by actors outside the healthcare system to improve the overall wellbeing of mothers.

Similarly, most causes of stillbirth are preventable. With a significant proportion of stillbirths occurring intrapartum, healthcare providers should be encouraged to conduct perinatal death reviews and act to improve the quality of care provided at the time of labour and birth. This includes intermittent fetal heart rate monitoring, identification and management of obstetric emergencies and resuscitation of the baby. This will ensure continuous improvements in the healthcare delivery system.

Many factors contribute to the wide variations in the reported proportions of stillbirth with unknown cause of death. Completeness and accuracy of records plays a major role in the ability of researchers to identify what the underlying cause of death is, as well as the capacity of healthcare facilities to conduct investigations to diagnose underlying diseases. The burden of disease in the population also contributes to this; a cause is more likely to be identified in populations with high disease burden. The most easily modifiable of all factors contributing to the high proportion of stillbirths with unknown cause is improvement in clinical records.

There seems to be confusion in how the terms “cause” and “risk factors” are used. While a cause is a clinical condition that has an established plausible mechanism to cause death, a “risk factor” is typically a maternal or paternal characteristic associated with stillbirth, which does not have a plausible mechanism leading to the death of the baby (McClure et al, 2009).

The frequent use of physical appearance or time of death to categorise stillbirth indicates that LMIC are likely to find the newly launched ICD-PM classification system useful and easy to apply since it requires categorising death by time (ante- or intrapartum) before fetal and maternal causes can

be assigned. To make the application of ICD-PM successful, better and practical methods of establishing time of death are required. This may also help address the problem of the large proportion of stillbirths whose time of death is unknown, as reported by Wilkins et al (Wilkins et al, 2015).

2A.5 Conclusion

Most causes of stillbirth are preventable and a significant proportion occurs during the intrapartum period. Prevention requires multi-level action to provide a better quality of care to all mothers and babies. Perinatal death reviews could provide the much-needed data for focused action. There is an urgent need to encourage and support the rapid adaptation of the ICD-PM classification system to facilitate consistent data collection across LMIC. More research should be focused on studying causes of stillbirth that are least reported, making a clear distinction between cause of and risk factors for stillbirth.

2A.6 Chapter Summary

This chapter has explored the major causes of and factors associated with stillbirth in LMIC. It has also described the classification systems used in those countries.

The review included a high number of papers (165) with a wide geographical distribution. The definition of stillbirth varies, but most developing countries tend to use a higher cut off point, i.e. 28 weeks of gestation or more. The stillbirth rate also varies among countries. The highest stillbirth rates were reported in sub-Saharan Africa and Southeast Asia.

Factors associated with stillbirth in LMIC could be grouped into the following categories: maternal factors, such as age and parity; fetal factors, such as gestational age, birthweight and sex; access to care, particularly antenatal and delivery services; socioeconomic factors, such as family income level, ethnicity and educational status; environmental pollution, such as water and air pollution, and; harmful social habits such as cigarette smoking.

The most frequently attributed causes of stillbirth were maternal diseases (8 - 50%) including hypertensive disorders, syphilis, positive HIV status with low CD4 count, malaria and diabetes. Congenital anomalies were reported to account for 2.1 - 33.3% of stillbirths; placental causes accounted for 7.4 - 42%; asphyxia and birth trauma (3.1 - 25%); umbilical problems (2.9 - 33.3%) amniotic and uterine factors (6.5 - 10.7%). A wide range of proportion of stillbirths remains “unclassified” (3.8 - 57.4%).

Seven different classification systems were identified but they were used in only 22% of studies that could have used a classification system.

In conclusion, there is the need to build capacity for perinatal death audit and make more use of existing guidelines such as the new WHO guidelines (WHO, 2016a). More research should be focused on reporting all categories of cause of stillbirth.

In another systematic review of literature, the next chapter explores classification systems used to categorise cause of stillbirth.

CHAPTER 2B: LITERATURE REVIEW II

2B.1 Introduction & Background

This chapter presents the second systematic review of literature conducted in this PhD programme. While the previous systematic review was aimed mainly at identifying causes of and factors associated with stillbirth in LMIC, this review focuses on summarising existing classification systems that could be used to categorise cause of stillbirth.

The chapter describes why and how the second review was conducted and presents its results. A brief discussion of the review results follows before the conclusion are drawn.

2B.1.1 Justification and objective of this review

Classification systems or frameworks are described as "passive construct systematically arranging similar entities with established criteria or differing characteristics" (Froen et al, 2009). To systematically and comprehensively extract relevant information from clinical records and/or verbal autopsy data to assign cause of death and contributing factors for each case of stillbirth reviewed, the use of standardised classification systems is very helpful. Such systems should also allow for uniform use of terminology and comparison within and between settings. It would be helpful to have an agreed classification system that can be applied across multiple settings to allow for comparability of findings.

Presently, there is a wide variety of classification systems used to categorise cause of perinatal death. Most of these classification systems show poor comparability (Lawn et al, 2011) and consistently report about two-thirds of stillbirths as "unexplained" or "cause unknown" (Gardosi et al, 2005). Some of the systems cannot be recommended for classification of cause of stillbirth as they were not designed for this and others are considered difficult to apply and have been reported to have high inter-observer variability (Flenady et al, 2009). Most systems were developed based on data from high-income countries. Thus, information required to use them successfully may not be available in low-resource settings.

In some countries with a high stillbirth rate, perinatal death audit has been introduced, but classification systems are rarely used during this process (Aminu et al, 2014). This is in part, at least, because it is difficult to know which of the classification systems is best suited to the local or national setting or healthcare level and partly because of lack of knowledge and understanding of often complex classification systems. Given that diagnostic and management pathways in most low-resource settings are different to those in high-income countries, it is also important to understand the minimum information required to be able to apply any of the systems.

As there was no comprehensive review of the available classification systems for stillbirth, this systematic review was conducted to identify and describe existing classification systems used to categorise cause of stillbirth. The advantages and limitations of each classification system were evaluated to provide healthcare providers and policy makers with information to enable informed choice of classification systems that are most appropriate in their setting, maternity unit, region or country.

2B.1.2 The ideal classification system for stillbirth

Preferably, a classification framework for stillbirth should have the following characteristics:

1) It should be structured to allow unambiguous allocation of cause of appropriate cause of death (Korteweg et al, 2006).
2) Use clear and uniform guidelines to allow comparisons within and across different settings (Korteweg et al, 2006).
3) Ability to retain important information about the death (Flenady et al, 2009).
4) It should be easy to use with low inter-observer variability (Flenady et al, 2009).
5) It should produce low proportion of stillbirths as unexplained.
6) There should be room for possible future amendments without disturbing the system (Korteweg et al, 2006).

2B.2 Methods (For Systematic Review)

2B.2.1 Search strategy and search terms

A review protocol was developed to guide the search for publications and define the inclusion and exclusion criteria.

Electronic databases (MEDLINE, CINAHL Plus, Global Health, Science Direct and Scopus) were searched for existing stillbirth or perinatal death classification systems published in English between 1950 (the period just before the first recorded classification system for stillbirth was published) and 2016 (inclusive).

The search terms (stillbirth OR "perinatal mortality") AND classification AND (system OR framework) were used to identify publications on classification systems and/or publications on cause of stillbirth and perinatal death that documented the use of a classification system. References of all identified relevant publications were hand-searched in a snowball fashion to find additional papers or documents (Figure 2B.1).

2B.2.2 Inclusion and exclusion criteria

We defined a classification system as any method of categorising cause of stillbirth. All published classification systems for stillbirth or perinatal death were included. Systems that were designed exclusively for neonatal, infant or general mortality were excluded. Decisions to include or exclude publications were made by the principal investigator, but closely checked by both supervisors. Disagreements were settled through consensus.

2B.2.3 Data extraction

All identified classification systems that met the inclusion criteria were obtained in their full electronic or printed versions, and reviewed. Using a pre-designed summary table, relevant information was extracted, and this was cross-checked by both supervisors. Information captured included: where and how the classification systems were first developed, and used, the major categories used in the classification system, type and range of information required for application and proportion of deaths reported as unknown. Where known, the number and distribution of identified cause of

stillbirths documented with the first application of the system were noted (Appendix 2).

2B.2.4 Assessment criteria and analysis

We assessed the applicability and ease of use of each system based on information requirements, proportion of unknown cause of stillbirth and overall complexity determined by exploring the structure of and terminology used in the systems.

Three criteria were used to assess each classification system:

i) Information requirement: Assessed by the depth of clinical information required to apply the system, including any special tests required for certain diagnoses;
ii) Proportion of stillbirths reported as unknown (or unclassified) by the authors of the system and;
iii) Complexity: Assessed by the number of categories and sub-categories and their hierarchical relationships within each system, use of terminology in the categories and sub-categories.

Studies were categorised by year of publication, their scope (stillbirths only or perinatal mortality) and level of complexity (as defined above). Narrative synthesis was used to report our findings.

2B.3 Results

A total of 118 documents were identified and screened, out of which 31 unique classification systems were included (Figure 2B.1).

2B.3.1 Development of classification frameworks

The included classification systems were published between 1954 and 2016. Only six of these were designed specifically for stillbirth (Gardosi et al, 2005; Hovatta et al, 1983; Fretts et al, 1992; Dudley et al, 2010; Varli et al, 2008; Reddy et al, 2009). Fourteen of the classification systems were designed to include perinatal mortality, three included neonatal death, two included infant mortality and one included “late abortions” (Whitfield et al, 1986).

The systems were developed and first applied using stillbirth data from a variety of settings, mostly regions with relatively low stillbirth rates (Figure

2B.2): Europe [16], Australasia [3], Scandinavia [3], North America [4], Africa [1], mixed locations [2] and from consensus [2].

Of the 31 systems included, 17 were developed using hospital data; six systems (WHO, 2004; Chan et al, 2004; PSANZ-PDC, 2009; Frøen, 2009; Reddy et al, 2009; WHO, 2016b) were developed through conference or expert consensus; five were modifications of previously developed systems (Baird & Thomson, 1969; CESDI, 2001; Hey et al, 1986; Cole et al, 1986; Keeling et al, 1989) and; three used data from surveys (Butler & Bonham, 1963; Cole et al, 1989; Alberman et al, 1994).

The studies' population sizes describing development of the system and/or first application varied and ranged from 239 (WHO, 2004) to 15,251 (Knutzen et al, 1975). Generally, the sample size of the studies was much higher in earlier compared to more recent studies.

Figure 2B.1: Flow chart showing process for selection of included studies

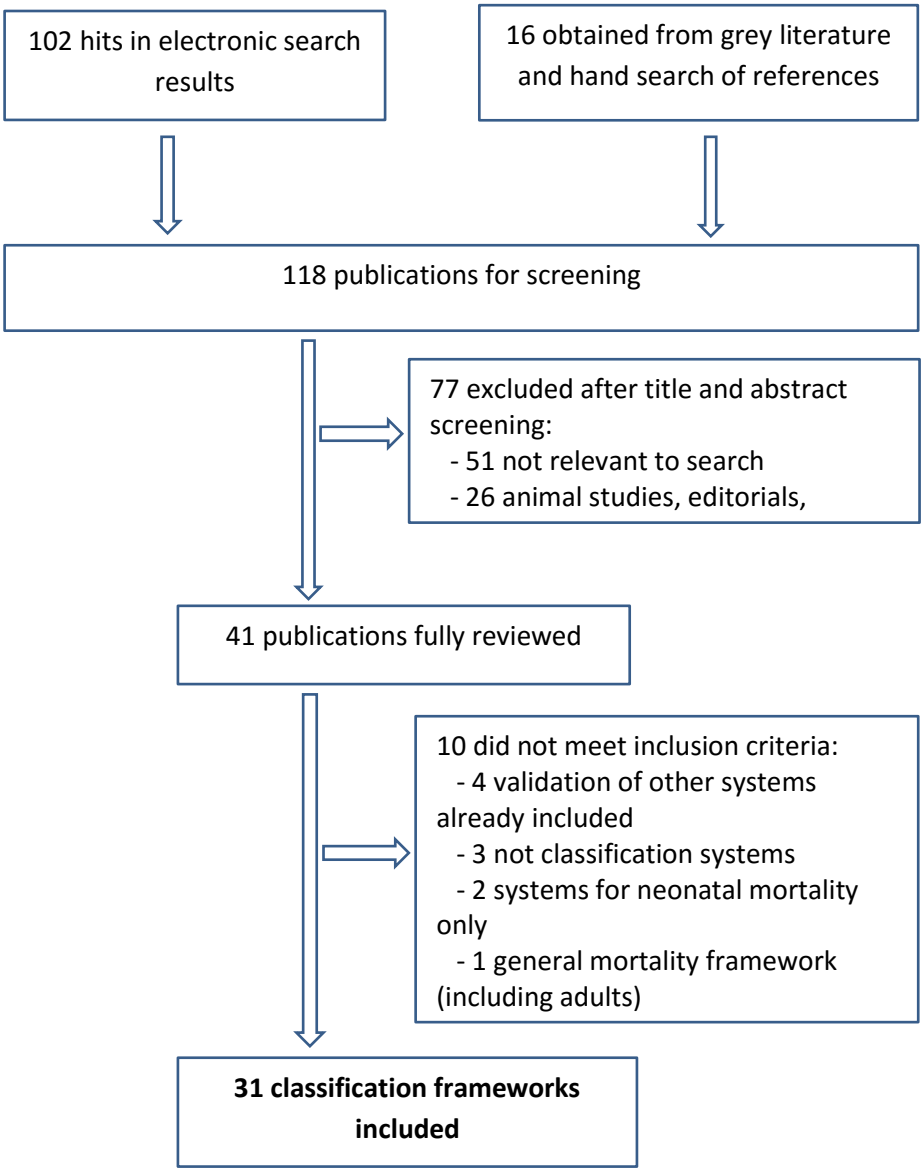
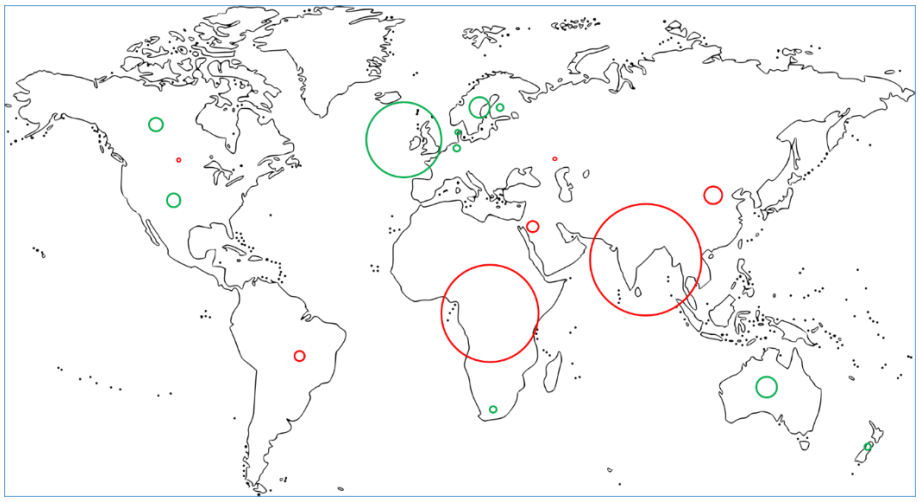


Figure 2B.2: Map showing global distribution of stillbirth (red circles; source: Lawn et al, 2011) and settings where classification systems were developed (green circles)



*Size of circles indicates stillbirth burden (red) or number of classification systems (green).

2B.3.2 Information requirement for application

Table 2B.1 summarises the type of information required to be able to apply each of the classification systems. In general, a clear majority of systems require information that would need to be obtained from comprehensive clinical records to be able to assign the cause of death and to identify factors associated with death or contribution conditions (but which are not the underlying cause of death).

Many of the systems reviewed, including ReCoDe (Gardosi et al, 2005), INCODE (Dudley et al, 2010) and TULIP (Korteweg et al, 2006) have categories that may require histological evidence to support certain diagnoses. INCODE has sub-categories for congenital abnormalities for various body systems – diagnosis of which may require a post-mortem. In addition, some systems may require chromosomal assays to enable a final diagnosis to be made (Keeling et al, 1989; Korteweg et al, 2006). In two of the systems, a specific, computerised system and programme for recording patient information was used in the development of the system and such a system may also be required for the application of the systems (Winbo et al, 1997; Winbo et al, 1998). The new ICD-PM (WHO, 2016b) was developed to allow for minimal data requirement and requires fewer clinical details compared to some other recently developed classification systems.

However, some systems such as Keeling et al, Langhoff-Roos et al and Korteweg et al require a substantial amount of detail for their application (Keeling et al, 1989; Langhoff-Roos et al, 1996; Korteweg et al, 2006).

Table 2B.1: Classification systems and the type of information required to assign cause of death and contributing factors

Classification System			Complexity			Source and type of information required to use classification system			
Name / Publication Title	***Authors***	***Year of development first publication or use***	***Scope***	***No. of main categories***	***No. of levels***	***Clinical records***	***Full Autopsy***	***Histological Autopsy***	***Other requirements***
Aberdeen classification	Baird	1954	Perinatal	8	1	√			Accurate gestational age or birth weight
Classification of causes of perinatal mortality	Bound et al	1956	Perinatal	11	1	√	√	√	
British Perinatal Mortality Survey - First Report	Butler and Bonham	1963	Perinatal	9	1	√	√		
Amended Aberdeen	Baird and Thomson	1969	Perinatal	10	2	√	√		
A clinical classification of the mechanisms of perinatal wastage	Low et al	1970	Perinatal	8	1	√			
Clinical classification of perinatal deaths	Knutzen et al	1975	Perinatal	8	1	√			

Classification System			Complexity			Source and type of information required to use classification system			
Name / Publication Title	***Authors***	***Year of development first publication or use***	***Scope***	***No. of main categories***	***No. of levels***	***Clinical records***	***Full Autopsy***	***Histological Autopsy***	***Other requirements***
Perinatal death: audit and classification	Chang et al	1979	Perinatal	15	3	√			
Wigglesworth	Wigglesworth	1980	Perinatal	5	1	√			
Causes of stillbirth: a clinico-pathological study of 243 patients	Hovatta et al	1983	Stillbirth	10	2	√	√		Serum enzymes assay; oral glucose tolerance test
Classifying perinatal death: fetal and neonatal factors	Hey, Lloyd and Wigglesworth	1986	Perinatal	11	2	√	√		
Perinatally related waste - a proposed classification of primary obstetric factors	Whitfield et al	1986	Perinatal	12	1	√	√		
Classifying perinatal death: an obstetric approach	Cole et al	1986	Perinatal	10	2	√			Rhesus compatibility test
International Collaborative Effort (ICE)	Cole et al	1989	Perinatal	8	1	√			
Classification of perinatal death	Keeling et al	1989	Perinatal	5	1	√	√	√	Chromosomal assay
Classification of Primary Cause of Fetal Death	Fretts et al	1992	Stillbirth	10	1	√	√	√	

Classification System			Complexity			Source and type of information required to use classification system			
Name / Publication Title	***Authors***	***Year of development first publication or use***	***Scope***	***No. of main categories***	***No. of levels***	***Clinical records***	***Full Autopsy***	***Histological Autopsy***	***Other requirements***
A new hierarchical classification of causes of infant deaths in England and Wales	Alberman et al	1994	Perinatal	9	1	√			
Nordic-Baltic	Langhoff-Roos et al	1996	Perinatal	13	1	√			Accurate gestational age
A computer-based method of cause of death classification in stillbirths and neonatal deaths	Winbo et al	1997	Perinatal	6	1	√			Computerised record system
Neonatal and Intrauterine Death Classification according to Etiology (NICE)	Winbo et al	1998	Perinatal	13	1	√			Computerised record system
Extended Wigglesworth	CESDI	2001				√			
Evaluation of 239 cases of perinatal death using a fundamental classification system	de Galan-Roosen et al	2002	Perinatal	7	2	√			
ICD-10	WHO	2004				√			
Perinatal Society of Australia and New Zealand - Perinatal Death Classification (PSANZ-PDC)	Chan et al	2004	Perinatal	11	1	√			

Classification System			Complexity			Source and type of information required to use classification system			
Name / Publication Title	***Authors***	***Year of development first publication or use***	***Scope***	***No. of main categories***	***No. of levels***	***Clinical records***	***Full Autopsy***	***Histological Autopsy***	***Other requirements***
Relevant Condition at Death (ReCoDe)	Gardosi et al	2005	Stillbirth	9	1	√	√		
Tulip	Korteweg et al	2006	Perinatal	6	2	√	√	√	Chromosomal assay
Stockholm classification of stillbirth	Varli et al	2008	Stillbirth	17	2	√			
National Institute of Child Health and Human Development (NICHHD)	Reddy et al	2009	Stillbirth	15	2	√			
Causes of death and associated conditions (CODAC) / Simplified CODAC	Frøen et al	2009	Perinatal	10	1	√			
Perinatal Society of Australia and New Zealand - Perinatal Death Classification (PSANZ-PDC) - Version 2.2	PSANZ	2009	Perinatal	11	3	√			
Initial Causes of Fetal Death (INCODE)	Dudley et al	2010	Stillbirth	6	1	√	√	√	Interview with mother/parents
ICD-PM	WHO	2016	Perinatal	3	3	√			

2B.3.3 Proportion of deaths with unknown cause

Table 2B.2 summarises the proportion of deaths reported as unknown and/or unclassified for each classification system at the time of the development and first application of the system. Only classification systems which reported proportion of unknown and/or unclassified cause of death were summarised (16 of 31). The lowest reported percentage of unknown cause of death was reported using the Nordic-Baltic classification (Langhoff-Roos et al, 1996) which reported 0.39% of deaths as cause unknown. The highest reported proportion of unknown cause of death was noted with application of the system by Keeling et al which reported 46.4% of stillbirths analysed as cause of death unknown (Keeling et al, 1989).

Generally, a decrease was noted in the proportion of stillbirths that remain classified as unexplained or unknown as new classification frameworks were developed over time.

Table 2B.2: Proportion of deaths reported as unknown or unclassified

Publication	Proportion unknown / unclassified (%)
Langhoff-Roos et al, 1996	< 1
Whitfield et al, 1986; Cole et al, 1986; Alberman, 1994; Winbo et al, 1997	< 5
Hovatta et al, 1983; de Galan-Roosen et al, 2002	5 – 10
Gardosi et al, 2005; Korteweg et al, 2006; Varli et al, 2008	11 – 20
Chang et al, 1979; Fretts et al, 1992	21 – 30
Baird et al, 1954	31 – 40
Knutzen et al, 1975; Winbo et al, 1998; Keeling et al, 1989	41 – 50

2B.3.4 Structural and terminological complexity

The more recently developed classification systems, such as the Stockholm classification (Varli et al, 2008), PSANZ-PDC (2009), and NICHHD (Reddy et al, 2009) have comprehensive provision for a wide range of categories, covering

most of the possible causes of death; (Table 2B.1). There were a few earlier systems, such as Chang et al, with a wide range of categories (Chang et al, 1979).

The category for unexplained deaths was absent in some of the systems, such as in Low et al (1970). However, some have too many different sub-levels for each category (Chang et al, 1979).

2B.3.5 Other key points

Many classification systems were developed using data from a large number and proportion of all recorded stillbirths in the populations studied, thus ensuring that the results are representative of the population and are, therefore, likely to be more generalisable in the settings for which these systems were developed (Gardosi et al, 2005; Dudley et al, 2010; Froen et al, 2009; Butler & Bonham, 1963; Winbo et al, 1997; Chang et al, 1979; Whitfield et al, 1986; Bound et al, 1956a; Bound et al, 1956b).

One system (Whitfield et al, 1986) was developed to be used for all "perinatally-related wastages", including late abortions. This has the advantage of presenting an opportunity to use a single system across many stages of pregnancy, although it is also complex to use and the terminology is outdated.

The use of highly inclusive definitions of stillbirth, such as "fetal losses from 16 completed weeks of gestation" (Tulip; Korteweg et al, 2006), or inclusion of "late abortions" in the case definition (Whitfield et al, 1986), may make application of systems more difficult where there is a lack of information about gestational age at time of death and/or birth.

2B.4 Discussion

This review was conducted to summarise existing classification systems used to assign cause of, and factors contributing, to stillbirth. The focus on papers published in the English language may have limited the number of papers included in the review. However, this may have been partly compensated for when the snowball approach was used to specifically search for papers found in references of other papers, which may otherwise have been missed through keyword searches.

Recently, some publications exploring classification of stillbirth have been published, but none focused on reviewing previous classification systems with a view to understanding how the systems have changed over the years, which could guide discussions on how best to approach the classification of stillbirth. However, a recent systematic review was conducted to summarise key features to classification systems for both stillbirths and neonatal deaths, but it was limited to the five-year period of 2009 to 2014 (Leisher et al, 2016). Even though they reported an overall higher number of classification systems, only 55 classification systems included stillbirth, which is less than the 118 we found in our review. Another study used Delphi method to establish a consensus on the important characteristics of ICD-PM (Wojcieszek et al, 2016).

Although focused on stillbirth only, this review offers a comprehensive summary of classification systems and their characteristics. It is hoped that it will help inform discussions on how best to approach the often-difficult task of assigning cause of, and factors contributing to, stillbirth during perinatal death reviews. In addition, we sought to provide clarity on which classification systems could be used in a standardised manner to provide comparable data across a variety of settings. These findings highlight that the type and range of information required to apply any of the existing systems may not be available in low- and middle-income countries where most stillbirths occur. This will require increased efforts to improve data collection and use as well as strengthening of perinatal death audit processes in these settings.

Cause of death and contributing factors

"Cause of death" and "contributing factors" are different. While "cause" refers to conditions that have a clear causal relationship with death, contributing factors refer to factors that are unlikely to have caused death directly but may have contributed to death. The new application of the International Classification of Death to deaths during pregnancy, childbirth and the puerperium (ICD-MM; WHO, 2012) was used to clarify this for maternal death and a similar approach was taken in case of perinatal deaths (McClure et al, 2009; WHO, 2016b). In this review, it was found that both

terminologies were still used erroneously and interchangeably by many authors.

Traditionally, classification systems were developed to address the specific disease pattern and practice in a population. However, only one classification system was developed using data from a middle-income country (South Africa) (Knutzen et al, 1975). Cause of death and associated conditions (CODAC) was developed with data included from two middle-income countries (Malaysia and South Africa) out of the seven countries included in the study (Froen et al, 2009). ICD-PM was developed with data from a middle-income country (South Africa) representing less than 10% of the overall data, while a high-income country (UK) represented over 90% of the overall data used to develop this system (WHO, 2016b). All other classification systems were developed using information pertaining to stillbirth data from high-income settings. There is likely to be a difference in distribution and range of causes of and factors contributing to stillbirth in low- compared to high-income countries. While a large proportion of stillbirths in low resources settings is associated with challenges in providing care for obstetric emergencies, maternal infections and fetal growth restriction (Aminu et al, 2014; Lawn et al, 2011), stillbirths in high-income countries are more often related to congenital abnormalities and factors such as obesity, smoking and advanced maternal age (Flenady et al, 2011).

Earlier systems generally included a category for stillbirth due to isoimmunisation. The absence of this category in more recent systems could be due to the improvement in antenatal care, particularly in high-income countries, where such cases are detected early and preventive measures taken to avoid adverse outcome.

The proportion of deaths for which a clear cause of death cannot be determined is important in any classification system. Generally, the proportion of stillbirths that remain unexplained or unknown has decreased as new classification systems were developed over time. This has been attributed mainly to improvements in the availability, range and use of diagnostic tests in countries where these classification systems were developed and used, as well as improvements in record keeping and in the

amount and detail of clinical information available in cases of stillbirths. Furthermore, the change in structure of classification systems, particularly the provision of more categories to accommodate more diagnoses, may have contributed to the reduction in the proportion of stillbirths categorised as unknown cause of death in more recent classification systems. The proportion of unexplained stillbirths also depends on the population upon which a classification system is applied, as cause of death is more likely to be found in populations with generally high disease burden.

Structure and complexity of classification systems

The structure and level of complexity of classification systems is potentially a limiting factor with regard to feasibility of application of the system. In many low-resource settings, mortality reviews are conducted by healthcare providers and managers with basic midwifery knowledge and skills (Ameh et al, 2014). The success of a system in such settings will, therefore, be dependent on how easy it is to understand and apply.

The simplicity of earlier systems, such as the Aberdeen classification (Baird et al, 1954), made these easy to use, but this is often at the expense of accurate assignment of a cause of death or may provide limited or no information on contributing factors. This would not support in-depth review and may not optimally allow healthcare providers to identify preventable factors or cause of death. Systems with less technical, simpler terminology, such as the Nordic-Baltic (Langhoff-Roos, 1996) and ReCoDe classifications (Gardosi et al, 2005), are easier to apply and more likely to be used consistently across settings, resulting in lower inter-observer variability.

Systems requiring a high level of detail (Keeling et al, 1989; Korteweg et al, 2006; Langhoff-Roos, 1996) may, in theory, have the advantage of being more accurate, but the feasibility of applying them in low resource settings, where such details simply do not exist, may be a major limitation with regard to recommendation for more global use.

The range of causes of stillbirth that are recognised and can be assigned has expanded over the years. More recently proposed systems tend to be more specific, with many more potential causes of stillbirth included. However, this has also led to the introduction of more sub-categories, making

classification systems more complex, which could increase inter-observer variability. The application of such systems may be particularly difficult in low- and middle-income countries where non-specialist healthcare workers provide the majority of maternal and newborn health care (Ameh et al, 2014; Owolabi et al, 2014). If these more complex systems are to be applied, it will require healthcare providers to be trained to understand how to apply such systems. In addition, patient records will need to be improved to ensure information required to apply the classification systems is documented and available at time of review.

Classification systems without a category for unexplained stillbirth present a challenge as it must be assumed that there will always be a proportion of deaths where cause of death cannot be ascertained and it is not clear how such cases could be included in aggregated information on stillbirths (i.e. those cases would presumably be unaccounted for or treated as "missing data") (Low et al, 1970). Having too many sub-categories as in Chang et al makes a system cumbersome to use and subject to higher inter-observer variability (Chang et al, 1979).

Although a broader, comprehensive system including all or most of the possible causes of death may be expected to result in a smaller proportion of deaths that are classified as unexplained or unknown, in practice, this is not always so. For example, despite the many categories and sub-categories of the system by Chang et al (Chang et al, 1979), 26.3% of stillbirths remained as unexplained. Similarly, the NICE classification has detailed provisions for almost all possible causes of perinatal death imaginable, but has reported up to 43.6% of perinatal deaths as unexplained (Winbo et al, 1998). We suggest that the availability of detailed clinical information and records is most likely the most important factor determining ability to assign a clear cause of death and apply any classification system, and that a broad and complex system in itself is insufficient.

Histological examination and autopsy

About a third (11/31) of classification systems include information that needs to be obtained via histological examination of tissue and/or autopsy. Although such information is not a requirement per se, the availability of this

information provides more clarity on cause of death and contributing factors. This is more often included in more recent systems that tend to move towards more accurate diagnoses involving histological and chromosomal examinations. However, autopsies are rarely conducted in low- and middle-income countries and pathology services are not usually available. For these settings, there should be a strong focus on obtaining as much clinical information as possible to help identify cause of death related to obstetric and maternal complications. Since perinatal (including stillbirth) audits are conducted to identify potentially avoidable priority areas for intervention and improvement in quality of care (Whitfield, 1986), it should be possible to at least identify factors contributing to, or associated with, stillbirth, even if a clear underlying cause of death cannot be assigned with certainty.

Recent systems rely on very specific patient details and laboratory investigations to enable increasingly more accurate diagnoses to be made. This means that in addition to ensuring detailed case notes are kept and are available and used for review, there is a need to improve healthcare providers' knowledge and understanding regarding causal pathways and aetiology of stillbirth. Information obtained via perinatal death or stillbirth review should also inform the care pathway for women and their partners who have had a stillbirth. This should include debriefing, support services (where available) and counselling for future pregnancies. Such support is still not available to most women who have had a stillbirth.

2B.5 Chapter Summary / Conclusion

The current stillbirth classification systems were designed to suit specific, population, disease pattern and needs, and this, at least in part, explains the variation in approach. There is currently no single agreed system that will suit every purpose and setting. If a classification system is to be applied successfully in low resource settings during stillbirth or perinatal death audit or review, it should strike a balance between details of information required, proportion of deaths for which a cause of death can be assigned and ease of use.

A layered classification system, such as the ICD-PM, that allows classification to a broad as well as more detailed level in a systematic manner is perhaps the most useful as it will allow for comparison within and between settings at least with regard to the main types and causes of stillbirth.

CHAPTER 3: METHODOLOGY

3.1 Introduction

To explore current literature on cause of, factors associated with, and classification systems used for stillbirth (objective 1), two systematic reviews were conducted on cause of stillbirth and classification systems used to categorise the cause. Methods used in the systematic reviews have been presented in Chapter 2 (Literature Review).

To assess cause of death (objective 2), classify the cause of death (objective 3), assess quality of care provided to mothers (objective 4) and formulate recommendations (objective 5), a descriptive cross-sectional study was conducted.

This chapter describes the methods used to conduct the study and achieve Objectives 2, 3, 4 and 5. It begins with definition of terms commonly used throughout the study; methods of data collection and analyses are described according to the objectives of the study. A description of how the sample size was obtained is then provided. Measures to ensure integrity and quality of the data is also described. Finally, ethical issues considered in the study are provided.

3.2 Definitions of Key Terms

Stillbirth: Stillbirth is the birth of a baby at ≥ 22 weeks of gestation or with birth weight of ≥ 500g or body length of ≥ 25cm who died before or during labour and birth. For international comparisons, stillbirth is a baby born dead at ≥ 28 weeks of gestation, or birth weight of ≥ 1000 g, or a body length of ≥ 35cm (WHO, 2004; Froen et al, 2011). In this study, the latter definition was used.

Stillbirth Rate: Stillbirth rate is the number of stillbirths per every 1,000 total births (live births + stillbirths).

Factor Associated with Stillbirth: A maternal/paternal characteristic is considered to be a risk factor for stillbirth when it is associated with stillbirth

but without an obvious causal relationship with the stillbirth (McClure et al, 2009).

Cause of Stillbirth: A cause of stillbirth is "any condition with a plausible mechanism likely to lead to the death of the fetus" (McClure et al, 2009).

Low-Income Country: A country with gross national income (GNI) per capita of $1,025 or less (World Bank, 2017).

Lower Middle-Income Country: A country with GNI per capita of $1,026 - $4,035 (World Bank, 2017).

Upper Middle-Income Country: A country with GNI per capita of $4,036 - $12,475 (World Bank, 2017).

High-Income Country: A country with GNI per capita of $12,476 or more (World Bank, 2017).

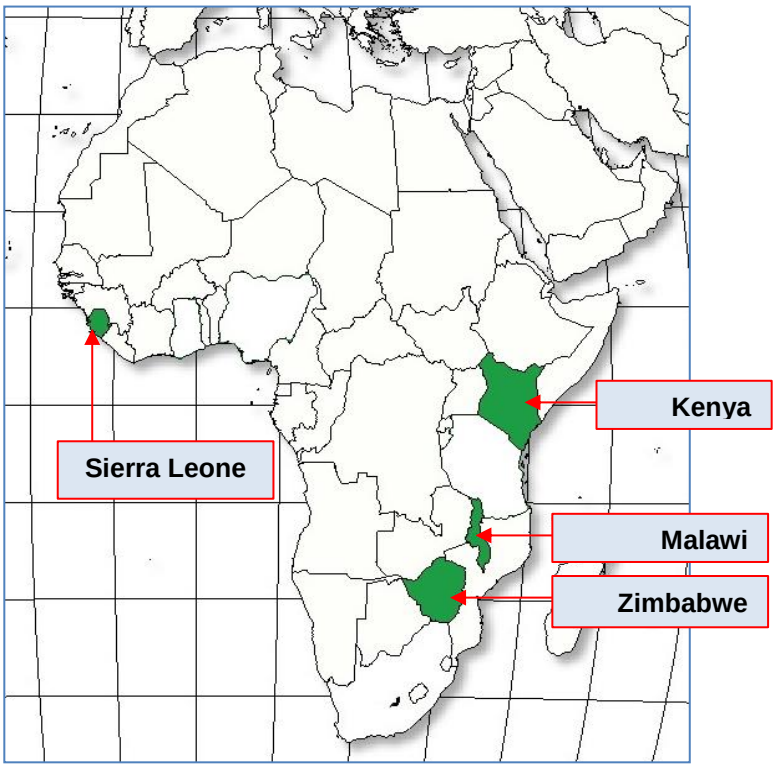
3.3 Methods

To achieve Objectives 2, 3, 4 and 5, a cross-sectional study was conducted. A cross-sectional study design was chosen because it offers a comparatively quick way to assess the causes of stillbirth and quality of care provided to mothers in the targeted countries. The methods are presented here following the STROBE guidelines for reporting cross-sectional studies.

3.3.1 Study settings

The study was conducted in four countries: Kenya, Malawi, Sierra Leone and Zimbabwe (Figure 3.1). The countries were part of the 'Making it Happen' (MiH) programme, which aimed to increase availability and to improve quality of Emergency Obstetric Care (EmOC) and early Newborn Care (NC). The MiH programme consisted of several components including trainings on quality improvement using audits. As part of the quality improvement package of the programme, perinatal death audit was introduced in the study countries.

Figure 3.1: Countries included in the study



These countries were selected for their poor maternal and newborn health indicators (Table 3.1). According to the demographic and health survey (DHS), maternal mortality ratio is generally high in all the four countries in this study; highest ratio of 1,165 per 100,000 live births reported from Sierra Leone (Table 3.1). Similarly, population perinatal mortality rate in all the countries was high, and Sierra Leone had the highest rate. Surprisingly, high proportions of mothers receive antenatal and delivery care from a skilled provider. However, there seems to be a larger service delivery gap for mothers in the postnatal period, with lowest proportion of mothers who receive postnatal checkup in the first two days after birth reported from Malawi (42.6%) and highest in Zimbabwe (73.4%). It should be noted that the DHS sampled from women who had live births only, excluding those who had stillbirth – the subject of this study.

Table 3.1: Key economic and health indicators for countries in the study

Indicator	Kenya (DHS, 2014)	Malawi (DHS, 2017)	Sierra Leone (DHS, 2013)	Zimbabwe (DHS, 2015)
Population (millions)	46.05	17.22	6.45	15.60
Gross national income per capita	$1,340*	$340*	$620*	$860*
Maternal mortality ratio (per 100,000 live births)	362	439	1,165	651
Perinatal mortality rate (per 1,000 pregnancies**)	29	35	39	34
HIV prevalence	6.0%	8.8%	2.0%	9.6%
Facility deliveries	61.0%	91.0%	54.0%	77.0%
Women (with a live birth) who received ANC	96.3%	94.8%	97.1%	93.3%
Women (with a live birth) who delivered with SBA	66.7%	90.4%	62.4%	80.6%
Women (with a live birth) who received PNC	54.2%	42.6%	72.3%	73.4%

* World Bank data (2015); ANC=antenatal care; SBA=skilled birth attendant; PNC=postnatal care

** "of 7 or more months' pregnancies", as described in the DHS reports.

Malaria is endemic in all the settings of this study, except in one facility in Zimbabwe, where annual parasite incidence was reported to be zero (DHS Zimbabwe, 2015). In Kenya, one facility served a population with low prevalence of malaria (1% – 5%), while the other two had prevalence of 20% – 40% (DHS Kenya, 2014). All the facilities targeted in this study in Malawi and Sierra Leone were in highly endemic malaria zones.

Data was collected from a total of 12 health facilities, selected purposively based on their high numbers of stillbirth in the MiH baseline survey. All the health facilities provided comprehensive emergency obstetric care (CEmOC) services. However, while the facilities in Kenya and Zimbabwe were tertiary, the facilities in Malawi and Sierra Leone were more at a secondary level, except Bwaila Hospital in Malawi, which was a major referral hospital.

I selected health facilities purposively based on their high numbers of stillbirth obtained from the "Making it Happen" monitoring and evaluation data:

- **Kenya (3 facilities)**:
    1) Jaramogi Oginga Odinga Teaching and Referral Hospital
    2) Kakamega Provincial Hospital
    3) Thika Level Five Hospital
- **Malawi (4 facilities)**:
    1) Bwaila Hospital
    2) Mulanje District Hospital
    3) Mwanza District Hospital
    4) Neno District Hospital

Bwaila Hospital was added later in the study when numbers of stillbirths from the other three facilities were found to be much lower than anticipated.

- **Sierra Leone (2 facilities)**:
    1) Bo Referral Hospital
    2) Makeni Government Hospital

Initially, I also selected another hospital (Lumley Government Hospital), but it was dropped out of the study due to lack of records for cases of stillbirth – all files were burnt down to contain the spread of Ebola virus during the outbreak of 2014/2015.

- **Zimbabwe (3 facilities)**:
    1) Harare Central Hospital
    2) Mpilo Central Hospital
    3) Parirenyatwa Hospital

3.3.2 Participants' eligibility criteria

Stillbirths: All babies born dead at 28 weeks' gestation or more, or birth weight of 1000 g or more, or a body length of 35 cm or more (WHO definition of stillbirth for international comparison; WHO, 2004; Froen et al, 2011).

Healthcare providers: Various cadres of healthcare providers involved in the delivery of maternal and newborn health services in their health facilities. These comprised of doctors, midwives, nurses, clinical officers who reviewed cases of stillbirth within the study countries.

Expert reviewers: Various cadres of healthcare professionals with advanced knowledge and skills in the field of maternal and newborn health, as well as international experience. These comprised of obstetricians, paediatricians, midwives and public health professionals who reviewed cases of stillbirth in Liverpool.

3.3.3 Data collection

I first informed and visited the reproductive health coordinators of the participating districts as well as the heads of the facilities and informed them about the study. In each health facility, I trained a team of eight to twelve healthcare workers – a total of 115 staff (midwives, nurses, doctors and other cadres of clinicians) – involved in provision of maternal and newborn care were trained to conduct perinatal death audit. Among the trained staff, I selected 33 who showed better grasp of the concept and were willing to take part in the review.

Identification of stillbirths

Starting from January 2015, all stillbirths identified sequentially from facility registers were included in the study until a predetermined sample size was reached (sampling is described in Section 3.3.5). I participated in the identification of cases from delivery registers, theatre registers and midwives' handover notes. Where these documents were deemed incomplete or inaccurate, the data collection team went through all patients records in the study period to identify cases of stillbirths.

Data collection process

In each country, I divided the sample between the selected facilities based on their numbers of births. Data was collected prospectively from patient records and facility registers using a specially designed data collection tool

(Appendix 3). I designed the tool by cross referencing of contents of perinatal death audit forms from different countries with results of literature review and existing classification systems. The tool was then checked and tested for feasibility by asking 22 healthcare workers from the participating countries to crosscheck it and give feedback, which was used to update the tool.

I personally took part (with healthcare providers) in the data extraction from available records and reviewed 758 (60%) of the included cases. Data collected comprised of date of delivery, maternal sociodemographic characteristics, pregnancy details, obstetric and medical history, baby's characteristics (sex, weight, and multiple gestation), cause of death (primary and secondary) and possible risk factors associated with the death. Other variables required for use as denominators in calculation of rates (such as total deliveries) were collected from labour ward and theatre registers.

I designed and used a facility assessment tool (Appendix 4) to collect basic information about the participating facilities (including facility level, signal functions available and any other relevant information) to obtain contextual background information for use in discussing the findings.

3.3.4 Outcomes

Primary outcomes:

- Distribution of causes of stillbirth by method of assessment and by country.
- Categories of causes of stillbirth according to ReCoDe and ICD-PM classification systems.
- Gaps in care provided to mothers identified via stillbirth audit.

Secondary outcome:

- Recommendations for the improvement of stillbirth audit process and classification; improvement of quality of maternal and newborn health services, and; areas of focus for future research.

3.3.5 Sample size

Based on data from the MiH baseline survey, I estimated that a total of about one thousand nine hundred (1,900) stillbirths would be recorded during the anticipated data collection period, with the following breakdown:

- Kenya: 450
- Malawi: 300
- Sierra Leone: 450
- Zimbabwe: 700

This information helped me to determine whether the study would be feasible within the estimated timeframe.

Using the '*StatCalc*' function in Epi Info (Version 7), I estimated that, at 95% confidence level, a total of **279 stillbirths** were required as the sample size in each country when the variable parameters were set as follows:

- Population: Kenya=42,000,000; Malawi=15,500,000; Sierra Leone=6,000,000 and Zimbabwe=6,800,000 (UNFPA data, 2014)
- Expected frequency = 3%
- Confidence limits = 2%
- Clusters = 3

However, I rounded up the sample to **300 per country,** making a total sample of **1,200 cases of stillbirth.** In each country, I divided the sample between the selected facilities based on their numbers of births from existing data.

3.3.6 Analyses

Statistical analyses are described in the individual sections for fulfilling each objective (below).

3.4 Fulfilling Objectives

3.4.1 Fulfilling Objective 2 (Assessing cause of stillbirth)

Cause of death was assessed using three methods as summarised in Figure 3.2:

Figure 3.2: Gantt chart showing time sequence for cause of death (CoD) assessment and classification

ACTIVITY	2015				2016			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Data extraction with HCPs								
Assessment of CoD with HCPs								
Assessment of CoD by expert panel								
Assessment of CoD with computer algorithms								
Classification of CoD by all 3 methods (by PI)								

1) Healthcare providers (HCPs)

I organised a workshop with the trained healthcare providers in each of the participating hospitals. During the workshops, the HCPs and I reviewed cases of stillbirth in batches within one month of death, and captured information from patient records and hospital registers into the specially designed data collection tool – I personally took part in the identification of 1,037 cases (82%), and participated in the review of 758 (60%) of the cases included in the analysis. Through group consensus, the HCPs and I then assigned the most likely cause of stillbirth, other possible cause(s) of stillbirth and modifiable factors which may or may not have made a difference to perinatal outcome.

In cases with multiple possible causes of death, we ranked the causes in order of likelihood of causing death.

2) Expert panel

The completed forms from all participating hospitals were reviewed by a group of eight experts in maternal and newborn health (midwives, doctors, obstetricians and a paediatrician).

I organised series a workshop with the expert panel where I introduced the study. Over several months, each case was reviewed by at least one expert who assigned the most likely cause of death. These were considered as the reference standards. I randomly selected one-quarter of the sample (324) for review by a second expert reviewer to observe inter-observer variations. Differences noted in 91 cases (31.5%) were resolved through consensus.

I obtained the proportion of cases for second review using Epi Info® (Version 7.2.0.1; CDC, 2016) by assuming 50% expected frequency of disagreement (to yield maximum sample) at 95% confidence level. This yielded 295 cases, but it was increased to 324 in case of possible case exclusions. Inter-observer differences noted in 91 cases (31.5%) were resolved through consensus.

3) Computer algorithms

Algorithms are set of rules that guide how decision is made on repetitive tasks. The algorithms used in this study were based on clinical signs, symptoms and investigation results of various conditions that are known to cause, or commonly associated with, stillbirth. The process of developing the algorithms was iterative.

I developed the proposal for the algorithms, and presented it to experts at two international conferences in Malawi (April, 2016) and in Liverpool (May, 2016) to identify missing areas in the design. A total of 86 experts attended the Malawi conference, while 69 attended the Liverpool conference, making a total of 155 experts. The experts were of various backgrounds in both clinical and health development fields, including obstetricians, midwives, paediatricians, nurses and public health physicians. Their feedback on the functions of the algorithms and user-friendliness was used to guide the overall design and presentation of the algorithms.

Initially, I wrote a list of common causes of stillbirth and neonatal mortality using ReCoDe (Gardosi et al, 2005) classification system and common causes of neonatal mortality listed by the WHO as guides (WHO, 2016c). Symptoms and signs of each of the cause of stillbirth and neonatal death, including

investigation results necessary for diagnoses, were determined from the literature.

I developed the algorithms and their decision-making pathways in plain language, which were converted into computer programming language (by a computer programmer) using Excel Macro® (Microsoft, 2016) to hierarchically diagnose various clinical conditions based on combinations of clinical symptoms, signs and results of laboratory investigations (Appendix 5). The hierarchy was a product of reiterative consultation with experts on which cause is more likely to be the final cause of death along the pathway to death. The ranking was necessary to inform the user what diagnosis is more likely to be the cause of death.

When data is entered, the algorithms check the data for entry errors and for fulfilment of the cause and contributing factors criteria. When a criterion is met, the algorithms return the diagnosis as a cause of death. If more than one cause of death criterion is met, the algorithms refer to the hierarchical list of diagnoses embedded in its decision-making process, and report the diagnosis at the highest level of the ranking as the most likely cause of death, while the rest of the diagnoses are reported as differential diagnoses.

The algorithms were subjected to an internal peer review process, where five experts with various backgrounds (3 obstetricians, 1 paediatrician and 1 midwife) scrutinised the algorithms for errors and gaps. Their feedback was used to develop the algorithms further and improve its presentation.

I also invited an external review panel, comprising of a paediatrician and two obstetricians with expertise in feto-maternal medicine, to review the decision-making process of the algorithms to determine cause of death and elements of poor care. Their feedback informed further changes in the algorithms and presentation of questions in the data collection form.

The algorithms were tested in three (3) stages:

1) **Initial Testing**: I applied the algorithms to the dataset to observe for variations with results from healthcare providers' consensus and

expert review. This helped in understanding how the algorithms worked, and changes needed to improve outputs were effected.

2) **Lay / Expert Feedback**: After improvements from the previous stage, I demonstrated the algorithms to a group of eight (8) users, comprising of experts in maternal and newborn health and people with no medical backgrounds. This was to identify any missing areas in the algorithms and to obtain feedback on user-friendliness from lay users. Their feedback helped particularly in adjusting the presentation of questions in the data collection form.
3) **Final Testing**: I created "dummy" cases of perinatal mortality with predictable outcomes for cause of death and its classification and elements of poor care to test the algorithms' ability to identify the desired outcomes. Observations were recorded and used to make final adjustments.

Data were then entered into the data capture form of the algorithms by the principal investigator. The Excel Macro® programme containing the algorithms was run to generate results.

Data analysis

I conducted a descriptive statistical analysis of the data using SPSS® (IBM, NY, Version 22). I also ran analysis of variance (ANOVA) whenever possible to compare results between the study countries. In instances where ANOVA could not be run due to deficiencies in the dataset, I used chi-square to compare results between countries. Statistical significance was determined at a p-value <0.05.

Antepartum stillbirth was defined as a macerated stillbirth whose mother arrived at the facility without a fetal heart sound, or a macerated stillbirth whose fetal heart sound was not documented on admission (shaded red in Table 3.2). Intrapartum stillbirth was defined as a stillbirth whose mother arrived at the health facility in labour with a fetal heart sound present irrespective of the physical appearance of the baby at birth (shaded green). Unspecified stillbirths were those that could not be categorised as either antepartum or intrapartum stillbirths (shaded grey).

Because of too many information gaps in some cases (52), the algorithms could not process them. Also, initial attempts to run Kappa analysis was not possible due to too many empty cells in the cross-tabulation needed to run the analysis. To run the analysis, the causes of stillbirth had to be categorised into fewer groups using the ReCoDe classification system (Gardosi et al, 2005).

Table 3.2: Determining time of death based on fetal physical appearance at birth and presence / absence of fetal heart sound on admission (as documented in case notes).

Fetal Heart Sound on Admission	**Appearance**		
	Fresh Stillbirth	**Macerated Stillbirth**	**Unspecified Stillbirth**
Present	Intrapartum Stillbirth	Intrapartum Stillbirth	Intrapartum Stillbirth
Absent	Intrapartum Stillbirth	Antepartum Stillbirth	Unknown Time of Death
Unknown	Intrapartum Stillbirth	Antepartum Stillbirth	Unknown Time of Death

3.4.2 Fulfilling Objective 3 (Applying classification systems)

Causes of death assigned via the three methods of assessment were categorised by the principal investigator using two classification systems:

1) Classification according to Relevant Condition at Death (ReCoDe; Gardosi et al, 2005) and;
2) The International Classification of Diseases for Perinatal Mortality (ICD-PM; WHO, 2016b).

I chose the ReCoDe classification system for its relatively good ability to keep information after coding, ease of use and low inter-observer variations (Flenady et al, 2009). The ReCoDe classification categorises cause of stillbirth into nine groups: fetus, umbilical cord, placenta, amniotic fluid, uterus,

mother, intrapartum, trauma and unclassified. Each category comprises of specific causes of stillbirth.

The ICD-PM was selected because it was new and this study would be the first to apply the system in multiple low-resource settings, giving valuable insight on how the system would work in such settings. This relatively new classification system uses a layered approach to categorise cause of perinatal mortality, including late neonatal mortality, often referred to as extended perinatal mortality.

In ICD-PM, each death is assigned a fetal cause and a contributing maternal condition. For fetal cause, mortality is categorised by time of death: antenatal stillbirth, intrapartum stillbirth and neonatal death. Antenatal deaths are further classified into six sub-categories (A1 to A6); intrapartum deaths are classified into seven sub-categories (I1 to I7), and; neonatal deaths are classified into 11 sub-categories (N1 to N11).

In this study, I used the following criteria to determine time of death:

- **Antepartum death**: Macerated stillbirths whose mothers arrived at the facility without fetal heart sound were categorised as antepartum deaths. Similarly, macerated stillbirths whose fetal heart sounds were not documented on admission were also categorised as antepartum deaths.
- **Intrapartum death**: All fresh stillbirths and stillbirths whose mothers arrived at the facility with fetal heart sound present were categorised as intrapartum deaths.
- **Unspecified death**: The remaining cases that could not be categorised either as antepartum or intrapartum deaths.

The contributing maternal condition are classified into five major categories: complications of placenta, cord and membranes (M1); maternal complications of pregnancy (M2); other complications of labour and delivery (M3); maternal medical conditions (M4), and; no maternal conditions (M5).

Analysis

Differences between the three methods of assessing cause of death were investigated using Kappa analysis, with p-value of <0.05 considered as significant.

3.4.3 Fulfilling Objective 4 (Assessing standard of care)

Antenatal interventions related to the prevention of stillbirth, as highlighted in the literature review, were assessed as per WHO antenatal care guidelines (WHO, 2002).

At antenatal care (ANC) level, I evaluated quality of care by assessing coverage of ANC interventions, as outlined in the WHO antenatal care guidelines (WHO, 2002), that were related to the prevention of stillbirth, including iron and folate supplements, anti-malarial prophylaxis, tetanus vaccination, HIV screening, syphilis screening and Rhesus (Rh) blood grouping.

Similarly, cases with diagnoses of any of the known causes of stillbirth or conditions associated with stillbirth were checked for documentation of treatment. This included treatment for hypertensive disorders, antepartum haemorrhage (APH), HIV infection, syphilis, malaria, prelabour rupture of membranes (PROM) and Rh incompatibility.

To assess delays during labour, I used two proxies: time between admission and birth, and; time between decision for emergency Caesarean section and actual birth. A 30-minute interval between decision and birth (McKenzie & Cooke, 2002) was used as a reference standard to assess for delay between decision for emergency CS and birth. In addition, a 60-minute interval is also reported.

I also used partograph use to assess quality of care during the intrapartum period. The participating healthcare providers and I assessed each partograph. A partograph was considered incorrectly used if any of the following criteria was met:

- Patient's details: incorrect or incomplete

- Fetal monitoring: incorrect or inadequate
- Cervical dilation plots: incorrect or inadequate
- Contractions monitoring: incorrect or inadequate
- Inaction after plot crosses action line
- Oxytocics / other drugs: not charted or wrongly charted
- Maternal vital signs: chart incorrect or inadequate

Finally, the 33 HCPs (alone) who took part in the management and review of the cases in the 12 study sites were asked about specific health system problems they encountered while managing each individual case of stillbirth. I asked them to report problems with any of the following: staff shortage; equipment and supplies; guidelines issues; wrong interventions, and; poor documentation.

Analysis

To compare findings between groups (e.g. countries) in normally distributed data, I used analysis of variance, while Pearson chi-square and Kruskal-Wallis test were used in case of non-parametric tests. I conducted a Kaplan-Meier survival analysis to explore the effect of country settings on the time between decision for CS and birth. In all analyses, I considered results significant when p-value was <0.05.

Criteria for assessing quality of ANC and documentation

Based on the WHO ANC guidelines (WHO, 2002), the following were considered as minimum ANC standards in this study: iron and folate supplementation, prophylactic anti-malarial treatment, tetanus vaccination, HIV screening, syphilis screening and Rhesus blood grouping.

The minimum documentation standard as outlined in the WHO guidelines for perinatal death review (WHO, 2016a) were used to assess documentation: parity, maternal age, pregnancy type, HIV status, LMP, date and time of birth, gestational age (and method of determination), place of birth, mode of delivery, baby's sex, birth weight and type of death (fresh/macerated).

Categorising care

Standard of care was categorised as follows:

- **Standard care – no improvement identified:** Defined as cases without a deficiency in any of the variables assessed: correct use of partograph, availability of staff, equipment and supplies, etc.
- **Sub-standard care in which better care may have made no difference to outcome:** Defined as cases admitted without fetal heart sound (FHS) on arrival in which at least one deficiency in care was found.
- **Sub-standard care which better care may have made a difference to outcome:** Cases admitted with FHS present on arrival and had at least one deficiency in care that could have made a difference to outcome, e.g. poor use of partograph, prolonged duration between admission and birth, etc.

3.4.4 Fulfilling Objective 5 (Formulating recommendations)

The results were discussed in light of other existing evidence, and recommendations were formulated and presented in the following categories:

- Improving stillbirth audit process
- Improving classification of stillbirth
- Improving quality of maternal and newborn health services
- Further research

3.5 Quality Assurance

3.5.1 Study Design and Data Collection

The study was designed to involve several experts in reviewing cases of stillbirth as well as in developing the computer algorithms. This ensured high level of standards were maintained at all stages of the study.

No personally identifiable information was collected, which reassured healthcare providers about the anonymity and confidentiality of the process,

making them more comfortable to volunteer important information. Completed data collection forms were checked on an ongoing basis by local research assistants and the principal investigator to ensure accuracy. Proportion of cases reviewed were reported to ensure transparency. Methods and procedures were fully documented; research records were kept up-to-date at all times.

3.5.2 Data Storage, Processing and Analysis

Data was anonymized right from the collection point, and stored in a secure password-protected system, ensuring and maintaining confidentiality and anonymity throughout the process of the study. Raw data has been stored and will be remain protected for at least 5 years before it is destroyed, as stipulated by the European Union data protection laws.

All entries were meticulously checked by the principal investigator. The data were then subjected to a rigorous cleaning process. Frequencies for all variables were generated to identify outliers. Reason for outliers was investigated to eliminate those that occurred due to data entry errors. Duplicate records were also identified and fixed. In line with the "no name, no blame" approach, the names of health facilities were also anonymized in the reporting of data.

3.6 Risks and Ethical Considerations

3.6.1 Healthcare Providers

Healthcare providers might have felt vulnerable due to the fear of being blamed for problems with the care provided to women who experienced stillbirths during antenatal or postnatal period especially where the care can be identified to have been sub-optimal.

During training on audit, I frequently reminded healthcare providers of the 'no shame, no blame' approach used during all audits. This approach has the advantage of encouraging the staff to volunteer more information, allowing more accurate diagnoses and identification of contributing factors. Most were familiar with the approach from practice of the more commonly

conducted maternal death audits. I also reassured them regarding confidentiality and anonymity.

3.6.2 Investigators

Data collectors may have become distressed by quality of care associated to stillbirth revealed during audit. Data collectors may have found that problems leading to stillbirth had not been properly addressed or may have discovered malpractice during data collection.

I debriefed the data collectors and none required counselling services. I also briefed the clinical lead of each healthcare facility on the general quality of care, with a view to facilitating areas for update training or communication of appropriate standards of care or clinical guidelines. At no point was identifiable information disclosed on any case of stillbirth or staff who managed the case.

3.6.3 Local Health Services

Data collection was scheduled at less busy times of the day or days of the week, as agreed with the local authorities, to avoid risk of disrupting service delivery. In facilities with very busy schedules, records were collected and moved to less busy locations within the facilities to conduct the reviews.

3.6.4 Compensation

Refreshments in the form of food and drinks were provided during training of healthcare workers, as well as during the reviews and data collection. Data collectors were reimbursed for their time and inconvenience.

3.6.5 Privacy and Confidentiality

Data was collected, stored and analysed anonymously without any information that was traceable to the affected women or their families. Confidentiality was maintained throughout the process.

3.6.6 Ethical Approval

I applied and obtained ethics approvals from the following ethics committees:

1) **Liverpool**: Ethics Committee, Liverpool School of Tropical Medicine. Reference number 14.026; dated 22nd October 2014, 6th January 2015, 15th January 2015 and 19th March 2015.
2) **Kenya**: Kenyatta National Hospital/University of Nairobi Ethics & Research Committee. Reference number KNH-ERC/A/398; dated 23rd December, 2014.
3) **Malawi**: College of Medicine Research & Ethics Committee (COMREC) Malawi. Reference number P.07/14/1601; dated 15th December, 2014.
4) **Sierra Leone**: Sierra Leone Ethics and Scientific Review Committee. Dated 9th October 2014 and 31st August, 2015.
5) **Zimbabwe**: Medical Research Council of Zimbabwe. Reference number MRCZ/A/1895; dated 9th March, 2015.

3.7 Dissemination

I gave preliminary feedback to the facilities and local authorities to help improve care. I also shared the results during the dissemination workshops held to wrap up the "Making it Happen" programme. Feedback will be shared with other relevant stakeholders in maternal and newborn health, such as the UNFPA and the UNICEF.

Final results of the study will be published in a peer-reviewed journal. Copies of the published work will be made available to relevant authorities.

3.7 Chapter Summary

- **Objective 1:** To explore literature on cause of, factors associated with, and classification of stillbirths, two separate systematic reviews were conducted and presented in Chapters 2A and 2B (Literature Review).
- **Objective 2:** To assess cause of stillbirth, a cross-sectional study was conducted in 12 health facilities across four sub-Saharan African countries (Kenya, Malawi, Sierra Leone and Zimbabwe).
- **Objective 3:** Causes of death were classified using ICD-PM and ReCoDe classification systems.
- **Objective 4:** Standard of care provided to women was assessed using proxies: coverage of ANC interventions; treatment for ailments known to cause or be associated with stillbirth; use of partograph, and; delays between admission to birth or between decision for Caesarean section and birth. Care was categorized as standard or sub-standard (outcome may or may not have been changed with better care).
- **Objective 5:** Recommendations were formulated in light of the results and discussion to improve stillbirth audit process, improve classification of stillbirth, improve quality of maternal and newborn health services, and for further research.

OVERVIEW OF RESULTS CHAPTERS (4, 5, 6 & 7)

The results of the primary study in this thesis are presented in four parts following the structure of the objectives of the study, as previously stated in Chapter 1:

1) To explore current literature on causes of, factors associated with, and classification systems used for stillbirth.
2) To assess cause of stillbirth in low- and middle-income countries and compare findings as identified by healthcare providers conducting stillbirth review at health facility level, an independent expert panel and computer algorithms.
3) To classify cases of stillbirth using two classification systems: The International Classification of Diseases for Perinatal Mortality (ICD-PM) and the classification of stillbirth according to Relevant Condition at Death (ReCoDe).
4) To assess standard of care provided to women who had stillbirth.
5) To formulate recommendations for improvement of quality of maternal and newborn health services.

While results for Objective 1 are presented in Chapters 2A and 2B (Literature Review), Objective 5 is fulfilled in Chapter 8 (Discussion and Recommendations). Thus, only the results for Objectives 2, 3 and 4 are presented in the results chapters (i.e. Chapters 4, 5, 6 and 7), as follows:

- Chapter 4 – Stillbirth rate and characteristics of mothers and babies.
- Chapter 5 – Cause of stillbirth: Related to Objective 2.
- Chapter 6 – Application of classification systems to cause of stillbirth: Related to Objective 3.
- Chapter 7 – Standard of care: Related to Objective 4.

CHAPTER 4: STILLBIRTH RATE & CHARACTERISTICS

4.1 Introduction

This chapter reports facility stillbirth rates in the selected facilities in the study, and describes the demographic and clinical characteristics of women and babies. It is related to objective #2, and focuses on the following research questions:

1) What is the stillbirth rate by health facility?
2) What are the characteristics of mothers and babies?
3) What characteristics of mothers and babies are similar or different across settings?
4) What proportion of the stillbirths were antepartum and intrapartum?

4.2 Stillbirth: Numbers and Rates

The calculated sample size was 279 per country, which was rounded to 300 per country, making a total of 1,200 cases for the study. During the study period, a total of 1,563 cases were recorded as stillbirths. However, a total of 1,329 (85.0%) were reviewed, which were evenly distributed between the four countries in the study (Figure 4.1).

An attempt was also made to obtain samples evenly from all health facilities within each country. However, because of differences in patient turn over, there was a disproportionate distribution of cases among facilities (Table 4.1). This was most markedly observed in Malawi, where one health facility (out of four) contributed 56.1% of all cases from the country. In facilities where fewer cases occurred than needed to meet the planned facility quota, all cases were reviewed, while in facilities where more cases occurred than needed, cases were reviewed until the country sample size was met.

The proportion of cases reviewed ranged from 70.4% in Zimbabwe to 100% in Sierra Leone. In Sierra Leone, one facility had no stillbirth case files available as all records were burnt to contain Ebola virus epidemic that occurred during the period. Thus, more cases than planned were obtained from the other two facilities to fill in the gap.

The inclusion/exclusion criteria have been described in the methodology. Briefly, babies born dead at 28 weeks of gestation or more or with a birth weight of 1000g or more were included. Of the 1,329 cases reviewed, 1,267 (95.3%) met the inclusion criteria, and these were included in the analysis. The proportion of cases that met the inclusion criteria slightly varied by country, with a range between 91.7% in Kenya and 97.7% in Sierra Leone.

Of all the four countries, health facilities in Sierra Leone had the highest stillbirth rate (118.1 per 1,000 births; 95% CI: 115.0 – 121.2), while facilities in Malawi had the lowest (20.3 per 1,000 births; 95% CI: 15.0 – 42.8). Health facilities in Kenya and in Zimbabwe had similar rates at 38.8 per 1,000 births (95% CI: 43.3 – 33.9) and 34.7 (95% CI: 31.8 – 39.2), respectively. Within individual countries, the stillbirth rate was similar among health facilities, except in Malawi, which had the highest disparity in the stillbirth rate among its facilities (Table 4.1) – hence, the widest confidence interval observed.

Figure 4.1: Cases selection process

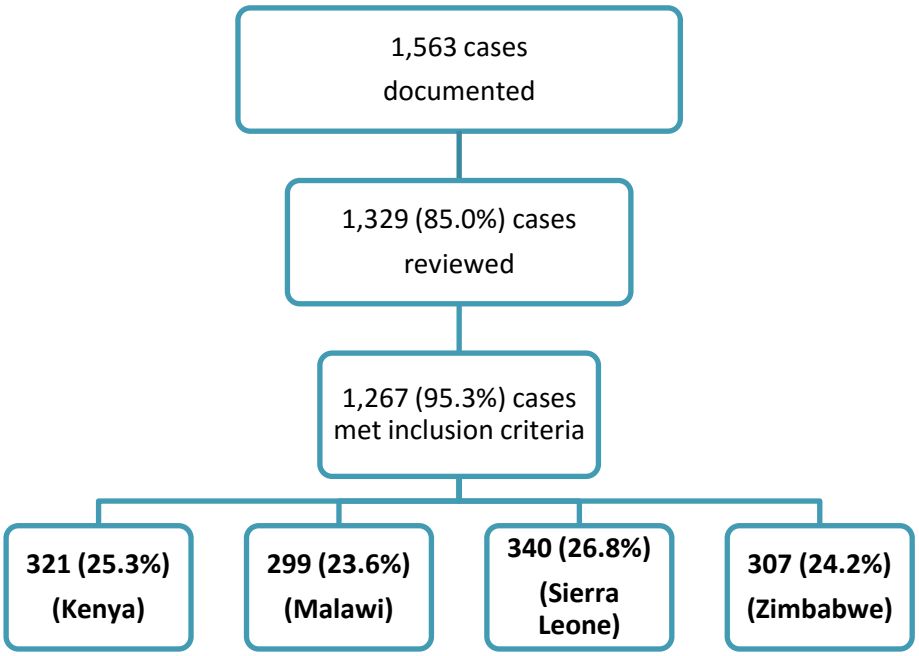


Table 4.1: Facility stillbirth rates (SBR) and proportion of stillbirths reviewed

Health Facility	Data Collection Period	Total Births	Total Stillbirths Recorded	SBR per 1,000 births (95% CI)	Proportion of Stillbirths Reviewed (%)	Met Criteria & Included in Analysis (% of Reviewed)
Kenya						
Hospital A	Jan – July 2015	3,416	127	37.2	83 (65.4%)	74 (89.2%)
Hospital B	Jan – July 2015	3,809	165	43.3	145 (87.9%)	133 (91.7%)
Hospital C	Jan – July 2015	3,451	122	35.4	122 (100%)	114 (93.4%)
Total	–	**10,676**	**414**	**38.8 (33.9 – 43.9)**	**350 (84.5%)**	**321 (91.7%)**
Malawi						
Hospital A	Jan – Oct 2015	12,449	216	17.4	180 (83.3%)	160 (88.9%)
Hospital B	Jan – July 2015	2,433	42	17.3	42 (100%)	41 (97.6%)
Hospital C	Jan – July 2015	2,123	73	34.4	73 (100%)	73 (100%)
Hospital D	Jan – July 2015	539	25	46.4	25 (100%)	25 (100%)
Total	–	**17,544**	**356**	**20.3 (15.0 – 42.8)**	**320 (89.9%)**	**299 (93.4%)**
Sierra Leone						
Hospital A	July 2014 – Sept 2015	1,403	168	119.7	168 (100%)	163 (97.0%)
Hospital B	July 2014 – Sept 2015	1,544	180	116.5	180 (100%)	177 (98.3%)
Total	–	**2,947**	**348**	**118.1 (115.0 – 121.2)**	**348 (100%)**	**340 (97.7%)**
Zimbabwe						
Hospital A	Jan – Mar 2015	3,519	135	38.4	104 (77.0%)	104 (100%)
Hospital B	Nov 2014 – Jun 2015	6,115	195	31.9	102 (52.3%)	88 (86.3%)
Hospital C	Jan – Apr 2015	3,178	115	36.2	115 (100%)	115 (100%)
Total	–	**12,812**	**445**	**34.7**	**311 (70.4%)**	**307 (95.6%)**

Health Facility	Data Collection Period	Total Births	Total Stillbirths Recorded	SBR per 1,000 births (95% CI)	Proportion of Stillbirths Reviewed (%)	Met Criteria & Included in Analysis (% of Reviewed)
				(31.8 – 39.2)		
STUDY TOTAL	–	**43,979**	**1,563**	–	**1,329 (85.0%)**	**1,267 (95.3%)**

4.3 Characteristics

4.3.1 Maternal characteristics

Maternal age

Maternal age was recorded in 1,231 (97.2%) of the 1,267 stillbirths (Table 4.2). The mean age of the mothers was 26.2 years (SD = 6.4).

A one-way between-groups analysis of variance (ANOVA) was conducted to explore age differences between countries. There was a statistically significant difference for age across the four countries: F (3, n = 1227) = 6.3, p = 0.0003. However, as per Cohen's Convention (Cohen, 1988), the actual difference between the mean age for each country was small, as observed in the individual countries' mean age and evident by an effect size of 0.02.

To appreciate which countries differed significantly, a post-hoc comparison using the Tukey HSD ("Honestly Significant Difference") was conducted, which indicated that the mean maternal age in Kenya was significantly higher than in Sierra Leone (p = 0.016), while mothers in Malawi were significantly younger than those in Zimbabwe (p = 0.032; Table 4.3). Similarly, mean age of mothers in Sierra Leone was significantly lower than that found in Zimbabwe (p = 0.0004). There was no statistically significant variation between Kenya and Malawi (p = 0.301); Kenya and Zimbabwe (p = 0.731), and; Malawi and Sierra Leone (p = 0.656).

However, the statistically significant differences observed between the countries may not be of clinical significance.

Parity

Of all mothers in the study, one-third (32.4%) were primi-para, more than half (57.0%) were para 2 – 4, and one-tenth (9.1%) were para 5 or more.

A variation in parity was observed across the four countries. To explore the statistical significance of the variation, a one-way between-groups ANOVA was conducted. There was a statistically significant difference between the countries ($p<0.0005$) for parity across the four countries: $F (3, n = 1240) = 18.4$, $p < 0.0005$. However, the actual difference between mean parity for each country was small (effect size of 0.04), and may be of little clinical significance.

Maternal education

About half (48.5%) of all women in the study completed at least primary school education. However, information on education was not available in 45% of the cases, majority of which were from Sierra Leone (Table 4.2). Proportion of women who completed various stages of education varied by country, and a chi-square test revealed that the variation was significant: $X^2 (9, n=700) = 258.34$, $p<0.0005$. Malawi and Sierra Leone had significantly more mothers who were uneducated than Kenya and Zimbabwe.

Maternal residence

Overall, 39% of mothers were from rural areas (Table 4.2). The proportions of mothers' residence also showed a wide variation between countries. A chi-square test indicated a significant difference in residence of mothers between the four countries, $X^2 (6, n = 1,222) = 334.68$, $p<0.0005$.

Compared to the other three countries, Kenya had significantly fewer mothers from urban regions, but more from semi-urban and rural areas, while Malawi had significantly fewer mothers from semi-urban areas. In Sierra Leone, there were significantly fewer mothers from semi-urban areas, but more from rural areas. Zimbabwe had significantly more mothers from urban areas and fewer from semi-urban and rural areas. This may have implications on design of public health programmes.

Referral status

Of the 1,267 cases, 44.9% of mothers were referred from other facilities, 53.1% arrived directly from home and information about the referral status of 2.0% was not available. Of those from rural areas, 56.1% were referrals.

Some differences were observed between countries, with most referrals observed in Zimbabwe (Table 4.2). When a chi-square test was conducted to explore the statistical significance of the variation between countries, it was significant: X^2 (3, n = 1,242) = 103.06, p<0.0005; but small (0.29 effect size, Cohen, 1988), and may have no clinical significance.

Type of pregnancy

Majority (90.7%) of the pregnancies were singletons, while 7.0% were multiple gestations. While some differences in the proportions of multiple pregnancies were observed between countries (Table 4.3), a chi-square test showed that the difference was not statistically significant: X^2 (3, n = 1,238) = 5.42, p = 0.14.

Table 4.2: Demographic and clinical characteristics of study population (n=1,267)

Characteristics		Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)	Statistic & p-value
Maternal age (years)	< 15	0 (0.0)	4 (1.3)	1 (0.3)	0 (0.0)	**5 (0.4)**	
	15 – 19	29 (9.0)	47 (15.7)	81 (23.8)	34 (11.1)	**191 (15.1)**	
	20 – 24	91 (28.1)	93 (31.1)	77 (22.7)	75 (24.4)	**336 (26.5)**	
	25 – 29	101 (31.5)	63 (21.1)	80 (23.5)	79 (25.7)	**323 (25.5)**	
	30 – 34	51 (15.9)	47 (15.7)	49 (14.4)	63 (20.5)	**210 (16.6)**	
	35 – 39	34 (10.6)	27 (9.0)	34 (10.0)	35 (11.4)	**130 (10.3)**	
	>= 40	8 (2.5)	10 (3.3)	7 (2.1)	11 (3.6)	**36 (2.8)**	
	No information	7 (2.2)	8 (2.7)	11 (3.2)	10 (3.3)	**36 (2.8)**	
	Mean (SD)	26.6 (5.8)	25.7 (6.6)	25.2 (6.4)	27.2 (6.5)	**26.2 (6.4)**	
	ANOVA (age by country)	-	-	-	-	**-**	F=6.3; p=0.0003
Parity	Para 1	103 (32.1)	101 (33.8)	101 (29.7)	105 (34.2)	**410 (32.4)**	
	Para 2 – 4	195 (60.8)	162 (54.2)	172 (50.6)	193 (72.9)	**722 (57.0)**	
	Para 5 or more	16 (5.0)	31 (10.4)	60 (17.7)	8 (2.6)	**115 (9.1)**	
	ANOVA (parity by country)	-	-	-	-	**-**	F=18.4; p=0.0005

Characteristics		Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)	Statistic & p-value
Mothers' educational level	None	18 (5.6)	47 (15.7)	18 (5.3)	2 (0.7)	**85 (6.7)**	
	Primary	115 (35.8)	110 (36.8)	0 (0.0)	55 (17.9)	**280 (22.1)**	
	Secondary	75 (23.4)	51 (17.1)	0 (0.0)	149 (48.5)	**275 (21.7)**	
	Tertiary	36 (11.2)	5 (1.7)	7 (2.1)	12 (3.9)	**60 (4.7)**	
	No information	77 (24.0)	86 (28.8)	315 (92.7)	89 (29.0)	**567 (44.8)**	
	Chi-square (country)	-	-	-	-	**-**	X^2=258.34; p<0.0005
Mothers' place of residence	Urban	63 (19.6)	127 (42.5)	157 (46.2)	260 (84.7)	**607 (47.9)**	
	Semi-urban	78 (24.3)	25 (8.4)	6 (1.8)	9 (2.9)	**118 (9.3)**	
	Rural	172 (53.6)	119 (39.8)	171 (50.3)	35 (11.4)	**497 (39.2)**	
	No information	8 (2.5)	28 (9.4)	6 (1.8)	3 (1.0)	**45 (3.6)**	
	Chi-square (country)	-	-	-	-	**-**	X^2=334.68; p<0.0005
Obstetric history	At least 1 surviving child	168 (52.3)	152 (50.8)	211 (62.1)	184 (59.9)	**715 (56.4)**	
	At least 1 previous abortion	39 (12.2)	37 (12.4)	26 (7.7)	32 (10.4)	**134 (10.6)**	
Antenatal visit	At least 1 visit	272 (84.7)	207 (69.2)	146 (42.9)	222 (72.3)	**847 (66.9)**	
	4 or more visits	113 (35.2)	29 (9.7)	4 (1.2)	75 (24.4)	**221 (17.4)**	

Characteristics		Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)	Statistic & p-value
	ANOVA (for mean no. of ANC visits by country)	-	-	-	-	-	F=41.8; p<0.0005
Referral status	Referral from other facility	118 (36.8)	99 (33.1)	139 (40.9)	213 (69.4)	**569 (44.9)**	
	Came from home	198 (61.7)	191 (63.9)	196 (57.7)	88 (28.7)	**673 (53.1)**	
	No information	5 (1.6)	9 (3.0)	5 (1.5)	6 (2.0)	**25 (2.0)**	
	Chi-square (country)	-	-	-	-	-	X^2=103.06; p<0.0005
Type of pregnancy	Singleton	294 (91.6)	269 (90.0)	302 (88.8)	284 (92.5)	**1,149 (90.7)**	
	Multiple	20 (6.2)	29 (9.7)	25 (7.4)	15 (4.9)	**89 (7.0)**	
	Chi-square (country)	-	-	-	-	-	X^2=5.42; p=0.14
Gestational age at birth	28 to 31 completed weeks	70 (21.8)	24 (8.0)	29 (8.5)	63 (20.5)	**186 (14.7)**	
	32 to 36 completed weeks	85 (26.5)	70 (23.4)	94 (27.6)	102 (33.2)	**351 (27.7)**	
	37 completed weeks or more	148 (46.1)	179 (59.9)	209 (61.5)	125 (40.7)	**661 (52.2)**	
	No information	18 (5.6)	26 (8.7)	8 (2.4)	17 (5.5)	**69 (5.5)**	
Mode of delivery	Spontaneous vaginal delivery	230 (71.7)	192 (64.6)	227 (66.8)	218 (71.0)	**867 (68.4)**	
	Caesarean section	76 (23.7)	69 (23.1)	77 (22.6)	81 (26.4)	**303 (23.9)**	

Characteristics		Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)	Statistic & p-value
	Laparotomy	8 (2.5)	23 (7.7)	22 (6.5)	7 (2.3)	**60 (4.7)**	
	Instrumental (assisted) vaginal delivery	1 (0.3)	9 (3.0)	8 (2.4)	0 (0.0)	**18 (1.4)**	
	Destructive operation (craniotomy)	0 (0.0)	4 (1.3)	0 (0.0)	0 (0.0)	**4 (0.3)**	
	No information	6 (1.9)	2 (0.7)	6 (1.8)	1 (0.3)	**15 (1.2)**	

4.3.2 Antenatal care (ANC) attendance

ANC information availability and booking status

Information about mothers' antenatal care (ANC) visits was available for 940 (74.2% of all) cases (Table 4.3). Availability of ANC information varied between the countries. While Zimbabwe had the highest proportion of women whose ANC information was available (96.1%), Sierra Leone had the lowest (44.4%).

Out of the 1,267 cases in this study, 847 (67%) of the mothers attended ANC at least once ("booked"). However, this ranged between 42.9% in Sierra Leone to 84.7% in Kenya. It should be noted that in Sierra Leone, mothers' ANC records were not available for 55.6% of cases. It was not clear whether the mothers without ANC record attended ANC but it was not documented, or the mothers did not attend at all. When only mothers for whom information was available were considered in the analysis for Sierra Leone, 91.4% had attended ANC at least once.

Table 4.3: Distribution of ANC attendance by country

Antenatal care status	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)
ANC information available	286 (89.1%)	208 (69.6%)	151 (44.4%)	295 (96.1%)	**940 (74.2%)**
ANC information unavailable	35 (10.9%)	91 (30.4%)	189 (55.6%)	12 (3.9%)	**327 (25.8%)**
Booked	272 (84.7%)	207 (69.2%)	146 (42.9%)	222 (72.3%)	**847 (66.9%)**
"Unbooked"	14 (4.4%)	1 (0.3%)	5 (1.5%)	73 (23.8%)	**93 (7.3%)**

Number of ANC visits

Figure 4.2 summarises antenatal clinic attendance by country. Overall, out of the 940 cases whose ANC information was available, 10.5% of their mothers had one visit; 24.3% had two visits; 16.9% had three visits, and; 23.5% had four or more visits. In all the four countries, there were some cases whose mothers evidently attended ANC, but the number of visits was not clear. This group constituted 14.9% of those whose information about ANC was

available. One-tenth (9.9%) were documented as “unbooked”, i.e. did not attend ANC at all.

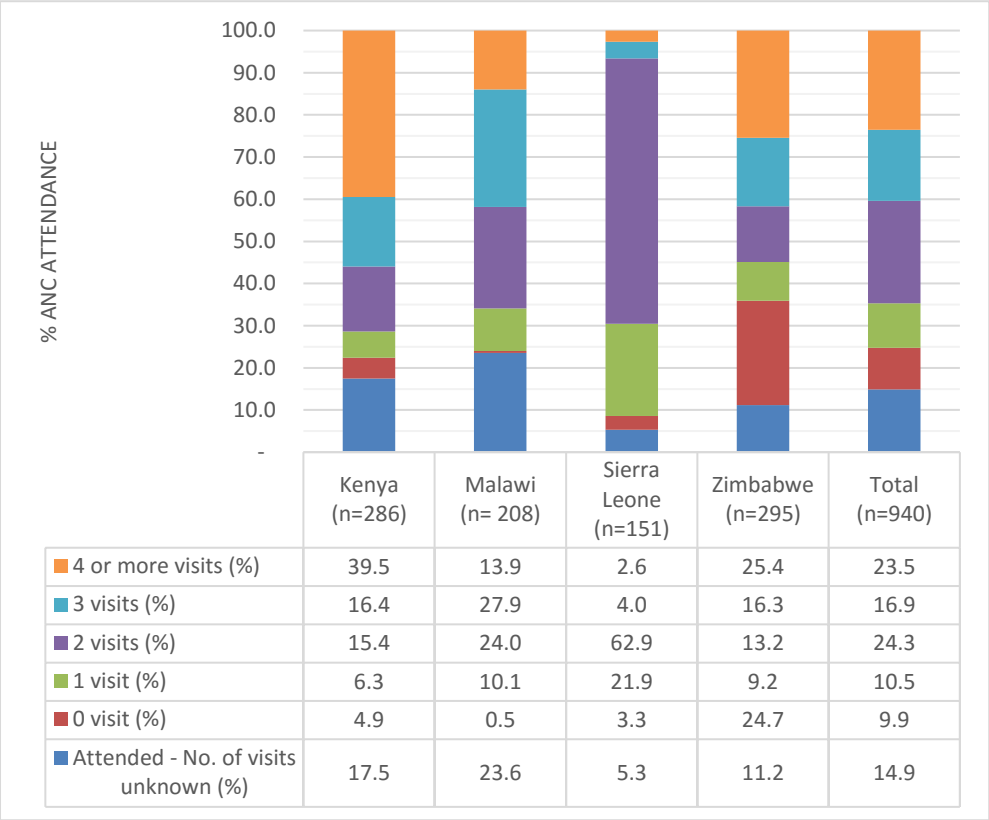
The mean number of ANC visits across all four countries was 3.0 (SD = 1.7). To explore differences in mean number of ANC visits between countries, a one-way between-groups ANOVA was conducted, which showed a statistically significant difference between the countries ($p<0.0005$) for number of ANC visits across the four countries: $F (3, n = 707) = 41.8$, $p < 0.0005$. The actual difference between the mean ANC visits for each country was large, with an effect size of 0.15.

A post-hoc comparison was conducted using the Tukey HSD to determine how countries differed with one another. Mothers in Kenya (M = 3.5, SD = 1.5) were significantly more likely to have attended ANC than mothers in Malawi (M = 2.6, SD = 1.0; $p<0.0005$) and Sierra Leone (M = 1.9, SD = 1.0; $p<0.0005$). Mothers from Malawi were also significantly more likely to have attended ANC than mothers from Sierra Leone. Similarly, Zimbabwean mothers (M = 3.3, SD = 1.8) were more likely to have attended ANC than Malawian ($p<0.0005$) and Sierra Leonean mothers ($p<0.0005$). There was no significant difference between ANC attendance in Kenya and in Zimbabwe ($p = 0.59$). However, the statistically significant differences observed between the countries may not be of clinical significance.

Several women had a record of attending ANC but did not have a record of number of visits. This was highest in Kenya (23.6%) and lowest in Sierra Leone (5.3%).

Across all settings, the number of women who did not attend any ANC represented a minority, except in Zimbabwe where up to 24.7% of women who had stillbirth did not attend. It is as low as 0.5% in Malawi, 3.3% in Sierra Leone and 4.9% in Kenya.

Figure 4.2: Distribution of ANC attendance by country



	Kenya (n=286)	Malawi (n= 208)	Sierra Leone (n=151)	Zimbabwe (n=295)	Total (n=940)
4 or more visits (%)	39.5	13.9	2.6	25.4	23.5
3 visits (%)	16.4	27.9	4.0	16.3	16.9
2 visits (%)	15.4	24.0	62.9	13.2	24.3
1 visit (%)	6.3	10.1	21.9	9.2	10.5
0 visit (%)	4.9	0.5	3.3	24.7	9.9
Attended - No. of visits unknown (%)	17.5	23.6	5.3	11.2	14.9

4.3.3 Gestational age at birth

The mean gestational age at birth was 35.8 weeks (95% CI: 35.6 – 36.0; SD = 3.5; median = 37). More than half (52.2%) of the babies were born at 37 completed weeks of gestation or later. The remaining babies were born before 37 completed weeks of gestation: very preterm (between 28 and 31 weeks of gestation; 14.8%), and late preterm (between 32 and 36 weeks; 27.7%).

A one-way between-groups ANOVA was conducted to explore mean difference in gestational age between countries. It showed a statistically significant difference between the countries ($p<0.0005$): $F (3, n = 1194) = 11.16$, $p < 0.0005$. The actual difference between the mean gestational age for each country was small, with an effect size of 0.03.

A post-hoc comparison using the Tukey HSD to examine differences between countries showed that the mean gestational age in Kenya (M = 36.3, SD = 4.0) was significantly lower than in Malawi (M = 36.4, SD = 3.0; p = 0.001) and Sierra Leone (M = 36.5, SD = 2.8; $p<0.0005$). The mean gestational age in

Malawi and Sierra Leone were also significantly higher than in Zimbabwe (M = 35.2, SD = 0.001, with a p-value of 0.001 and <0.0005, respectively). There was no significant difference between Kenya and Zimbabwe (p = 0.99), and between Malawi and Sierra Leone (p = 0.99). Even among countries with statistically significant differences, the difference was small, and may not be of any clinical importance.

Among the countries, proportion of preterm stillbirths ranged from 31.4% in Malawi to 53.7% in Zimbabwe.

However, only 29 cases (2.3%) had their gestational age determined by ultrasound; the rest were estimated by last menstrual period (LMP) and/or clinical examination. Out of those with gestational age estimated by LMP or abdominal examination, 173 (15.8%) were simply documented as "term", most of which (170 out of 173) were found in Sierra Leone. There were no records gestational age assessment after birth.

4.3.4 Mode of delivery

Most babies (68.2%) were born vaginally without assistance, while 303 (23.9%) were delivered by caesarean section. There was a striking similarity in caesarean section rate for stillbirth among the four countries, ranging from 22.6% in Sierra Leone to 26.4% in Zimbabwe. A total of 60 (4.7%) of the babies were delivered via laparotomy for ruptured uterus. The proportions of laparotomies observed in Malawi (23; 7.7%) and Sierra Leone (22; 6.5%) were more than double the proportions found in Kenya (8; 2.5%) and Zimbabwe (7; 2.3%). A chi-square test could not be used to explore differences between countries as one of the test's assumptions, to have at least 80% of cells with expected frequencies of 5 or more, was not fulfilled by the data.

There was low use of assisted instrumental vaginal delivery; only 18 cases (1.4%) were delivered by vacuum or forceps. Four cases (0.3% of all cases) were delivered via destructive procedures (craniotomy), all of which were recorded in a single health facility (Hospital C) in Malawi.

4.3.5 Type of stillbirth

Conventionally, stillbirths are recorded based on their physical appearance: fresh (indicating intrapartum death) or macerated (indicating antepartum death). In this section, the consistency of using physical appearance in determining time of death is explored.

Figure 4.3 below summarises conditions of babies at birth and status of their fetal heart sound on admission to the labour ward, the main method of assessing whether a baby is alive or not during third trimester in the study settings.

Overview

Four hundred and fifty-five (455) fresh stillbirths were recorded, accounting for 35.9% of all cases included in this analysis. Of these, review of case notes showed that 49.7% had fetal heart sound documented as present on admission to the labour ward. Similarly, 674 cases of macerated stillbirths accounted for 53.2% of all cases in this analysis. However, up to 21.1% of the cases recorded to be macerated had fetal heart sound documented as present on admission to the labour ward. The condition of the remaining 138 cases (10.9%) was not specified.

It should be noted that because of the long duration of labour without action (discussed in more detail in Chapter 7), some mothers were admitted into the labour ward with fetal heart sound present, but they gave birth to macerated stillborn babies.

Differences between settings

When the data was analysed by country (Table 4.4), all four countries showed some similarities, with fresh and macerated stillbirths recorded whether the mother arrived at the facility with fetal heart sound present or absent. However, there were differences in the proportions of fresh/macerated stillbirths whose mothers were admitted to the labour ward with fetal heart sound present or absent.

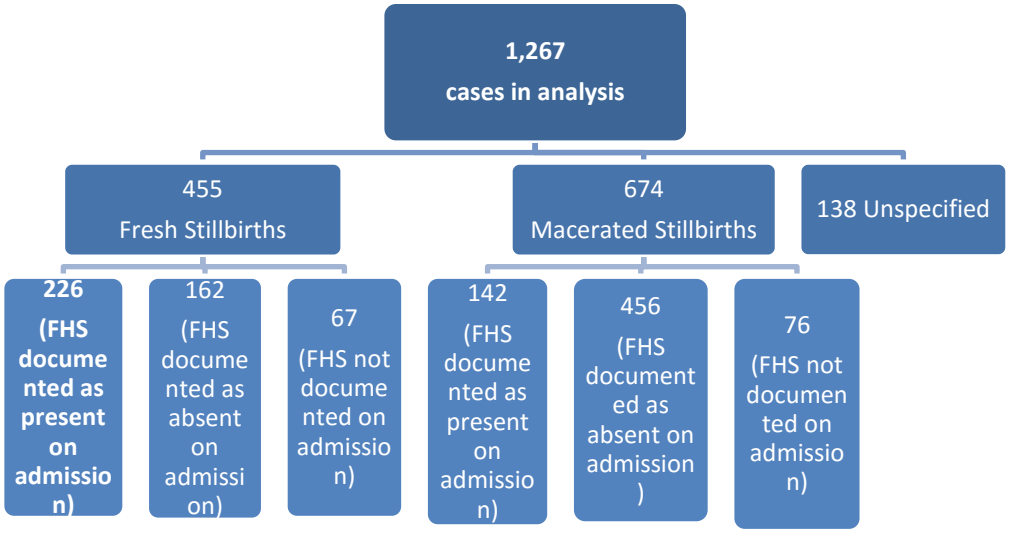
Sierra Leone had the highest number of unspecified stillbirths (Table 4.4), comprising 35.9% of all cases from the country. Furthermore, Sierra Leone

also had the highest number of stillbirths whose fetal heart sound was not documented at the time of admission, with 27.4% in that category.

A chi-square test revealed that although the difference in the proportion of women admitted with fetal heart sound present across the four countries was small (effect size = 0.21), it was statistically significant: X^2 (3, n=1093) = 45.97, p<0.0005. Thus, the difference may not be of clinical importance.

Similarly, a chi-square test was conducted after excluding cases without a fresh/macerated classification to explore variations in type of stillbirth between countries. It showed a significant difference, X^2 (3, n=1129) = 66.98, p<0.0005, and a small effect size of 0.24 was observed, indicating little, if any, clinical significance.

Figure 4.3: Documentation of fetal appearance and fetal heart sound (FHS) on admission to the labour ward



4.4 Time of death

Antepartum death

In this study, macerated stillbirths whose mothers arrived at the facility without fetal heart sound were categorised as antepartum deaths. Similarly, macerated stillbirths whose fetal heart sounds were not documented on admission were also categorised as antepartum deaths. These constituted a total of 532 cases of antepartum deaths, representing 42.0% of all cases, with variation between countries (Figure 4.4 and Table 4.4). The highest proportion of antepartum stillbirths were recorded in Zimbabwe.

Intrapartum death

All fresh stillbirths and stillbirths whose mothers arrived at the facility with fetal heart sound present were categorised as intrapartum deaths (Figure 4.4 and Table 4.4). This category constituted a total of 643 of the 1,267 cases (50.7%). Malawi had the highest proportion in this category, while Zimbabwe had the lowest.

Unspecified death

The remaining 92 cases (7.3%; Figure 4.4 and Table 4.4) could not be categorised either as antepartum or intrapartum deaths. Sierra Leone had the highest proportion of stillbirths that could not be categorised by time of death.

Figure 4.4: Time of death by country

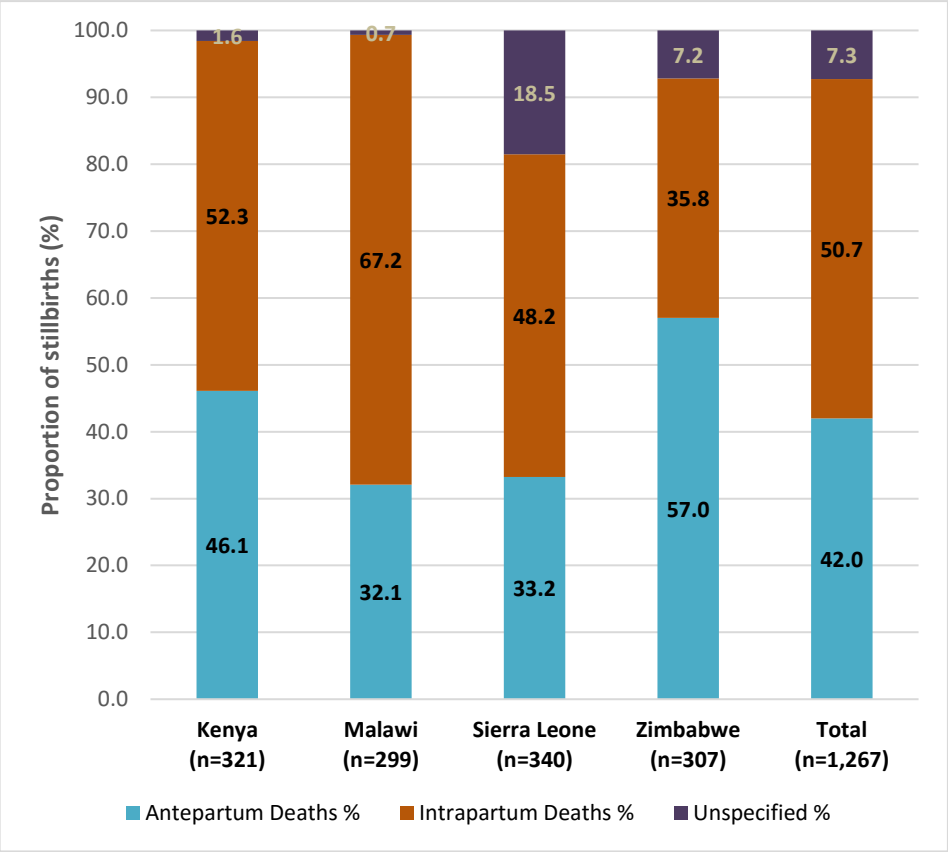


Table 4.4: Fetal physical appearance at birth and fetal heart sound (FHS) on admission (as documented in case notes).

Facility	Fetal Heart Sound on Admission	Fresh SB (%)	Macerated SB (%)	Unspecified (%)	Total (%)
Kenya					
Hospital A n=74 (%)	Present	13 (17.6)	7 (9.5)	1 (1.4)	**21 (28.4)**
	Absent	8 (10.8)	36 (48.6)	2 (2.7)	**46 (62.2)**
	Unknown	2 (2.7)	5 (6.8)	0	**7 (9.5)**
Hospital B n=133 (%)	Present	29 (21.8)	13 (9.8)	3 (2.3)	**45 (33.8)**
	Absent	30 (22.6)	53 (39.8)	2 (1.5)	**85 (63.9)**
	Unknown	1 (0.8)	2 (1.5)	0	**3 (2.3)**
Hospital C n=114 (%)	Present	16 (14.0)	11 (9.6)	0	**27 (23.7)**
	Absent	29 (25.4)	47 (41.2)	1 (0.9)	**77 (67.5)**
	Unknown	5 (4.4)	5 (4.4)	0	**10 (8.8)**
Total n=321 (%)	**Present**	**58 (18.1)**	**31 (9.7)**	**4 (1.2)**	**93 (29.0)**
	Absent	**67 (20.9)**	**136 (42.4)**	**5 (1.6)**	**208 (64.8)**
	Unknown	**8 (2.5)**	**12 (3.7)**	**0 (0.0)**	**20 (6.2)**
Malawi					
Hospital A n=160 (%)	Present	57 (35.6)	26 (16.3)	1 (0.6)	**84 (52.5)**
	Absent	17 (10.6)	56 (35.0)	0	**73 (45.6)**
	Unknown	2 (1.3)	0 (0)	1 (0.6)	**3 (1.9)**
Hospital B n=41 (%)	Present	10 (24.4)	5 (12.2)	0	**15 (36.6)**
	Absent	4 (9.8)	13 (31.7)	1 (2.4)	**18 (43.9)**
	Unknown	4 (9.8)	4 (9.8)	0	**8 (19.5)**
Hospital C n=73 (%)	Present	26 (35.6)	7 (9.6)	1 (1.4)	**34 (46.6)**
	Absent	11 (15.1)	17 (23.3)	0	**28 (38.4)**

Facility	Fetal Heart Sound on Admission	Fresh SB (%)	Macerated SB (%)	Unspecified (%)	Total (%)
	Unknown	9 (12.3)	2 (2.7)	0	**11 (15.1)**
Hospital D n=25 (%)	Present	10 (40.0)	3 (12.0)	0	**13 (52.0)**
	Absent	7 (28.0)	4 (16.0)	0	**11 (44.0)**
	Unknown	1 (4.0)	0 (0)	0	**1 (4.0)**
Total n=299 (%)	**Present**	**103 (34.4)**	**41 (13.7)**	**2 (0.7)**	**146 (48.8)**
	Absent	**39 (13.0)**	**90 (30.1)**	**1 (0.3)**	**130 (43.5)**
	Unknown	**16 (5.4)**	**6 (2.0)**	**1 (0.3)**	**23 (7.7)**
Sierra Leone					
Hospital A n=163 (%)	Present	13 (8.0)	17 (10.4)	22 (13.5)	**52 (31.9)**
	Absent	13 (8.0)	30 (18.4)	26 (16.0)	**69 (42.3)**
	Unknown	6 (3.7)	20 (12.3)	16 (9.8)	**42 (25.8)**
Hospital B n=177 (%)	Present	21 (11.9)	10 (5.6)	8 (4.5)	**39 (22.0)**
	Absent	18 (10.2)	32 (18.1)	8 (4.5)	**58 (32.8)**
	Unknown	36 (20.3)	31 (17.5)	13 (7.3)	**80 (45.2)**
Total n=340 (%)	**Present**	**34 (10.0)**	**27 (7.9)**	**30 (8.8)**	**91 (26.8)**
	Absent	**31 (9.1)**	**62 (18.2)**	**34 (10.0)**	**127 (37.4)**
	Unknown	**42 (12.5)**	**51 (15.0)**	**29 (8.5)**	**122 (35.9)**
Zimbabwe					
Hospital A n=104 (%)	Present	18 (17.3)	19 (18.3)	6 (5.8)	**43 (41.3)**
	Absent	3 (2.9)	43 (41.3)	12 (11.5)	**58 (55.8)**
	Unknown	0	3 (2.9)	0 (0)	**3 (2.9)**
Hospital B n=88 (%)	Present	5 (5.7)	10 (11.4)	4 (4.5)	**19 (21.6)**
	Absent	7 (8.0)	55 (62.5)	6 (6.8)	**68 (77.3)**
	Unknown	0	1 (1.1)	0	**1 (1.1)**

Facility	Fetal Heart Sound on Admission	Fresh SB (%)	Macerated SB (%)	Unspecified (%)	Total (%)
Hospital C n=115 (%)	Present	8 (7.0)	14 (12.2)	0	**22 (19.1)**
	Absent	15 (13.0)	70 (60.9)	3 (2.6)	**88 (76.5)**
	Unknown	1 (0.9)	3 (2.6)	1 (0.9)	**5 (4.3)**
Total n=307 (%)	**Present**	**31 (10.1)**	**43 (14.0)**	**10 (3.3)**	**84 (27.4)**
	Absent	**25 (8.1)**	**168 (54.7)**	**21 (6.8)**	**214 (69.7)**
	Unknown	**1 (0.3)**	**7 (2.3)**	**1 (0.3)**	**9 (2.9)**
All countries					
All Facilities n=1,267 (%)	Present	226 (49.7%)	142 (21.1%)	**46 (33.3%)**	**414 (32.7%)**
	Absent	162 (35.6%)	456 (67.7%)	**61 (44.2%)**	**679 (53.6%)**
	Unknown	67 (14.7%)	**76 (11.3%)**	**31 (22.5%)**	**174 (13.7%)**

Green=Intrapartum stillbirths; Blue=Antepartum stillbirths; Red=Unknown time of death

4.5 Chapter Summary

Facility stillbirth rate is high and varies between countries. However, between health facilities within the same country, the rate is similar in all countries, except in Malawi, where the rate varied between facilities.

Overall, the mean age of mothers was 26.2 years (SD = 6.4). Although the mean age showed a tight range across the countries (25.2 – 27.2), the difference was statistically significant. Most mothers who had stillbirth came from urban areas, and arrived at health facilities directly from home.

Only about one-third of mothers who had stillbirth were primipara. Although there is a variation in mothers' parity across settings, the proportion of mothers who were primipara was similar across all four countries. About 9% of mothers were grand-multiparous, with wide variations between countries.

Mothers typically attended antenatal care at least once, and the mean number of ANC visits across all four countries was 3 (SD = 1.7). However, only about one-fifth of mothers attended ANC four or more times.

About half of all babies were born at term, and about two-thirds were born through spontaneous vaginal delivery. More than one-third (35.9%) of cases were documented as fresh stillbirth and 32.7% were documented to have fetal heart sound present on admission. Overall, using the combination of physical appearance and status of fetal heart sound on admission, half of all stillbirths could be classified as intrapartum deaths, ranging between 35.8% in Zimbabwe and 67.2% in Malawi.

CHAPTER 5: CAUSE OF STILLBIRTH

5.1 Introduction

This chapter presents results of cause of stillbirth in the four countries using the three methods for assessment of cause of death discussed in the methodology: cause of death as assigned by healthcare providers; cause of death as assigned by an expert panel, and; cause of death as determined using computerised algorithms.

This chapter is related to objective #2, and it focuses on the following research questions:

1) What are the major causes of stillbirth by method of assessment?
2) Are their differences in the distribution of causes of stillbirth between countries?
3) What is the distribution of cause based on time of death (antepartum / intrapartum death)?
4) What are the advantages and disadvantages of each method of cause assessment?

5.2 Cause of Death as Assigned by Healthcare Providers (HCPs)

5.2.1 Most likely (underlying) cause of death by country

Table 5.1 summarises the most likely cause of stillbirth as assigned by healthcare providers (HCPs) in the field using a process of perinatal death review. Out of the total 1,267 cases, the providers could assign a cause of death for 990 (78.1%). For the remaining 277 (21.9%) cases, no underlying cause of death could be identified. In all cases whose cause of death could not be identified, some information was missing. The proportion of stillbirths with unknown cause was 33.4% in Malawi, 24.7% in Sierra Leone, 22.1% in Kenya and 7.2% in Zimbabwe.

The leading cause of death assigned was asphyxia (18.5%). Other main cause of stillbirth was placental disorders (mainly antepartum haemorrhage and others) accounted for 15.1%. This is followed by hypertensive disorders in pregnancy (hypertension, pre-eclampsia and eclampsia) with 13.6%, infections (6.6%) and cord-related problems contributing 6.5%.

Causes accounting for 5% or less each included ruptured uterus (5.2%), amniotic problems (3.7%), prematurity (3.3%) and anaemia in pregnancy (1.4%). Congenital fetal anomalies accounted for 2.4% of the cases, and included: anencephaly, gastroschisis, hydrocephalus, spina bifida, sacrococcygeal teratoma and some unspecified thoraco-abdominal anomalies.

Maternal infections (pneumonia, tuberculosis, urinary tract infections and others) accounted for 1% of all cases.

There were other causes contributing less than one percent of the total cases, including diabetes, external trauma, Rhesus isoimmunisation and so on.

There was a wide variation among countries in the proportion of some causes of stillbirth, but not in others. For example, cord problems showed a narrow range among the countries (5.5% to 7.2%). On the other hand, asphyxia was most reported from Sierra Leone, accounting for 27.1% of all cases, while it accounted for 21.0% in Malawi, 15.5% in Kenya and 9.4% in Zimbabwe.

Table 5.1: First most likely cause of stillbirth assigned by HCPs.

Cause of death	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Loene n=340 (%)	Zimbabwe n=307 (%)	Total N=1267 (%)
Asphyxia					
Asphyxia (Unspecified cause)	37 (11.5)	24 (8.0)	20 (5.9)	11 (3.6)	**92 (7.3)**
Asphyxia due to prolonged labour	1 (0.3)	18 (6.0)	33 (9.7)	1 (0.3)	**53 (4.2)**
Asphyxia due to obstructed labour	10 (3.1)	6 (2.0)	17 (5.0)	15 (4.9)	**48 (3.8)**
Asphyxia due to prolonged second stage of labour	2 (0.6)	12 (4.0)	8 (2.4)	1 (0.3)	**23 (1.8)**
Asphyxia due to prolonged obstructed labour	0 (0.0)	3 (1.0)	14 (4.1)	1 (0.3)	**18 (1.4)**
Sub-total	**50 (15.6)**	**63 (21.1)**	**92 (27.1)**	**29 (9.4)**	**234 (18.5)**
Placental Disorders					
APH (Unspecified)	25 (7.8)	6 (2.0)	48 (14.1)	22 (7.2)	**101 (8)**
APH (Placenta abruptio)	11 (3.4)	14 (4.7)	6 (1.8)	29 (9.4)	**60 (4.7)**
APH (Placenta previa)	5 (1.6)	2 (0.7)	9 (2.6)	6 (2.0)	**22 (1.7)**
Placental insufficiency	1 (0.3)	0 (0.0)	0 (0.0)	6 (2)	**7 (0.6)**
Placental anomaly	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	**1 (0.1)**
Sub-total	**42 (13.1)**	**22 (7.4)**	**64 (18.8)**	**63 (20.5)**	**191 (15.1)**
Hypertensive Disorders					
Hypertension in pregnancy	27 (8.4)	5 (1.7)	9 (2.6)	34 (11.1)	**75 (5.9)**
Pre-eclampsia	13 (4.0)	10 (3.3)	2 (0.6)	52 (16.9)	**77 (6.1)**
Eclampsia	1 (0.3)	2 (0.7)	10 (2.9)	7 (2.3)	**20 (1.6)**
Sub-total	**41 (12.8)**	**17 (5.7)**	**21 (6.2)**	**93 (30.3)**	**172 (13.6)**
Infectious Conditions					
HIV	9 (2.8)	8 (2.7)	0 (0.0)	19 (6.2)	**36 (2.8)**
Malaria in pregnancy	12 (3.7)	6 (2.0)	6 (1.8)	0 (0.0)	**24 (1.9)**

Cause of death	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Loene n=340 (%)	Zimbabwe n=307 (%)	Total N=1267 (%)
Syphilis	0 (0.0)	1 (0.3)	1 (0.3)	9 (2.9)	**11 (0.9)**
Infection / Sepsis	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.7)	**6 (0.5)**
UTI	1 (0.3)	0 (0.0)	4 (1.2)	0 (0.0)	**5 (0.4)**
Pneumonia during pregnancy	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Pulmonary TB	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	**1 (0.1)**
Sub-total	**25 (7.8)**	**16 (5.4)**	**12 (3.5)**	**31 (10.1)**	**84 (6.6)**
Cord Problems					
Cord prolapse	10 (3.1)	16 (5.4)	24 (7.1)	13 (4.2)	**63 (5.0)**
Cord around the neck	9 (2.8)	3 (1.0)	2 (0.6)	2 (0.7)	**16 (1.3)**
Cord anomaly	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.7)	**2 (0.2)**
Cord knotting	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Sub-total	**20 (6.2)**	**19 (6.4)**	**26 (7.6)**	**17 (5.5)**	**82 (6.5)**
Amniotic Problems					
PROM	18 (5.6)	6 (2.0)	1 (0.3)	2 (0.7)	**27 (2.1)**
Chorioamnionitis	2 (0.6)	0 (0.0)	2 (0.6)	4 (1.3)	**8 (0.6)**
Polyhydramnios	5 (1.6)	2 (0.7)	1 (0.3)	0 (0.0)	**8 (0.6)**
Oligohydramnios	2 (0.6)	1 (0.3)	1 (0.3)	0 (0.0)	**4 (0.3)**
Sub-total	**27 (8.4)**	**9 (3.0)**	**5 (1.5)**	**6 (2.0)**	**47 (3.7)**
Others					
Ruptured uterus	7 (2.2)	25 (8.4)	24 (7.1)	10 (3.3)	**66 (5.2)**
Prematurity	9 (2.8)	6 (2.0)	3 (0.9)	24 (7.8)	**42 (3.3)**
Congenital fetal anomaly	8 (2.5)	15 (5.0)	0 (0.0)	8 (2.6)	**31 (2.4)**
Anaemia in pregnancy	6 (1.9)	6 (2.0)	4 (1.2)	2 (0.7)	**18 (1.4)**
Diabetes	6 (1.9)	0 (0.0)	0 (0.0)	1 (0.3)	**7 (0.6)**

Cause of death	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Loene n=340 (%)	Zimbabwe n=307 (%)	Total N=1267 (%)
Trauma (external)	4 (1.2)	1 (0.3)	1 (0.3)	1 (0.3)	**7 (0.6)**
Rhesus isoimmunisation	2 (0.6)	0 (0.0)	1 (0.3)	0 (0.0)	**3 (0.2)**
Sickle cell disease	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	**2 (0.2)**
Deep vein thrombosis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Iatrogenic ("criminal abortion")	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Post maturity	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Traditional abortive herbs	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	**1 (0.1)**
Unknown	71 (22.1)	100 (33.4)	84 (24.7)	22 (7.2)	**277 (21.9)**

5.2.2 Cause by time of death

When cause of death assigned by HCPs were analysed by time of death (Table 5.2), it was interesting to note that up to 4.0% of all cases were due to asphyxia and occurred during the antepartum period. On the other hand, congenital anomalies, which are more likely to cause death during the antepartum period, caused more deaths during the intrapartum period than antepartum.

It is also important to note that although most deaths due to ruptured uterus occurred during intrapartum period, some occurred during antepartum period, highlighting issues with records of fetal heart sound on admission and physical appearance of babies (fresh / macerated).

As expected, more deaths due to placental disorders occurred during the intrapartum period than antepartum. Similarly, there were more cases with unknown cause of death during antepartum than intrapartum period.

Table 5.2: Most likely cause of death as assigned by HCPs by time of death.

CAUSE OF DEATH	Antepartum Death n=1,267	Intrapartum Death n=1,267	Unknown Time of Death n=1,267	Total n=1,267 (%)
Asphyxia				
Asphyxia (unspecified)	21	68	3	92 (7.3)
Asphyxia due to obstructed labour	18	25	5	48 (3.8)
Asphyxia due to prolonged labour	4	46	3	53 (4.2)
Asphyxia due to prolonged obstructed labour	4	13	1	18 (1.4)
Asphyxia due to prolonged second stage of labour	4	19	0	23 (1.8)
Sub-total (%)	**51 (4.0)**	**171 (13.5)**	**12 (0.9)**	**234 (18.5)**
Placental Disorders				
APH (unspecified)	33	49	19	101 (8.0)
APH (Placenta abruptio)	24	34	2	60 (4.7)
APH (Placenta praevia)	8	11	3	22 (1.7)
Placental anomaly	0	1	0	1 (0.1)
Placental insufficiency	4	2	1	7 (0.6)
Total (%)	**69 (5.4)**	**97 (7.7)**	**25 (2.0)**	**191 (15.1)**
Hypertensive Disorders				
Hypertension in pregnancy	39	32	4	75 (5.9)
Pre-eclampsia	33	40	4	77 (6.1)
Eclampsia	5	13	2	20 (1.6)
Sub-total (%)	**77 (6.1)**	**85 (6.7)**	**10 (0.8)**	**172 (13.6)**
Cord Problems				
Cord around the neck	10	6	0	16 (1.3)
Cord knotting	0	1	0	1 (0.1)
Cord prolapse	17	43	3	63 (5.0)
Cord anomaly	1	1	0	2 (0.2)
Sub-total (%)	**28 (2.2)**	**51 (4.0)**	**3 (0.2)**	**82 (6.5)**
Infectious Conditions				
HIV	24	10	2	36 (2.8)
Malaria in pregnancy	11	12	1	24 (1.9)

CAUSE OF DEATH	Antepartum Death n=1,267	Intrapartum Death n=1,267	Unknown Time of Death n=1,267	Total n=1,267 (%)
Syphilis	11	0	0	11 (0.9)
Infection / Sepsis (unspecified)	3	3	0	6 (0.5)
Urinary tract infection	3	2	0	5 (0.4)
Pneumonia during pregnancy	1	0	0	1 (0.1)
Pulmonary tuberculosis	0	1	0	1 (0.1)
Sub-total (%)	**53 (4.2)**	**28 (2.2)**	**3 (0.2)**	**84 (6.6)**
Amniotic Problems				
PROM	11	16	0	27 (2.1)
Chorioamnionitis	4	3	1	8 (0.6)
Oligohydramnios	1	3	0	4 (0.3)
Polyhydramnios	5	3	0	8 (0.6)
Sub-total (%)	**21 (1.7)**	**25 (2.0)**	**1 (0.1)**	**47 (3.7)**
Others				
Congenital anomaly	9	20	2	31 (2.4)
Ruptured uterus	14	45	7	66 (5.2)
Diabetes	5	2	0	7 (0.6)
Deep vein thrombosis	1	0	0	1 (0.1)
Iatrogenic ("criminal abortion")	0	1	0	1 (0.1)
Post-maturity	0	1	0	1 (0.1)
Prematurity	31	9	2	42 (3.3)
Rhesus isoimmunisation	1	2	0	3 (0.2)
Sickle cell disease	1	1	0	2 (0.2)
Anaemia in pregnancy	9	9	0	18 (1.4)
Traditional abortive herbs	1	0	0	1 (0.1)
Trauma (external)	4	3	0	7 (0.6)
Unknown (%)	157 (12.4)	93 (7.3)	27 (2.1)	277 (21.9)

5.2.3 Aggregate contribution of conditions to cause of death

Overall, 399 cases had more than one cause of death assigned (Table 5.3). When the contribution of each cause of death in all the ranks were combined, asphyxia contributed the most, accounting for 24.5%. This is followed by hypertensive disorders in pregnancy (17.8%). Placental problems (mainly antepartum haemorrhage) accounted for 17.5%, followed by cord problems (7.6%) and amniotic problems (5.5%).

Other major causes were: infections (13.3%), prematurity (13.2%). Congenital anomalies and anaemia in pregnancy accounted for 3.6% each. Conditions that contributed less than one percent of the causes were: diabetes, Rhesus isoimmunisation, external trauma and sickle cell disorders.

The assignment of unknown cause of death only changed from 21.9% in the first rank to 22.2% in the cumulative total.

Table 5.3: First, second, third and fourth most likely cause of death as assigned and ranked by HCPs.

Cause of Death	1st Cause n=1267 (%)	2nd Cause n=399 (%)	3rd Cause n=70 (%)	4th Cause n=6 (%)	Aggregated Contribution to Cause n=1267 (%)
Asphyxia					
Asphyxia (Unspecified cause)	92 (7.3)	22 (5.5)	3 (4.3)	0 (0.0)	**117 (9.2)**
Asphyxia due to prolonged labour	53 (4.2)	20 (5)	3 (4.3)	0 (0.0)	**76 (6.0)**
Asphyxia due to obstructed labour	48 (3.8)	16 (4)	2 (2.9)	0 (0.0)	**66 (5.2)**
Asphyxia due to prolonged second stage of labour	23 (1.8)	6 (1.5)	1 (1.4)	0 (0.0)	**30 (2.4)**
Asphyxia due to prolonged obstructed labour	18 (1.4)	3 (0.8)	0 (0.0)	0 (0.0)	**21 (1.7)**
Sub-total	**234 (18.5)**	**67 (16.8)**	**9 (12.9)**	**0 (0.0)**	**310 (24.5)**
Hypertensive Disorders					
Hypertension	75 (5.9)	38 (9.5)	1 (1.4)	0 (0.0)	**114 (9.0)**
Pre-eclampsia	77 (6.1)	6 (1.5)	1 (1.4)	0 (0.0)	**84 (6.6)**
Eclampsia	20 (1.6)	8 (2)	0 (0.0)	0 (0.0)	**28 (2.2)**
Sub-total	**172 (13.6)**	**52 (13.0)**	**2 (2.9)**	**0 (0.0)**	**226 (17.8)**
Placental Problems					
APH (Unspecified)	101 (8)	13 (3.3)	0 (0.0)	0 (0.0)	**114 (9.0)**
APH (Placenta abruptio)	60 (4.7)	9 (2.3)	1 (1.4)	0 (0.0)	**70 (5.5)**
APH (Placenta praevia)	22 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	**22 (1.7)**
Placental insufficiency	7 (0.6)	6 (1.5)	0 (0.0)	0 (0.0)	**13 (1.0)**
Placental anomaly	1 (0.1)	1 (0.3)	1 (1.4)	0 (0.0)	**3 (0.2)**
Sub-total	**191 (15.1)**	**29 (7.3)**	**2 (2.9)**	**0 (0.0)**	**222 (17.5)**
Cord Problems					
Cord prolapse	63 (5.0)	7 (1.8)	0 (0.0)	0 (0.0)	**70 (5.5)**
Cord around the neck	16 (1.3)	5 (1.3)	0 (0.0)	0 (0.0)	**21 (1.7)**
Cord anomaly	2 (0.2)	0 (0)	0 (0.0)	1 (16.7)	**3 (0.2)**
Cord knotting	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	**2 (0.2)**
Sub-total	**82 (6.5)**	**13 (3.3)**	0 (0.0)	**1 (16.7)**	**96 (7.6)**
Amniotic Problems					

Cause of Death	1st Cause n=1267 (%)	2nd Cause n=399 (%)	3rd Cause n=70 (%)	4th Cause n=6 (%)	Aggregated Contribution to Cause n=1267 (%)
PROM	27 (2.1)	3 (0.8)	5 (7.1)	0 (0.0)	**35 (2.8)**
Chorioamnionitis	8 (0.6)	5 (1.3)	0	0 (0.0)	**13 (1.0)**
Oligohydramnios	4 (0.3)	3 (0.8)	3 (4.3)	1 (16.7)	**11 (0.9)**
Polyhydramnios	8 (0.6)	3 (0.8)	0 (0.0)	0 (0.0)	**11 (0.9)**
Sub-total	**47 (3.7)**	**14 (3.5)**	**8 (11.4)**	**1 (16.7)**	**70 (5.5)**
Infectious Diseases					
HIV	36 (2.8)	22 (5.5)	4 (5.7)	0 (0.0)	**62 (4.9)**
Syphilis	11 (0.9)	4 (1.0)	1 (1.4)	0 (0.0)	**16 (1.3)**
STI (unspecified)	0 (0.0)	3 (0.8)	0 (0.0)	0 (0.0)	**3 (0.2)**
Malaria in pregnancy	24 (1.9)	13 (3.3)	3 (4.3)	0 (0.0)	**40 (3.2)**
Infection / Sepsis (unspecified)	6 (0.5)	8 (2.0)	3 (4.3)	0 (0.0)	**17 (1.3)**
UTI	5 (0.4)	18 (4.5)	3 (4.3)	0 (0.0)	**26 (2.1)**
Pneumonia/LRTI in pregnancy	1 (0.1)	1 (0.3)	0 (0.0)	1 (16.7)	**3 (0.2)**
Pulmonary TB	1 (0.1)	0 (0.0)	0 (0.0)	1 (16.7)	**2 (0.2)**
Sub-total	**84 (6.6)**	**69 (17.3)**	**14 (20.0)**	**2 (33.3)**	**169 (13.3)**
Others					
Prematurity	42 (3.3)	108 (27.1)	17 (24.3)	0 (0.0)	**167 (13.2)**
Ruptured uterus	66 (5.2)	14 (3.5)	1 (1.4)	0 (0.0)	**81 (6.4)**
Congenital fetal anomaly	31 (2.4)	3 (0.8)	9 (12.9)	2 (33.3)	**45 (3.6)**
Anaemia in pregnancy	18 (1.4)	22 (5.5)	5 (7.1)	0 (0.0)	**45 (3.6)**
Diabetes	7 (0.6)	1 (0.3)	1 (1.4)	0 (0.0)	**9 (0.7)**
Rhesus isoimmunisation	3 (0.2)	2 (0.5)	2 (2.9)	0 (0.0)	**7 (0.6)**
Trauma (external)	7 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	**7 (0.6)**
Sickle cell disease	2 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	**3 (0.2)**
Deep vein thrombosis	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Iatrogenic ("criminal abortion")	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Post maturity	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Traditional abortive herbs	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Unknown	277 (21.9)	4 (1.0)	0 (0.0)	0 (0.0)	**281 (22.2)**

5.3 Cause of Death Assigned by Expert Panel

5.3.1 Cause of death by country

Table 5.4 summarises cause of death as assigned by expert panel. Out of the 1,267 cases, the experts assigned a cause of death for 938 cases (74.0%), while the remaining 329 (26.0%) remained unknown.

Like the results obtained by HCPs, the leading cause of death as assigned by the experts was asphyxia (20.8% of all cases). This showed a marked variation between countries, with the highest proportion of stillbirth due to asphyxia observed in Sierra Leone (35.3%) and the lowest in Zimbabwe (9.4%).

Hypertensive disorders (hypertension, pre-eclampsia and eclampsia) accounted for 13.3% of all cases. This also varied between 4.3% in Malawi and 33.9% in Zimbabwe. Deaths due to placental and cord problems showed more even distributions across the four countries. However, lower proportions of death due to infections were noted in Sierra Leone than in the rest of the countries.

Deaths due to ruptured uterus showed similar proportions, except in Malawi where a much higher proportion was found. No cause due to congenital anomalies was documented in Sierra Leone by the expert panel.

Table 5.4: Most likely cause of stillbirth as assigned by expert panel.

Cause of death	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)
Asphyxia					
Asphyxia (Unspecified)	53 (16.5)	50 (16.7)	113 (33.2)	25 (8.1)	**241 (19)**
Asphyxia due to obstructed labour	2 (0.6)	8 (2.7)	6 (1.8)	4 (1.3)	**20 (1.6)**
Asphyxia due to prolonged labour	1 (0.3)	1 (0.3)	1 (0.3)	0 (0.0)	**3 (0.2)**
Sub-total	**56 (17.4)**	**59 (19.7)**	**120 (35.3)**	**29 (9.4)**	**264 (20.8)**
Hypertensive Disorders					
Hypertension in pregnancy	35 (10.9)	8 (2.7)	9 (2.6)	66 (21.5)	**118 (9.3)**
Pre-eclampsia	0 (0.0)	3 (1)	0 (0.0)	36 (11.7)	**39 (3.1)**
Eclampsia	0 (0.0)	2 (0.7)	8 (2.4)	2 (0.7)	**12 (0.9)**
Sub-total	**35 (10.9)**	**13 (4.3)**	**17 (5.0)**	**104 (33.9)**	**169 (13.3)**
Placental Disorders					
APH (Placenta abruptio)	13 (4.0)	16 (5.4)	2 (0.6)	29 (9.4)	**60 (4.7)**
APH (Placenta previa)	3 (0.9)	1 (0.3)	2 (0.6)	5 (1.6)	**11 (0.9)**
APH (Unspecified)	24 (7.5)	4 (1.3)	54 (15.9)	10 (3.3)	**92 (7.3)**
Placental insufficiency	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.0)	**3 (0.2)**
Sub-total	**40 (12.5)**	**21 (7.0)**	**58 (17.1)**	**47 (15.3)**	**166 (13.1)**
Cord Problems					
Cord prolapse	16 (5.0)	18 (6)	24 (7.1)	11 (3.6)	**69 (5.4)**
Cord around the neck	0 (0.0)	4 (1.3)	0 (0.0)	4 (1.3)	**8 (0.6)**
Cord anomaly	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	**1 (0.1)**
Sub-total	**16 (5.0)**	**22 (7.4)**	**24 (7.1)**	**16 (5.2)**	**78 (6.2)**
Infectious Diseases					
HIV	3 (0.9)	6 (2)	0 (0.0)	11 (3.6)	**20 (1.6)**
Infection (Unspecified)	1 (0.3)	2 (0.7)	1 (0.3)	3 (1)	**7 (0.6)**
Malaria	12 (3.7)	1 (0.3)	0 (0.0)	0 (0.0)	**13 (1.0)**
Pneumonia in pregnancy	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Syphilis	0 (0.0)	1 (0.3)	0 (0.0)	11 (3.6)	**12 (0.9)**

Cause of death	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)
UTI	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Sub-total	**18 (5.6)**	**10 (3.3)**	**1 (0.3)**	**25 (8.1)**	**54 (4.3)**
Amniotic Problems					
Chorioamnionitis	6 (1.9)	3 (1)	2 (0.6)	3 (1)	**14 (1.1)**
PROM	8 (2.5)	2 (0.7)	2 (0.6)	2 (0.7)	**14 (1.1)**
Polyhydramnios	4 (1.2)	2 (0.7)	1 (0.3)	0 (0.0)	**7 (0.6)**
Oligohydramnios	4 (1.2)	1 (0.3)	1 (0.3)	1 (0.3)	**7 (0.6)**
Other amniotic problems	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	**1 (0.1)**
Sub-total	**22 (6.9)**	**8 (2.7)**	**7 (2.1)**	**6 (2.0)**	**43 (3.4)**
Others					
Ruptured uterus	12 (3.7)	30 (10.0)	20 (5.9)	15 (4.9)	**77 (6.1)**
Congenital fetal anomaly	9 (2.8)	14 (4.7)	0 (0.0)	9 (2.9)	**32 (2.5)**
Prematurity	1 (0.3)	4 (1.3)	1 (0.3)	15 (4.9)	**21 (1.7)**
Birth trauma	1 (0.3)	7 (2.3)	0 (0.0)	1 (0.3)	**9 (0.7)**
External trauma	3 (0.9)	0 (0.0)	1 (0.3)	2 (0.7)	**6 (0.5)**
IUGR	1 (0.3)	3 (1.0)	0 (0.0)	2 (0.7)	**6 (0.5)**
Anaemia in pregnancy	2 (0.6)	2 (0.7)	0 (0.0)	2 (0.7)	**6 (0.5)**
Diabetes	3 (0.9)	0 (0.0)	0 (0.0)	2 (0.7)	**5 (0.4)**
Abdominal pregnancy	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Traditional herbs	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	**1 (0.1)**
Unknown	97 (30.2)	108 (35.5)	87 (26.5)	37 (10.4)	**329 (26.0)**

5.3.2 Cause of death by time of death

When cause of death assigned by the expert panel was analysed by time of death (ante- or intrapartum), 4.3% of the cases were due to asphyxia and occurred during the antepartum period (Table 5.5). Deaths due to hypertensive and placental disorders showed equal distributions between antepartum and intrapartum periods.

As expected, there were more deaths due to cord problems during the intrapartum period and fewer due to infections at the same period. Cases with unknown causes occurred twice as many in the antepartum period than intrapartum.

Table 5.5: Most likely cause of stillbirth (expert panel) by time of death

Cause of death	Antepartum Death n=1,267	Intrapartum Death n=1,267	Unknown Time of Death n=1,267	Total n=1,267 (%)
Asphyxia				
Asphyxia (unspecified cause)	33	107	5	**145 (11.4)**
Asphyxia due to obstructed labour	12	21	4	**37 (2.9)**
Asphyxia due to prolonged labour	4	40	3	**47 (3.7)**
Asphyxia due to prolonged obstructed labour	3	10	0	**13 (1.0)**
Asphyxia due to prolonged second stage	3	13	0	**16 (1.3)**
Sub-total (%)	**55 (4.3)**	**191 (15.1)**	**12 (0.9)**	**258 (20.4)**
Hypertensive Disorders				
Hypertension in pregnancy	43	29	4	**76 (6)**
Pre-eclampsia	32	36	4	**72 (5.7)**
Eclampsia	5	14	2	**21 (1.7)**
Sub-total (%)	**80 (6.3)**	**79 (6.2)**	**10 (0.8)**	**169 (13.3)**
Placental Disorders				
APH (Unspecified)	30	42	19	**91 (7.2)**
APH (Placenta abruptio)	20	34	2	**56 (4.4)**
APH (Placenta praevia)	6	8	2	**16 (1.3)**
Placental insufficiency	1	2	0	**3 (0.2)**
Sub-total (%)	**57 (4.5)**	**86 (6.8)**	**23 (1.8)**	**166 (13.1)**
Cord Problems				
Cord prolapse	21	45	4	**70 (5.5)**
Cord anomaly	0	1	0	**1 (0.1)**
Cord around the neck	3	3	0	**6 (0.5)**
Cord knotting	0	1	0	**1 (0.1)**
Sub-total (%)	**24 (1.9)**	**50 (3.9)**	**4 (0.3)**	**78 (6.2)**

Cause of death	Antepartum Death n=1,267	Intrapartum Death n=1,267	Unknown Time of Death n=1,267	Total n=1,267 (%)
Infectious Conditions				
HIV	15	4	1	**20 (1.6)**
Infection	1	1	0	**2 (0.2)**
Malaria in pregnancy	7	6	0	**13 (1.0)**
Infection / Sepsis (unspecified)	6	4	0	**10 (0.8)**
Syphilis	11	1	0	**12 (0.9)**
Pneumonia during pregnancy	1	0	0	**1 (0.1)**
Pulmonary tuberculosis	0	1	0	**1 (0.1)**
UTI	0	1	0	**1 (0.1)**
Sub-total (%)	**41 (3.2)**	**18 (1.4)**	**1 (0.1)**	**60 (4.7)**
Amniotic Problems				
Chorioamnionitis	7	6	1	**14 (1.1)**
Oligohydramnios	4	3	0	**7 (0.6)**
Polyhydramnios	3	4	0	**7 (0.6)**
PROM	4	10	0	**14 (1.1)**
Amniotic fluid - other problem	0	1	0	**1 (0.1)**
Sub-total (%)	**18 (1.4)**	**24 (1.9)**	**1 (0.1)**	**43 (3.4)**
Others				
Congenital anomaly	10	20	2	**32 (2.5)**
Ruptured uterus	16	50	6	**72 (5.7)**
Prematurity	18	3	0	**21 (1.7)**
Birth trauma	4	5	0	**9 (0.7)**
Diabetes	3	2	0	**5 (0.4)**
IUGR	2	4	0	**6 (0.5)**
Anaemia in pregnancy	3	3	0	**6 (0.5)**
Traditional abortive herbs	1	0	0	**1 (0.1)**
Trauma (external)	4	2	0	**6 (0.5)**
Unknown	196	106	33	**335 (26.4)**

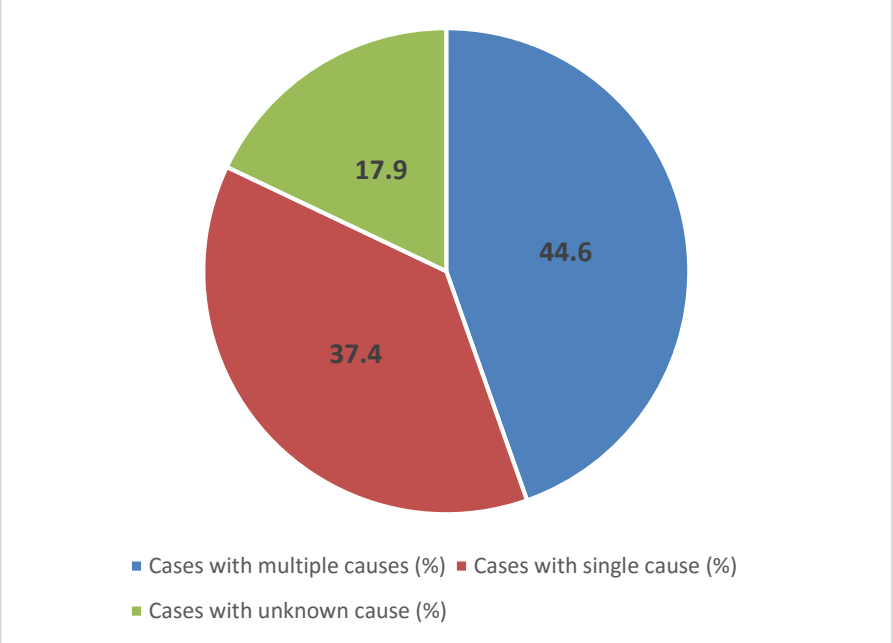
5.4 Cause of Death Determined by Computer Algorithms

5.4.1 Overview

The computer algorithms used in this study were programmed to assign multiple causes of death simultaneously. Only 455 cases (37.4%) had a single cause; 542 (44.6%) had two or more causes. No cause of death was identified by the algorithms in the remaining 218 cases (17.9%; Figure 5.1).

For case with multiple causes, the algorithms identified the most likely cause based on a hierarchical model described in the methodology chapter (and attached in Appendix 5). Briefly, the model ranks cause of death based on pathway to death as well as findings of the results of systematic literature review on cause of stillbirth (Chapter 2). Thus, the most likely cause of death was identified.

Figure 5.1: Proportions of cause of death by computer algorithms



5.4.2 Most likely causes of stillbirth

Table 5.6 summarises the most likely cause of stillbirth reported by the algorithms. Like the previous methods of assessing cause of death, the leading cause of stillbirth was asphyxia, accounting for 37.4% of the cases. The result for asphyxia is similar across the countries, except in Malawi where it accounted for more than half (52.2%) of the cases.

Accounting for 15.7% of stillbirth, fetal causes came second. The major fetal cause was fetal growth restriction, defined as birth weight less than 10th centile for gestational age, which was notably unreported by either HCPs or the expert panel. Proportion of deaths due to fetal causes was similar across countries, except in Sierra Leone where fetal causes accounted for a remarkably higher proportion (22.6%).

Stillbirths due to placenta disorders (mainly placenta praevia) represented 11.4% of the cases. This has also shown wide variation among countries, from 3.3% in Malawi to 11.4% in Zimbabwe. Stillbirths due to hypertensive disorders also showed a similar variation across the counties.

The highest proportion of stillbirths with unknown cause was found in Kenya (33.1%) and the lowest was in Sierra Leone (9.7%). The low proportion of cases with unknown cause of death in Sierra Leone may not be unrelated to the high proportions of fetal growth restriction found in the country, which is at least twice what is found in the other countries. Possible reasons for the high proportion of fetal growth restriction in Sierra Leone are discussed in the Discussion Chapter.

Table 5.6: Most likely cause of stillbirth as determined by computer-based algorithms.

Cause	Kenya n=269 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1215 (%)
Asphyxia	82 (30.5)	156 (52.2)	118 (34.7)	99 (32.2)	455 (37.4)
Fetal Causes					
Congenital anomaly	6 (2.2)	4 (1.3)	1 (0.3)	11 (3.6)	22 (1.8)
Fetal growth restriction	26 (9.7)	27 (9.0)	70 (20.6)	34 (11.1)	157 (12.9)
Twin-twin transfusion	2 (0.7)	2 (0.7)	6 (1.8)	2 (0.7)	12 (1.0)
Sub-total	**34 (12.6)**	**33 (11.0)**	**77 (22.6)**	**47 (15.3)**	**191 (15.7)**
Placental Disorders					
Placenta abruptio	3 (1.1)	0 (0.0)	1 (0.3)	1 (0.3)	5 (0.4)
Placenta praevia	16 (5.9)	10 (3.3)	37 (10.9)	34 (11.1)	97 (8.0)
Sub-total	**19 (7.1)**	**10 (3.3)**	**38 (11.2)**	**35 (11.4)**	**102 (8.4)**
Hypertensive Disorders					
Hypertension	12 (4.5)	7 (2.3)	7 (2.1)	32 (10.4)	58 (4.8)
Eclampsia	0 (0.0)	0 (0.0)	4 (1.2)	0 (0.0)	4 (0.3)
Sub-total	**12 (4.5)**	**7 (2.3)**	**11 (3.2)**	**32 (10.4)**	**62 (5.1)**
Others					
Infections	19 (7.1)	27 (9.0)	29 (8.5)	34 (11.1)	109 (9.0)
Cord prolapse	6 (2.2)	4 (1.3)	19 (5.6)	11 (3.6)	40 (3.3)
Ruptured uterus	4 (1.5)	10 (3.3)	14 (4.1)	4 (1.3)	32 (2.6)
Diabetes	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.2)
External trauma	2 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
Iatrogenic	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.1)
Isoimmunisation	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Unknown	89 (33.1)	52 (17.4)	33 (9.7)	44 (14.3)	218 (17.9)

5.4.3 Most likely causes of stillbirth by time of death

In Table 5.7, cause of death assigned by computer algorithms are presented by time of death. A smaller proportion of deaths than found by HCPs and experts were found by the algorithms to be due to asphyxia during antepartum period. There were more deaths due to hypertensive and placental disorders occurring in the antepartum period than in intrapartum period.

As expected, there were more stillbirths due to fetal causes (mainly fetal growth restriction) in the antepartum period than in the intrapartum period. Similarly, infections caused more deaths in the antepartum period than in the intrapartum period. One would expect most cases of stillbirth due to ruptured uterus in the intrapartum period, but this was not the case.

Cases with unknown causes were four times more in antepartum period than intrapartum period.

Table 5.7: Most likely cause of stillbirth (computer algorithms) by time of death

Cause	Antepartum Death n=1,215 (%)	Intrapartum Death n=1,215 (%)	Unknown Time of Death n=1,215 (%)	Total n=1,215 (%)
Asphyxia	33 (2.7)	416 (34.2)	6 (0.5)	455 (37.4)
Fetal Causes				
Congenital anomaly	16 (1.3)	4 (0.3)	2 (0.2)	22 (1.8)
Fetal growth restriction	102 (8.4)	30 (2.5)	25 (2.1)	157 (12.9)
Twin-twin transfusion	3 (0.2)	5 (0.4)	4 (0.3)	12 (1.0)
Sub-total	**121 (10.0)**	**39 (3.2)**	**31 (2.6)**	**191 (15.7)**
Placental Disorders				
Placenta abruptio	3 (0.2)	1 (0.1)	1 (0.1)	5 (0.4)
Placenta praevia	53 (4.4)	30 (2.5)	14 (1.2)	97 (8.0)
Sub-total	**56 (4.6)**	**31 (2.6)**	**15 (1.2)**	**102 (8.4)**
Hypertensive Disorders				
Hypertension	45 (3.7)	8 (0.7)	5 (0.4)	58 (4.8)
Eclampsia	1 (0.1)	1 (0.1)	2 (0.2)	4 (0.3)
Sub-total	**46 (3.8)**	**9 (0.7)**	**7 (0.6)**	**62 (5.1)**
Others				
Infections	76 (6.3)	23 (1.9)	10 (0.8)	109 (9.0)
Cord prolapse	15 (1.2)	20 (1.6)	5 (0.4)	40 (3.3)
Ruptured uterus	15 (1.2)	10 (0.8)	7 (0.6)	32 (2.6)
Diabetes	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)
External trauma	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.2)
Iatrogenic	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
Isoimmunisation	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
Unknown	166 (13.7)	41 (3.4)	11 (0.9)	218 (17.9)

5.4.4 Aggregate contribution to cause of stillbirth

Overall, when the contribution of each cause of stillbirth irrespective of rank were combined (Table 5.8), fetal growth restriction appeared to contribute the most, observed in 41.5% of 1267 cases of stillbirth. Because of the high position of asphyxia in the algorithms, it contributed to 37.4% of all cases as the first cause, but no contribution to the subsequent ranks.

Up to 14.7% of the cases met the criteria for placenta praevia as a cause of death in the algorithms. Much fewer cases of placenta abruptio than praevia were found by the algorithms as the diagnosis of the former required presence of abdominal pain, which was not documented in most case notes of cases of antepartum haemorrhage.

Conditions such as malaria and birth trauma did not appear as cause of death in the first rank because of their position in the hierarchical model. However, on aggregate, both have contributed to some of the cases.

Table 5.8: Aggregate cause of stillbirth as determined by computer algorithms.

Cause of Death	1st Cause n=1215 (%)	2nd Cause n=1215 (%)	3rd Cause n=1215 (%)	4th Cause n=1215 (%)	Aggregate n=1215 (%)
Asphyxia	455 (37.4)	0 (0.0)	0 (0.0)	0 (0.0)	**455 (37.4)**
Fetal Causes					
Congenital anomaly	22 (1.8)	23 (1.9)	0 (0.0)	0 (0.0)	**45 (3.7)**
Fetal growth restriction	157 (12.9)	227 (18.7)	102 (8.4)	18 (1.5)	**504 (41.5)**
Twin-twin transfusion	12 (1.0)	27 (2.2)	16 (1.3)	8 (0.7)	**63 (5.2)**
Sub-total	**191 (15.7)**	**277 (22.8)**	**118 (9.7)**	**26 (2.1)**	**612 (50.4)**
Placental Disorders					
Placenta abruptio	5 (0.4)	2 (0.2)	0 (0.0)	0 (0.0)	**7 (0.6)**
Placenta praevia	97 (8.0)	66 (5.4)	15 (1.2)	0 (0.0)	**178 (14.7)**
Vasa praevia	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.2)	**3 (0.2)**
Sub-total	**102 (8.4)**	**69 (5.7)**	**15 (1.2)**	**2 (0.2)**	**188 (15.5)**
Hypertensive Disorders					
Hypertension	58 (4.8)	33 (2.7)	5 (0.4)	0 (0.0)	**96 (7.9)**
Pre-eclampsia	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	**1 (0.1)**
Eclampsia	4 (0.3)	2 (0.2)	3 (0.2)	0 (0.0)	**9 (0.7)**
Sub-total	**62 (5.1)**	**36 (3.0)**	**8 (0.7)**	**0 (0.0)**	**106 (8.7)**
Others					
Infections	109 (9.0)	85 (7.0)	14 (1.2)	2 (0.2)	**210 (17.3)**
Cord prolapse	40 (3.3)	28 (2.3)	0 (0.0)	0 (0.0)	**68 (5.6)**
Ruptured uterus	32 (2.6)	25 (2.1)	1 (0.1)	0 (0.0)	**58 (4.8)**
Malaria	0 (0.0)	11 (0.9)	31 (2.6)	4 (0.3)	**46 (3.8)**
Birth trauma	0 (0.0)	2 (0.2)	10 (0.8)	3 (0.2)	**15 (1.2)**
External trauma	2 (0.2)	5 (0.4)	1 (0.1)	1 (0.1)	**9 (0.7)**
Diabetes	2 (0.2)	3 (0.2)	0 (0.0)	0 (0.0)	**5 (0.4)**
Isoimmunisation	1 (0.1)	1 (0.1)	3 (0.2)	0 (0.0)	**5 (0.4)**
Iatrogenic	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.1)**
Unknown	218 (17.9)	0 (0.0)	0 (0.0)	0 (0.0)	**218 (17.9)**
GRAND TOTAL	**1215 (100.0)**	**542 (44.6)**	**201 (16.5)**	**38 (3.1)**	

5.6 Comparison Between Methods of Assigning Cause of Stillbirth

Initial attempt to run statistical (Kappa) analysis to compare the results between different methods of assessment was unsuccessful due to a large number of empty cells when the data was cross-tabulated, failing to meet one of the basic requirements of the analysis. This only became possible after grouping the different causes of death, and it is presented in the chapter on classification (section 6.2.4).

However, based on experience in this study, the different methods of cause of death assessment could be compared to highlight their advantages and disadvantages (Table 5.9). It is difficult to conclude which method of assessment will generally perform better than the others. Each method may be more relevant than the others in different contexts.

While reviews by healthcare providers provided opportunities to hospital staff to learn to identify problems quickly and act to solve them, this method took longer time to conduct and was most likely to be affected by possibility of bias in data analysis. HCPs had the tendency to discount some important pieces of information or attach more importance to unimportant information in their analysis.

Experts, on the other hand, were more knowledgeable in the field, and often quicker than healthcare providers in finding cause of death. They were unlikely to be biased in their assessments of cause of death. However, they had the highest proportion of cases with unknown cause and were more difficult to get to conduct the reviews.

Computer algorithms had the lowest proportion of cases with unknown cause. Experts contributing to the algorithms were even more knowledgeable than experts participating in reviews. Algorithms also have the added advantage of taking human bias out of data analysis. The major drawback for algorithms was the elimination of human interaction and discussions, which often highlight important issues that could affect the outcomes of a review.

Table 5.9: Comparison between methods of cause assessment

Characteristics	Healthcare Providers	Expert Panel	Computer Algorithms
Proportion of cases with unknown cause	22.2% (aggregate)	26.4%	17.9% (aggregate)
Observed speed	20 – 30 minutes per case	10 – 20 minutes per case	Only a few seconds to process thousands of cases.
Reasoning process	Discussions may highlight important points in review.	Discussions may highlight important points in review.	Algorithms are pre-set and applied equally to every case.
Possibility of bias in data analysis	Exists due to fear of consequences of the review.	Exists, but to a lesser degree than HCPs (experts less attached to the data).	Non-existent
Resources needed	Initial data collector and minimum of three healthcare providers to discuss case and identify cause and contributing factors.	Initial data collector and minimum of two experts in maternal and newborn health to discuss case and identify cause and contributing factors.	Experts needed initially to develop algorithms; a data collector and; one data clerk to enter and clean data.
Affordability	Healthcare providers are always required, but they are generally less expensive than experts.	Experts' time always required, which is expensive.	High capital costs; low recurring costs.

5.7 Chapter Summary

The major causes of stillbirth were: asphyxia, hypertensive disorders, antepartum haemorrhage, ruptured uterus, infections and cord problems. Asphyxia was the most common cause of stillbirth irrespective of method of assessment used. The causes were similar across the four countries in this study, but there were differences in distribution.

As expected, causes of death differed in their distribution by time of death. However, some causes such as asphyxia and ruptured uterus, that are expected to occur almost exclusively during the intrapartum period, were found to have also occurred in the antepartum period. This was found irrespective of the method of assessment used.

The three methods used to assess cause of death showed some similarities and differences. It is difficult to conclude which method is the best; this depends on the purpose of the review and resources available to conduct it. For health facilities with a few perinatal deaths in a month, reviews by healthcare providers present a cost-effective way of identifying problems and proffering solutions to improve care. For research purposes, however, computer algorithms seem to offer a faster and effective way of analysing thousands of cases and achieving acceptable results.

Comparison between the methods of assessment on how each method assigned cause of death is explored in the next chapter on classification of death.

CHAPTER 6: APPLICATION OF CLASSIFICATION SYSTEMS

6.1 Introduction

This is the third of the four results chapters. In this chapter, two stillbirth classification systems are applied to the cause of stillbirth presented in the previous chapter.

The systems to be applied are:

1) Classification according to Relevant Condition at Death (ReCoDe; Gardosi et al, 2005) and;
2) International Classification of Diseases for Perinatal Mortality (ICD-PM; WHO, 2016b).

The chapter focuses on objective #3, and answers the following research question:

1) Which category of causes accounts for most stillbirths?
2) What are the similarities and/or differences in the classification of causes of stillbirth by different methods of assessment?
3) Which classification is more useful based on a set of criteria?
    a) accuracy
    b) proportion of unknown
    c) ease of use
    d) inter-method agreement
    e) resources required for application or feasibility in LMIC

6.2 ReCoDe Classification

Details of classification systems have been highlighted earlier in the literature review and the methodology chapters. Briefly, the ReCoDe classification categorises cause of stillbirth into nine groups: fetus, umbilical cord, placenta, amniotic fluid, uterus, mother, intrapartum, trauma and unclassified.

Each category comprises of specific causes of stillbirth.

6.2.1 ReCoDe application to cause of death assigned by healthcare providers

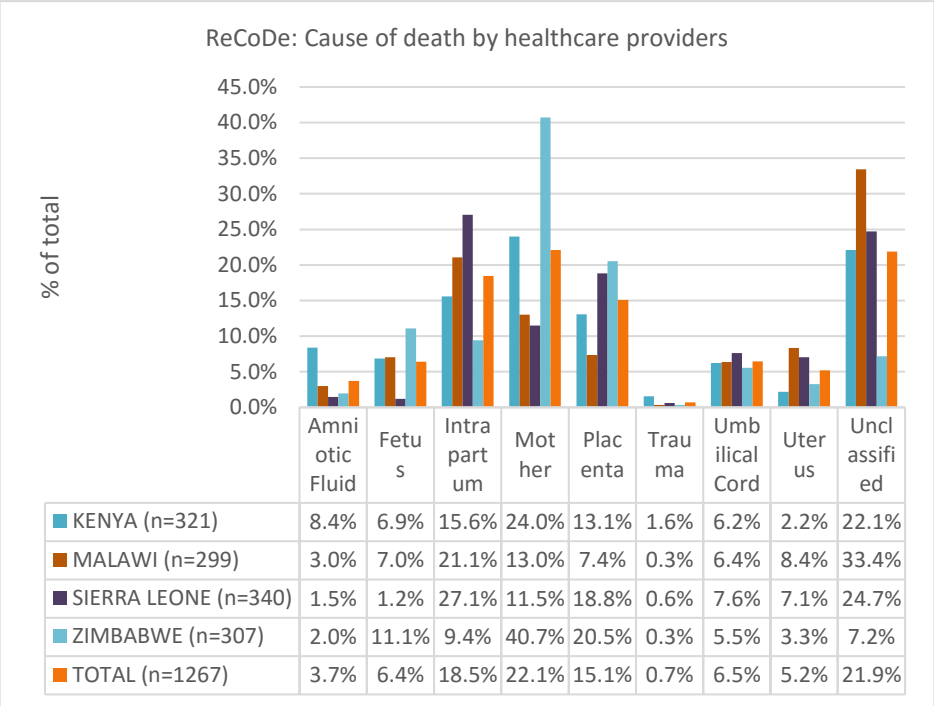
Figure 6.1 summarises the findings after applying ReCoDe classification system to cause of stillbirth assigned by HCPs. The four countries showed some variations for the different categories of cause of stillbirth. Overall, however, maternal conditions, such as hypertensive disorders, diabetes, infections, etc, are the leading cause of stillbirth, accounting for 22.1% of the causes. Across the four countries, the proportions accounted for by these conditions varied; it was highest in Zimbabwe (40.7%) and lowest in Sierra Leone (11.5%).

Intrapartum causes, mainly intrapartum asphyxia, accounted for 18.5% of all cases. Although this also varied among countries, the variation is contrary to the finding for maternal conditions. Intrapartum causes were highest in Sierra Leone (27.1%) and lowest in Zimbabwe (9.4%).

Placental causes, including placenta abruptio and praevia, accounted for 15.1%, with variations between countries. The rest of the categories also showed variations among countries, except for umbilical causes, which were similar across all four countries.

Cases where cause of death could not be assigned by the HCPs were categorised under “Unclassified” in the ReCoDe classification. These represented a total of 21.9%. This also varied between the countries, ranging between 7.2% in Zimbabwe and 33.4% in Malawi.

Figure 6.1: ReCoDe classification for cause of death by HCPs



	Amniotic Fluid	Fetus	Intrapartum	Mother	Placenta	Trauma	Umbilical Cord	Uterus	Unclassified
KENYA (n=321)	8.4%	6.9%	15.6%	24.0%	13.1%	1.6%	6.2%	2.2%	22.1%
MALAWI (n=299)	3.0%	7.0%	21.1%	13.0%	7.4%	0.3%	6.4%	8.4%	33.4%
SIERRA LEONE (n=340)	1.5%	1.2%	27.1%	11.5%	18.8%	0.6%	7.6%	7.1%	24.7%
ZIMBABWE (n=307)	2.0%	11.1%	9.4%	40.7%	20.5%	0.3%	5.5%	3.3%	7.2%
TOTAL (n=1267)	3.7%	6.4%	18.5%	22.1%	15.1%	0.7%	6.5%	5.2%	21.9%

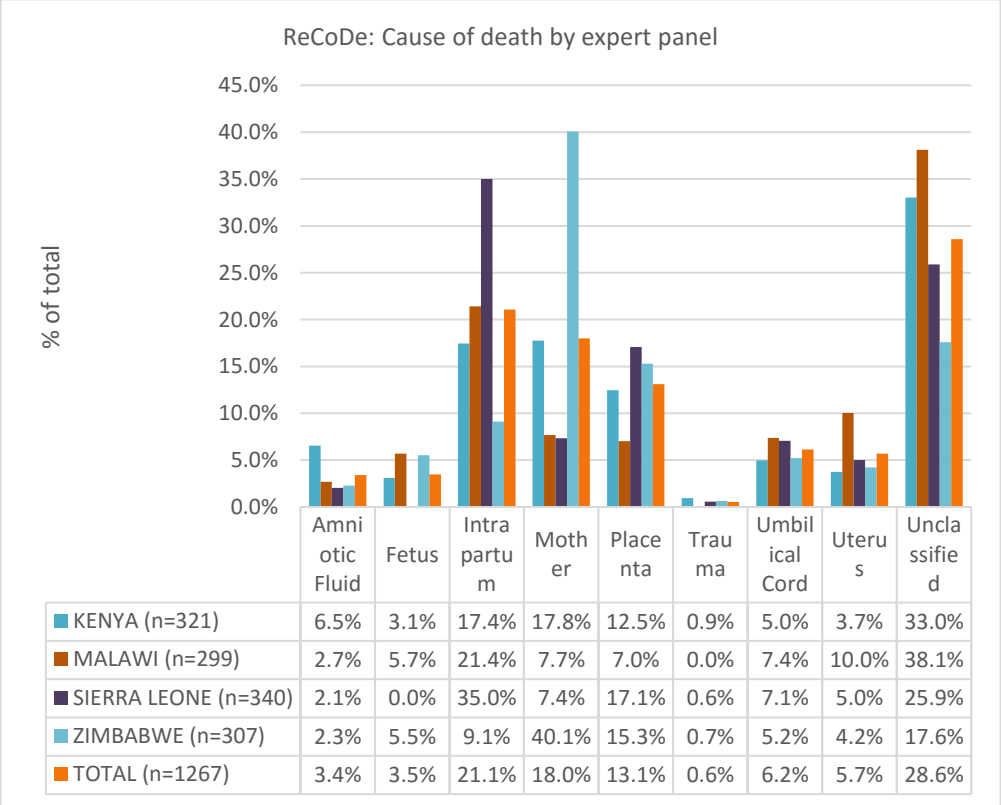
6.2.2 ReCoDe application to cause of death assigned by expert panel

When ReCoDe classification was applied to cause of death assigned by expert panel (Figure 6.2), the leading cause of death was intrapartum conditions, accounting for 21.1% of the cases, with variations between countries.

Even wider variations were observed for maternal conditions, which accounted for 18.0%, with lowest range of 7.4% in Sierra Leone and highest of 40.1% in Zimbabwe.

Other categories also varied among countries. Uterine cause in Malawi were observed to account for 10%, which is at least double the proportion in the other countries. However, umbilical causes showed similarities across all four countries.

Figure 6.2: ReCoDe classification for cause of death by expert panel



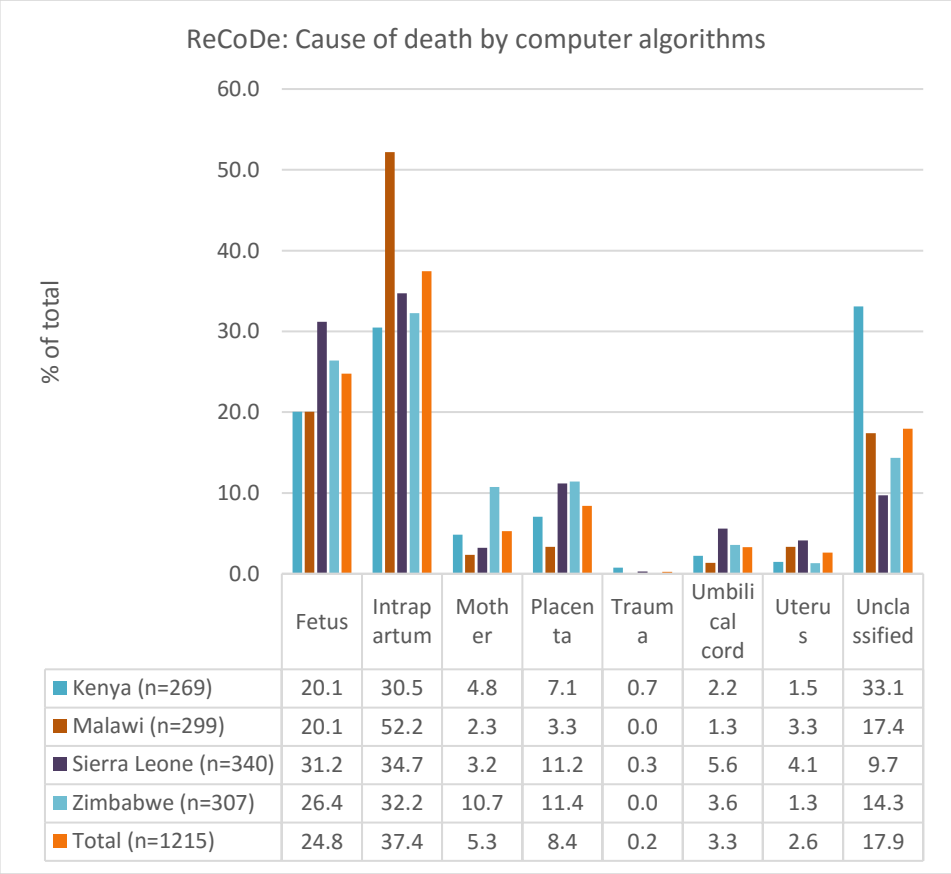
	Amniotic Fluid	Fetus	Intrapartum	Mother	Placenta	Trauma	Umbilical Cord	Uterus	Unclassified
KENYA (n=321)	6.5%	3.1%	17.4%	17.8%	12.5%	0.9%	5.0%	3.7%	33.0%
MALAWI (n=299)	2.7%	5.7%	21.4%	7.7%	7.0%	0.0%	7.4%	10.0%	38.1%
SIERRA LEONE (n=340)	2.1%	0.0%	35.0%	7.4%	17.1%	0.6%	7.1%	5.0%	25.9%
ZIMBABWE (n=307)	2.3%	5.5%	9.1%	40.1%	15.3%	0.7%	5.2%	4.2%	17.6%
TOTAL (n=1267)	3.4%	3.5%	21.1%	18.0%	13.1%	0.6%	6.2%	5.7%	28.6%

6.2.3 ReCoDe application to cause of death determined by computer algorithms

Figure 6.3 summarises ReCoDe classification of cause assigned by algorithms. The highest proportion was in intrapartum cases, accounting for 37.4%, and Malawi had the highest proportion of 52.2%. Similarly, the category for fetal causes accounted for 24.8%, and Sierra Leone had the highest proportion of 31.2%. For causes related to the mother, the countries showed similar results, with slight lead by Zimbabwe. Causes related to the placenta showed more variation between the countries.

Cases whose cause of death could not be found constituted 17.9%. This also varied between the countries. Kenya had the highest proportion (33.1%), while Sierra Leone had the lowest (9.7%).

Figure 6.3: ReCoDe classification for most likely cause of death by computer algorithms



	Fetus	Intrapartum	Mother	Placenta	Trauma	Umbilical cord	Uterus	Unclassified
Kenya (n=269)	20.1	30.5	4.8	7.1	0.7	2.2	1.5	33.1
Malawi (n=299)	20.1	52.2	2.3	3.3	0.0	1.3	3.3	17.4
Sierra Leone (n=340)	31.2	34.7	3.2	11.2	0.3	5.6	4.1	9.7
Zimbabwe (n=307)	26.4	32.2	10.7	11.4	0.0	3.6	1.3	14.3
Total (n=1215)	24.8	37.4	5.3	8.4	0.2	3.3	2.6	17.9

6.2.4 Comparison of ReCoDe classification for the different methods of assigning cause of death

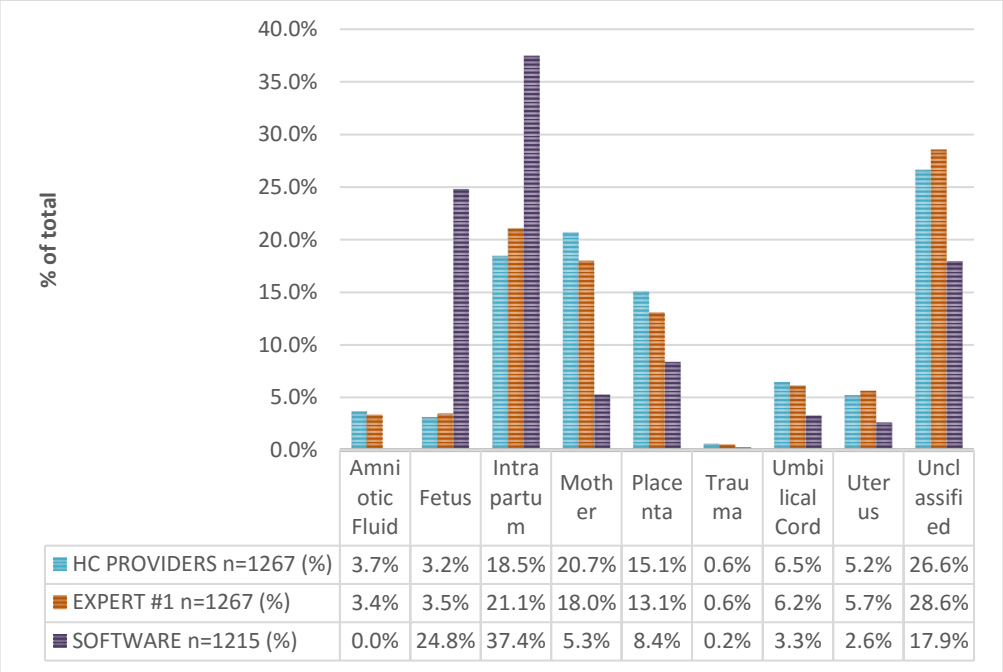
To explore the level of agreement between the three methods of assigning cause of death, Kappa analyses were conducted.

The analysis showed a statistically significant agreement between ReCoDe classification of cause of death assigned by HCPs and that assigned by expert panel ($p<0.0005$), with an agreement value (k) of 0.69, representing a good level of agreement (Peat, 2001). The analysis between cause of death assigned by expert panel and cause assigned by computer algorithms showed a much lower, but still statistically significant agreement, with k-value of 0.34 ($p<0.0005$). Similarly, the results obtained from HCPs and from the algorithms showed low, but statistically significant agreement ($k=0.31$; $p<0.0005$).

Interestingly, when the 324 cases that were randomly selected for second expert review were analysed, the agreement rate between the experts was only moderate ($k=0.61$; $p<0.0005$), and it was lower than that between experts and HCPs.

Although the agreement rates were statistically significant among the methods of assessment, there were some differences in the proportions for individual categories (Figure 6.4). For example, in the “fetus” category, HCPs had almost double what the expert panel reported (6.4% and 3.5%, respectively). Similarly, the computer algorithms reported 24.8% to be due to fetal causes, which was approximately seven-fold more than the result obtained via the expert panel.

Figure 6.4: Bar chart comparing ReCoDe classification applied to most likely cause of death by HCPs, experts and computer algorithms.



	Amniotic Fluid	Fetus	Intrapartum	Mother	Placenta	Trauma	Umbilical Cord	Uterus	Unclassified
HC PROVIDERS n=1267 (%)	3.7%	3.2%	18.5%	20.7%	15.1%	0.6%	6.5%	5.2%	26.6%
EXPERT #1 n=1267 (%)	3.4%	3.5%	21.1%	18.0%	13.1%	0.6%	6.2%	5.7%	28.6%
SOFTWARE n=1215 (%)	0.0%	24.8%	37.4%	5.3%	8.4%	0.2%	3.3%	2.6%	17.9%

6.3 ICD-PM Classification of Cause of Death

Details about the International Classification of Diseases for Perinatal Mortality (ICD-PM; WHO, 2016b) has been presented in the literature review and the methodology chapters. Briefly, this new classification system uses a layered approach to categorise cause of perinatal mortality, including late neonatal mortality, often referred to as extended perinatal mortality.

In this system, each death is assigned a fetal cause and a contributing maternal condition. For fetal cause, mortality is categorised by time of death: antenatal stillbirth, intrapartum stillbirth and neonatal death. Antenatal deaths are further classified into six sub-categories (A1 to A6); intrapartum deaths are classified into seven sub-categories (I1 to I7), and; neonatal deaths are classified into 11 sub-categories (N1 to N11).

The contributing maternal condition are classified into five major categories: complications of placenta, cord and membranes (M1); maternal complications of pregnancy (M2); other complications of labour and delivery (M3); maternal medical conditions (M4), and; no maternal conditions (M5).

In this study, a special category ("stillbirths of unknown time of death") was created to accommodate stillbirths whose time of death was unknown.

6.3.1 ICD-PM application for cause of death assigned by healthcare providers

Table 6.1 summarises results for ICD-PM application to cause of death by HCPs. Antepartum cause of death assigned by HCPs were mostly classified as unspecified (89.7%). Other significant categories were: infections (7.0%), congenital anomalies (3.6%).

Most (61.1%) intrapartum deaths were classified as unspecified. Other categories were: acute intrapartum events, such as asphyxia (31.3%), congenital anomalies (3.7%), and infections (3.6%).

Similarly, 81.5% of stillbirths that could not be classified as ante- or intrapartum deaths did not have a fetal cause. However, some were classified into acute events (14.7%), infections (2.2%) and congenital anomalies (2.2%).

Generally, co-existing maternal conditions were more evenly distributed than fetal causes of death. Complications of placenta, cord and membranes (M1) were found in 22.3%, while maternal complications of pregnancy (M2) such as oligohydramnios and premature rupture of membranes, were reported in 8.6%. Other categories were: complications of labour (M3; 37.6%) and maternal medical conditions (M4; 11.6%). No maternal conditions (M5) were reported for 19.8% of the stillbirths.

In total, 174 (13.7% of all) cases could not be assigned into either a fetal category or maternal contributing condition.

6.3.2 ICD-PM application for cause of death assigned by expert panel

Like the results of ICD-PM classification of cause of death assigned by HCPs, the majority (83.1%) of antepartum deaths assigned by expert panel were unspecified (Table 6.2). Other categories in the antepartum death category were: congenital anomalies (1.9%), infections (4.3%) and antepartum hypoxia (10.3%).

For intrapartum deaths, the major cause of death assigned by the expert panel were categorised as: congenital anomalies (3.3%), acute intrapartum events (29.7%) and infections (1.1%). However, 64.5% were classified as unspecified for fetal cause.

Stillbirths that could not be classified as ante- or intrapartum deaths were classified into the following ICD-PM groups: congenital anomalies (2.2%), hypoxia (13.0%) and unspecified fetal cause (84.8%).

Co-existing maternal conditions were found in most cases: complications of placenta, cord and membranes were reported in 12.0%, and; maternal complications of pregnancy found in 5.4%. Other categories were: complications of labour (50.7%); maternal medical conditions (6.8%), and; no maternal conditions were reported in 25.1% of the cases.

In total, 197 (15.5% of all) cases could not be assigned into either a fetal category or maternal contributing condition.

6.3.3 ICD-PM application for cause of death determined with computer algorithms

For antepartum deaths, there was more variety of categories for cause by algorithms than with the two previous methods of assigning cause of death used (Table 6.3). The major categories were: fetal growth disorders (29.5%), infections (17.5%), hypoxia (6.3%) and unknown (42.6%).

Intrapartum deaths were categorised as acute intrapartum events (69.6%), fetal growth disorders (9.3%). As expected, there were fewer cases in the unspecified category in intrapartum deaths than in antepartum deaths (13.4%).

Stillbirths that could not be categorised as antepartum or intrapartum deaths belonged to various groups, mainly fetal growth disorders (44.4%) and infections (16.7%).

For co-existing maternal conditions, the majority (66.7%) were not associated with any contributing maternal condition. Commonly associated maternal conditions were: complications of placenta, cord and membranes were reported (18.4%), maternal medical conditions (9.0%); and other complications of labour (5.9%).

In total, 218 (17.9% of all) cases could not be assigned into either a fetal category or maternal contributing condition.

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Table 6.1: Application of ICD-PM to cause of stillbirth by HCPs

	M1: Complications of placenta, cord and membranes	M2: Maternal complications of pregnancy	M3: Other complications of labour and delivery	M4: Maternal medical and surgical conditions	M5: No maternal condition	Total (%)
Antepartum Death						
A1: Congenital malformations, deformations and chromosomal abnormalities	1	1	7	2	3	**14 (2.6)**
A2: Infection	4	2	9	22	0	**37 (7.0)**
A3: Antepartum hypoxia	0	0	0	0	0	**0 (0.0)**
A4: Other specified antepartum disorder	1	0	3	0	0	**4 (0.8)**
A5: Disorders related to fetal growth	0	0	0	0	0	**0 (0.0)**
A6: Antepartum death of unspecified cause	95	33	188	55	106	**477 (89.7)**
Total n=532 (%)	**101 (19.0%)**	**36 (6.8%)**	**207 (38.9%)**	**79 (14.8%)**	**109 (20.5%)**	**532 (100.0)**
Intrapartum Death						
I1: Congenital malformations, deformations and chromosomal abnormalities	2	2	10	1	9	**24 (3.7)**
I2: Birth trauma	0	0	0	0	0	**0 (0.0)**
I3: Acute intrapartum event	12	19	98	14	58	**201 (31.3)**
I4: Infection	1	5	5	12	0	**23 (3.6)**

	M1: Complications of placenta, cord and membranes	M2: Maternal complications of pregnancy	M3: Other complications of labour and delivery	M4: Maternal medical and surgical conditions	M5: No maternal condition	Total (%)
I5: Other specified intrapartum disorder	0	0	0	1	1	**2 (0.3)**
I6: Disorders related to fetal growth	0	0	0	0	0	**0 (0.0)**
I7: Intrapartum death of unspecified cause	139	38	134	30	52	**393 (61.1)**
Total n=643 (%)	**154 (24.0)**	**64 (10.0)**	**247 (38.4)**	**58 (9.0)**	**120 (18.7)**	**643 (100.0)**
Stillbirth of Unknown Time of Death*						
U1: Congenital malformations, deformations and chromosomal abnormalities	0	0	2	0	0	**2**
U2: Hypoxia and other acute events	0	3	4	0	6	**13 (14.1)**
U3: Infection	1	0	0	1	0	**2 (2.2)**
U4: Other specified disorder	0	0	0	0	0	**0 (0.0)**
U5: Disorders related to fetal growth	0	0	0	0	0	**0 (0.0)**
U6: Death of unspecified cause	27	6	17	9	16	**75 (81.5)**
Total n=92 (%)	**28 (30.4)**	**9 (9.8)**	**23 (25.0)**	**10 (10.9)**	**22 (23.9)**	**92 (100.0)**
GRAND TOTAL – n=1267 (%)	**283 (22.3)**	**109 (8.6)**	**477 (37.6)**	**147 (11.6)**	**251 (19.8)**	**1267 (100.0)**

Table 6.2: Application of ICD-PM to cause of stillbirth by expert panel

	M1: Complications of placenta, cord and membranes	M2: Maternal complications of pregnancy	M3: Other complications of labour and delivery	M4: Maternal medical and surgical conditions	M5: No maternal condition	Total (%)
Antepartum Deaths						
A1: Congenital malformations, deformations and chromosomal abnormalities	0	0	7	0	3	**10 (1.9)**
A2: Infection	0	2	10	9	2	**23 (4.3)**
A3: Antepartum hypoxia	0	1	34	0	20	**55 (10.3)**
A4: Other specified antepartum disorder	0	0	0	0	0	**0 (0.0)**
A5: Disorders related fetal growth	0	0	2	0	0	**2 (0.4)**
A6: Antepartum death of unspecified cause	59	18	210	43	112	**442 (83.1)**
Total n=532 (%)	**59 (11.1)**	**21 (3.9)**	**263 (49.4)**	**52 (9.8)**	**137 (25.8)**	**532 (100.0)**
Intrapartum Deaths						
I1: Congenital malformations, deformations and chromosomal abnormalities	0	0	10	0	11	**21 (3.3)**
I2: Birth trauma	0	0	4	0	1	**5 (0.8)**
I3: Acute intrapartum event	0	10	102	0	79	**191 (29.7)**
I4: Infection	0	2	2	3	0	**7 (1.1)**

	M1: Complications of placenta, cord and membranes	M2: Maternal complications of pregnancy	M3: Other complications of labour and delivery	M4: Maternal medical and surgical conditions	M5: No maternal condition	Total (%)
I5: Other specified intrapartum disorder	0	0	0	0	0	**0 (0.0)**
I6: Disorders related to fetal growth	0	1	3	0	0	**4 (0.6)**
I7: Intrapartum death of unspecified cause	75	29	221	23	67	**415 (64.5)**
Total n=643 (%)	**75 (11.7)**	**42 (6.5)**	**342 (53.2)**	**26 (4.0)**	**158 (24.6)**	**643 (100.0)**
Stillbirth of Unknown Time of Death*						
U1: Congenital malformations, deformations and chromosomal abnormalities	0	0	2	0	0	**2 (2.2)**
U2: Hypoxia and other acute events	0	1	6	0	5	**12 (13.0)**
U3: Infection	0	0	0	0	0	**0 (0.0)**
U4: Other specified disorder	0	0	0	0	0	**0 (0.0)**
U5: Disorders related to fetal growth	0	0	0	0	0	**0 (0.0)**
U6: Death of unspecified cause	18	4	30	8	18	**78 (84.8)**
Total n=92 (%)	**18 (19.6)**	**5 (5.4)**	**38 (41.3)**	**8 (8.7)**	**23 (25.0)**	**92 (100.0)**
GRAND TOTAL – n=1215 (%)	**152 (12.0)**	**68 (5.4)**	**643 (50.7)**	**86 (6.8)**	**318 (25.1)**	**1267 (100.0)**

Table 6.3: Application of ICD-PM to cause of stillbirth by computer algorithms

	M1 - Complications of placenta, cord and membranes	M2 - Maternal complications of pregnancy	M3 - Other complications of labour and delivery	M4 - Maternal medical and surgical conditions	M5 - No maternal condition	Total (%)
Antepartum Deaths						
A1 - Congenital anomalies	0	0	0	5	11	**16 (3.0)**
A2 - Infection	7	0	4	9	72	**92 (17.5)**
A3 - Antepartum hypoxia	5	0	8	1	19	**33 (6.3)**
A4 - Other specified antepartum disorder	0	0	1	0	5	**6 (1.1)**
A5 - Fetal growth disorders	35	0	4	15	101	**155 (29.5)**
A6 - Unspecified cause	30	0	6	22	166	**224 (42.6)**
Total n=526 (%)	**77 (14.6)**	**0 (0.0)**	**23 (4.4)**	**52 (9.9)**	**374 (71.1)**	**526 (100.0)**
Intrapartum Deaths						
I1 - Congenital anomalies	0	0	0	0	4	**4 (0.7)**
I2 - Birth trauma	0	0	0	0	0	**0 (0.0)**
I3 - Acute intrapartum event	61	0	30	36	290	**417 (69.6)**
I4 - Infection	16	0	2	1	15	**34 (5.7)**
I5 - Other specified intrapartum disorder	2	0	0	1	5	**8 (1.3)**

	M1 - Complications of placenta, cord and membranes	M2 - Maternal complications of pregnancy	M3 - Other complications of labour and delivery	M4 - Maternal medical and surgical conditions	M5 - No maternal condition	Total (%)
I6 - Fetal growth disorders	18	0	2	6	30	**56 (9.3)**
I7 - Unspecified cause	25	0	7	7	41	**80 (13.4)**
Total n=599 (%)	**122 (20.4)**	**0 (0.0)**	**41 (6.8)**	**51 (8.5)**	**385 (64.3)**	**599 (100.0)**
Stillbirth of Unknown Time of Death						
U1 - Congenital anomalies	0	0	0	0	2	**2 (2.2)**
U2 - Acute events	0	0	2	0	4	**6 (6.7)**
U3 - Infection	7	0	2	1	5	**15 (16.7)**
U4 - Other specified disorder	0	0	0	0	4	**4 (4.4)**
U5 - Fetal growth disorders	11	0	3	1	25	**40 (44.4)**
U6 - Unspecified cause	7	0	1	4	11	**23 (25.6)**
Total n=90 (%)	**25 (27.8)**	**0 (0.0)**	**8 (8.9)**	**6 (6.7)**	**51 (56.7)**	**90 (100.0)**
GRAND TOTAL n=1215 (%)	**224 (18.4)**	**0 (0.0)**	**72 (5.9)**	**109 (9.0)**	**810 (66.7)**	**1215 (100.0)**

6.3.4 Comparison of ICD-PM classification for the different methods of assigning cause of death

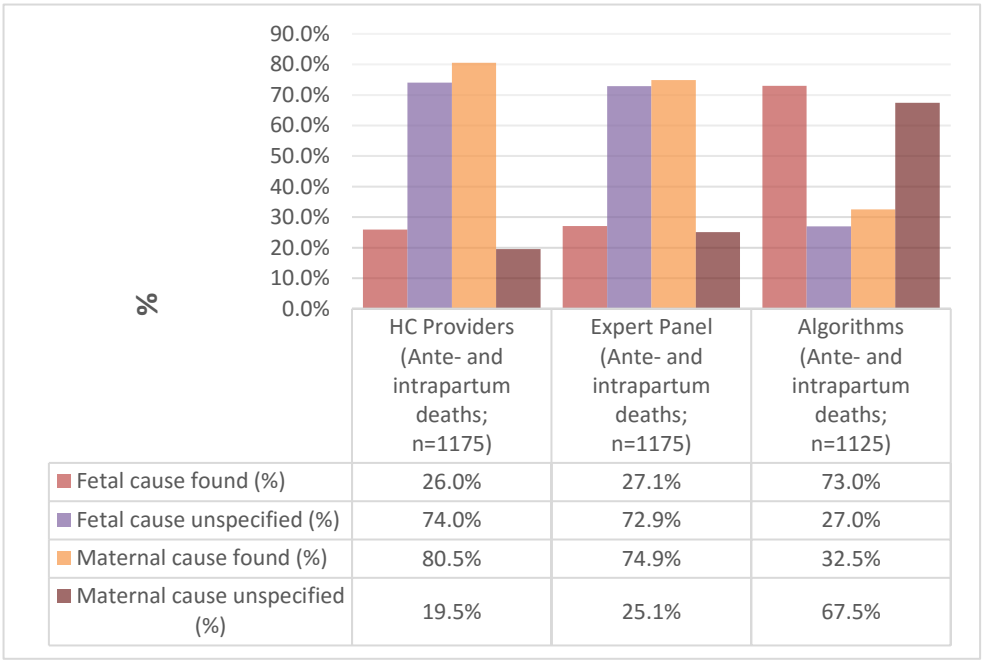
When compared side by side, all three methods returned a variety of causes responsible for death. In many of the categories, the similarities are shared more commonly between HCPs and expert panel than with the algorithms.

Fetal causes of death were more frequently reported by the algorithms than by any of the other two methods (Figure 6.5). Conversely, more associated maternal conditions were reported by HCPs and expert panel than by the algorithms (Tables 6.5-6.7).

When all cases classified as unknown were aggregated together, the lowest proportion of unknown was observed from the algorithms results (17.2%), followed by HCPs (22.2%) and expert panel (29.0%).

To explore differences between the three methods of assigning cause of death, a Kappa analysis was conducted. However, no two methods of assessing cause of death had enough similarities to satisfy the test's requirements and produce meaningful results: k-value was less than 0.0005, and no significance value was returned.

Figure 6.5: Bar chart comparing fetal and maternal cause of death according to ICD-PM classification



	HC Providers (Ante- and intrapartum deaths; n=1175)	Expert Panel (Ante- and intrapartum deaths; n=1175)	Algorithms (Ante- and intrapartum deaths; n=1125)
Fetal cause found (%)	26.0%	27.1%	73.0%
Fetal cause unspecified (%)	74.0%	72.9%	27.0%
Maternal cause found (%)	80.5%	74.9%	32.5%
Maternal cause unspecified (%)	19.5%	25.1%	67.5%

6.4 Chapter Summary

Using ReCoDe classification system, intrapartum events (mainly intrapartum asphyxia) contributed the most deaths, followed by maternal diseases (mainly hypertensive disorders and infections), placental and fetal conditions. The proportion of cases classified as unknown using the ReCoDe classification ranged from 17.9% by computer algorithms to 28.6% by expert panel.

The simple structure of ReCoDe classification allowed statistical analysis of differences in the categories by different methods of cause assessment. It showed that despite the observed differences in proportions of the categories, there was a statistically significant agreement between cause assigned by expert panel (which was treated as the reference standard) and the other two methods of assessment.

With ICD-PM, the major categories accounting for the death were: intrapartum hypoxia and fetal growth restriction. For contributing maternal conditions, M1 (placental, cord and membranes) and M3 (other complications of labour and delivery) dominated the groups.

Overall, the proportion of cases that could not be assigned into either a fetal cause category or a contributing maternal condition in ICD-PM ranged from 13.7% to 17.9%.

CHAPTER 7: STANDARD OF CARE

7.1 Introduction

This chapter presents results related to standard of care provided to women who had stillbirths that may have affected outcome of birth. It relates to objective #4 of the study. Elements of care presented are categorised as follows:

- Coverage and quality of antenatal care (ANC) interventions
- Quality of intrapartum care
- Health system factors

Finally, the chapter categorises quality of care based on sets of criteria (described in Chapter 3 – Methodology).

Research questions addressed in this chapter are:

1) What is the coverage and quality of care provided to mothers and babies?
2) What proportion of stillbirths could have been saved with better care (using a set of criteria)?
3) What proportion of cases meet standard of care?

7.2 Coverage and Quality of ANC Interventions among Mothers with Stillbirth

7.2.1 Antenatal visits (summary)

Details of antenatal care (ANC) has been presented earlier in Section 4.3.2. Briefly, of the 1,267 cases, 940 (74.2%) had ANC information available. Of those whose information was available, 847 (90.1% or 66.9% of total) attended ANC at least once: 10.5% had one visit; 24.3% had two visits; 16.9% had three visits; 23.5% had four or more visits, and; 14.9% attended but their number of visits was unknown. One-tenth (9.9%) did not attend ANC at all.

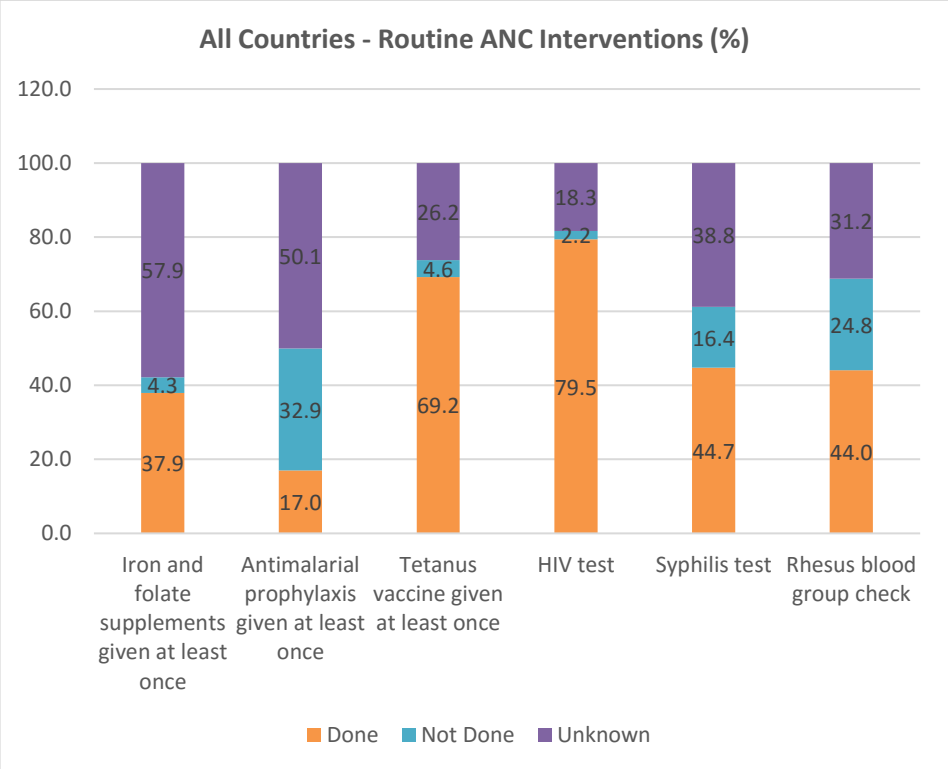
However, those who attended at least once ranged between 42.9% in Sierra Leone to 84.7% in Kenya. Zimbabwe had 72.3% booked and Malawi had 69.2%. The highest proportion of mothers who attended ANC four or more

times was found in Kenya (39.5%), followed by Zimbabwe (25.4%), Malawi (13.9%) and Sierra Leone (2.6%).

7.2.2 Coverage of routine ANC interventions

Figures 7.1 through 7.5 summarise performance of routine antenatal interventions. Selected antenatal interventions known to prevent or reduce the risk of stillbirth, as highlighted in the literature review, were assessed as per WHO antenatal care guidelines (WHO, 2002), namely: iron and folate supplements, anti-malarial prophylaxis, HIV and syphilis screening and Rhesus blood group check.

Figure 7.1: Performance of routine antenatal interventions (all countries; n=847)



Iron and folate supplements

Out of the 847 mothers who attended antenatal care at least once, 321 (37.9%) had iron and folate supplements at least once; 36 (4.3%) did not have any supplements recorded. In 490 (57%) of the cases, it was not clear whether women were given supplements or not as there was no documentation of the intervention.

A chi-square test indicated a significant difference in iron and folate supplements between countries, X^2 (3, n = 427) = 10.20, p = 0.17, with Cramer's V value of 0.16, indicating a small effect size (Cohen, 1988; Figures 7.2 through 7.5).

Anti-malarial prophylaxis

Of the 847 mothers who attended ANC at least once, only 17% had antimalarial prophylaxis, one-third (32.9%) had no antimalarial prophylaxis and the data was not available for about half (50.1%) of them. Malawi had the highest coverage for anti-malarial prophylaxis, with 42% of women having documented evidence of the intervention.

In Zimbabwe, one of the three study sites was not considered malaria-endemic, and antimalarial prophylaxis was not part of their antenatal care protocol.

Tetanus vaccination

Although not directly linked with stillbirth, tetanus vaccination was assessed to explore completeness of antenatal services. Overall, 69.2% of women who attended ANC had at least one dose of tetanus vaccine. This varies between the countries, with the highest coverage (95.2%) recorded in Sierra Leone and the lowest recorded in Kenya, although the figures for Kenya may have been influenced by the larger proportion (48.5%) of women whose vaccination status was unknown.

A chi-square test indicated a significant variation in tetanus vaccination between countries, X^2 (3, n = 704) = 50.16, p<0.0005, with Cramer's V value of 0.27, indicating a small-to-medium effect size.

HIV screening

With almost 80% coverage across all four countries, HIV screening is by far the most delivered antenatal care intervention among the cases studied. Malawi had the highest documented coverage (97.1%), followed by Zimbabwe (94.1%) and Kenya (92.6%). In Sierra Leone, only 11 (3.2%) out of the 340 cases had information about their HIV status, and all of them were

negative; there was no documentation of HIV screening in the remaining 329 (96.8%).

A chi-square test indicated a significant variation in HIV screening coverage between countries, X^2 (3, n = 882) = 44.87, p<0.0005, with Cramer's V value of 0.23, indicating a small effect size as the countries had high coverage.

Syphilis screening

Of the 847 women who attended ANC, 416 (44.7%) were screened for syphilis. This also showed a wide variation between countries, with highest documented coverage found in Kenya (75.7%), followed by Zimbabwe (72.2%), Malawi (4.8%) and Sierra Leone (1.4%).

A chi-square test indicated a significant variation in syphilis screening between countries, X^2 (3, n = 629) = 44.87, p<0.0005, with Cramer's V value of 0.43, indicating a medium effect size.

Rhesus blood grouping

About 44% of the women who had antenatal care had their Rhesus blood group checked. With almost 81% coverage, Kenya had the highest proportion of women who had this test done. It is followed by Sierra Leone (62.3%), then Zimbabwe (26.6%) and Malawi (1.4%), although in most the cases in Malawi (77.3%) this information was not available.

A chi-square test indicated a significant difference in Rhesus blood group typing between countries, X^2 (3, n = 746) = 359.04, p<0.0005, with a large effect size (0.69).

Results of HIV, syphilis and Rhesus screening are presented in the next section.

Figure 7.2: Kenya – Performance of routine antenatal interventions (n=272)

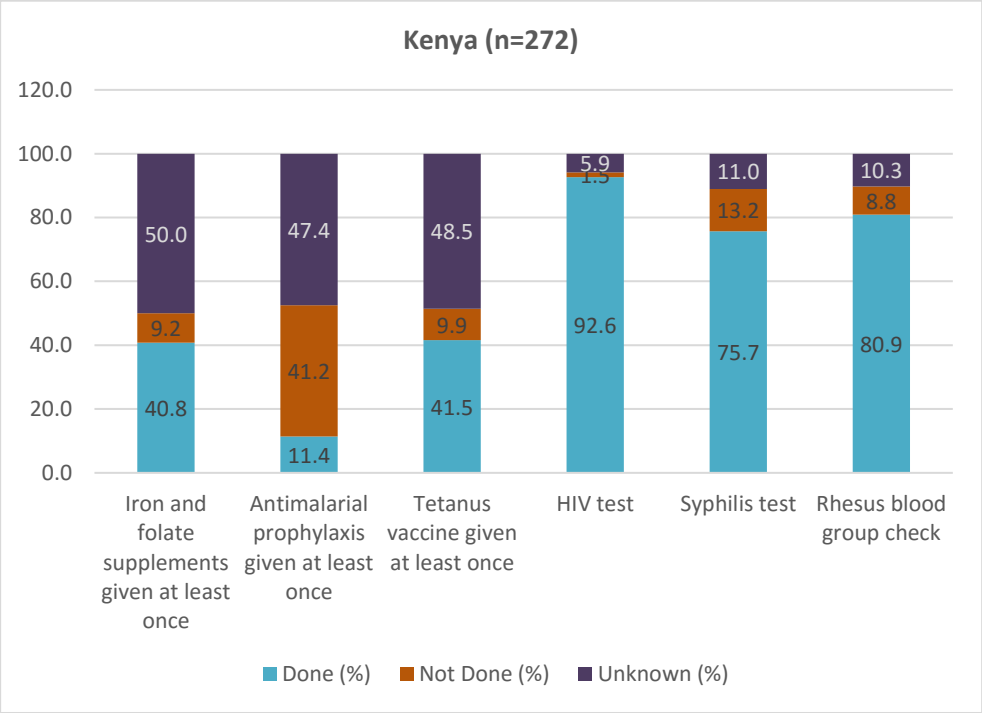


Figure 7.3: Malawi – Performance of routine antenatal interventions (n=207)

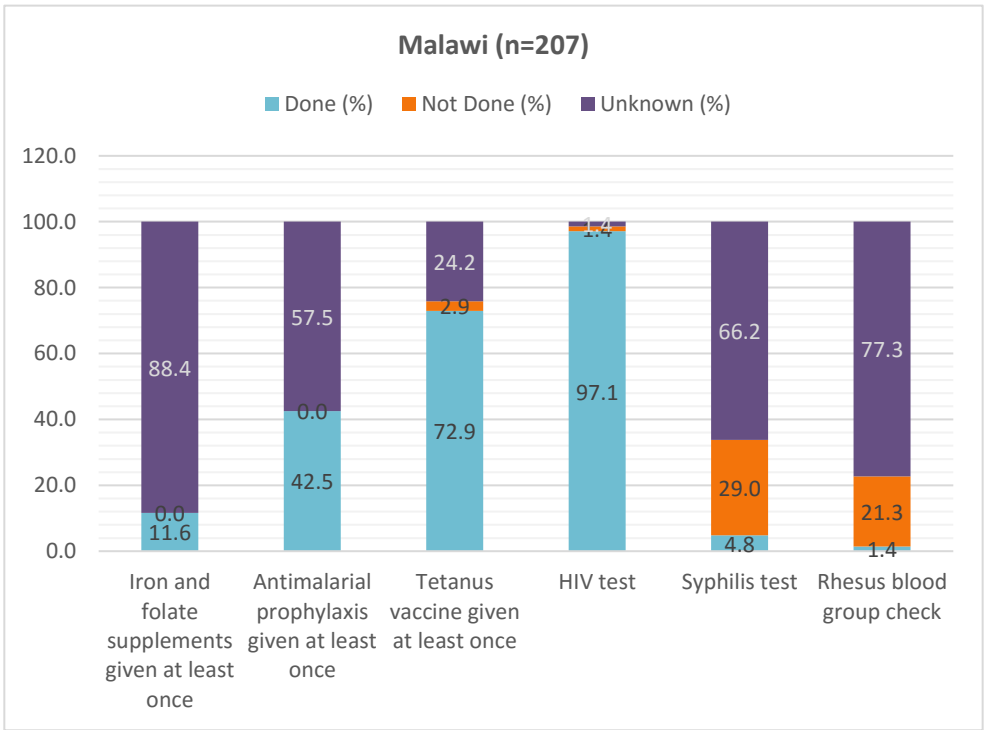


Figure 7.4: Sierra Leone – Performance of routine antenatal interventions (n=146)

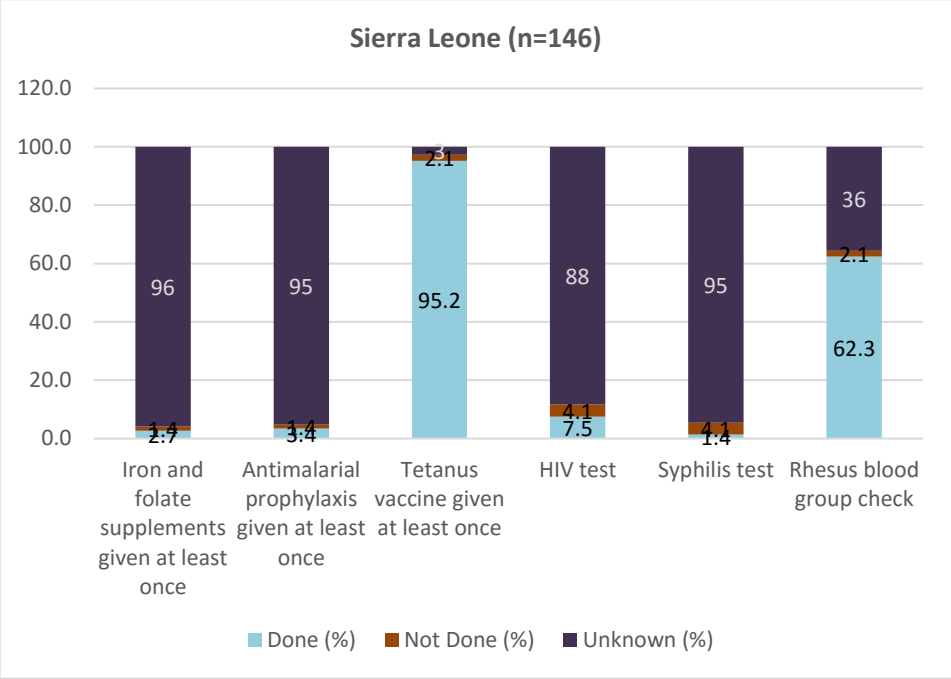
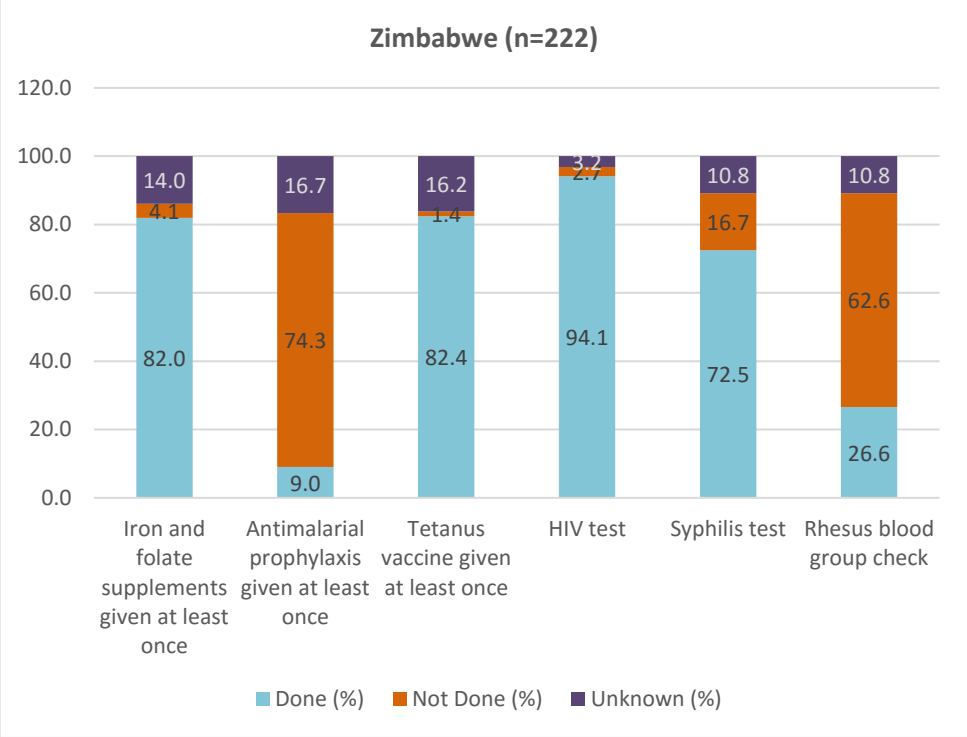


Figure 7.5: Zimbabwe – Performance of routine antenatal interventions (n=222)



7.2.3 Identification and management of antenatal morbidity

Antenatal diagnoses of common clinical conditions that have been established to cause stillbirth from the literature were included: infections such as malaria, HIV and syphilis; hypertensive disorders in pregnancy; antepartum haemorrhage; diabetes; Rhesus incompatibility, and; external trauma. Of the 1267 women, 704 (55.6%) were diagnosed with at least one of the conditions before birth. The remaining 563 (44.4%) had none of the clinical conditions.

Figure 7.6 summarises common antenatal (maternal) morbidity in pregnancy and their treatment status.

Hypertensive disorders

Of the 1,267 cases included in this analysis, hypertensive disorders in pregnancy (gestational hypertension, pre-eclampsia and eclampsia) were the most diagnosed conditions during antenatal period, affecting 236 (18.5%) of the cases. However, only 126 (53.4%) of the cases of hypertension diagnosed had documented evidence of treatment, with relative variations between countries (Table 7.1).

Table 7.1 Hypertensive disorders in pregnancy

	Kenya n=321 (%)	**Malawi n=299 (%)**	**Sierra Leone n=340 (%)**	**Zimbabwe n=307 (%)**	**Total n=1267 (%)**
Number of cases diagnosed of hypertensive disorders	48 (15.0)	26 (8.7)	33 (9.7)	129 (42.0)	**236 (18.5)**
Number of cases of hypertensive disorders with documented treatment	28 (58.3)	12 (46.2)	19 (57.6)	67 (51.9)	**126 (53.4)**

Antepartum haemorrhage (APH)

A total of 198 cases (15.6% of 1267) had documented antepartum haemorrhage: 43 (13.4%) in Kenya, 25 (8.4%) in Malawi, 68 (20.0%) in Sierra Leone and 62 (20.2%) in Zimbabwe.

While all women with APH were hospitalised, only 75 (37.9%) had records of active intervention, including blood transfusion and Caesarean section. Among the remaining 123 who had no record of active intervention after admission, 24 (19.5%) were admitted with fetal heart sound present, 74 (60.1%) were admitted with absent fetal heart sound, while 25 (20.3%) were not assessed for fetal heart sound on admission.

HIV infection

A total of 803 women (63.4%) had their HIV screening test result documented: 266 (82.9%) in Kenya, 269 (90.0%) in Malawi, 11 (3.2%) in Sierra Leone and 257 (83.7%) in Zimbabwe.

Among those whose information on HIV test was available, 113 (14.1%) were positive (Figure 7.6). Zimbabwe had the highest proportion of women who were positive (18.7%), followed by Malawi (16.4%), while Kenya had 7.9%. In Sierra Leone, all the 11 cases whose HIV test result was available were negative.

Overall, 59.3% of HIV-positive mothers were on anti-retroviral treatment at the time of the antenatal visit, but this varied by country: 50% in Malawi, 60% in Zimbabwe and 75.9% in Kenya. There were scanty details regarding the reasons for lack of treatment. While some of the mothers were not on treatment because they were diagnosed at the time of birth, some may not have been on treatment because they had not met the criteria for commencement of treatment.

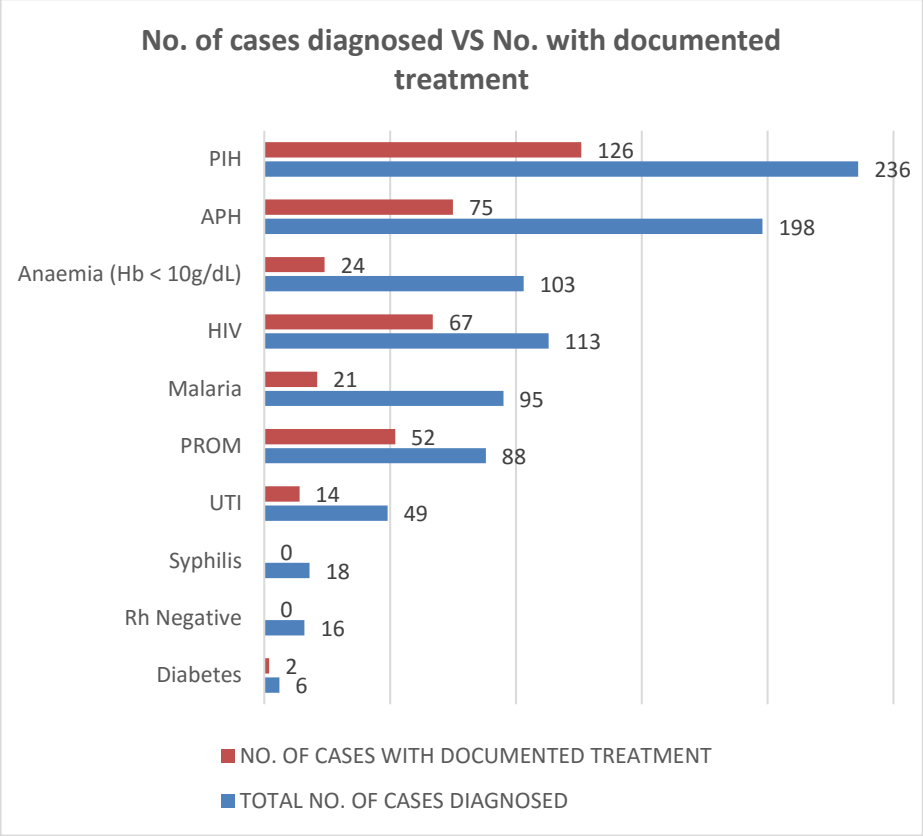
Syphilis

Overall, 417 women (32.9%) had their syphilis test results documented. Availability of information on syphilis test varied: 211 (65.7%) in Kenya, 193 (62.9%) in Zimbabwe, 11 (3.7%) in Malawi and only 2 (0.6%) in Sierra Leone.

In all four countries, 18 (4.3%) tests were positive: 2 in Kenya, 1 in Malawi, 2 in Sierra Leone and 13 in Zimbabwe.

None of those who tested positive had a documentation of treatment for the disease (Figure 7.6).

Figure 7.6: Clinical conditions present during antenatal period and treatment status.



PIH = pregnancy-induced hypertension; APH = antepartum haemorrhage; HIV = human immunodeficiency virus infection; PROM = premature rupture of membranes; UTI = urinary tract infection; Rh = Rhesus.

Malaria

Test for malaria was widely documented – 1189 mothers (93.8%) had record of malaria test. Among them, 95 (8.0%) were positive. Of those who were positive, only 21 (22.1%) had any documentation of treatment.

PROM

A total of 88 mothers had prelabour rupture of membranes (PROM). Of those who had PROM, 41 (46.6%) were gave birth to premature babies. However, only 24 (27.2%) of the 88 mothers had any form of intervention before birth,

which included antibiotics, tocolytics and steroids “to enhance the baby’s lung maturity”.

Rhesus (Rh) incompatibility

Information about Rhesus blood group for mothers was available for 430 (33.9%) of the women in this study. Availability of this information varied across countries: 70.4% in Kenya, 2.0% in Malawi, 40.3% in Sierra Leone and 19.9% in Zimbabwe.

Of those mothers who were tested for Rhesus blood group, 16 (3.7%) were Rhesus negative. Among the Rh-negative women, 7 were primi gravida; the rest were gravida 1 or more. Nevertheless, none of the 16 women who were Rh negative had any record of treatment with anti-D immunoglobulin for prevention of Rh incompatibility for future pregnancies.

However, it is noteworthy that there were no records of the Rhesus blood group of fathers or babies in any of the countries in this study, making it difficult to confirm the diagnosis of Rhesus incompatibility.

Other clinical conditions in pregnancy

A total of 158 (12.4%) of mothers had a record of their haemoglobin checked, and 103 mothers (8.1% of total) were anaemic (haemoglobin less than 10mg/dL). However, only 24 (23.3% of 103) had any documented intervention for anaemia, which varied from oral iron and folate supplements to blood transfusion.

Diabetes was less frequently diagnosed. Of the six cases of diabetes diagnosed before or during antenatal period, only two were on treatment.

Similarly, there were relatively lower cases of urinary tract infection, although it was not a routinely tested diagnosis. Of the 49 cases diagnosed, only 29% had a record of treatment.

7.3 Quality of Intrapartum Care

7.3.1 Late arrival at facility (1st and 2nd delays)

Cervical dilatation and fetal heart sound on admission were used as proxies for late arrival at the health facility. In this section of the analysis, mothers referred from other facilities who may have arrived late due to referral delays were discounted.

Results about referral status of cases has been presented in Table 4.2 in Section 4.3. Briefly, 569 cases (44.9% of 1267) were referrals from other facilities, while 673 (53.1%) arrived from home. There was no information about the referral status of 25 cases (2.0%).

Of the 1267 women in this study, 802 mothers (63.3%) had vaginal examination on admission documented, while the remaining 465 (36.7%) did not have a record of vaginal examination on admission.

Of the 673 women who came from home, 414 (61.5%) had a record of vaginal examination on admission. The cervical dilatation data for this group did not show a normal distribution; they were skewed on both extremes, with a skewness value of 0.05 (SE of 0.12). Thus, parametric techniques of analysis were inappropriate. The median was calculated instead, which was 5 (IQR = 2, 9).

As shown in Figure 7.7, it is worth noting that more than one-fifth (22%) of mothers arrived at the facility at full cervical dilatation of 10 cm.

Similarly, of the 673 women who arrived from home, 98 (15%) did not have information about the status of fetal heart sound on admission (Figure7.8). Only 249 (37%) had fetal heart present. For the remaining 326 (48%), the fetal heart sound of their babies was absent on admission.

Figure 7.7: Cervical dilatation on admission (non-referrals only)

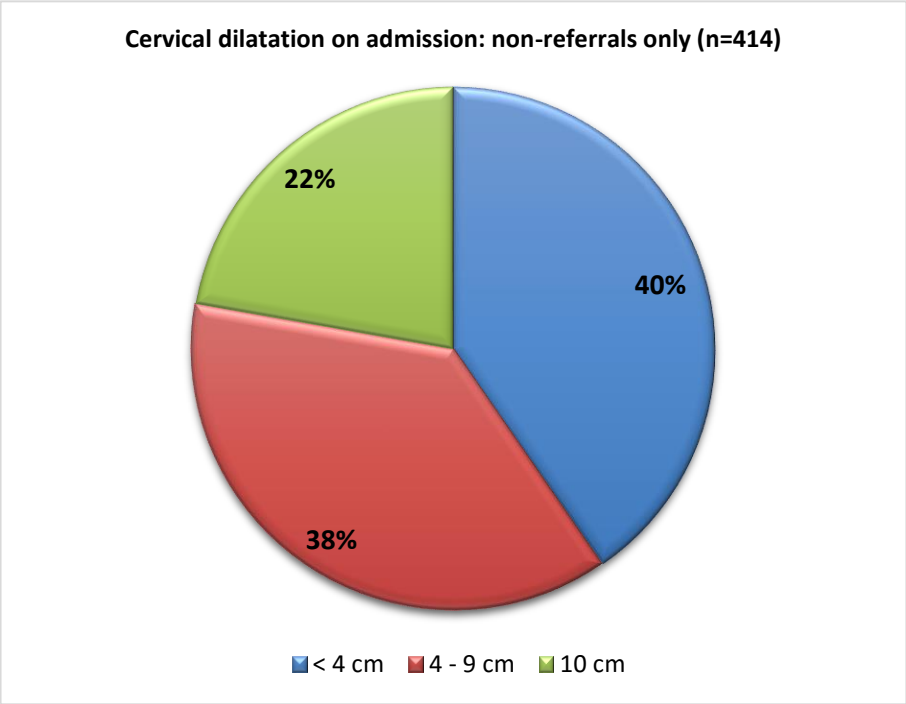
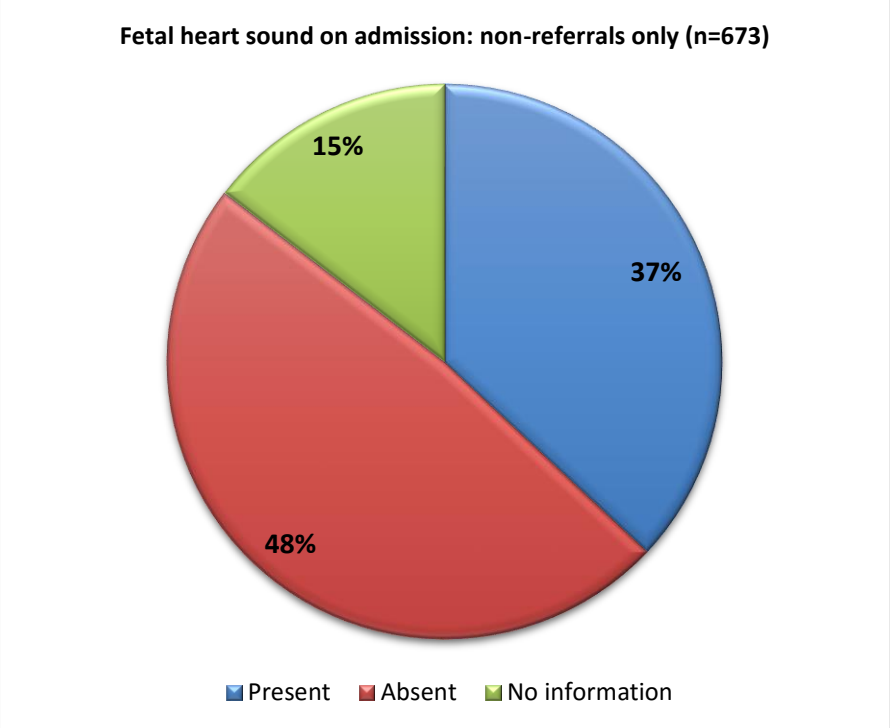


Figure 7.8: Fetal heart sound on admission (non-referrals only)



Overall, since mothers are admitted in active labour (cervical dilatation of 4 – 9cm), it could be concluded that the 22% of the mothers who arrived at full cervical dilatation were late. Similarly, using fetal heart sound on admission as a proxy, it could be said that at least 48% of mothers who arrived without fetal heart sound were late.

However, the accuracy of the results from the above proxies depends largely on the accuracy of the clinical assessments.

7.3.2 Delay at the health facility (3rd delay)

To assess delay at the health facility, two proxies were used:

1) Time between admission and birth, and;
2) Time between decision for Caesarean section and actual birth.

Time interval between admission and birth

A total of 989 (78.1% of total) had their admission and birth time documented. However, to remove cases of wrong diagnosis of labour, women admitted with cervical dilatation of less than 4 cm were excluded in this analysis. Thus, the total sample in this section was 450 cases.

Parametric statistical tests were inappropriate for the data due to skewness; it had a skewness value of 26.79 (SE = 0.08). Thus, the median and inter-quartile range (IQR) were calculated instead. The median time between admission and birth for all women admitted at 4 cm of cervical dilatation or more was 176 minutes (or 2 hours, 54 minutes), with an IQR of 384 minutes (Table 7.2), bearing in mind, as presented in the previous section, that up to one-quarter of women arrived at health facilities at 9 to 10 cm cervical dilatation (Figure 7.7).

By country, Sierra Leone had the longest time interval between admission and birth for mothers admitted at 4 cm dilatation or more, with a median of 214 minutes (IQR: 573).

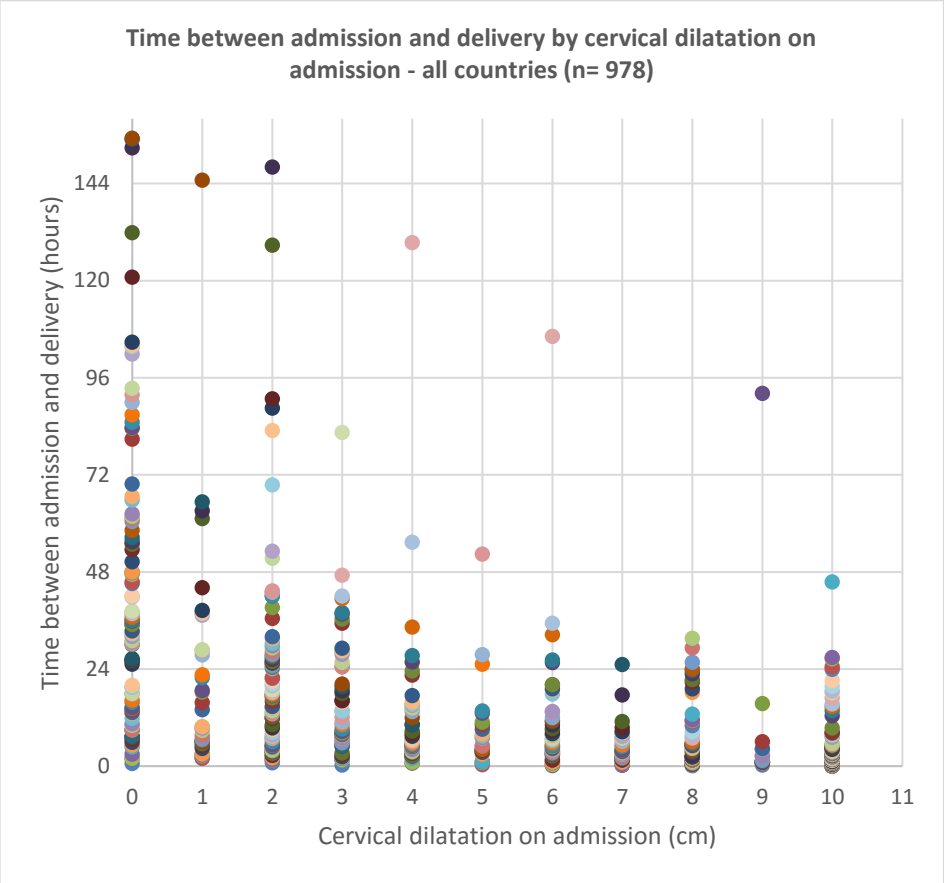
A Kruskal-Wallis test was conducted after excluding women admitted at cervical dilatation of less than 4 cm to exclude possible cases of false labour.

It showed that the difference between the countries (Table 7.2) was statistically significant (n = 450, p = 0.001).

Table 7.2: Median and inter-quartile range for time between admission and birth.

Cervical dilatation (CD) on admission / Country	Sample size	Median time between admission and birth (minutes)	Inter-quartile range
CD = 4 cm (all countries)	59	379	639
CD = 5 cm (all countries)	27	300	411
CD = 6 cm (all countries)	54	365	552
CD = 7 cm (all countries)	39	191	298
CD = 8 cm (all countries)	71	208	444
CD = 9 cm (all countries)	24	74	199
CD = 10 cm (all countries)	176	68	173
Kenya (CD >= 4 cm)	104	159	327
Malawi (CD >= 4 cm)	46	168	345
Sierra Leone (CD >= 4 cm)	192	214	573
Zimbabwe (CD >= 4 cm)	108	125	255
All countries (CD >= 4 cm)	**450**	**176**	**384**

Figure 7.9: Time between admission and birth by cervical dilatation on admission. Outliers removed from graph to allow majority of data points to be visible.



Time interval between decision for emergency Caesarean section (CS) and birth

A total of 303 mothers underwent a Caesarean section. Of those, 219 were emergencies that had information about their date and time of decision for the procedure and date and time of actual birth. A 30-minute interval between decision and birth (McKenzie & Cooke, 2002) was used as a reference standard to assess for delay between decision for emergency CS and birth.

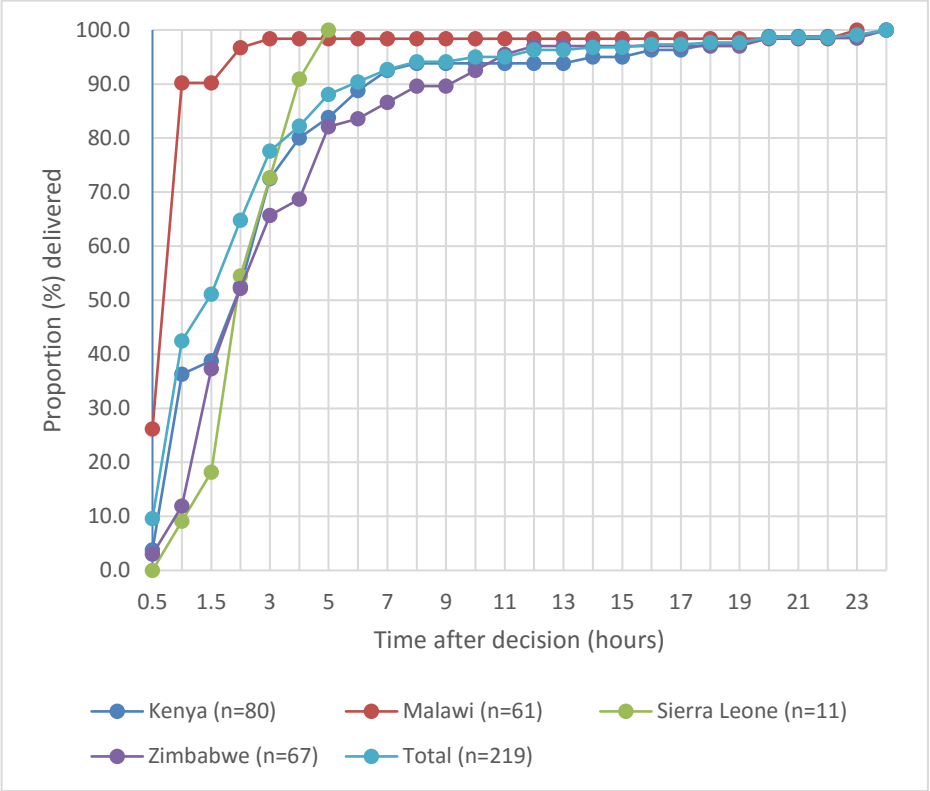
Overall, the median time between decision and birth was 90 (IQR: 120; Table 7.3). The median time interval was similar across the countries, except in Malawi, where a shorter period of 60 minutes was observed.

A Kaplan-Meier survival analysis was conducted to explore the effect of country settings on the time between decision for emergency CS and birth. There was a statistically significant variation between the countries ($p<0.0005$). Figure 7.10 is a reversed Kaplan-Meier plot to demonstrate variations between the countries.

Table 7.3: Time interval between decision for emergency CS and birth

Country	Sample size	Median time between admission and birth (minutes)	Interquartile range	95% Confidence Interval	
				Lower Bound	Upper Bound
Kenya	80	120	175	146.4	261.6
Malawi	61	60	30	32.4	120.2
Sierra Leone	11	120	72	106.2	199.3
Zimbabwe	67	120	225	63.5	288.0
All countries	**219**	**90**	**120**	141.0	204.1

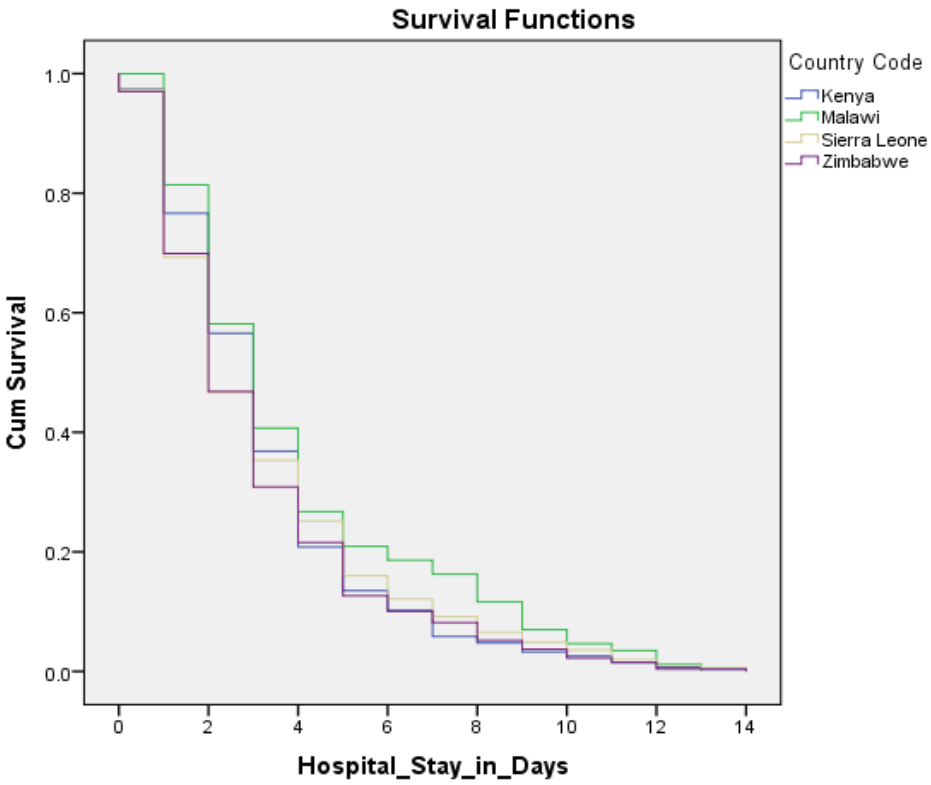
Figure 7.10: Proportion of women delivered after decision for CS.



Hospital stay

The overall median hospital stay for mothers who had stillbirths was 3 days, with a close range of 2 to 3 days. A Kaplan-Meier survival analysis (Figure 7.11) showed no statistically significant difference between countries (p = 0.174).

Figure 7.11: Kaplan-Meier survival analysis graph for hospital stay



7.3.3 Use of partograph

It was assumed that all women in active labour are commenced on a partograph (WHO, 2008). However, mothers who arrived during the second stage of labour and those who were rushed to the theatre immediately after admission were excluded from this part of the analysis. These two groups constituted 208 mothers (16.4% of total).

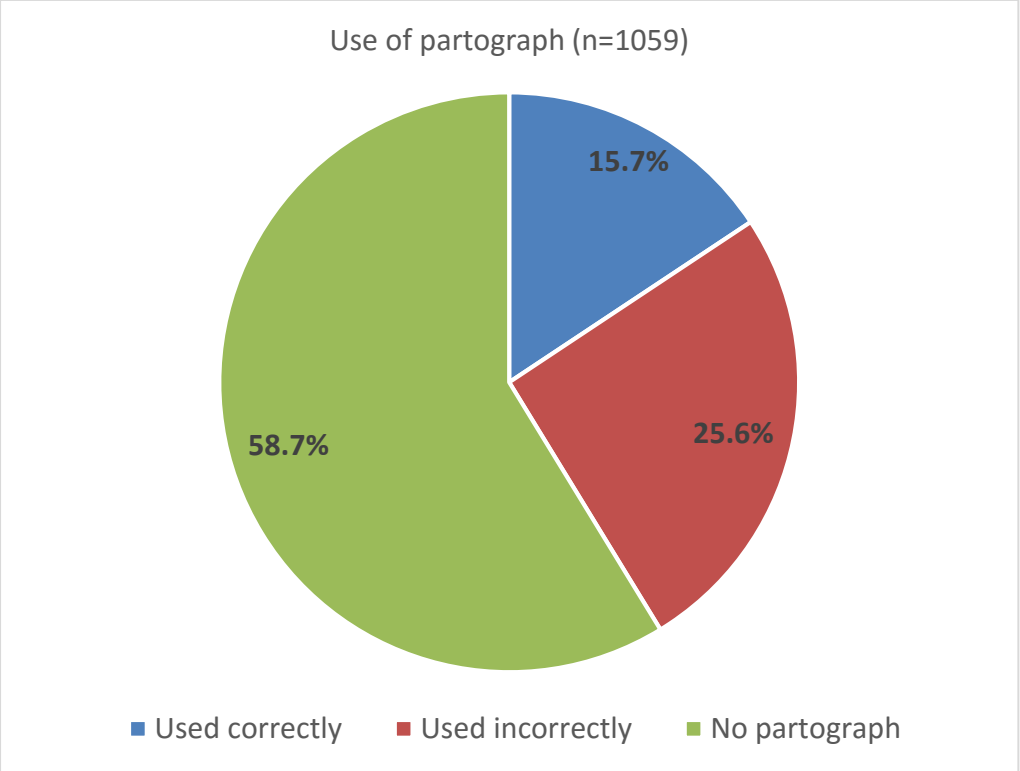
Thus, after accounting for the above two groups, a total of 1059 (83.6%) were eligible for use of partograph (Figure 7.12). Of those cases, only 445 (42%) had a partograph.

When healthcare providers studied the partographs for completeness and correct usage (criteria as described in the methodology chapter), of the 445 cases that had a partograph, the graph was used correctly in only 166 cases (37.3% of those with a partograph or 15.7% of total). Common errors found in the partographs were:

- Patient's details incorrect/incomplete

- Fetal monitoring incorrect/inadequate
- Cervical dilation plots incorrect or inadequate
- Contractions monitoring incorrect/ inadequate
- Inaction after plot crosses action line
- Oxytocics/other drugs not charted or wrongly charted
- Maternal vital signs chart incorrect/ inadequate
- Urine tests not done or not recorded
- Partograph not signed

Figure 7.12: Partograph use (eligible cases only)



7.4 Health System Factors

The 33 HCPs who took part in the management and review of the cases in the 12 study sites were asked about specific health system problems they encountered while managing each individual case of stillbirth. This section presents their responses (Table 7.4). HCPs were asked in a questionnaire format whether they had experienced any of the following over period the stillbirths occurred: staff shortage, equipment and supplies problems and guidelines issues. When they reported a challenge, they were also asked to explain why they had the challenge.

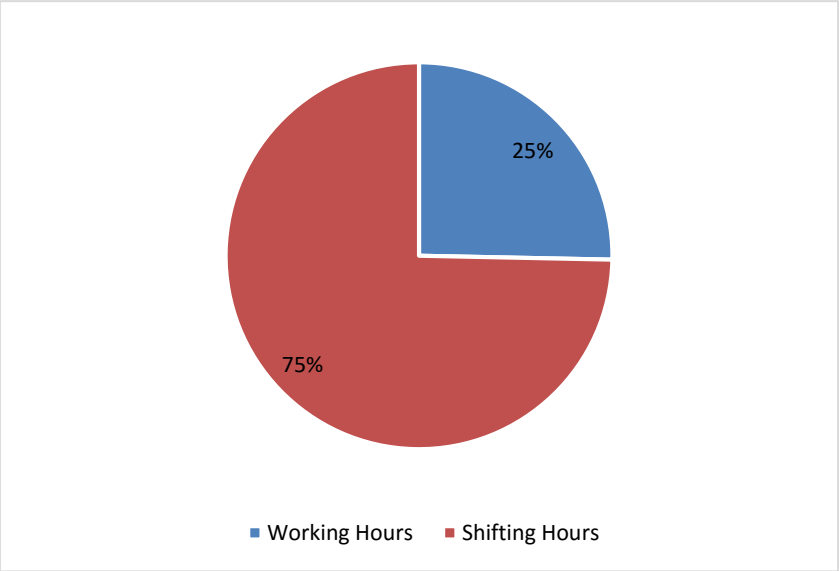
This section also reports on the findings of the HCPs' discussions on each case for appropriateness of interventions used in its management, and the adequacy of relevant documentation (Table 7.4).

Staff shortage

When HCPs were asked whether there was shortage of staff at the period of birth when the stillbirth occurred relative to other periods, ignoring the prevailing global lack of human resources, they reported shortage of staff in only 6.2% of the cases. In Sierra Leone, report of relative shortage of staff was due to reduction in services during the Ebola outbreak of between 2014 and 2015. For other countries, relative shortage was reported to be due to absenteeism from sick or annual leave.

Similarly, since hospitals in the study settings were generally better staffed to handle emergencies during normal working hours (generally between 8.00am to 3.00pm), the proportion of stillbirth during working hours and the proportion during shifting hours (3.00pm to 8.00am) were compared. Of the 1090 cases whose time of birth was available, 814 (74.7%) occurred during evening and night shifts (Figure 7.13). Since the normal working hours are about 8 hours (33%) of a day, the result in the pie chart was as expected, but it may still be useful in guiding practice, for example, to underscore the importance of balancing duty rosters to meet demands.

Figure 7.13: Proportion of stillbirths during working hours (8.00am to 3.00pm) compared to shifting hours (3.00pm to 8.00am)



Equipment and supplies

Surprisingly, HCPs reported lack of equipment and supplies for faster and effective management of mothers in only a small proportion of stillbirths – only 2.1% of the stillbirths reviewed were affected by the lack of or dysfunctional equipment; 2.5% were affected by lack of supplies. The four countries show similar proportions, except Sierra Leone, which showed slightly higher proportions affected by equipment problems, while Zimbabwe had slightly higher proportions of cases affected by supplies.

Table 7.4: Elements of care related to health system as reported by HCPs

Health System Factors	Kenya n=321 (%)	Malawi n=299 (%)	Sierra Leone n=340 (%)	Zimbabwe n=307 (%)	Total n=1267 (%)
Staff Shortage	29 (9.0)	8 (2.7)	38 (11.2)	4 (1.3)	**79 (6.2)**
Equipment problems	5 (1.6)	6 (2.0)	11 (3.2)	4 (1.3)	**26 (2.1)**
Supplies problems	7 (2.2)	7 (2.3)	6 (1.8)	12 (3.9)	**32 (2.5)**
Guidelines issues	70 (21.8)	50 (16.7)	58 (17.1)	61 (19.9)	**239 (18.9)**
Wrong intervention	57 (17.8)	26 (8.7)	27 (7.9)	28 (9.1)	**138 (10.9)**
Poor documentation	213 (66.4)	204 (68.2)	319 (93.8)	132 (43.0)	**868 (68.5)**

Guidelines issues

When asked for the availability of guidelines for the management of major conditions that contribute to stillbirth, HCPs agreed that the management of 18.9% of the total cases were affected by lack of clear management guidelines available to staff. The proportions were similar across the four countries.

Inappropriate interventions

HCPs deliberated on the appropriateness of interventions used in the management of each case of stillbirth. Overall, they agreed that the interventions used in the management of 10.9% of the cases were inappropriate. This figure was most reported in Kenya, where up 17.8% of the cases were reported to be managed using at least one wrong intervention at one time or another during the management of the cases.

Poor documentation

HCPs assessed case files of stillbirth for completeness and accuracy of information needed to determine cause of death or assess quality of care, and reported 68.5% to be incomplete, inaccurate or both.

However, this varied by country. In Sierra Leone, for example, as high as 93.8% of the cases had evidence of poor documentation.

7.5 Standard of Care

7.5.1 Deficiencies in care

The criteria for classifying standard of care has been described in the methodology. The following is a brief description:

- ANC minimum standards for selected interventions as highlighted in the WHO ANC guidelines (WHO, 2016a): iron and folate supplementation, prophylactic anti-malarial, tetanus vaccination, HIV screening, syphilis screening and Rhesus blood grouping.
- WHO minimum documentation standards as outlined in the WHO guidelines for perinatal death review (WHO, 2016a): parity, maternal age, pregnancy type, HIV status, LMP, date and time of birth, gestational age (and method of determination), place of birth, mode of delivery, baby's sex, birth weight and type of death (fresh/macerated).

Overall, only 2.2% of mothers who were booked for antenatal care had all interventions as set out in the criteria for ANC (Table 7.5). In Malawi and Sierra Leone, no mother met the criteria.

For minimum perinatal data, one-third (34.5%) met the criteria. However, this showed wide variation across countries. Zimbabwe had the highest proportion of cases meeting the WHO minimum data criteria with 60.6%, while Sierra Leone had the least (0.6%).

Births within 12 hours of admission while in active labour was 78.2%. The proportion was similar across the countries, except in Zimbabwe where a higher proportion was observed. When time taken from decision to perform a Caesarean section and actual birth was analysed using 30 minutes as reference standard (MacKenzie & Cooke, 2002), only 6.9% of the cases of Caesarean section met the criteria. When this criterion was relaxed to 60 minutes, the overall proportion improved to about one-third (30.7%).

Table 7.5: Deficiencies in care

Quality of Care	Kenya	Malawi	Sierra Leone	Zimbabwe	Total
Met ANC minimum standards	16	0	0	3	19
Denominator for ANC minimum standards: Total booked	272	207	146	222	847
Proportion meeting minimum ANC standards	**5.9%**	**0.0%**	**0.0%**	**1.4%**	**2.2%**
Met WHO minimum perinatal indicators (WHO, 2016a)	173	76	2	186	437
Denominator for WHO minimum perinatal indicators: All cases	321	299	340	307	1,267
Proportion meeting minimum ANC standards	**53.9%**	**25.4%**	**0.6%**	**60.6%**	**34.5%**
Birth within 12 hours of admission	90	40	149	102	381
Denominator for deliveries within 12 hours: All mothers arriving with cervical dilatation of 4cm or more	122	56	199	110	487
Proportion delivered within 12 hours of admission	**73.8%**	**71.4%**	**74.9%**	**92.7%**	**78.2%**
Delivered within 30 minutes of decision for CS (MacKenzie & Cooke, 2002)	3	16	0	2	21
Denominator for deliveries within 30 min of decision: All CS deliveries	76	69	77	81	303
Proportion of CS deliveries within 30 minutes of decision	**3.9%**	**23.2%**	**0.0%**	**2.5%**	**6.9%**
Delivered within 60 minutes of decision for CS	29	55	1	8	93
Denominator for deliveries within 60 min of decision: All CS deliveries	76	69	77	81	303
Proportion of CS deliveries within 60 minutes of decision	**38.2%**	**79.7%**	**1.3%**	**9.9%**	**30.7%**

7.5.2 Care in relation to outcome

The criteria for classifying standard of care has been described in the methodology. The following is a brief description:

- Standard care – no improvement identified: Defined as cases without an identified deficiency in any of the variables assessed: correct use of partograph, availability of staff, equipment and supplies.
- Sub-standard care in which better care may have made no difference to outcome: Defined as cases admitted without fetal heart sound (FHS) on arrival and had at least one deficiency in care.
- Sub-standard care which better care may have made a difference to outcome: Cases admitted with FHS on arrival and had at least one deficiency in care that could have made a difference to outcome, e.g. lack of use of partograph, too long duration between admission and birth, etc.

None of the cases in this study had a standard care where no improvement was identified (Table 7.6). Thus, all cases had one form of deficiency in care or another. Overall, 62.1% arrived too late for healthcare providers to make any difference to the outcome. However, with better care, the outcome of 414 cases (37.9%) may have been changed.

Table 7.6: Preventable stillbirths

Quality of Care	Kenya n=301 (%)	Malawi n=276 (%)	Sierra Leone n=218 (%)	Zimbabwe n=298 (%)	Total n=1,093 (%)
Standard care; no improvements identified	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**0 (0.0)**
Sub-standard care; better care may have made no difference to outcome	208 (69.1)	130 (47.1)	127 (58.3)	214 (71.8)	**679 (62.1)**
Sub-standard care; better care may have made a difference to outcome	93 (30.9)	146 (52.9)	91 (41.7)	84 (28.1)	**414 (37.9)**

7.6 Chapter Summary

Coverage for antenatal care interventions differed by country and by intervention. While HIV screening had relatively higher coverage, the coverage for anti-malarial prophylaxis seemed low. By far, the facilities in Zimbabwe had the highest coverage for antenatal interventions, while information was scanty in Sierra Leone. Furthermore, for mothers diagnosed of various ailments, there was a wide gap in coverage for their treatment.

A large proportion of mothers (25%) who came from their homes arrived at the health facility late, with cervical dilatation of 9 – 10cm. And about half (48%) of non-referrals arrived too late, without fetal heart sound on admission.

Some elements of third delay were also observed at the health facilities. Only 78.2% of mothers admitted in active labour gave birth within 12 hours of admission. For mothers who had Caesarean section, median time between decision for the procedure and birth ranged from 60 to 120 minutes. Only 15.7% of eligible mothers had a partograph correctly used for them.

Health system problems also contributed to some of the stillbirths, but not as much as initially thought from the literature.

The overall quality of care was poor, with deficiencies identified in both antepartum and intrapartum care. In total, the outcome of 414 (37.9%) stillbirths could have been altered with better care.

CHAPTER 8: DISCUSSION & RECOMMENDATIONS

8.1 Introduction

This study was conducted to identify underlying cause of stillbirth using three different methods, and to identify areas of care that would require action at various levels to improve quality of maternal and newborn health. In addition, two classification systems were applied, including the new WHO ICD-PM (applied for the first time on data from low-resource settings), to formulate recommendations to improve stillbirth review process, classification of stillbirths and maternal and newborn services.

Following the structured discussion format for scientific results (Docherty and Smith, 1999), this chapter discusses the study's principal findings, identifying its strengths and weaknesses, and comparing results found with those of previous studies. Throughout the chapter, an attempt is also made to identify implications of the results for clinicians, managers and policymakers, and to provide direction for future research. It fulfils objective #5 of the study.

8.2 Stillbirth Rate

The stillbirth rate is an important indicator of quality of care, giving insight into the success rate of management of pregnancy and childbirth. Sadly, the stillbirth rate (SBR) remains unacceptably high in low- and middle-income countries (LMIC). At the population level, the mean SBR could be as high as 29 per 1,000 births in sub-Saharan Africa, compared to 3.1 per 1,000 births estimated in high-income countries (Lawn et al, 2011).

It is hoped that the large sample size in this study and selection of various regions of each country make the findings more generalizable at least to other facilities in the countries studied and possibly other countries with similar settings.

However, in sub-Saharan Africa where it is estimated that only two-thirds of mothers give birth in health facilities and only half of all stillbirths occur in the facility (Lawn et al, 2016), many stillbirths remain unaccounted for in

facility data. Therefore, the results of this study may not represent the full picture of the problem in the population.

There are only a few studies reporting on stillbirth rates from the countries included in this study, most of which were conducted more than a decade ago. However, the studies available could be compared with this study to some extent since they were also mostly hospital-based. They could also serve as a benchmark for observing change in stillbirth rates over time.

Kenya

In Kenya, a hospital-based cohort study of 18 stillbirths in 411 births to investigate the role of placental inflammation in adverse obstetrical outcome reported a stillbirth rate of 43.8 per 1,000 births (Mwanyumba et al, 2003), which is similar to what we found (38.8 per 1,000 births; 95% CI: 33.9 – 43.9) despite the time gap between the two studies.

The latest Kenya Demographic and Health Survey (DHS) reported a population stillbirth rate of 13.3 per 1,000 births (DHS, 2014), indicating a wide variation between hospital and population stillbirth rate. Since 61.2% of births occur in health facilities (DHS, 2014), focusing on reducing facility stillbirths is likely to cause a remarkable reduction in the overall population stillbirth rate.

Malawi

In a hospital-based study of 54 stillbirths in 1,571 births in Malawi, Kalanda et al (2006) reported a stillbirth rate of 34.4 per 1,000 births, which is higher than our finding of 20.3 per 1,000 births. The difference between their result and ours could be because they studied one hospital while we studied four. Nevertheless, their finding falls within the range of the stillbirth rates found among the four hospitals in Malawi (i.e. between 17.3 and 46.4 per 1,000 births), as well as within the confidence limits of this study (95% CI: 15.0 – 42.8).

Like Kenya, Malawi also has a relatively high proportion of facility births, with up to 73.2% of births occurring in hospitals, and an estimated population

stillbirth rate of 13.5 per 1,000 births (DHS, 2015-16), which is even lower than the 15.8 per 1,00 births reported earlier (DHS, 2010).

Sierra Leone

For Sierra Leone, there were no similar studies to enable comparison of results. However, the DHS reported a population stillbirth rate of 8.1 per 1,000 births (DHS, 2013), which is much lower than the hospital stillbirth rate we found (118 per 1,000 births; 95% CI: 115.0 – 121.2). The high stillbirth rate found in this study could be partly because the data collection coincided with the period of Ebola virus outbreak of 2014/2015 in the region. Although hospitals included in this study did not treat confirmed cases of Ebola, there was a remarkable scale down of maternal and newborn health services to control the epidemic, with a 34% increase in facility maternal mortality ratio and 24% increase in stillbirth rates observed (Jones et al, 2016). In one of the hospitals studied, maternal and newborn health services were only provided between morning and evening. Mothers in labour were discharged every evening and asked to come back the following morning if they had not given birth.

With only half (54.4%) of mothers giving birth in hospitals in Sierra Leone (DHS, 2013), there is the need to increase both the demand for maternal and newborn health services and the quality of services provided in facilities.

Zimbabwe

A large retrospective study involving 986 stillbirths in Zimbabwe investigating birth patterns and birth outcomes in a hospital reported a stillbirth rate of 57.4 per 1,000 births (Feresu et al, 2004), which was higher than our finding of 34.7 per 1,000 births in the country. However, it is noteworthy that while they included cases of stillbirth "after 20 weeks of gestation", we defined stillbirth from 28 weeks. The low cut-off point they used was likely to have increased the rate.

Among the four countries in this study, Zimbabwe relatively has the highest proportion of mothers who deliver in hospitals (77%; DHS, 2015). This high proportion of hospital deliveries, coupled with the relative low population stillbirth rate (12 per 1,000 births; DHS, 2015), presents an opportunity to

further reduce the overall population stillbirth rate by focusing interventions on improving quality of care in health facilities.

Overall

Higher hospital-based stillbirth rates than reported in this study are not uncommon in the literature. However, most of such reports are usually from studies of high risk groups. For example, in a hospital study of 19 stillbirths in 52 births to investigate sero-positivity of toxoplasmosis in women with 'bad obstetric history' in India, Sarkar et al reported a stillbirth rate of 365 per 1,000 births (Sarkar et al, 2012). Similarly, in another hospital-based study of 38 stillbirths among 148 births, a stillbirth rate of 257 stillbirths per 1,000 births was reported among women with sickle cell disorder in Tanzania (Muganyizi & Kidanto, 2013).

Nevertheless, a few studies from other countries have reported similarly high stillbirth rates in relatively healthy populations. While Jammeh et al reported 156 stillbirths per 1,000 births in a rural hospital in The Gambia (Jammeh et al, 2010), Begum reported a stillbirth rate of 104 per 1,000 births in another hospital in Dhaka, Bangladesh (Begum, 2010). Even higher rate of 170 per 1,000 births was reported from a tertiary hospital in Nigeria (Ugwa & Ashimi, 2015).

The variation in stillbirth rate between the countries in this study could partly be explained by the differences in the capacity of the hospitals in the study. While all the facilities in this study offered comprehensive obstetric and newborn care, in reality, there were disparities in their levels. For example, whereas all the three hospitals in Zimbabwe were tertiary facilities, which provided the highest level of care in the country, there was a mixture of both district level and regional health facilities in the other three countries. The latter had fewer specialist staff and equipment.

8.3 Time of Death

More than one-third (35.9%) of cases were documented as fresh stillbirth and 32.7% were documented to have fetal heart sound present on admission. Overall, using the combination of physical appearance and status of fetal heart sound on admission, half of all stillbirths could be classified as

intrapartum deaths, ranging between 35.8% in Zimbabwe and 67.2% in Malawi.

Clinicians around the world rely on the classification of stillbirths into “fresh” or “macerated” as an indication of time of death. This categorisation enables a quick assessment of whether a baby died during the ante- or intrapartum period, with implications on priorities for improvement of care.

Determining time of death is, however, difficult, especially in low-resource settings with huge challenges in quality of antenatal and emergency obstetric care. Using fetal appearance alone (i.e. fresh/macerated categorisation), a large proportion of stillbirths in this study were initially misclassified in terms of their time of death. Healthcare providers tended to classify fewer stillbirths (35.9%) as “fresh”, implying fewer intrapartum deaths than antepartum. Several studies in LMIC (as discussed in the literature review – Chapter 2A) that used this method of determining time of death have reported similar proportions of stillbirths as intrapartum, ranging from 34.9% to 45.5% (Guidotti et al, 2009; Edmond et al, 2008a and 2008b; Baqui et al, 2011; Bhattacharyya & Pal, 2012; Kuti et al, 2003).

However, a study in Ghana that evaluated the reliability of provider assessment of fetal maceration by appearance found that 30% of babies expected to be reported as fresh stillbirths were misclassified as macerated (Gold et al, 2014). The study concluded that provider-reported fetal appearance alone may be an unreliable indicator for assessing time of fetal death.

Using a combination of both fetal appearance and presence/absence of fetal heart sound on admission, 50.7% of the stillbirths in this study were categorised as intrapartum. These results agree with the findings of Lawn et al. who used regression models and reported up to 51% of all stillbirths as intrapartum (Lawn et al, 2016). It is noteworthy, however, that despite a seemingly comprehensive search for data, the estimates reported by Lawn et al were limited by the “quantity and quality of available data”, which impeded identification of a satisfactory model.

Visible signs of maceration begin to show 6-12 hours post-mortem (Genest & Singer, 1992). Thus, for mothers admitted in active labour with a live baby (fetal heart sound present), a stillbirth outcome would be expected to be fresh rather than macerated, unless there is a delay in providing care. In this study, some mothers remained in labour for even longer than 24 hours. Therefore, some intrapartum deaths were likely to be born macerated. Moreover, the subtle early signs of maceration are less likely to be recognised by low skilled healthcare providers, giving more room for misclassification of time of death.

Aside these difficulties, 7.3% could not be categorised as either ante- or intrapartum deaths. This was, however, much less than what was reported by Wilkins et al (2015), who found that as high as 31.4% of 153 stillbirths in a hospital in East Timor had unknown time of death.

These findings imply that in low-resource settings, the use of fetal appearance to determine time of death may be misleading. Since the new WHO classification for perinatal mortality (ICD-PM; WHO, 2016b) requires that stillbirths are classified by time of death before a fetal and maternal cause of death can be identified, it will be challenging to apply the ICD-PM classification in LMIC where most global stillbirths occur (Lawn et al, 2016). The consequence of misclassifying stillbirths (by their time of death) may result in programmes focusing attention away from areas of care with the most problems.

8.4 Cause of Stillbirth

This study has demonstrated that cause of stillbirth can be successfully assigned using any of the three methods used, with advantages and disadvantages for each method. The following section discusses why large differences were observed in some of the results with regard to method of assessment used, and compares the results with findings from other studies.

8.4.1 Major cause of death

Asphyxia

The leading cause of death (by all three methods of assessment) was asphyxia, accounting for 18.5% determined via HCP review, 20.8% by expert panel review and 37.4% using computer-based algorithms. The relatively high proportion of asphyxia found by the algorithms was because asphyxia was prioritised in the hierarchical model. When the algorithms diagnosed asphyxia simultaneously with other conditions (such as hypertension, diabetes, etc), the algorithms considered asphyxia more important. This was because the baby was considered to have made it to labour alive despite the existence of the other conditions, i.e. for intrapartum deaths.

There is paucity of information on proportion of stillbirths due to asphyxia from the countries studied. However, in a prospective cohort study of 60 stillbirths in neighbouring Tanzania using hospital records and verbal autopsy, asphyxia-related death was reported to account for 25% of stillbirths (Hinderaker et al, 2003). In Zambia, Turnball et al reported in a population-based survey involving 50 stillbirths that asphyxia was responsible for 18% of stillbirths (Turnball et al, 2011).

In a more recent study that used computer-based algorithms to assign cause of stillbirth in six low- and middle-income countries (including Kenya), McClure et al reported as high as 46.6% of stillbirths to be due to asphyxia (McClure et al, 2017). Their findings were closer to the findings of the algorithms used in this study than that of HCP reviews or expert panel review. This is despite the difference in the placement of asphyxia in the hierarchical models of the algorithms used in the two studies. While our algorithms considered asphyxia first for reasons discussed above, their algorithms placed asphyxia at the fourth position, after trauma, congenital anomalies and infection.

Since asphyxia is in principle preventable, it is important to ensure mothers are attended to by skilled birth attendants. Correct use of the partograph for all mothers in active labour, as recommended by the WHO (WHO, 2016d), could help in identifying early signs of fetal distress.

Placental disorders

Placental disorders, comprising mainly of placenta abruptio and praevia, also contributed significantly to stillbirth (by all three methods of assessments), accounting for between 8.4% and 15.1% depending on method of assessment. For cause assigned by computer algorithms, it was observed that the proportion of stillbirths due to placenta praevia was much higher than that of placenta abruptio. This was because, to meet the criteria for placenta abrutio, the algorithms required presence of abdominal pain in addition to vaginal bleeding. This piece of information was not available in many of the cases reviewed. Thus, the algorithms diagnosed cases of antepartum haemorrhage (APH) without abdominal pain to be due to placenta praevia. This is likely to have caused an over-representation of stillbirths due to placenta praevia, as placenta abruptio is a much more common cause of stillbirth, and suggests an area for improving the algorithms.

The proportion of stillbirth due to APH varies widely in the literature. For example, whereas Bhattacharya and Pal (2012) reported 8.4% of stillbirths to be due to APH in a population-based cross-sectional study involving 5,257 stillbirths in India, Edmond et al (2008a) reported as high as 32% among 661 stillbirths in a population-based cross-sectional study nested in a trial in Ghana. However, the Ghanaian study was conducted via community verbal autopsy. Diagnosis of APH is likely to be more accurate in hospital settings where trained healthcare providers make and document diagnoses, thus more reliable than what can be discerned from community informants.

Hypertensive disorders

Healthcare providers assigned hypertensive disorders (hypertension, pre-eclampsia and eclampsia) as the cause of 13.6% of the stillbirths reviewed; the expert panel assigned 13.3%, and; the computer algorithms assigned 5.1% (8.7% on aggregate).

The reason for the disparity between the proportions assigned by the algorithms and the other two methods was twofold. First, information about proteinuria was mostly unavailable. Thus, the data could not meet the

algorithms' criteria for the diagnosis of pre-eclampsia. In other words, failure of the algorithms to diagnose pre-eclampsia may not necessarily mean absence of the diagnosis, but absence of objective information to fulfil its strict criteria. It is not clear how HCPs and the expert panel made the diagnosis without this information. One possible reason may be because it was ignored.

Secondly, the algorithms' hierarchical model gives more priority to causes that occur closer to death than those more likely to occur further away from death in the pathway to death. This means that when hypertensive disorders (which usually cause antepartum death) co-exist with such causes as asphyxia (which usually causes intrapartum death), the algorithms returned the causes closer to death as the most likely cause and hypertensive disorders as one of the other possible causes. This also explains why the aggregate contribution of hypertensive disorders by the algorithms (8.7%) was higher than the proportion for its most likely cause (5.1%; Tables 5.6 and 5.8 in results).

Hypertensive disorders have been established to pose a significant risk of stillbirth. In a clinical trial involving 195 stillbirths in Bangladesh, which investigated patterns of antepartum complications and the risk of perinatal deaths associated with such complications in rural Bangladesh, pregnancy-induced hypertension was found to increase significantly the risk of stillbirth (IRR: 1.8; 95% CI: 1.3–2.5) (Khanam et al, 2017).

None of the studies from the literature review reported proportions of stillbirth due to hypertensive disorders in the study countries. In other countries, varying proportions have been reported. In Nigeria, a similar hospital-based study of 158 stillbirths reported 12.7% of stillbirths to be due to hypertensive disorders (Mutihir & Eka, 2011). A lower proportion (5%) was found in another hospital-based study of 143 stillbirths in Liberia (Lori et al, 2014). However, proportions as high as 29.3% have also been reported in a hospital-based study in Pakistan (Munim et al, 2011).

Improving availability and quality of antenatal services is key to identifying women with hypertensive disorders and preventing adverse outcomes. The

new WHO guidelines for antenatal care recommend regular measurement of mothers' blood pressure and screening for pre-eclampsia (WHO, 2016d).

Congenital anomalies

All the three methods of assigning cause of death used in this study returned low proportions of stillbirths due to congenital anomalies, ranging from 1.8% to 2.5%, depending on method.

In Sierra Leone, only one case of stillbirth was assigned by the algorithms to be due to a congenital anomaly; HCPs and experts did not assign any case of stillbirth to be due to congenital anomaly in Sierra Leone. The almost total absence of congenital anomalies as cause of stillbirth in Sierra Leone does not necessarily imply lower incidence of congenital anomalies in Sierra Leone than in the other countries. It may be explained by lack of capacity of HCPs to recognise such cases or lack of recognition of such findings as important enough to be documented, or both. In settings such as these, healthcare providers rarely examine a stillborn after birth; they often diminish the existence of the baby to help cope with bereaving parents (Froen et al, 2011).

Globally, congenital anomalies are estimated to account for 7.4% of stillbirths (Lawn et al, 2016). These figures are generally higher in high-income countries. In Canada, for example, congenital anomalies are estimated to account for up to 11% of stillbirths, while in Ireland it is as high as 21% (Lawn et al, 2016).

In low-resource settings, where more preventable causes of stillbirth proportionally account for most deaths, it is common to have a low proportion of stillbirths due to congenital anomalies. In a similar study of 2,064 births in Nigeria, Ezugwu et al reported 2.1% of stillbirths to be due to congenital anomalies (Ezugwu et al, 2011). However, even in LMIC, there are some reports of high proportions of stillbirths due to congenital anomalies: 21.8% has been reported in Pakistan (Munim et al, 2011) and 15.1% in Thailand (Tannirandorn & Jatuparisuth, 2004). A wide range of anomalies have been reported, including central nervous system-related congenital anomalies (Edmond et al, 2008b; Mo-suwan et al, 2009; Uroos et al, 2014; Kaistha et al, 2016), cardiovascular (Edmond et al, 2008b) musculoskeletal

(Aboualsoltani et al, 2009) renal, pulmonary and cord anomalies (Vijayan et al, 2012; Uroos et al, 2014).

Some congenital anomalies are preventable. However, it is difficult to focus interventions on congenital anomalies of public health importance without proper documentation of anomalies to enable identification of those that are preventable and their distribution pattern. Thus, there is the need to improve documentation of such cases, and the need for more research to report types of anomalies causing stillbirth in LMIC.

The WHO recommends commencement of folic acid supplementation as early as possible during pregnancy (ideally before conception) to prevent neural tube defects (WHO, 2016d). A carefully planned elective Caesarean section could prevent adverse outcomes following obstructed labour as a result of congenital anomalies such as hydrocephalus.

Cord problems

Proportions of stillbirths due to cord problems (mainly cord prolapse) ranged from 3.3% to 6.5%. And more than one-third (35.4%) of mothers who had stillbirths due to cord accidents were considered to have been admitted with a live baby, i.e. with fetal heart sound present.

The major difference between the methods of assigning cause of death lies in the importance attached to the cause by the different methods. While the healthcare providers may consider cord prolapse as the cause of death in the presence of other causes, the computer algorithms were programmed to prioritise other more important causes along the pathway to death, such as asphyxia and placental abruption. In the absence of evidence for the other more likely causes, the algorithms diagnosed cord accidents, when its criteria were met.

Low quality studies from LMIC suggest that the incidence of cord prolapse is low in those settings, with rates of 0.3% or less reported (Umar & Gaya, 2015). A higher rate of 1.7% was reported from a large retrospective study of 1,424 cases of cord prolapse in Ireland (Gibbons et al, 2014). However, there is a marked difference in survival rates between low- and high-resource

settings. While as high as 45% of cases of 42 cases of cord prolapse resulted in stillbirth in a low-resource setting (Umar & Gaya, 2015), only 6% of the 1,424 cases in the Irish study ended up as stillbirth (Gibbons et al, 2014).

A similar hospital-based study in Nigeria reported that cord accidents accounted for 7% of the 158 stillbirths they studied (Mutihir & Eka, 2011).

Increasing availability and quality of emergency obstetric and newborn health services will enable faster action for women who need emergency Caesarean section to save their babies. Mothers should be educated to be able to recognise common danger signs in pregnancy and encouraged to report to a facility early.

Fetal growth restriction

Neither HCPs nor expert panel attributed any case of stillbirth to intrauterine growth restriction (IUGR). Yet, the computer algorithms attributed as high as 12.9% of the stillbirths to IUGR. The diagnosis also contributed to 41.5% of all the stillbirths, using 3288 grams as reference mean weight for babies born at 40 weeks of gestation (Hadlock et al, 1991). However, since the method of diagnosis of IUGR used in this study is dependent on accurate records of gestational age and birth weight, it should be noted that only a small proportion (2.3%) of the cases in this study had gestational age confirmed by ultrasound.

The HCPs and the expert panel did not consider IUGR as a cause of death perhaps because the diagnosis involves placing the birth weight of each baby in a centile chart, which could be a tedious task when done manually, but easily accomplished by the computer algorithms.

This perhaps also explains why there are few studies reporting IUGR as a cause of stillbirth in LMIC. The only study found from LMIC which reported proportion of stillbirths due to IUGR was conducted in a hospital in Pakistan, where Munim et al reported IUGR to account for 18% of the 278 cases of stillbirth in the study (Munim et al, 2011).

IUGR is the single largest condition associated with stillbirth (Gardosi et al, 2005), thus cannot be ignored. Its inclusion into classification systems for

causes of stillbirth is said to reduce the proportion of stillbirths with unknown causes from 40-50% to less than 20% (Gardosi et al, 2005; Vergani et al, 2008).

In a study to estimate the gestational age for 620 stillbirths in the United States, Conway et al concluded that fetal foot length is relatively accurate in measuring gestational age at death, and they recommend collecting such data in all stillbirths (Conway et al, 2013). This may be feasible in LMIC, and could potentially improve the accuracy of the diagnosis of IUGR during perinatal death reviews.

Early detection is the key to tackling IUGR. The WHO recommends regular fetal growth monitoring through: daily fetal movement counting by mothers; measurement of symphysis-fundal height during antenatal visits; routine antenatal cardio-tocography; ultrasound monitoring, and; Doppler ultrasound. In settings where ultrasound is not available, fetal growth should be monitored by regular check of symphysis-fundal height during antenatal visits, but this shouldn't replace abdominal palpation (WHO, 2016d).

However, if these strategies are to succeed, staff shortages and lack of equipment in LMIC are some of the challenges that must be overcome.

Twin-twin transfusion

Twin-twin transfusion syndrome (TTTS) is another cause of stillbirth only diagnosed by the algorithms. It accounted for 1% of the stillbirths, or 13.5% of the 89 cases with multiple gestation. It is not unusual for healthcare professionals to miss the diagnosis of TTTS. Baud et al has reported failure to identify TTTS in 33% of 323 cases of referrals to a hospital in Canada (Baud et al, 2014).

Although rare, TTTS is a potentially fatal condition that occurs when abnormal placental blood vessels cause an uneven blood flow to identical twin fetuses sharing a placenta (Duryea et al, 2016). A systematic review and meta-analysis of 361 studies (Danon et al, 2013) found that the condition substantially increases the risk of stillbirth throughout the third trimester, but even more so at 36 weeks of gestation (OR: 8.5; CI 1.6–44.7). The

diagnosis is suspected in a monochorionic twin gestation when one twin (usually a stillbirth) has a birth weight which is 25% less than the other twin (stillbirth or live born).

There are scanty previous reports of proportion of stillbirths due to TTTS in LMIC. In the only study found, which investigated causes of hydrops fetalis among 492 fetal deaths in Thailand, Taweevisit & Thorner found that TTTS was responsible for 10.2% of the deaths (Taweevisit & Thorner, 2010). The much larger proportion in their study could have resulted from their focus on hydrops fetalis only, excluding all intrapartum deaths and other causes of antepartum deaths.

While there is currently little that can be done to prevent TTTS, early identification of multiple pregnancies could help in the monitoring of high risk cases. Interventions such as amnio-reduction and laser surgery have been favoured to remarkably improve survival chances of one or both twins (Duryea et al, 2016).

Infections

The proportions of stillbirths due to infections (HIV, malaria, syphilis, UTI and other infections) were within a close range across the three methods of assessment: 6.8% by HCPs, 4.3% by experts and 9.0% by computer algorithms. It should be noted, however, while HCPs and expert panel assigned some cases to HIV, the computer algorithms did not recognise HIV as a direct cause of death as evidence suggests that there is no increased risk of stillbirth due to HIV infection per se (OR: 1.5; 95% CI: 0.7 – 3.0; Chi et al, 2007).

In Sierra Leone, the low proportion of stillbirths due to syphilis and none due to HIV were as a result of lack of information on these diagnoses rather than absence of the diagnoses.

A large study of 19,791 births and 495 stillbirths in multiple countries in West Africa showed that infections significantly increase the risk of stillbirth (OR: 9.7; CI: 6.3 – 15.1; Chalumeau et al, 2012). Another study in a hospital in

Brazil reported that up to 9.3% of stillbirths were due to infections (Andrade et al, 2009), which is similar to the findings in this study.

Malaria is a major threat to pregnant women and their babies. The WHO recommends a package of interventions to control malaria, including the use of insecticide-treated nets (ITN), intermittent prophylactic treatment and appropriate case detection and management. High quality evidence suggests that intermittent prophylactic treatment of malaria with sulfadoxine-pyrimethamine (SP) is beneficial in pregnancy (WHO, 2016d).

However, demographic and health surveys in this study's countries indicate that the malaria control strategies outlined by the WHO (above) are not producing the desired results. For example, ownership and use of ITN among pregnant women ranges from 13.1% in Zimbabwe (DHS, 2015) to 57% in Malawi (DHS, 2017). Similarly, the proportion of pregnant women who had 2 or more doses of SP is low: 16.9% in Kenya (DHS, 2014), 63% in Malawi (DHS, 2017) and 45.1% in Sierra Leone (DHS, 2013). This was not reported in Zimbabwe DHS. Although there is a general gradual improvement of these indicators over time, if the desired 100% ITN distribution is to be achieved, stakeholders should prioritise, re-strategize and share success stories for other countries to adapt. Educative communication strategies and campaigns should be targeted at women, especially in rural areas, on the importance of use of ITN (Sangare et al, 2012).

Integrating screening for syphilis with HIV screening during antenatal visits will strengthen existing health systems for maternal and newborn care. Low-certainty evidence suggests that vitamin A supplementation could reduce the risk of infections during pregnancy (WHO, 2016d). Routine hand washing by healthcare practitioners before and after procedures will reduce nosocomial infections. Making penicillin available to all mothers with syphilis could help to prevent as many as 37,822 stillbirths globally each year (Taylor et al, 2016).

Ruptured uterus

Uterine rupture is a catastrophic intrapartum event. It accounted for 5.2% of the stillbirths according to HCPs; 6.1% by expert panel, and; 2.6% by

computer algorithms. The difference between the proportions by method of assessment was mainly because uterine rupture frequently leads to asphyxia, which is higher in the algorithms' hierarchical model. This also explains why the cumulative contribution of uterine rupture by the algorithms was higher (4.8%).

However, the three methods of assessment seem to agree that there were more cases of ruptured uterus in Malawi and Sierra Leone than in Kenya and Zimbabwe. Although all the facilities in this study provided comprehensive emergency obstetric care, the facilities in Kenya and Zimbabwe generally had more capacity in terms of skilled manpower and equipment availability. They were better positioned to detect imminent rupture of uterus.

There is paucity of literature reporting proportions of stillbirth resulting from ruptured uterus as most literature tend to use asphyxia as cause of stillbirth. Although, without intervention, uterine rupture ultimately leads to hypoxia and death, it should be recognised as an independent cause of death in perinatal death reviews (Gardosi et al, 2005). This is because if all stillbirths due to uterine rupture are documented to be due to intrapartum hypoxia, information about the underlying causes of the hypoxia may be lost. Thus, action to improve quality of care may not necessarily address the underlying cause of death.

Uterine rupture is an avoidable event. Hospitals should be able to identify high risk groups and remain alert for possible emergencies. Correct use of the partograph could help identify obstruction early and allow for more timely intervention. All mothers must be encouraged to deliver with a skilled birth attendant. Mothers with a history of previous Caesarean section should give birth preferably close to or in a facility to enable repeat CS, if necessary. Clinicians should be cautious when using oxytocics in such mothers and in grand-multiparous mothers.

Amniotic causes

Amniotic causes of stillbirth include oligohydramnios, polyhydramnios, chorioamnionitis and prelabour rupture of membranes (Gardosi et al, 2005). They accounted for 3.6% of all stillbirths according to HCPs and 3.4%

according to the expert panel. This category of causes was not identified by the algorithms as ultrasound details required to meet its criteria were rarely available.

Oligo- and polyhydramnios usually result from congenital anomalies in the baby, especially gastrointestinal and renal anomalies, that impede the baby's normal digestion and excretion of the fluid. Routine measurement of symphysis-fundal height could prove useful in detecting oligo- and polyhydramnios in settings without ultrasound (WHO, 2016d).

More research is needed to determine any direct role of these conditions as independent causes of stillbirth.

Unknown cause

Stillbirths categorised to have "unknown" cause form an important part of any death review. While HCPs assigned 21.9% of all the stillbirths in this study to this category, the expert panel assigned 26%, and the computer algorithms assigned 17.9% as unknown.

Assigning a case to the "unknown" category could be because of either lack of information to reach a reasonable conclusion on the cause of death or simply due to inability to identify a cause despite availability of all information needed to make a diagnosis. In this study, most cases classified to have "unknown" cause were due to lack of information.

By country, Zimbabwe had the least proportion of stillbirth assigned as cause unknown by HCPs and expert panel, and Malawi had the highest. Because all the three hospitals in Zimbabwe were teaching hospitals located in urban areas, the clinical records were generally more complete, thus, allowing the reviewers to assign a cause to most cases reviewed. On the other hand, three of the four hospitals in Malawi were district hospitals located in semi-urban and often remote locations. Their records were not as complete as the those found in an urban hospital.

Nevertheless, the computer algorithms found the lowest proportion of unknown in Sierra Leone due to high proportion of deaths due to IUGR, cord prolapse and ruptured uterus, all of which are diagnosed from information

that is more readily available, e.g. gestational age and birth weight for IUGR and presence of a prolapsed cord in the case of cord prolapse.

Overall, the algorithms also found the least proportion of cases with unknown causes when compared to HCPs and expert panel. This may be because the software does not "forget" information once entered, while humans are likely to forget certain details or their importance, and are therefore more likely to assign a case as unknown. The high proportion of stillbirths due to IUGR (12.9%) found by the algorithms, none of which were found by either HCPs or experts, might have also contributed to the lower proportion of cases with unknown cause since inclusion of IUGR is known to reduce proportions of cases with unknown cause to less than 20% (Gardosi et la, 2005; Vergani et al, 2008). On the other hand, this could be an indication of an over-representation of IUGR by the algorithms.

Several previous studies have reported varying proportions of stillbirths due to unknown causes. While Engmann et al reported 12% as unknown in a multi-national, population-based study of 143 stillbirths (Engmann et al, 2011), two different population-based studies involving 1,748 and 661 stillbirths from Bangladesh and Ghana, respectively, have reported at least half of stillbirths to be due to unknown causes (Baqui et al, 2011; Edmond et al, 2008b). A small, hospital-based study of 17 stillbirths in Nepal reported 47% as unknown (Manandhar et al, 2003). The study of cause of stillbirth involving 2,847 cases of stillbirth in six LMIC using computer algorithms (discussed earlier) reported 17.1% as unknown (McClure et al, 2017).

These variations in the proportion of stillbirth with unknown cause reflect the variation in capacity of the various hospitals where the studies were conducted. Like the diagnosis in living subjects, hospitals with more skilled staff, diagnostic equipment and better records are more likely to identify a cause of death. Differences in disease burden in various populations also affect the proportion of stillbirth with unknown cause; a cause is more likely to be found in populations with high disease burden.

8.4.2 Methods of cause assignment

Despite differences observed in the proportion of individual cause of death for the different methods of assessment, when the cause of death was categorised using the ReCoDe classification, there was a statistically significant agreement across the three methods (Results Chapter, Section 6.2.4). This implies that any of the methods could be used to produce essentially the same results when cause of death is classified using the ReCoDe classification. The choice of which method to use, therefore, depends on other factors that favour or disfavour the purpose of the review.

The three methods showed some strengths and weaknesses. While HCPs and the expert panel had higher proportions of stillbirths with unknown cause and took more time and resources to conduct the reviews than the computer algorithms, the two methods still provided opportunities for problems in care to be discussed in detail, and for recommendations to be formulated. This way, perinatal death review helps to generate ideas for development of pertinent action plans.

However, perinatal mortality audit can be a tedious process. Because of the subjective nature of assessments during reviews, inter-observer bias also exists. It should be noted that even between experts, the agreement rate was lower than what one would expect ($k=0.61$; $p<0.0005$), indicating inconsistencies in assigning cause of death even among the experts.

The sheer numbers of perinatal mortality in LMIC make perinatal death reviews overwhelming in such settings. Staff shortage also compounds this problem, and where staff are available, they often lack the capacity to conduct reviews and identify causes, factors contributing to the death and elements of poor care. Eliminating human influence in information analysis could help reduce bias, and make the review process faster and easier even in settings with staff shortages. When reviewing all cases of perinatal death is not practical, the new WHO guidelines on perinatal death review (WHO, 2016a) recommend reviewing as many cases as possible. Thus, research is needed to establish minimum proportions of stillbirths that should be reviewed when all cases cannot be done.

The algorithms were faster, and once set up, the system required smaller time and resource investment than HCPs and experts. However, this method eliminated opportunities for discussions. Since the primary purpose of death reviews is to improve care, therefore, algorithms should be used in research and to complement facility reviews, but not as replacement for discussions during hospital reviews. In settings where there are only a few staff in a health facility, algorithms could prove useful in providing a second opinion on the cause of death and elements of poor care.

8.5 Classification of Stillbirth

8.5.1 ReCoDe classification

When cause of stillbirth was categorised using ReCoDe classification, intrapartum causes (mainly asphyxia) and maternal conditions (mainly hypertensive disorders and infections) were the leading categories of death. The category for unknown accounted for 17.9% by computer algorithms to 28.6% by expert panel.

Although the result of Kappa analysis to compare agreement between the three methods of assessment showed some level of agreement between all three methods, there were also differences in the proportions assigned by the methods. The most differences were observed between the proportions found by the algorithms and the other two methods. This emanated partly from prioritisation of certain diagnoses in the hierarchical model of the algorithms (Appendix 5). For example, while HCPs and expert panel assigned 18.5% and 21.1%, respectively, to the intrapartum category, the algorithms assigned as high as 37.4%. The relative high proportion in the intrapartum category assigned by the algorithms was largely accounted for by asphyxia which is ranked highly in the hierarchical model of the algorithms.

Another reason for the differences between the results obtained by the algorithms and the other two methods was the unavailability of specific information required by the algorithms to make certain diagnoses. For example, the algorithms required ultrasound evidence to make the diagnosis of oligo- or polyhydramnios, which was rarely available.

In addition, the remarkable differences observed between the results of the algorithms and other two methods in the fetus category was due to the almost total absence of certain key diagnoses, such as fetal growth restriction, in cause assigned by HCPs and the expert panel (as discussed previously in section 8.4.1). While HCPs and expert panel assigned 6.3% and 3.5%, respectively, to the fetus category, the algorithms assigned as high as 18.7%. The relative high proportion in the fetus category assigned by the algorithms was mostly due to fetal growth restriction and twin-twin transfusion, both of which were not diagnosed by the HCPs or the expert panel.

Some differences were also observed between proportion of cause assigned as unknown and proportion categorised as "unclassified" using ReCoDe classification. This is particularly so in cause assigned by HCPs and experts. The difference emanated from diagnoses assigned as causes which are not recognised to cause stillbirth in ReCoDe classification. For example, anaemia in pregnancy and prematurity were reported as cause of stillbirth, but are not recognised by ReCoDe classification as causes, and were, therefore, categorised as unclassified.

When ReCoDe classification was first published (Gardosi et al, 2005), the leading cause of death was fetal growth restriction (43%) and lethal congenital anomalies (14.9%). Intrapartum asphyxia, which played a major role in our study, only accounted for 3.4%. The total proportion for unclassified was 16%.

These discrepancies with our study were not unexpected as Gardosi et al conducted their study using data from maternity units in a high-income country (the UK), where the distribution of cause of stillbirth differs from that in a LMIC (Flenady et al, 2011). The relatively low proportion of stillbirths due to uterine cause (0.1%) compared to the findings in this study (2.6% to 5.7%, depending on method of assessment) is an indicator of the discrepancy in quality of obstetric care between high-and low-resource settings.

Furthermore, the high priority given to fetal growth restriction in the ReCoDe classification has been reported to significantly influence the overall distribution of causes of stillbirth (Ego et al, 2013).

8.5.2 ICD-PM classification

With ICD-PM, the major categories accounting for the death were: intrapartum hypoxia and fetal growth restriction. For contributing maternal conditions, M1 (placental, cord and membranes) and M3 (other complications of labour and delivery) dominated the groups. Overall, the proportion of cases that could not be assigned into either a fetal cause category or a contributing maternal condition in ICD-PM ranged from 13.7% to 17.9%.

No cause was allocated to M2 (maternal complications of pregnancy) by using the algorithms. As discussed earlier, the algorithms required ultrasound information to diagnose conditions in that group (e.g. oligohydramnios, polyhydramnios, incompetent cervix, etc). However, ultrasound information was not available.

Generally, many categories were blank as some conditions considered as causes by healthcare providers and the expert panel, such as HIV, prematurity and anaemia in pregnancy, are not considered as cause of death in ICD-PM. Thus, these diagnoses ended up as unknown. Moreover, diagnostic capabilities of facilities in LMIC to make some diagnoses was also limited.

Apart from the difficulty in determining time of death (which has been discussed in Section 8.3), there was a further difficulty with regard to deciding how a case with multiple causes should be classified. For example, when more than one fetal causes are diagnosed which belong to different categories, the decision regarding which category the case goes depends on the reviewers. In this study, it was assigned alphabetically, i.e. A1 then A2, then A3, etc. However, it would be more accurate if this was based on a clearly defined pathway to death to avoid subjective interpretation and ensure more uniform application of the classification.

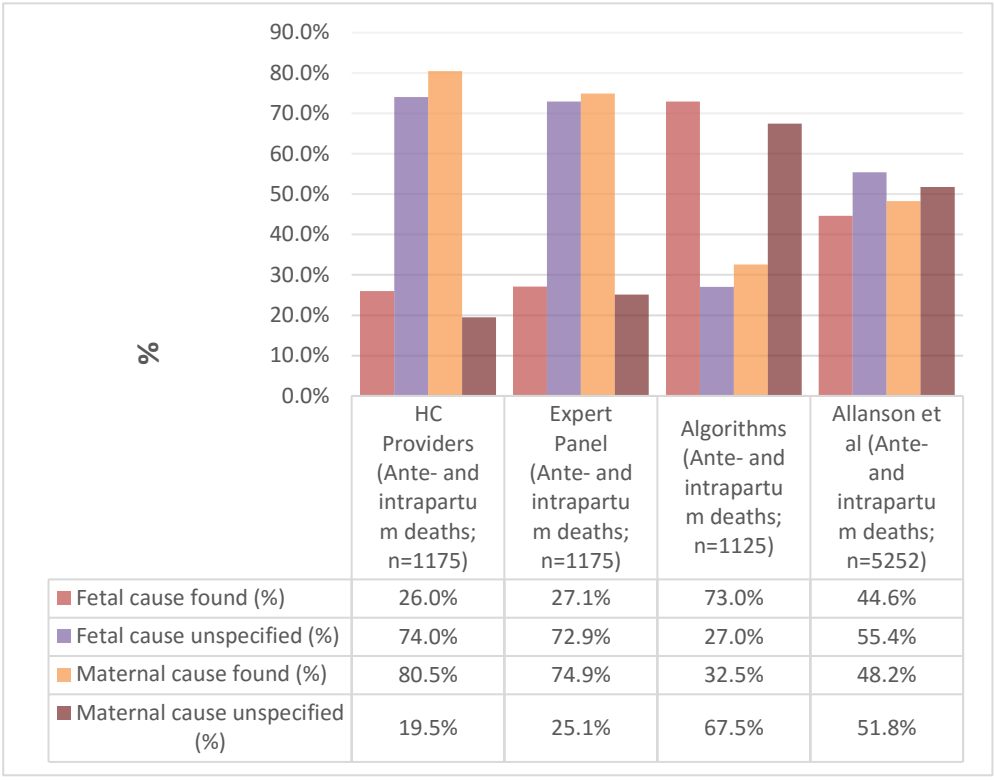
In comparison with the first (and only) publication on the application of ICD-PM on stillbirth data, Allanson et al (2016) reported 50% and 48.3% as antepartum, and 39% and 5% as intrapartum in South Africa and the UK, respectively. It is noteworthy, however, that they reported perinatal deaths, i.e. including early neonatal deaths. When the reported figures for stillbirths were isolated, intrapartum deaths represented 17.7% and 9.4% in South Africa and the UK, respectively.

In their study, Allanson et al found 59.1% and 22.4% of antepartum and intrapartum deaths, respectively, to be due to unspecified fetal cause. And 53.3% of the antepartum deaths had no associated maternal condition, while 37.9% of the intrapartum deaths had no associated maternal cause. Thus, for intrapartum death, Allanson et al reported a relatively smaller proportion with unspecified fetal cause (22.4%), and a larger proportion without associated maternal conditions (37.9%). Figure 8.1 (below) is an extension of Figure 6.5 (section 6.3.4) to compare this study's results with that of Allanson et al (2016).

The discrepancies with this study were not surprising – the study settings differed. While most of the data (93%) in the study by Allanson et al came from the UK, a high-income country, all datasets in this study were from LMIC, where obstetric emergencies still account for most of the stillbirths.

To further improve ICD-PM, therefore, some features of ReCoDe classification, such as the simple structure and use of simple terms, could be adapted. (More detailed suggestions to improve ICD-PM are highlighted in the recommendations section.)

Figure 8.1: ICD-PM classification: this study vs Allanson et al (2016)



	HC Providers (Ante- and intrapartum deaths; n=1175)	Expert Panel (Ante- and intrapartum deaths; n=1175)	Algorithms (Ante- and intrapartum deaths; n=1125)	Allanson et al (Ante- and intrapartum deaths; n=5252)
Fetal cause found (%)	26.0%	27.1%	73.0%	44.6%
Fetal cause unspecified (%)	74.0%	72.9%	27.0%	55.4%
Maternal cause found (%)	80.5%	74.9%	32.5%	48.2%
Maternal cause unspecified (%)	19.5%	25.1%	67.5%	51.8%

8.6 Standard of Care

Coverage for antenatal care interventions differed by country and by intervention. While HIV screening had relatively higher coverage, the coverage for anti-malarial prophylaxis seemed low. For mothers diagnosed of various ailments, there was a wide gap in coverage for their treatment.

A large proportion of mothers (25%) who came from their homes arrived at the health facility late, with cervical dilatation of 9 – 10cm. And about half (48%) of non-referrals arrived too late, without fetal heart sound on admission.

Some elements of third delay were also observed at the health facilities. Only 78.2% of mothers admitted in active labour gave birth within 12 hours of admission. For mothers who had Caesarean section, median time between decision for the procedure and birth ranged from 60 to 120 minutes. Only 15.7% of eligible mothers had a partograph correctly used for them.

8.6.1 Antepartum care

Using the WHO guidelines for antenatal care (WHO, 2002), every pregnant mother in the countries included in this study should receive iron and folate supplementation, prophylactic anti-malarial (except in some regions of Zimbabwe not considered as malaria-endemic) and tetanus vaccination. In addition, mothers should be screened for hypertensive disorders, HIV and syphilis, and assessed for Rhesus blood grouping.

Overall, only 2.2% of mothers who attended ANC had all these services provided to them. In Malawi and Sierra Leone, none of the mothers had all services provided. For mothers diagnosed with certain conditions during their antenatal visits, the majority are not receiving the care that should follow their diagnoses.

However, there seems to be wide disparity between the results of this study and the findings of the Demographic and Health Surveys (DHS) conducted in these countries in terms of coverage of antenatal care (Table 8.1). These differences might have resulted from the differences in study populations. While the DHS is a population study using random sampling, this study was hospital-based and targeted mothers with an adverse birth outcome only.

Table 8.1: DHS findings for some selected health outcomes

DHS Outcomes	Kenya DHS (2014)	Malawi DHS (2017)	Sierra Leone DHS (2013)	Zimbabwe DHS (2015)
Women with a live birth in the past five years who took iron and folate supplements	69.7%	89.4%	93.8%	83.3%
Women who received 1 or more doses of SP/Fansidar at ANC	29.5%	88.6%	62.1%	Not available
Women who received 3 or more doses of SP/Fansidar at ANC	10.1%	30.0%	45.1%	Not available
Women receiving two or more tetanus toxoid injections during last pregnancy	51.1%	73.0%	86.9%	40.0%
Women whose last birth was protected against neonatal tetanus	75.6%	90.2%	90.0%	54.3%
Women who received counselling on HIV and an HIV test during ANC	66.9%	79.7%	42.9%	71.3%

8.6.2 Intrapartum care

A large proportion of mothers arrived late at the health facility during childbirth, with up to one-quarter arriving at full cervical dilatation.

However, mothers' delay in arrival at the facility wasn't the only delay factor in the findings. There were indications of delays at the facility as well. Women who arrived early enough spent too long in labour or too long waiting for an emergency Caesarean section (CS), except in Malawi where the median time interval between decision for CS and actual birth was around 60 minutes. This is clearly below acceptable standards for time between decision and birth, i.e. 30 minutes (McKenzie & Cooke 2002).

Across all four countries, 29.7% to 51.2% of stillbirths whose mothers were admitted with fetal heart sound (FHS) present were classified as macerated stillbirths, indicating possible delays in providing care at the facility. Likewise, some cases with absent FHS on admission were classified as fresh stillbirths. This may indicate first and second delays, and gives insight into the populations' health seeking behaviour.

Similarly, the clear majority of women (84.3%) either did not have a partograph or it was used incorrectly. Poor use of the partograph has been linked to poor knowledge of the partograph. Fawole et al reported that only 37.3% of HCPs in a tertiary health facility in Nigeria could mention at least one component of the partograph (Fawole et al, 2008). A similar study in Cameroon reported that less than one-third of non-physician obstetric care providers had good knowledge of the partograph (Sama et al, 2017). Thus, in-service education should complement efforts to improve the use of the partograph in the management of labour (Pettersson et al, 2000).

In a study comparing the WHO composite partograph with a latent phase with a simplified one without the latent phase, Mathews et al reported that up to 85% of healthcare providers experienced difficulties with the former (Mathews et al, 2007). Therefore, simplifying the standard WHO partograph in country adaptations could make it easier to use, especially among low cadre health staff.

The documentation for cases reviewed was poor. Generally, poor documentation of clinical information is a common problem in LMIC. In study that assessed the adequacy of medical records in a hospital in Nepal, Mishra et al reported many gaps in hospital records, including 96.9% of in-patients not given any instructions on discharge (Mishra et al, 2009).

Standard-based audit (SBA) could be used to address areas of care needing urgent attention. It also has the advantage of being less threatening to healthcare providers. Thus, healthcare providers should be encouraged to conduct SBA, which could also help develop their competencies in conducting death reviews.

8.7 Strengths and Limitations

8.7.1 Study design

This study was the first to use different methods of assessing cause of stillbirth and triangulate the findings, highlighting the advantages and disadvantages of each method. It is also the first to use data from multiple LMIC to test the new ICD-PM classification, providing important insights into the applicability of the classification system in settings where most global stillbirths occur.

However, this study was designed as hospital-based. With only half of all stillbirths occurring in health facilities in sub-Saharan Africa (Lawn et al, 2016), hospital-based stillbirth studies only tell half of the story. The design also missed the opportunity to explore factors contributing to stillbirth in the community, such as reasons for delays in seeking care and referral delays. The quantitative nature of the design also did not allow exploration of reasons for poor care from healthcare providers.

Although many aspects of stillbirth and neonatal mortality overlap, the focus of this study on stillbirth alone, without including neonatal mortality, limits the generalisability of its findings to neonatal mortality. Thus, even the application of ICD-PM, which includes neonatal deaths, was limited to stillbirth. Similarly, the lack of inclusion of data from live births to serve as a comparison group has limited the study analysis, especially in exploring factors associated with stillbirth.

Nevertheless, the design also gave the study some advantages. In terms of cause of death assignment, the hospital-based design gave the study the advantage of assigning cause more accurately than would have been possible with verbal autopsy, for example.

The study was conducted in multiple countries, which enabled comparison between the countries. The multiple sites in each country also allowed comparison between different settings within each country, identifying problems that were peculiar to certain settings and some that were common in all settings.

With the benefit of retrospection, the sample size could have been smaller if it was calculated based on frequency of cases with known cause rather than stillbirth rate, as I did in the study. For example, assuming an expected frequency of 78% of cases with known cause (as found in this study), using the same parameters as above, the sample would have been 264 per country or a total of 1,056 cases. Thus, it is hoped that the accidentally larger sample size has given the study even more statistical power to detect rare problems and make the findings more generalizable.

The use of standard WHO definitions and guidelines wherever possible will make findings more acceptable to many LMIC.

8.7.2 Data collection and analysis

One of the major strengths of this study was the chronological sampling of cases until the sample size was achieved, which eliminated chances of selection bias. However, the low number of cases in some facilities obliged the research team to obtain uneven number of cases from facilities to meet the country sample size. Although this may have caused unbalanced distribution of cases between facilities in the same country, the review of all cases in the facilities with low numbers of stillbirth meant there was no sampling bias in those facilities. In the facilities with higher stillbirths than needed to meet the sample, the chronological sampling mitigated against selection bias.

During the data collection, healthcare providers participated in the review of cases from the same facility, which could potentially introduce the risk of bias

in cause assignment. However, the training given to the healthcare providers and the participation of the principal investigator during the review of most of the cases helped to mitigate against this risk. The independent expert review of cases, which showed a high level of agreement with the HCPs ($k=0.69$; $p<0.0005$), confirmed that the risk of bias was negligible, if any.

Furthermore, the data collection tools were subjected to several rounds of peer review and preliminary testing involving stakeholders from the study countries before they were deployed. This gave many opportunities for improvement of the tools and ensured that a more robust data was collected.

Ultimately, the inherent limitation of the methods used to assess cause of death was the dependence on hospital records, which were often incomplete, inaccurate or both. In cases with more than one possible cause of death, arriving at the most likely cause was often difficult. The lack of autopsy data to validate cause of death made the cause of death less certain. However, the involvement of several experts in the cause of death assessment as well as in the development of the computer-based algorithms used might have boosted the reliability of the results. Additionally, it is hoped that the agreement of the three methods of assessing cause of death in some areas may be a strong indication of the validity of the findings.

In the analysis, all cases that met the definition of stillbirth were included; this further reduced the chances of selection bias. However, there were few previous studies with which to compare the results; the few available often had differing methods. Therefore, all efforts were made to discuss findings carefully without over-generalisation.

8.8 Recommendations

8.8.1 Improving the stillbirth audit process

At the facility level, with half of stillbirths occurring intrapartum, there is a need to encourage perinatal death reviews. Perinatal mortality audit is an effective strategy for improving quality of care and could reduce perinatal mortality by up to 30% (Pattinson et al, 2009). This could be conducted by either an existing quality improvement or maternal death review team or by

a sub-committee dedicated to the exercise. In settings with too many deaths, where reviewing all deaths is not feasible, the new WHO guidelines on perinatal death review recommend focusing on intrapartum deaths (WHO, 2016a).

To conduct the reviews well, healthcare providers need to be trained on how to conduct perinatal death audit using the "no blame, no shame" approach, identify elements of poor care and initiate action to change practice.

At least for mothers admitted with fetal heart sound present, fetal appearance should be considered simultaneously with status of fetal heart sound on admission and duration of labour before a decision is made on the time of death. This will ensure more accurate and universally consistent results. Healthcare providers should be trained to be able to identify early signs of maceration.

Ultimately, since the cause of death for a proportion of stillbirths will always remain unknown, the prospect of reducing the proportion of stillbirths with unknown cause lies in our ability to reduce the subset of cases with unknown cause due to lack of information – which was reported in two-thirds of the cases in this study. Therefore, improving hospital records is the key to reducing the proportion of stillbirths of unknown cause. Improvements in staffing levels and diagnostic capabilities in health facilities will also help reduce the proportion of stillbirths whose cause is unknown.

At national and international levels, stakeholders in LMIC should advocate to make stillbirth a notifiable event. This will facilitate improvement in information documentation, collection and reporting; it will also encourage more reviews.

8.8.2 Improving classification of cause of stillbirth

Using the ICD-PM, some stillbirths could not be categorised as either ante- or intrapartum death. Without the creation of another category to accommodate them, information regarding these cases could have been lost. It is, therefore, recommended that the ICD-PM is amended to create a category for cases whose time of death could not be determined.

The lack of definition and understanding of a clear pathway to death leaves gaps for subjective interpretation of the ICD-PM. Thus, the classification system should clearly define diagnoses for consistency of reporting. There should also be a guide on how cases with multiple potential causes of death should be handled.

Global stakeholders should advocate for the adoption of the new ICD-PM to facilitate consistent reporting of cause of stillbirth to enable more focused global interventions.

8.8.3 Improving quality of maternal and newborn health services

Immediate action to reduce stillbirth that could yield quick results, the so-called 'low-hanging fruits', should address the following areas:

- Despite the finding that two-third of mothers who had stillbirth attended antenatal care at least once, more than half arrived too late for birth. This calls for better health education during antenatal visits. Healthcare providers should work with mothers to develop feasible birth plans, and mothers should be educated on the importance of skilled birth attendance. Community engagement strategies should address challenges relating to transport to the hospital for mothers and babies.
- Lack of guidelines and/or inappropriate interventions observed in one-fifth of the cases should prompt action toward development of local protocols for the management of common conditions in pregnancy. This should be adequately communicated to all staff involved in the provision of care to mothers and babies.
- HCPs should be encouraged to develop and implement standards for ANC and EmONC services. For example, standards on the use of the partograph could help reduce delay to intervene and ultimately reduce stillbirths due to asphyxia and possibly ruptured uterus. Other areas where standards should be developed include: ANC services, resuscitation, record keeping and management of common conditions in pregnancy.
- Hospitals should be ready with staff, supplies and other resources needed to conduct emergency procedures, especially Caesarean

section, to reduce delays observed in conducting the procedure. Actions should also address other delays identified in the facility.

- To improve recognition of IUGR, HCPs should be trained on how to use growth monitoring charts so they can recognise the condition early and intervene. This will also increase their ability to identify the condition during perinatal death reviews and focus actions to improve quality of care accordingly.

The overall high stillbirth rate observed in these countries is indicative of the quality of care mothers and babies receive in health facilities. If the Every Newborn Action Plan (ENAP; WHO, 2014) target of reducing stillbirth rate in every country to less than 12 per 1,000 births is to be achieved by 2030, there is the need for an urgent and coordinated action at local, national and international levels to improve the quality of care provided to mothers and babies in health facilities.

8.8.4 Further research

Researchers reporting findings of stillbirth studies should make a clear distinction between cause of death, risk factors and contributing factors.

Unlike maternal death reviews, the sheer numbers of stillbirths make reviews overwhelming for most health facilities in low-resources settings, a problem compounded by the inadequate human resources in such settings. Therefore, future research should focus on determining the proportion of stillbirths that should be reviewed for optimal results.

Algorithms developed to complement perinatal death reviews should be tested on different datasets to explore their utility, and should be refined for use in facility- as well as community-based audits.

Purposefully designed studies to assess the quality of antenatal and intrapartum care given to women (including those with live babies) in LMIC would give a better indication of the quality of maternal and newborn health services. Reasons behind mother's late arrival as well as for the poor care they receive at the facility should be explored.

More studies should be conducted in LMIC with a view to testing the new ICD-PM to check for its feasibility, consistency of reporting across different settings and ease of use. More research is need to further explore methods of determining time of death to suit the realities in LMIC where mothers are rarely monitored closely.

Case studies are relevant and important study design that could be used to report rare cases in a relatively more timely manner (Carey, 2010), allowing in-depth explorations of complex issues (Crowe et al, 2011). While recognising the limitations of a case study as a scientific methodology, it could play a significant role in improving our understanding cause of, and factors contributing to, stillbirth. Researchers could use the methodology to report rare conditions causing stillbirth or circumstances contributing to the death.

8.9 Chapter Summary / Conclusions

The stillbirth rate remains unacceptably high in low- and middle-income countries (LMIC). In this study, it ranged between 20.3 per 1,000 births in Malawi and 118.1 per 1,000 births in Sierra Leone. Half of all the stillbirths (50.7%) were classified as intrapartum stillbirths.

Even with minimal datasets, healthcare providers could identify the cause of stillbirth in 77.8% of cases, as well as elements of sub-standard care. This information is useful to guide action for the improvement of care.

The major causes of stillbirth were asphyxia, placental disorders, hypertensive disorders, infections, cord problems and ruptured uterus. Asphyxia was the most common cause of stillbirth irrespective of method of assessment used.

Antenatal and intrapartum care delivered to mothers who had stillbirth was poor. Up to 97.8% of cases had sub-standard antenatal care; only 30.7% of cases of all Caesarean deliveries were conducted within one hour of the decision. Up to 37.9% of cases could potentially be prevented with improved access to, and quality of, antenatal care, skilled birth attendance and emergency obstetric and newborn care. HCPs should be encouraged to conduct stillbirth review and act upon the findings to improve quality of care.

Although there was a statistically significant agreement between results obtained through computer-based algorithms and those obtained through HCPs and the expert panel, the agreement was weak. Differences observed in the three methods of assessing cause of death emanated partly from prioritisation of certain diagnoses, such as asphyxia, in the hierarchical model of the algorithms. In addition, some specific information required by the algorithms to make certain diagnoses was not available. For example, the algorithms require evidence from an ultrasound to make the diagnosis of oligo- or polyhydramnios, which was rarely available. Thus, some changes in the algorithms' hierarchical model for assigning cause of death may be necessary.

Using the ReCoDe classification system, intrapartum events (mainly intrapartum asphyxia) contributed the most deaths, followed by maternal diseases (mainly hypertensive disorders and infections) and placental and fetal conditions.

With the ICD-PM system, the major categories accounting for the death were: intrapartum hypoxia and fetal growth restriction. For contributing maternal conditions, M1 (placental, cord and membranes) and M3 (other complications of labour and delivery) dominated the groups. It was challenging classifying stillbirths whose time of death could not be determined. Therefore, the new ICD-PM could work in LMIC, but it needs to be improved to accommodate stillbirths that cannot be categorised either as ante- or intrapartum death. Guidance is also needed on how to handle cases with multiple possible causes.

More researchers should apply the new ICD-PM with a view to testing its performance, especially in low-resource settings where there are more challenges with clinical records.

Further research should also focus on exploring the use of computer algorithms in community-based reviews. This will have the potential to process large amounts of data easily and provide a more objective and consistent assessment of cause of, and especially community-related factors contributing to, stillbirth.

Studies exploring quality of perinatal care should include both stillbirth and neonatal to get a better understanding of factors contributing to perinatal mortality. More research is needed to further explore methods of determining time of death to suit the realities in LMIC where mothers are rarely monitored closely.

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APPENDIX 1: SUMMARY TABLE FOR SYSTEMATIC REVIEW I

See accompanying Excel spreadsheet

APPENDIX 2: SUMMARY TABLE FOR SYSTEMATIC REVIEW II

See accompanying Excel spreadsheet

APPENDIX 3: DATA COLLECTION FORM

PERINATAL DEATH REVIEW FORM

Instructions: Fill in this form for every perinatal death (i.e. stillbirth and neonatal death in the 1st week of life). The example of code below (SRL/FRT/01/01) represents "Sierra Leone/Freetown/January/1st case of perinatal death in the month of January".

Country	Date of Audit	Date of Data Collection	Code (E.g. SRL/FRT/01/01)

SECTION 1: HEALTH FACILITY

Name of Health Facility: ……

County / District / Region: ……..

Type of Health Facility (tick one):

National	Referral / Teaching	Regional	District	General	Health Centre	Other (specify) ……

Level of Health Facility (tick one): BEmONC ☐ CEmONC ☐

Is this a Helping Baby Breath (HBB) Facility? Yes ☐ No ☐

SECTION 2: MOTHER

Mother's Initials: …….. **Mother's Age:**

…… (in years)

Mother's Address (tick one): Rural ☐ Semi-urban ☐ Urban ☐

Mother's County / District:

……

Educational Level <u>Completed</u> (tick one):

None ☐

Primary ☐

Secondary ☐

Tertiary ☐

Was mother referred from another facility? Yes ☐ No ☐

If Yes, from which facility?

……..

<u>SECTION 3: PREGNANCY</u>

Mother's Parity: Para …….. + ……. No. of Children Alive

……..

Type of pregnancy (tick one): Singleton ☐ Multiple Gestation ☐

Antenatal Care Attendance: Yes ☐ No ☐

If yes, how many visits? ……..

Date of 1st Booking: ……..

ANC Interventions (tick all that apply):

Interventions	Yes	No	Follow-Up Questions	Response to Follow-Up Questions
Iron and Folate given?			If yes, for how long?	
Anti-malaria prophylaxis given?			If yes, how many doses?	
Tetanus Toxoid given?			If yes, how many doses?	
HIV test done?			If yes, +ve or –ve result? If +ve, on ARV?	
Syphilis test done?			If yes, +ve or –ve result?	

			If +ve, any treatment?	
Rhesus blood group checked?			If yes, +ve or –ve result? If RhD –ve, treatment?	

Conditions present during this pregnancy (tick all that apply)

Conditions	Yes	No	Follow-Up Questions	Response to Follow-Up Questions
Antepartum haemorrhage			If yes, mention treatment	
Malaria			If yes, mention treatment	
Hypertensive disorders (PIH, pre-eclampsia, eclampsia)			If yes, mention treatment	
Diabetes			If yes, mention treatment	
Pre-mature rupture of membranes			If yes, mention treatment	
Anaemia (Hb)			If yes, mention treatment	
Urinary tract infection			If yes, mention treatment	
Trauma (due to accident or gender-based violence)			If yes, mention treatment	
Other (specify)			If yes, mention treatment	

SECTION 4: LABOUR AND BIRTH

Gestational Age (in weeks): …….. **Cervical Dilatation on Admission:** ……. cm

Reason for Admission:

……

Date of Admission (DD/MM/YYYY): …… **Time of Admission**: ……

Date of Delivery (DD/MM/YYYY): …….. **Time of Delivery**: ……

Date of Discharge (DD/MM/YYYY): ……..

Place of delivery (tick one):

Health facility ☐ (specify)

……

Home ☐

TBA ☐

Other ☐ (specify)

……..

On admission, was fetal sound present? Yes ☐ No ☐ Not assessed ☐

Was partograph used? Yes ☐ No ☐ Unknown ☐

If 'Yes', was partograph used correctly? Yes ☐ No ☐

If 'No', mention error:

……..

Any Obstetric Complications?

……..

……..

Presentation (tick one)**:**

Cephalic ☐

Breech ☐

Others (specify):

……

Mode of Delivery (tick one)**:**

Spontaneous Vaginal Delivery ☐

Caesarean Section ☐

Vacuum ☐

Forceps ☐

Others (specify):

……

Indication(s) for Instrumental / Caesarean Delivery:

……

……

Time between decisions for CS / instrumental and actual delivery of the baby:

Less than 30 minutes ☐ 30 minutes - 1 hour ☐

Greater than 1 hour ☐ How Long? ……. Not documented ☐

Mother's Outcome: Alive ☐ Died ☐

Any Morbidity? (Specify)

……

SECTION 5: BABY'S CONDITION

Weight of the baby (in grams): ……

Sex: Female ☐ Male ☐

Baby's Condition at Birth:

Alive ☐ Fresh SB ☐ Macerated SB ☐

Any congenital anomaly noted:

……

Apgar Score: At 1 min:…… At 5 min:…….. At 10 min: …….

Resuscitation attempted with Ambu bag? Yes ☐ No ☐

If born alive, select one: Kept with Mother ☐ Referred ☐

If born alive, state when the baby died: …… (days or hours after delivery)

SECTION 6: CAUSES AND AVOIDABLE FACTORS

Probable Cause(s) of Death:

(E.g. congenital anomaly, HIV, hypertension, placenta previa, asphyxia, umbilical prolapse, ruptured uterus, etc.). If more than one cause, list the most likely cause(s) first.

1. ……
2. ……

3. ……

4. ……

Avoidable Factors: Use comment section for clarifications.

Factors	Yes	No	Support with facts
Delay to seek health care			
Delay to reach the health facility			
Delay to provide care after arrival at health facility			
Was full complement of staff available during mother's stay?			
Functional resuscitation equipment (e.g. ambu bag) available?			
Supplies and drugs (including blood) available?			
Were instructions, guidelines and/or protocols followed?			
Was the right intervention used?			
Was relevant and adequate documentation made?			
Others (specify):			

SECTION 7: PLAN OF ACTION

ACTION POINT	PERSON RESPONSIBLE	TIMEFRAME

Comments:

……..

……

……..

Form Completed by:

Name: …… Sign: …… Date: ……..

APPENDIX 4: HEALTH FACILITY ASSESSMENT TOOL

'MAKING IT HAPPEN' PROGRAMME

FACILITY ASSESSMENT TOOL

(One form to be completed per facility)

Country	**Date of Data Collection**	**Code** **(E.g. SRL-01)**

Name of Health Facility:

……

County / District / Region:

……

Type of Health Facility (tick one):

National	Referral / Teaching	Regional	District	General	Health Centre	Other (specify) ……

Level of Health Facility (tick one): BEOC ☐ CEOC ☐

Distance to nearest Referral Facility (Km):

……

Availability of Signal Functions

EmOC Signal Function	Available 24hrs/day? (Y/N)	Performed in the last 3 months? (Y/N)	Reason for non-performance (tick all that apply)
a) Administration of parenteral antibiotics			☐ No clients ☐ No drugs available ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Other (please specify in section 'j' below)
b) Administration of uterotonic drugs (e.g. oxytocin)			☐ No clients ☐ No drugs available ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Other (please specify in section 'j' below)
c) Administration of parenteral anti-convulsants (e.g. magnesium sulphate)			☐ No clients ☐ No drugs available ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Other (please specify in section 'j' below)

EmOC Signal Function	Available 24hrs/day? (Y/N)	Performed in the last 3 months? (Y/N)	Reason for non-performance (tick all that apply)
d) Manual removal of placenta			☐ No clients ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Staff uncomfortable or unwilling to perform procedure for reasons unrelated to training ☐ National or facility policies do not allow function to be performed ☐ Other (please specify in section 'j' below)
e) Removal of retained products (e.g. MVA, D&C)			☐ No clients ☐ No equipment available / equipment not functional ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Staff uncomfortable or unwilling to perform procedure for reasons unrelated to training ☐ National or facility policies do not allow function to be performed

EmOC Signal Function	Available 24hrs/day? (Y/N)	Performed in the last 3 months? (Y/N)	Reason for non-performance (tick all that apply)
			☐ Other (please specify in section 'j' below)
f) Assisted vaginal delivery (e.g. vacuum extraction, forceps delivery)			☐ No clients ☐ No equipment available / equipment not functional ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Staff uncomfortable or unwilling to perform procedure for reasons unrelated to training ☐ National or facility policies do not allow function to be performed ☐ Other (please specify in section 'j' below)
g) Newborn resuscitation with bag and mask			☐ No clients ☐ No equipment available / equipment not functional ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Staff uncomfortable or unwilling to perform

EmOC Signal Function	Available 24hrs/day? (Y/N)	Performed in the last 3 months? (Y/N)	Reason for non-performance (tick all that apply)
			procedure for reasons unrelated to training ☐ National or facility policies do not allow function to be performed ☐ Other (please specify in section 'j' below)
h) Blood transfusion			☐ No clients ☐ No blood available / no blood bank ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Other (please specify in section 'j' below)
i) Caesarean section			☐ No clients ☐ No Caesarean section facilities available ☐ Staff shortage ☐ Staff do not have the skills to perform procedure ☐ Staff are not confident to perform procedure ☐ Other (please specify in section 'j' below)

Service delivery data:

	Jan	Feb	Mar	Apr	May	June	July	Aug	Sep	Oct
Fresh SB										
Macerated SB										
Total Stillbirths										
Total Deliveries (All)										

Comments:

……
……
……
……
……
……
……
……
……
……
……

APPENDIX 5: COMPUTER HIERARCHICAL MODEL FOR ASSIGNING CAUSE OF DEATH

Ranking for Stillbirth	Rank
Asphyxia	1
Lethal congenital anomaly	2
Abruptio placentae	3
Ruptured uterus	4
Eclampsia	5
Pre-eclampsia	6
Cord prolapse	7
Gestational Hypertension	8
Chronic Hypertension	9
Syphilis	10
Placenta praevia	11
Diabetes	12
Chorioamnionitis	13
Oligohydramnios	14
Polyhydramnios	15
Fetal growth restriction	16
Twin-twin transfusion	17
Fetomaternal haemorrhage	18
Birth Trauma	19
Acute Infection	20
Malaria	21
HIV-Related complications	22
External trauma	23
Isoimmunisation	24
Placental insufficiency /infarction	25
Constricting loop or knot	26
Iatrogenic	27
Non-immune hydrops	28
Chronic Infection – e.g. TORCH	29
Vasa Praevia	30
Velamentous insertion	31
Thyroid diseases	32
Lupus/Antiphospholipid Syndrome	33
Cholestasis	34
Drug abuse	35
Unknown - Inadequate information available	36
Unknown - No relevant condition identified	37
Ranking for Neonatal Death*	**Rank**
Birth asphyxia	1
Intrapartum trauma	2

Fatal congenital anomaly	3
Possible severe bacterial infection	4
Meningitis	5
Pneumonia	6
Sepsis	7
Tetanus	8
Diarrhoea	9
Complication of prematurity (RDS)	10
Unknown - Inadequate information available	11
Unknown - No relevant condition identified	12

* Not relevant to this study.