Counting the smallest: data to estimate global stillbirth, preterm birth and low birthweight rates

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Thesis submitted in accordance with the requirements for the degree of

Doctor of Philosophy
of the
University of London

January 2020

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Work funded by Children's Investment Fund Foundation, Save the Children (Saving Newborn Lives Program), the World Health Organization and the Bill & Melinda Gates Foundation

Declaration of own work

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

Signed:  Date: 6th January 2020

Abstract

Background

Stillbirth, preterm birth and low birthweight are important indicators of global burden of disease, status of maternal health and healthcare, and predictors of health throughout the life-course. Data are available through Civil Registration and Vital Statistics (CRVS), Health Management Information Systems (HMIS) and household surveys. Comparisons of data by country or over time requires standard definitions and comparable data quality. Data gaps and inconsistencies necessitate adjustments and use of modelled estimates in many settings.

Methods

Systematic data searches were undertaken to compile available data on these outcomes for 195 countries. Where no reliable data were available, statistical models were used to generate national estimates. Data quantity and quality were summarised for each outcome, with implications for improvement and research**.**

Results

The estimated burden remains large: 2.6 million stillbirths (2015), 14.9 million preterm births (2010) and 20.5 million low birthweight babies (2015) based on 4,392 data-points from 148 countries. Common data quality challenges include use of non-standard definitions, omission, and misclassification. Targeted data quality assessments are required to detect these. Five data gaps identified to address are: (1) coverage of data systems (2) accurate assessment of vital status at birth, birthweight and gestational age for every birth, (3) accurate recording of these key data elements (4) comparable collation within and across data systems and (5) use of data to inform programmes and policy. Evidence exists across all data platforms of examples of solutions to close these gaps. Systematic data linkage could increase efficiency.

Conclusion

Data availability has increased over the last decade, even in the poorest countries. Data quality issues currently hamper the use of these data to improve outcomes in many settings, but could be addressed with political will and targeted investment. Ending preventable deaths among the world's smallest babies requires that these data are accurate, available and used.

Acknowledgements

I am immensely grateful to a wide group of people for their patient support over the course of my PhD. Firstly, I would particularly like to thank Joy Lawn, my supervisor and mentor throughout the last decade. Without her vision for improving the health of every newborn worldwide, and her encouragement for us all to be part of this, I would not be working in the field of global newborn health.

Thank you also to my advisory committee, Oona Campbell and Simon Cousens for your invaluable support in providing guidance, advice, support and encouragement to keep going throughout this PhD.

Thank you to all the newborn health team at LSHTM, past and present, for your hard work, patience and support throughout – it is a privilege to be a part of this team; especially to Sarah Moxon for her invaluable support and encouragement. Thank you also to other London School colleagues from the wider MARCH centre, for excellent research and many thought provoking discussions which have helped shaped this work.

Throughout this PhD I have had the privilege of working with a wide network of colleagues worldwide. I would especially like to thank colleagues at UNICEF, World Health Organization, Saving Newborn Lives, Johns Hopkins and the EN-INDEPTH study team. It has been both an honour and a pleasure to be part of these amazing teams and to work with such dedicated experts. The work presented in this PhD would not have happened without their collaboration.

I would like to thank the funders of this work: Children's Investment Fund Foundation (CIFF), Save the Children (Saving Newborn Lives Program), the World Health Organization and the Bill & Melinda Gates foundation.

Finally, I would like to thank Marko, Toma, Millie, and Teo and my wider family and friends for their unwavering support.

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Abbreviations

ANC	Antenatal Care
CRVS	Civil Registration and Vital Statistics
DHIS-2	District Health Information System-2
DHS	Demographic and Health Surveys
DHSS	Demographic and Health Surveillance Site
ENAP	Every Newborn Action Plan
ENMR	Early Neonatal Mortality Rate
GA	Gestational Age
GATHER	Guidelines for Accurate and Transparent Health Estimates Reporting
HIC	High Income Countries
HMIS	Health Management Information Systems
ICD-10	International Classification of Disease 10th Revision
ICD-11	International Classification of Disease 11th Revision
ICD-MM	International Classification of Disease – Maternal Mortality
ICD-PM	International Classification of Disease – Perinatal Mortality
LBW	Low Birthweight
LIC	Low Income Countries
LMIC	Low and Middle Income Countries
LMP	Last Menstrual Period
MDG	Millennium Development Goals
MIC	Middle Income Country
MICS	Multiple Indicator Cluster survey
MPDSR	Maternal and Perinatal Death Surveillance and Response
NMR	Neonatal Mortality Rate
RHS	Reproductive and Health Surveys
SBR	Stillbirth Rate
SDG	Sustainable Development Goals
SGA	Small for Gestational Age
UNICEF	United Nations International Children's Fund
UN-IGME	United Nations Inter-agency Group for Child Mortality Estimation
USS	Ultrasound Scan
WHO	World Health Organization

Definition of key terms

Live birth	A baby born with any signs of life, irrespective of the duration of pregnancy
Fetal death	A death prior to the complete expulsion or extraction from its mother of a product of human conception, irrespective of the duration of pregnancy
Stillbirth	A fetal death at ≥1000g, or ≥28 weeks, or crown-to-heel length ≥35cm
Preterm Birth	A live birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the women's Last Menstrual Period (LMP)
Low birthweight	A live birth with a weight at birth of less than 2500g

SECTION I. INTRODUCTION

This section comprises of two chapters. Chapter 1 provides a background on the importance of adverse outcomes around the time of birth and why information is needed for all countries. It presents an overview of relevant global targets and goals and the rationale for the focus of the thesis on three selected birth outcomes: stillbirth, preterm birth and low birthweight. An introduction to some of the data gaps for stillbirth, preterm birth and low birthweight is presented and the current need for global estimates to fill these is discussed. This information was gathered through a broad reading of the literature on the topic and searching for specific information regarding outcomes, global targets, goals and estimates. In addition, throughout the course of this PhD I participated in global and regional meetings hosted by WHO and UNICEF, including Every Newborn Action Plan (ENAP) and the Mother and Newborn Information for Tracking Outcomes and Results (MONITOR) groups. These meetings provided further insights and information which I have used to contextualise the thesis.

The second chapter in this section reviews in further detail the requirements for measuring stillbirth, preterm birth and low birthweight outcomes – including definitions, data sources and platforms and potential measurement challenges. It draws on the information collected as part of the background reading for chapter 1 and participation in global meetings. In addition, targeted searches were undertaken to further explore specific aspects of the measurement of these outcomes. The introduction to measurement and data platforms, expands on work that I undertook as part of this PhD which sought to present challenges associated with maternal, fetal and neonatal mortality.[1]

1. Background, rationale, aims and objectives

1.1. Background

1.1.1. Adverse outcomes around the time of birth

Great importance has traditionally been given to the time around birth – with potential for new life, but also for great hazard for both the mother and the baby as it transitions from intra- to extra-uterine life. Throughout most of history, maternal causes of mortality have remained the commonest cause of death for women of reproductive age. As maternal mortality has decreased, increased attention has been given to the importance of maternal 'near-miss' and associated morbidity originating around the time of birth, of which obstetric fistula is an important example.[2] Similarly, rates of mortality both in-utero and in the early period after birth have remained high for newborns throughout most of history. Perinatal epidemiology has traditionally therefore focused on the time around birth. However, increasingly, the importance of adequate length of gestation and growth in-utero on the baby's chance to survive and thrive free from morbidity have been recognised.

In this thesis, the term 'baby' is used to refer to the fetus or neonate in discussions around adverse birth outcomes in pregnancies ≥22 completed weeks of gestation. Whilst the epidemiological terms will be used where necessary, the term 'baby' is used by mothers and avoids repetition of 'fetus or neonate' throughout these discussions. The use of the word 'baby' does not imply any specific rights to the fetus or neonate. Much discussion has previously been had on this.[3,4] Whilst detailed discussion on the rights of the fetus or neonate is outside the remit of this thesis, they will be considered briefly in terms of the effect that the perceptions of personhood and babies' rights have on legislation around registration and recording practices.

This thesis will focus on three outcomes for the baby measured at the time of birth – stillbirth, preterm birth and low birthweight (Table 1-1).

Table 1-1 Three focus outcomes of PhD - stillbirth, preterm birth and low birthweight

Outcome	Definition
Stillbirth	A death prior to the complete expulsion or extraction from its mother of a product of human conception at ≥1000g, or ≥28 weeks, or crown-to-heel length ≥35cm
Preterm birth	A live birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's Last Menstrual Period (LMP)
Low birthweight	A live birth with a weight at birth of less than 2500g

The direct determinants of these three outcomes are maternal, fetal or placental factors during pregnancy, or, in the case of intrapartum stillbirths, the process of labour itself. This is in contrast to other perinatal outcomes, such as neonatal mortality, where postnatal factors, such as

immaturity and environmental infectious agents, also play an important role. All three of these outcomes are also closely linked to maternal outcomes around the time of birth.

In recent years, there has been increasing policy attention to outcomes around the time of birth for the baby including neonatal mortality[5] and preterm birth.[6] However, stillbirths remain relatively invisible, hidden in the shadows and lacking global policy attention.[7]

Adverse birth outcomes are a reality experienced by many women and families. However, in a world of many issues competing for attention and finite resources, why is it important for public health to also consider these outcomes of stillbirth, preterm birth and low birthweight?

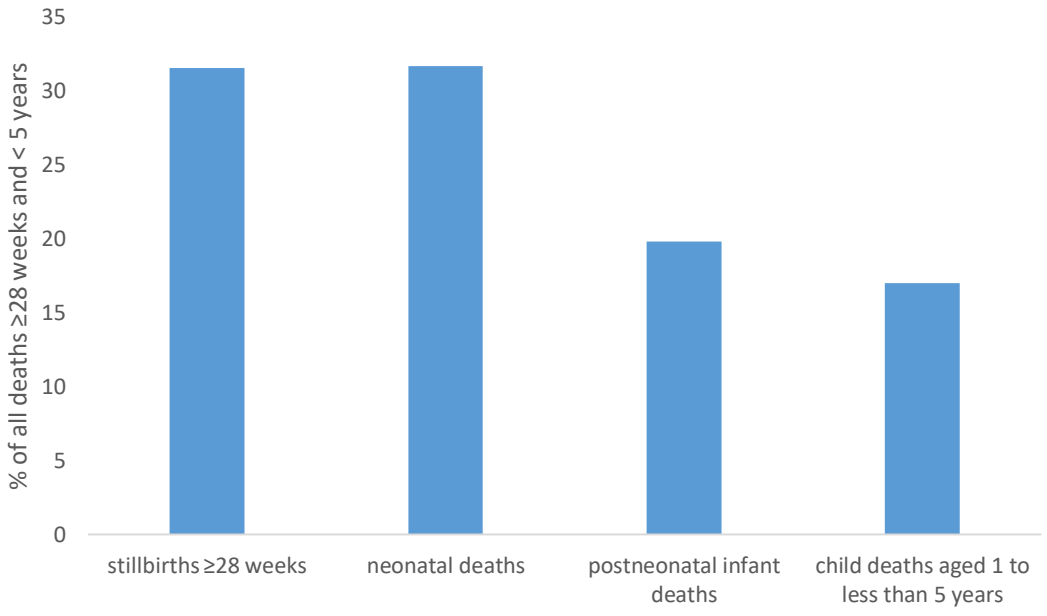
1.1.2. Why are adverse outcomes around the time of birth important?

Epidemiology

Mortality

Adverse birth outcomes have a large impact on child mortality. Recently, the concept of 'total under five deaths' has been introduced, which includes all deaths in the first 5 years of life for any live born baby and all stillbirths of 28 or more completed weeks of gestation.[8] Globally around 60% of all 'total under five deaths' occur in-utero (stillbirth) or during the first 28 days of life (neonatal death) (Figure 1-1). This proportion would be even greater if fetal deaths at earlier gestations were included. It has recently been highlighted in the US that there are many more fetal deaths in utero at ≥20 weeks gestation than infant deaths.[9]

Figure 1-1 Age distribution of stillbirths and deaths of children under five in 2016



The risk of neonatal mortality is highest for babies born at the lowest gestational ages, falls sharply as gestational age increases, but rises again after 41 weeks.[10] This U-shaped relationship has also been shown to hold true for birthweight, with higher mortality in babies born at <2500g or >4000g.[11] More than 80% of neonatal deaths are estimated be in low birthweight babies. Two-thirds of low birthweight associated neonatal deaths are preterm and one-third are small-for-gestational-age.[12-14] Those born preterm or small-for-gestational-age also remain at higher risk of mortality throughout early childhood.

Morbidity

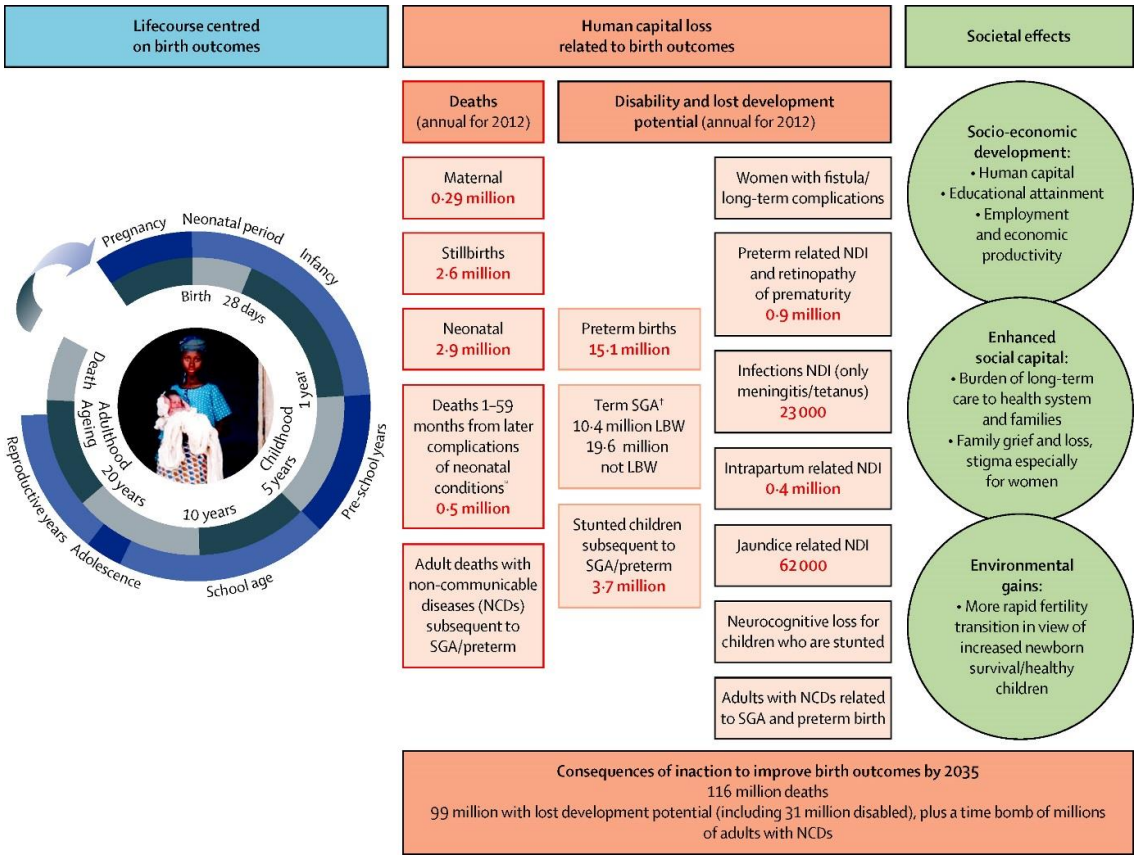
Being born preterm is associated with a substantially increased risk of short term morbidity, such as respiratory distress syndrome, jaundice, intraventricular haemorrhage, necrotising enterocolitis and infection, with the risks greatest for those most preterm.[15,16] Even in those born at term, in-utero growth restriction is associated with increased risks of perinatal asphyxia, hypothermia and hypoglycaemia.[17] These adverse birth outcomes are also associated with short term maternal morbidity from obstetric complications, infections, placental conditions such as pre-eclampsia and poor maternal mental health.[2]

The impact of early growth and development in-utero on later health outcomes is increasingly recognised.[18-20] Processes such as preterm birth or low birthweight secondary to in-utero growth restriction are therefore important markers of potential long-term consequences, including impaired growth and development, and long-term development of non-communicable diseases.[21,22] The long-term impact of adverse birth outcomes on maternal health is also important. For example, following a stillbirth, this can include both physical morbidity e.g. obstetric fistula, and psychological morbidity e.g. depression and abnormal grief reaction.[23]

Wider impact

Some of the short- and long-term morbidity and mortality effects of adverse birth outcomes on the baby and mother have been detailed above. However, the impact of these adverse outcomes on women, families and wider society goes beyond these effects. Figure 1-2 summarises the estimated overall consequences of adverse birth outcomes on loss of human capital and wider societal effects. As such, adverse birth outcomes for the baby, including stillbirth, preterm birth and low birthweight, have the potential to be valuable public health indicators reflecting maternal health, nutrition, access to healthcare and poverty. Disaggregated tracking of these outcomes can be a useful barometer of equity in any given population.

Figure 1-2 Estimated consequences of inaction to improve birth outcomes in terms of human capital loss by 2035, and wider societal effects



SGA – Small for gestational age; LBW – Low birthweight; NDI – Neurodevelopmental impairment; NCD – Non-communicable disease
Source: Lawn et al 2014.[14] Reproduced with permission. (Analyses undertaken by H. Blencowe)
[1]Term SGA – Small for gestational age at ≥37 weeks.

Preventability

Despite the persisting large burden in terms of numbers and associated adverse consequences for the baby, family and wider society, many stillbirths, preterm and low birthweight births are preventable with high quality care along the continuum – preconception, antenatal, childbirth, postnatal.[24-27] Improving coverage of care along the continuum that meets minimum quality standards for all women and their babies globally needs to be prioritised if these outcomes are to be improved. Investing in this care will improve outcomes, not only for the baby around the time of birth, but also for the mother, her offspring and society in the longer term.

1.1.3. Why do we need information on birth outcomes for all countries?

Information on birth outcomes is essential to inform clinical care at an individual level, but as highlighted above, there are also important epidemiological, programmatic, and rights-based arguments for the measurement and collation of information on adverse birth outcomes, including stillbirth, preterm birth and low birthweight at a population level. These include:

1. Monitoring the health of the population – these indicators are sensitive markers of both maternal health and the health of her baby, and therefore important markers for monitoring Universal Healthcare Coverage targets within the SDGs.[28]
2. Monitoring the quality of obstetric received care[29,30] – for example, intrapartum stillbirth rates of more than 1 per 1,000 total births may be indicative of issues in quality of childbirth care, and should prompt further investigation.[31]
3. Monitoring the impact of any public health interventions to improve maternal and perinatal health.
4. Allowing comparisons of burden to other health priorities to enable appropriate allocation of resources to maternal and newborn health.
5. Data on levels and causes can help drive programmatic action and investment, including informing investment cases. Informing maternal and newborn policies and obstetric and neonatal health programming in light of the epidemiology can help target the most important challenges in a given setting; for example, the majority of low birthweight babies in South Asia are growth restricted term babies, compared to in other regions where the majority are preterm.
6. Advocacy and accountability – research has shown that these outcomes are important to women and their families. Tracking these outcomes can help hold governments accountable to providing appropriate healthcare provision, both to reduce occurrence of these outcomes and to provide ongoing care as appropriate. Appropriate ongoing care may include women's and child health services providing appropriate physical and psychological support, physiotherapy, occupational therapy and education services. Advocacy, often driven by affected families, has played an important role in driving the awareness of need for both stillbirth and preterm birth global estimates.[32]

In recognition of the importance of obtaining such information from all settings, and to hold governments accountable, many groups have lobbied for global targets and the setting of goals to which all countries commit. These have been set for many topics across differing sectors including health, education and environment. Below the global goals that have been set with relevance to stillbirth, preterm birth and low birthweight are reviewed.

1.1.4. Global targets and goals

In the Millennium Development Goal (MDG) era, the MDG-4 target for child mortality played an important role in driving improvements in measurement and tracking of under-five child mortality. It also highlighted the important contribution of deaths in the first 28 days of life (neonatal mortality) to overall child mortality. This led to investment in interventions to improve neonatal outcomes, not only by donors, but also governments, driven by political pressure

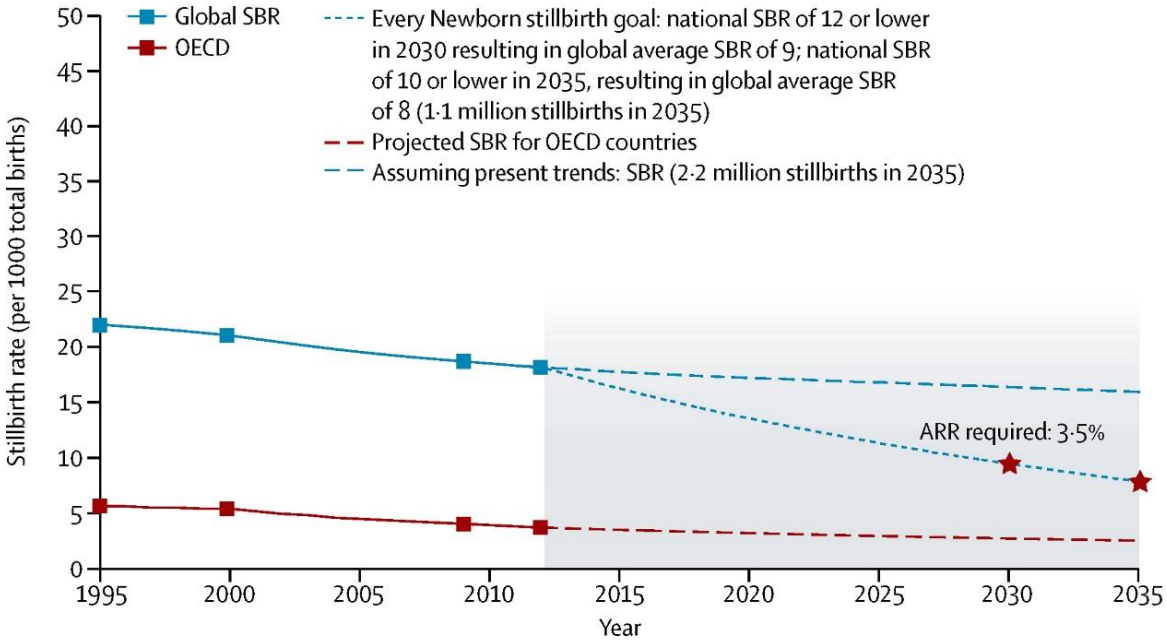
within countries. Between 2003 and 2013, official development assistance and private grant funding to child health increased by 286%, with an 18-fold increase for newborn health. However, specific funding for stillbirths, which were not included in the MDG target, was negligible throughout this time period.[33,34]

In the wake of the recognition of the importance of targets and goals to drive investment and action, several targets and goals have subsequently been set that relate to the outcomes of stillbirth, preterm birth and low birthweight. These will be important in tracking improvements in perinatal health during the SDG era.

Stillbirths

In 2014 the Every Newborn Action Plan (ENAP), a global multi-partner movement to end preventable maternal and newborn deaths and stillbirths, set a target for national stillbirth rates (SBRs) of 12 or fewer stillbirths per 1,000 total births in all countries by 2030, accompanied by action in countries to address disparities.[35] This stillbirth target was included alongside the neonatal mortality target in response to the requests from many countries during the ENAP consultation process.[14]

Figure 1-3 Stillbirth reduction target by 2030



Source: Lawn et al 2014.[14] Reproduced with permission. (Analyses undertaken by H. Blencowe with M. Lalli)
ARR=Average Annual Rate of Reduction. Red stars denote the 2030 and 2035 targets

The initial ENAP targets were set to 2035, to align with the 2035 targets already set for child survival in 'A promise renewed'.[36] Figure 1-3 shows both the original 2035 ENAP target, and the revised 2030 target to align with the time frame of the SDGs. The targets are denoted by red stars.

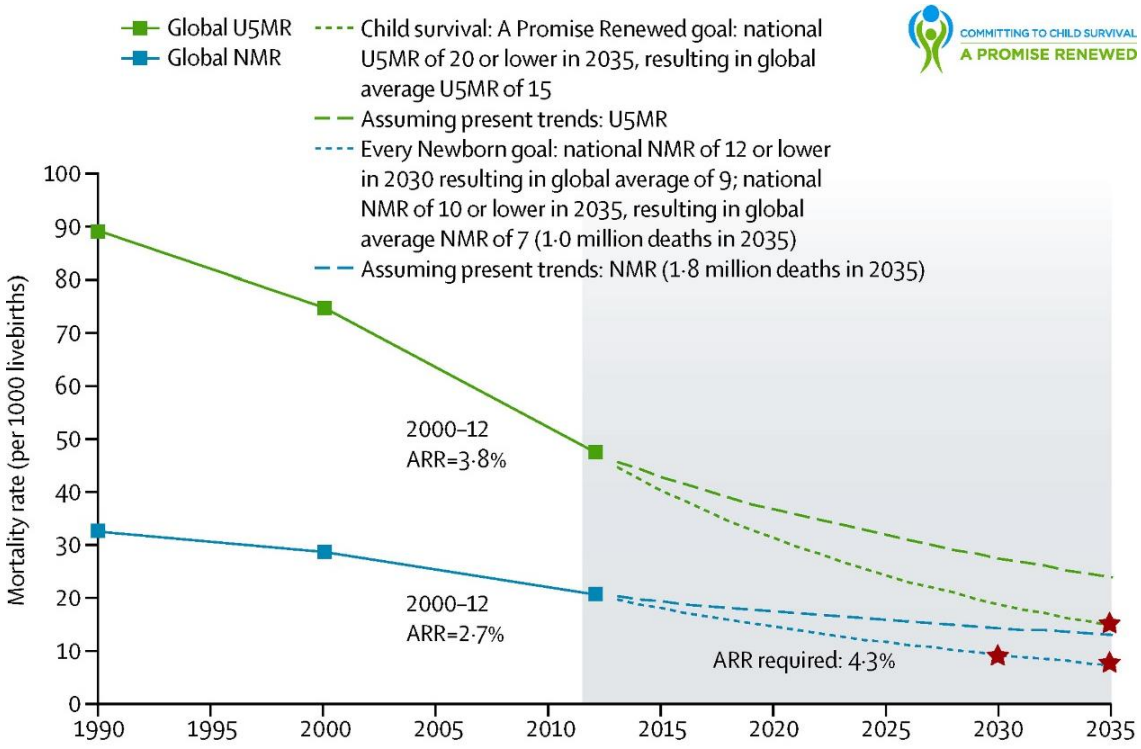
The stillbirth rate target was not included as an SDG indicator, however it is included as a core indicator for tracking in the United Nations' Global Strategy for Women's, Children's and Adolescents' Health 2016-2030.[37] Data availability to track progress towards stillbirth targets are limited in many settings. The inclusion of stillbirth rate for the first time as a global core indicator requires investment to improve data to track this outcome.

Neonatal Mortality

Figure 1-4 shows both the original 2035 ENAP neonatal mortality target, and the revised 2030 target to align with the time frame of the SDGs. The targets are denoted by red stars. The revised 2030 target was included as an SDG target under SDG Goal 3 (Ensure healthy lives and promote well-being for all at all ages). The SDG target relating to neonatal mortality is:

3.2. 'By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births.'[38]

Figure 1-4 Neonatal mortality reduction target by 2030



Source: Lawn et al 2014.[14] Reproduced with permission.
ARR=Average Annual Rate of Reduction. Red stars denote the 2030 and 2035 targets

The SDG goal indicators state that these mortality rates should be heavily disaggregated (including by subnational geographical location) so as to identify particularly vulnerable populations, whilst recognising that data collection on neonatal mortality rates will need to be improved. As will be argued throughout this thesis, improving the counting of every birth,

including stillbirths, is key to improving neonatal mortality rate data. This is important as, in all settings, approximately a third to one half of neonatal deaths occur on the first day of life and may be at risk of misclassification as stillbirths;[39,40] and around three quarters of all neonatal deaths are estimated to be in preterm or low birthweight babies who are at higher risk of being omitted from the data system.[14]

Preterm birth

Preterm birth is estimated to account for 1.01 million under 5 deaths, 90% of these occurring in the first 28 days of life.[41] Hence, whilst there are no specific global targets for preterm birth, it is very closely linked to meeting SDG targets for neonatal mortality reduction. The proportion of all child deaths that are directly attributed to preterm birth varies from 13% (including 29% of all neonatal deaths) in low income countries (LIC), around 20% (34 - 37% of all neonatal deaths) in middle income countries (MIC), to 26% (41% of all neonatal deaths) in high income countries (HIC).[41] However, as the overall mortality rates are much higher outside of HICs, most deaths related to preterm birth happen in low and middle income countries (LMIC). Achieving neonatal mortality targets will therefore necessitate tackling the underlying issue of preterm birth – both in terms of preterm birth prevention and improved survival through access to high quality care.

Low birthweight

In 2012, the World Health Assembly, recognizing that accelerated action was needed to address the persisting problem of the double burden of malnutrition in all countries, endorsed a Comprehensive Implementation Plan on maternal, infant and young child nutrition. This plan specified six global nutrition targets for 2025, including a 30% reduction in the number of babies born Low Birth Weight (LBW; <2500g) from a 2012 baseline.[42] LBW is a key outcome indicator to measure progress towards the achievement of the global nutrition targets and monitoring LBW trends is therefore an essential component of the Global Monitoring Framework approved by Member States at the World Health Assembly in May 2015.

Unfortunately, at the time of the target setting, there was no baseline data or estimate on low birthweight prevalence for many countries for around the year 2012. The only available data from most LMICs are from nationally representative household surveys, such as Demographic and Health Surveys, which are known to have limitations in their capture of information about birthweight.[43,44]

Substantial data gaps exist to inform tracking of progress towards stillbirth and low birthweight targets. Global estimates are an important short- to mid-term attempt to use available

information to monitor progress, although this must be coupled with improvements in quality and timeliness of relevant data to enable more accurate tracking.

1.1.5. Global estimates

In general, it has long been recognised that data for important health indicators are seldom available for all populations, across all time periods. Adverse birth outcomes indicators are no exception to this. To obtain estimates, data of variable quality and completeness often need to be aggregated to construct an overall picture of likely trend at a population level.[45] In reality, data on outcomes around the time of birth are frequently even more sparse and of lower quality than for other health outcomes. To meet this gap, modelled estimates of relevant health indicators have often been used. These modelled estimates have been used by governments, non-governmental organisations and funders to provide a timely, fuller picture of the health of populations; provide comparisons between populations and within populations over time; report programme performance to international agencies; identify emerging international health priorities; and generate interest in and advocate for condition-specific programmes.[46] Another advantage of estimates is their relative low cost when compared to the long-term capacity and system strengthening required to generate high-quality empirical data.

However, the use of modelled estimates can have adverse consequences such as diminishing country ownership and masking data gaps thus reducing investment by governments and donors to strengthen national information and statistical systems.[47] In addition, the limitations of the differing processes used to assimilate input data, modelling methods and assumptions on the interpretation of the estimates have been increasingly recognised. These limitations, coupled with the confusion faced at a national or sub-national level by numerous differing estimates of the same indicator, have led to calls for increasing collaboration and transparency in global health estimation.[48-50]

In response to this, in 2014, the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) Working Group was convened to define and promote good practice in the reporting of global health estimates.[51] It recognised the need for standardization, transparency and comparability of approaches, where possible, to enable inter-country comparisons and facilitate the understanding and proper use of global estimates. The group published its guidance in 2016 (Table 1-2).

As the GATHER guidance was under development throughout the period of the work for this PhD, it did not guide the reporting of the earlier preterm birth estimates work detailed in this thesis. However, a draft version of the guidance was used to guide the reporting for the later

stillbirth estimates, and the LBW estimates presented were reported using the final version of GATHER.

Table 1-2 GATHER checklist of information to be included in reports of global health estimates

Item #	Checklist item
Objectives and funding	
1	Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made.
2	List the funding sources for the work.
Data Inputs	
For all data inputs from multiple sources that are synthesized as part of the study:	
3	Describe how the data were identified and how the data were accessed.
4	Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.
6	Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5).
For data inputs that contribute to the analysis but were not synthesized as part of the study:	
7	Describe and give sources for any other data inputs.
For all data inputs:	
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.
Data analysis	
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).
11	Describe how candidate models were evaluated and how the final model(s) were selected.
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.
13	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.
14	State how analytic or statistical source code used to generate estimates can be accessed.
Results and Discussion	
15	Provide published estimates in a file format from which data can be efficiently extracted.
16	Report a quantitative measure of the uncertainty of the estimates (e.g. uncertainty intervals).
17	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.
18	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.

Source: Stevens et al,[51] reproduced with permission

There has been little previous work undertaken in the area of estimation of adverse birth outcomes compared to other health outcomes. The first published peer-reviewed systematic estimates of national-level prevalence of many adverse birth outcomes for countries worldwide were published relatively recently: stillbirths (published 2006),[52] neonatal cause of death (2006),[53] neonatal mortality (2010),[54,55] small-for-gestational age (2013)[13], preterm birth (2012)[56] and low birthweight (2019). The latter two were undertaken as part of this thesis, as was a 2016 update of stillbirth estimates.

1.2. Rationale for focus on stillbirth, preterm birth and low birthweight

This PhD focuses on three important birth outcomes, namely stillbirth, preterm birth and low birthweight. They are good case studies for illustrating some of the major measurement challenges in birth outcome data. The rationale for the choice to focus on these three outcomes was driven by three factors. Firstly, they are all important causes of mortality and morbidity; secondly, they all require assessment at the time of birth; finally, they are all relatively under-researched areas compared to other global estimates. These will be discussed in more detail below. Other outcomes of similar burden such as overall neonatal or infant mortality could have been considered, however these face different measurement challenges. Many of neonatal and infant deaths occur outside of health facilities, and have different underlying causes and programmatic action requirements. In addition, more previous research has been undertaken on the measurement of overall neonatal and infant mortality, and at the time of starting this work both of these measures were already included in routine annual UN child mortality estimates.

Stillbirth, preterm birth and low birthweight are important causes of mortality and morbidity globally, and are responsible for at least 70% of the 5.2 million deaths in babies from 28-weeks of gestation to 28 days of life. Stillbirths are responsible for around a third of total deaths in children from 28-weeks of gestation to 5 years of age ranging from 25.4% in sub-Saharan Africa to 34% in East Asia and the Pacific.[8] Stillbirths are associated with substantial maternal mortality and morbidity, both physical such as obstetric fistula, but also psychological with an estimated 4.2 million women living with depression globally following a stillbirth.[23,57]

Direct complications of preterm birth are estimated to account for 1.01 million under 5 deaths annually, 90% of these occurring in the first 28 days of life.[41] In addition, 0.9 million survivors of preterm birth are estimated to have long-term neuro-cognitive impairment.[14,21] Preterm birth is also an important factor associated with long-term morbidity. In 2012 7.4 million children under five were estimated to be stunted after preterm birth.[14]

No global estimates to date have quantified the estimated underlying contribution of low birthweight to neonatal and child mortality. Low birthweight babies comprise appropriately grown preterm babies, and preterm and term growth restricted babies. Low birthweight preterm babies, whether appropriately grown or growth restricted, dying of direct complications of their preterm birth are included in the preterm causal category for child cause of death. For term babies growth restriction is not usually coded as a primary cause of death and hence less information is available to inform estimates of how many term neonatal deaths have underlying growth restriction resulting in them being low birthweight. Whilst few neonatal

deaths in high income countries are likely to be attributable to term low birthweight it remains an important cause of mortality and morbidity in low and middle income countries. Estimates for South Asia and sub-Saharan Africa suggested that there were 10.4 million term low birthweight babies and over 300,000 neonatal deaths in these regions were attributable to term low birthweight, and a further 7 million children were stunted.[14]

All of these outcomes have overlapping technical measurement and data challenges. All require measurement of key data elements at the time of birth, namely vital status, gestational age and birthweight. An accurate assessment of vital status at birth is required for all these outcomes as preterm birth and low birthweight rate definitions only include live births in the numerator and denominator, whilst stillbirth rate only includes babies with no signs of life at birth in the numerator and all babies born in the denominator. Ascertainment of vital status at birth is strongly affected by health professionals, women's and societal perceptions of fetal viability and personhood. Identification of low birthweight babies requires an accurate birthweight, ideally within an hour of birth. Accurate measurement of both vital status and birthweight requires skilled healthcare workers, with an enabling environment, including functioning equipment. With more than 80% of all births worldwide in facilities, reviewing and taking steps to overcome the challenges of measuring these key data elements in health facilities is of public health importance to enable improved monitoring of interventions and programmes to address these adverse outcomes.

Determining whether a fetal death without a birthweight meets the requirements to be registered as a stillbirth or whether a live birth is preterm or not preterm requires accurate gestational age assessment. Whilst gestational age assessment should ideally be undertaken and recorded earlier in pregnancy, for example at antenatal clinic attendance, this is used to calculate the gestational age at delivery. It therefore also requires measurement and recording at the time of birth. In addition to the technical measurement challenges common to all three outcomes, stillbirth is a very sensitive issue with associated ethical and legal considerations as well as other factors, such as stigma, affecting reporting. In many settings, all of these measurement challenges result in substantial data gaps and reliance on modelled estimates to track these three outcomes.

Once these three key data elements (vital status at birth, birthweight and gestational age) are routinely collected and captured in the data system for all births it will be possible to generate stillbirth, low birthweight, preterm birth and small-for-gestational age estimates from these, all of which are of public health importance.

Finally, there remains a substantial gap in terms of existing work on measurement of stillbirth, preterm birth and low birthweight outcomes compared to for instance neonatal or child mortality that since 2011 have been included in annual child mortality estimates of the United Nations Inter-agency Group for Child Mortality Estimation (UN-IGME).[58] As described above, all three outcomes are included in this thesis in view of their large burden, similar measurement challenges, and data gaps. Whilst many stillbirths will be born before 37 completed weeks of gestation, weighing less than 2500g, there is no overlap between stillbirth and preterm birth or low birthweight as the latter two indicators only include live births. There is some overlap between the two outcomes for live births, namely preterm and low birthweight. Most preterm births will also be low birthweight, however, growth restricted low birthweight term babies also have an increased risk of neonatal and post neonatal mortality and longer term morbidity including stunting and increased adult cardiovascular risk.[12,14] These are therefore also an important group to identify and focus public health interventions for, to seek to improve growth in utero, but also to optimise the nutritional environment for the child.[59-61] In the future when accurate gestational age and birthweight assessments are recorded for all births, using small for gestational age indicators could provide a better proxy for in-utero growth restriction, but until this is possible, and as reflected in global target setting there remains a role for low birthweight as an indicator.[42]

1.3. Aims and objectives

The overall aim of this thesis is to describe the current status of the available data on stillbirth, preterm birth and low birthweight, and to provide recommendations to improve input data to support estimation of the burden of these conditions.

The overall aim is achieved through the following objectives:

Objective 1: Review the requirements for measuring stillbirth, preterm birth and low birthweight outcomes – including definitions, indicators, measurement challenges and data sources and platforms.

Objective 2: Conduct three separate in-depth analyses of the availability of stillbirth, preterm birth and low birthweight rate data for all countries worldwide.

Objective 3: Develop and implement methods to produce national estimates of stillbirth, preterm birth and low birthweight rate, with time trends where possible.

Objective 4: Summarise lessons learnt regarding birth outcome data through estimation exercises for stillbirth, preterm birth and low birthweight.

Objective 5: Present an overview of measurement gaps and propose solutions for improving the data for stillbirth, preterm birth and low birthweight. Make data platform specific recommendations for the implementation of these principles.

1.4. Thesis structure

This thesis follows the book style, although several of the chapters have been published as articles in peer-reviewed journals. It is divided into three sections. An overview of the component sections is provided below. Further details of the component chapters are provided in Table 1-3, including related objectives, research themes and questions, and methods.

Section I: Comprises two chapters.

Chapter 1 provides a background on stillbirth, preterm birth and low birthweight outcomes, including their public health importance, global targets, data gaps and current reliance on global estimates. The rationale, aims and objectives of the thesis are included.

Chapter 2 addresses ***Objective 1***. It seeks to review in further detail the requirements for measuring stillbirth, preterm birth and low birthweight outcomes – including definitions, data sources and platforms and potential measurement challenges.

Section II: Comprises four chapters addressing ***Objectives 2, 3 and 4***.

Chapters 3, 4 and 5 address ***Objectives 2 and 3*** and detail the systematic analysis of data available to inform estimates of stillbirth, preterm birth and low birthweight birth rate for all countries worldwide. For each of the outcomes the process for the development and implementation of methods to produce estimates is described. The resultant national, regional and worldwide estimates are presented. Chapters 3, 4 and 5 have been published in peer-reviewed journals (Lancet and Lancet Global Health).

Chapter 6 addresses ***Objective 4***. It draws together lessons learnt from data analyses for stillbirth, preterm birth and low birthweight. It provides a summary of the current status of the data to inform stillbirth, preterm birth and low birthweight estimates, and discusses data quality challenges.

Section III: Discussion and conclusion. The final section comprises two chapters.

Chapter 7 addresses ***Objective 5***. An overview of the measurement gaps for stillbirth, preterm birth and low birthweight are presented. Proposed solutions to close measurement gaps for birth outcome data and improve the input data for stillbirth, preterm birth and low birthweight estimates across key data platforms are discussed.

Chapter 8 provides an overall summary of the work including recommendations for policy, practice and research.

1.5. Table of overview of thesis chapters, research questions and methods

Table 1-3 Overview of thesis chapters, research questions and methods

Section and chapter	PhD objectives	Research themes and questions	Methods
Section I: Chapter 1	Background	○ Why are adverse outcomes around the time of birth important? Why do we need information on these for all countries? Why global estimates? Global targets and goals. ○ Introduction to some of the measurement gaps and current need for global estimates to fill these. General estimation principles and GATHER guidelines. Need for standardization/comparability of approaches to enable inter-country comparisons and facilitate global estimates. ○ Rationale for focus on stillbirth, preterm birth and low birthweight.	Targeted review of relevant literature to contextualise thesis. Broad reading around the topic.
Section I: Chapter 2	***Objective 1:*** Review the requirements for measuring stillbirth, preterm birth and low birthweight outcomes – including definitions, data sources and platforms and potential measurement challenges.	○ Definitions and indicators for measuring stillbirth, preterm birth and low birthweight outcomes. ○ Introduction to potential measurement challenges including case ascertainment, measuring vital status at birth, gestational age, birthweight, and timing of death. ○ Data sources and platforms for measuring stillbirth, preterm birth and low birthweight outcomes.	Targeted review of the literature and normative guidance. Wider reading around the topic.
Section II: Chapter 3	***Objective 2:*** Conduct an in-depth analysis of the availability of **stillbirth rate** data for all countries worldwide	○ Overview of available data from national statistical websites, DHS surveys, published literature and unpublished sources. ○ Preparation of estimation input database including developing inclusion/ exclusion criteria and covariate data.	Systematic Review

	Objective 3: Develop and implement methods to produce national **stillbirth rate** estimates, with time trends where possible.	○ Identification of countries with more reliable data where country-level data can be used alone to estimate stillbirth rates. ○ Fitting of regression model with country-level random effect to estimate stillbirth rates for countries without reliable time series data. ○ Describing the worldwide burden of stillbirth estimated using these methods.	Loess Regression Regression Prediction Model
Section II: Chapter 4	***Objective 2:*** Conduct an in-depth analysis of the availability of **preterm birth rate** data for all countries worldwide ***Objective 3:*** Develop and implement methods to produce national **preterm birth rate** estimates, with time trends where possible.	○ Overview of available data from national statistical websites, DHS surveys and published literature. ○ Preparation of estimation input database including developing inclusion/ exclusion criteria and covariate data. ○ Identification of countries with more reliable data where country-level data can be used alone to estimate preterm birth rates. ○ Fitting of regression model with country-level random effect to estimate preterm birth rates for countries without reliable time series data. ○ Describing the worldwide burden of preterm birth estimated using these methods	Systematic Review Loess Regression Regression Prediction Model
Section II: Chapter 5	***Objective 2:*** Conduct an in-depth analysis of the availability of **low birthweight rate** data for all countries worldwide ***Objective 3:*** Develop and implement methods to produce	○ Overview of available data from national statistical website and nationally representative surveys. ○ Preparation of estimation input database including developing inclusion/ exclusion criteria and covariate data.	Systematic Review Country consultation

	national **low birthweight rate** estimates, with time trends where possible.	○ Identification of countries with more reliable data where country-level data can be used alone to estimate low birthweight rates. ○ Fitting of regression model with country-level random effect to estimate low birthweight rates for countries without reliable time series data. ○ Describing the worldwide burden of low birthweight estimated using these methods	bSpline Regression Regression Prediction Model
Section II: Chapter 6	***Objective 4:*** Summarise lessons learnt through estimation exercises for stillbirth, preterm birth and low birthweight.	○ Where are the data gaps for stillbirth, preterm birth and low birthweight? ○ What are the main challenges to data quality currently for stillbirth preterm birth and low birthweight? ○ What are the options for assessing data quality for stillbirth, preterm birth and low birthweight? ○ Strengths and limitations of this thesis	Descriptive Analysis Literature review
Section III: Chapter 7	***Objective 5:*** Present an overview of measurement gaps and propose solutions for improving the data for stillbirth, preterm birth and low birthweight. Make data platform specific recommendations for the implementation of these principles.	○ Overview of measurement gaps for birth outcome data ○ Proposed solutions for improving stillbirth, preterm birth and low birthweight data across data platforms	
Section III: Chapter 8		○ Overall summary and practical implications going forward ○ Recommendations for policy and research	

2. Measuring birth outcomes

The previous chapter provided an overview of the importance of birth outcomes in general from an epidemiological and programmatic standpoint. Perinatal epidemiology as a specialised branch of epidemiology focusing on the distribution, determinants and sequelae of perinatal events has emerged gradually as a field over the past 100 years. Perinatal mortality data, comprising stillbirths and early neonatal deaths, have been collected since the 1800s in Nordic countries. Interest in birthweight measurement grew during the 19th century, whilst measurement of preterm birth has been a more recent focus during the 20th century.

Whilst it is generally agreed that these outcomes are important, their measurement has not always been straightforward. In addition to the usual challenges with epidemiological data collection, such as data comparability, overburdened data platforms and limited funding, measurement of birth outcomes is challenged by cultural perceptions of viability and personhood, as well as by stigma associated with these conditions. These affect the design of data systems, data collection and reporting of events.

This chapter also discusses some of the issues associated with the measurement of stillbirth, preterm birth and low birthweight. The work presented in this chapter draws from material on 'Measuring maternal, foetal and neonatal mortality: Challenges and solutions' published in Best Practice and Research Clinical Obstetrics and Gynaecology in October 2016 (see Annex A.2. for details).[1] I led the fetal and neonatal aspects of that paper, which seeks to present the overlapping challenges with the measurement of maternal, fetal and neonatal mortality. In this chapter, the text from the original publication has been expanded to provide further details regarding the measurement of mortality outcomes for the baby that were collected as part of work undertaken for the initial overview that could not be included within the tight word limit of the original publication. For definitions and indicators, United Nation's normative guidance such as WHO's International Classification of Diseases was prioritised, including reviewing current and historical definitions. Potential sources of data were identified by reviewing data sources from previous work seeking to understand the burden of these outcomes, and other sources identified through widespread background reading. In addition to discussing the measurement of fetal mortality and stillbirths, the measurement of the other outcomes, preterm birth and low birthweight, which are the focus of this thesis, are also included here. Targeted searches of peer reviewed qualitative and quantitative literature, programme reports, information from web sites, using key words including variations of "stillbirth", "low birthweight", "preterm birth", "measurement", "data" and "assessment" were undertaken to further explore specific aspects of the measurement of these outcomes. This was supplemented

with information from personal communication with experts familiar with the measurement of these outcomes through global and regional newborn health meetings I attended. Work that I had previously undertaken around the measurement of gestational age was updated and expanded, alongside work I undertook as part of a new systematic review on accuracy of gestational age assessment.[62,63] In many cases there is overlap between the components of information required to capture a given birth outcome, such as vital status at birth, gestational age and birthweight.

2.1. Definitions

To enable valid comparisons between populations and within populations over time, it is imperative that statistical data should be collected in such a way as to enable data to be extracted and reported according to standard definitions. This applies to all indicators, and the need to adhere to standard definitions in perinatal statistics, at national, regional, district, or local level has long been recognised.[64] The World Health Organization (WHO), through the International Classification of Diseases (ICD), has developed common definitions which when adopted and applied can facilitate comparisons across countries and data sources.[65] In recent years, in recognition of the importance of the standard application of this coding system for both defining and coding deaths, WHO have developed guidelines for coding maternal mortality (ICD-MM) and perinatal mortality (ICD-PM).[66,67] Individual countries often have their own definitions to allow collection of additional information for programmatic purposes or to meet legal requirements.

Table 2-1 contains the ICD-10 definitions for a selected group of key birth outcomes, which are linked to the main outcomes of this thesis, namely stillbirth, preterm birth and low birthweight. This is followed by a detailed description of the definitions, indicators and data platforms required for the capture of comparable data on stillbirth, preterm birth and low birthweight. A high-level introduction to some of the challenges in the application of these definitions will be introduced later in this chapter. These will be further expanded on later in the thesis.

Table 2-1 ICD-10 definitions for selected birth outcomes

Birth outcome	Definition
Fetal Death	Death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles
Early Fetal Death	Fetal death occurring from 500 to 999grams, or if birthweight not available from 22^{+0} to 27^{+6} weeks, or 25 to <35cms crown-heel length
Late Fetal Death	Fetal death occurring at ≥1000 grams, or if birthweight not available at ≥28 weeks, or ≥35cms crown-heel length Commonly referred to as stillbirth
Antepartum Fetal Death	Fetal death occurring prior to the onset of labour[a]
Intrapartum Fetal Death	Fetal death occurring after the onset of labour but before birth[a]
Live birth	The complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached[b]
Neonatal Death (NND)	Death of a live born infant in the first 28 days of life regardless of gestational age or birthweight
Early Neonatal Death (ENND)	Death of a live born infant in the first 7 days of life regardless of gestational age or birthweight
Late Neonatal Death (LNND)	Death of a live born infant between day 7 - 27 of life regardless of gestational age or birthweight
Perinatal Death	Composite indicator including all late fetal deaths and early neonatal deaths
Preterm Birth	Any birth[c] before 37 completed weeks of gestation, or fewer than 259 days since the first day of the women's Last Menstrual Period (LMP)
Low Birthweight (LBW)	Weight at birth of less than 2500 grams (up to and including 2499g)[c,d]
Small-for-gestational age (SGA)	Weight at birth below the 10th percentile for the gestational age in a standard population[c,e,f]
Large-for-gestational age (LGA)	Weight at birth greater than the 90th percentile for the gestational age in a standard population, or 4000g or more at term

[a] Antepartum or intrapartum denotes only the time of death in relation to labour. To ensure comparability it should be specified if includes late fetal deaths only or also early fetal deaths. [b] Notes on previous versions: Heartbeats are to be distinguished from transient cardiac contractions; respirations are to be distinguished from fleeting respiratory efforts or gasps. [c] 'birth' is specified, but definition usually only applied to live births [d] Further sub-groupings within LBW include very low birthweight(VLBW): less than 1500g and extremely low birthweight (ELBW): less than 1000g [e] ICD-10 specifies weight and length below 10th centile for gestational age (P05.1), but definition usually applied to weight criteria only. [f] Includes both growth restricted babies and those constitutionally small

2.1.1. Live birth

Live birth = baby born with any signs of life, irrespective of the duration of pregnancy

Live birth is defined in ICD-10 as "the expulsion or extraction from its mother of a product of human conception, irrespective of the duration of the pregnancy, which, after such expulsion or extraction, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached. Heartbeats are to be distinguished from transient cardiac contractions; respirations are to be distinguished from fleeting respiratory efforts or gasps."[65]

Live birth is a crucial definition, and it is important to distinguish a live birth from a baby with no signs of life at birth, as it forms the denominator for most of the outcomes around the time of birth for the baby, including preterm birth, low birthweight and neonatal mortality. In the first attempts at standardising the definition, the Committee for Hygiene of the League of Nations defined a live birth by the presence of breathing. It was adapted by WHO to the current definition in the 1950s in recognition that breathing may not always be present at birth even if the baby shows signs of life. In some countries a lower limit of length of life was specified for survival to be registered as a live birth.[68] These included: being alive at the time of registration if <28 weeks in France or <1000g in Romania; being alive for at least 24 hours if ≤1000g in Poland or <500g in Czechoslovakia; and being alive for at least 7 days if <28 weeks or <1000g in the former USSR. These alternative definitions do not capture early neonatal deaths in the most vulnerable of live births, and hence limit comparisons between countries.

There is now widespread agreement on the definition of a live birth. In almost all settings now, the intention is that data are collected using the International Classification of Disease 10th revision (ICD-10) criteria. However, variation in practice in the application of this definition still exists. This is discussed in more detail in Chapter 6.

2.1.2. Stillbirth /Fetal Death

Stillbirth = fetal death at ≥1000g, or ≥28 weeks, or crown-to-heel length ≥35cm

Fetal death is "death prior to the complete expulsion or extraction from its mother of a product of human conception, irrespective of the duration of pregnancy and which is not an induced

termination of pregnancy." Death is indicated by the fetus not showing signs of being a live birth, as described above. ICD-10 defines fetal deaths as occurring from ≥500 grams, or if birthweight is not available ≥22 weeks, or if birthweight and gestational age are not available a crown-to-heel length of ≥25cms.[65] Deaths before this period are spontaneous abortions, or miscarriages in lay terminology. However, in practice, definitions and terminology for fetal deaths are applied inconsistently, especially amongst high-income countries where thresholds range from 20 weeks gestational age upwards.[69,70] ICD-10 distinguishes early fetal deaths (Table 2-1) from late fetal deaths (commonly referred to as stillbirths) using birthweight, gestational age, or length criteria. ICD-10 recommends reporting both early and late fetal mortality rates, while WHO recommends using the late fetal death (stillbirth) rate for international comparisons.

Although a minority of countries have recorded fetal deaths at earlier gestations for many years, e.g. in the US fetal deaths at ≥20 weeks have been reported since 1945, the thresholds for definitions of stillbirth adopted by most countries are based on perceptions of viability. Until the relatively recent advent of neonatal intensive care and its scale-up in well-resourced settings since the 1970s, 28 weeks was viewed as the limit of viability. However, substantial advances have been made in the field of perinatal and neonatal care over the past 50 years. This limit has been pushed ever lower in well-resourced high-income settings, with survival possible from 22 or 23 weeks gestation upwards.[71-76] However, in any given setting, the recording of both births and deaths is most problematic around the threshold of viability for that setting. Whilst this is usually now not a problem for stillbirth reporting using the late fetal death international comparison definition in HICs where the threshold of viability is around 23 – 24 weeks, this remains an important data challenge in many LMICs where, in settings without neonatal intensive care, babies less than around 30 weeks may not be perceived as viable.

Before the advent of routine ultrasound dating of pregnancies, measurement of gestational age was frequently problematic in all settings, and greater importance was therefore placed, both clinically and for public health purposes, on birthweight. ICD-10 was developed several decades ago when gestational age assessment relied on often highly uncertain recall of last menstrual periods.[77] In contrast, birthweight was readily measureable, and therefore the fetal death thresholds were set to be based first on the birthweight criterion, then gestational age only if birthweight is not available, and finally on length. However, birthweight and gestational age thresholds do not give equivalent results (see Chapter 3 for details), with most high-income countries now favouring the use of gestational age as the primary definition.[10,78,79]

In understanding the development of the concept of 'stillbirth', it is important to recognise that the term has most frequently been used to capture the concept of a viable fetus born dead or dying before the society recognises it as being a living entity – which may vary substantially by time, place, culture, religion and other societal factors. In contrast, the term fetal death captures the death of a fetus in-utero, which may occur minutes, hours, days, or occasionally longer before its delivery. The term 'stillbirth' is often used in clinical practice and common parlance to refer to any fetal death; however, it is used in global estimates to refer to late fetal deaths only. Some have suggested that the term 'stillbirth' or born dead is outdated and creates confusion, especially in terms of the varying ways that the term is used with different lower gestational age limits and inclusion or exclusion of terminations of pregnancy.[80,81] They argue that knowing when the fetus died in-utero, i.e. gestation at fetal death, is more important in terms of understanding the aetiology and in providing a prognosis for the risk of stillbirth in the next pregnancy. In most cases the interval between fetal death and delivery is days at most, and such distinctions are therefore of less importance. However, in some cases this interval can be more prolonged. For example, if fetal reduction is undertaken at 12 weeks, but the fetal remains are delivered at term, current definitions and legal status require that the stillbirth be registered, even if the fetal remains are not-identifiable. Another instance with a potential long time lag between fetal death in-utero and birth, is a twin pregnancy when one twin dies and is either not recognised, or the clinical decision is made that the living twin has a better chance of survival by remaining closely monitored in-utero than by being delivered preterm.[82] In this case the parents have to register the second twin as a stillbirth, even if the twin died early in the second trimester, if the surviving twin is born after the threshold for stillbirth registration. However, these cases are relatively rare, and from the perspective of overall stillbirth rate data, will have little effect at a population level.

In this thesis the term 'stillbirth' is used throughout to apply to late fetal deaths, recognising the measurement and data challenges detailed also apply to fetal deaths at earlier gestational ages. However, as the purpose of this thesis is to review data to inform estimates for global comparison, the late fetal death definition is used.

2.1.3. Preterm birth

Preterm birth = a birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's Last Menstrual Period (LMP)

'Prematurity or immaturity' was initially defined by WHO at the first World Health Assembly in 1948 as "a birthweight of 2500g or less, or live born specified as immature. If birthweight is not specified, a live born infant with a period of gestation of less than 37 weeks or specified as "premature".[83,84] It was not until 1961 that the WHO expert Committee recommended switching to the use of a gestational age cut off.[85] This was followed by confirmation of the boundary between preterm and term at 37 completed weeks of gestation in 1970 at the Second European Congress of Perinatal Medicine.[86] This meeting also discouraged the use of the term 'immaturity/ prematurity'; however, despite this, the terms 'prematurity' and 'preterm birth' are still often used synonymously, however in this thesis, the epidemiological term 'preterm birth' will be used.

Preterm birth is defined by WHO as 'any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the women's Last Menstrual Period (LMP)'.[65,87] It is subdivided by gestational age into extremely preterm (<28 weeks); very preterm (28 - <32 weeks) and moderate or late preterm (32 - <37 weeks).[6] The definition is usually applied to preterm live births only, which is of importance in terms of identifying early mortality risk,[88] needs for neonatal intensive and special care,[89,90] and estimating long term consequences in terms of developmental outcomes, increased medical and educational needs.[21,91,92] All these are important at the individual clinical level, and also for public health programming and appropriate resource allocation.

The definition, in accordance with the ICD-10 live birth definition, does not include a lower limit to differentiate between a spontaneous abortion and a viable live birth. However, in practice the lines between the two are frequently blurred at the extremes of viability, and the reporting of these births as live births will depend in large part on the skills of the birth attendant and on resuscitation practices. Therefore, a renewed call has been made to record every birth, both live and stillbirth for the purposes of international comparisons, in view of the widespread differences in access to and quality of obstetric care, variations in policies and practice for active resuscitation of extremely preterm infants, and challenges in the recognition of vital signs at the time of birth especially in low-resource settings.[93,94]

2.1.4. Low birthweight

Low birthweight = A live birth with a weight at birth of less than 2500g[a]

[a] low birthweight definition includes all babies with a birthweight of <2500g, however in practice and in this thesis this is applied only to live births

Birthweight is defined as the first weight of the fetus or newborn obtained after birth.[65] Additional notes in ICD-10 state that "for live births birthweight should be measured preferably

within the first hour of life before significant postnatal weight loss has occurred. While statistical tabulations include 500g groupings for birthweight, weights should not be recorded in those groupings. The actual weight should be recorded to the degree of accuracy to which it is measured."[65]

Ideally, a birth outcome indicator that captured fetal growth well would be desirable, as fetal growth provides evidence of a healthy in-utero environment and predicts postnatal healthy survival and development. Birthweight is simply the mass of a baby at birth, and as such is affected by nutritional, maternal, environmental and genetic underlying factors, as well as by gestational age at birth.[95-97] However, low birthweight has remained an attractive indicator due to its relative ease of measurement and interpretation, and its ability to predict newborn survival and a range of other health outcomes.

A cut off of 2500g was first proposed by Dr Arvo Ylppö in 1919 to define what he called 'premature infants.'[98,99] At the time, this represented a large shift in philosophy to distinguish 'congenital weaklings' where death in infancy was the norm from 'premature infants' where the high risk of mortality could be in part mitigated by extra care. Initially different cut-offs were used, however in recognition of the importance of standardisation of definitions, a *2500g or less cut off* was accepted by the American Academy of paediatrics in 1935, and by the WHO at the 1st World Health Assembly in 1948.[84] In 1976, the current definition of low birthweight *as less than 2500g* was agreed upon at the 29th World Health Assembly.[100] Low birthweight can be further categorised into extremely low birthweight (birthweight <1000g) and very low birthweight (birthweight <1500g).[65]

Moreover, despite its widespread acceptance and use amongst researchers and public health professionals, including the WHO, the appropriateness of low birthweight alone as a predictor of high risk has come under some criticism.[101] These arguments are based on observations which show that at a population level the distribution of birthweight can be viewed as a dominant distribution of predominantly healthy newborns (which is normally distributed), and a residual tail comprising very small newborns who fall outside the dominant distribution.[102-104] It is argued that it is those babies in the residual tail, the majority of whom are preterm as well as small,[102] that are at high risk of mortality and adverse outcomes. Hence, using the 2500g does not distinguish well between those healthy newborns at the tail end of the normal distribution (not necessarily at increased mortality risk), and those in the residual tail (at increased risk). In addition, those in the residual tail may be small because of sub-optimal in-utero growth, normal in-utero growth but delivered preterm and those genetically small, all having very different

prognosis. However, despite this, in part due to the challenges of measuring gestational age data, low birthweight has remained an important, measurable public health and nutrition indicator, with recent Nutrition Goal targets, and hence is included in this thesis.

Throughout the second half of the 20th century there was increasing understanding that birthweight was a composite measure of length of gestation and fetal growth.[105] As the accuracy of methods to measure gestational age increased, it became more feasible to create a measurable indicator that took into account both birthweight and gestational age. This was beneficial in that it provided further discrimination in prediction of need for care, mortality risk and longer term prognosis.[106,107] The commonest measure in use as a proxy for fetal growth restriction at any given gestational age is small-for-gestational age. This is defined as weight at birth below the 10th percentile for the gestational age.[108] Previous attempts to develop charts to define normal growth were limited as they were based only on live born newborns. Especially at earlier gestational ages, those who are delivered differ substantially in their health status from those who remain in-utero. Hence, recent attempts have been made to seek to define fetal and newborn growth standards. However, lack of consensus on appropriate growth standards, in particular whether it is appropriate to use a single standard or whether population-specific standards are required, currently limits the comparability of this as an outcome.[109-111]

2.2. Indicators

2.2.1. Stillbirth and Fetal Mortality Indicators

Mortality indicators for outcomes in babies are usually measured per 1,000 births. Fetal mortality rates use total births as a denominator: (number fetal deaths)/ (live births + fetal deaths) X 1,000. Stillbirth rate is a subsample of the overall fetal death rate, including only late fetal deaths at ≥1000g, ≥28 weeks or ≥35cm.

$$Stillbirth\ rate = \frac{(fetal\ deaths\ at\ \geq 1000g, \geq 28\ weeks\ or\ \geq 35cm)}{(live\ births + \ fetal\ deaths\ at\ \geq 1000g, \geq 28\ weeks\ or\ \geq 35cm)} X1000$$

A combined indicator for all 'perinatal deaths',[65] is used: (late fetal deaths + early neonatal deaths (days 0 – 6))/ (live births + late fetal deaths) X 1,000. The perinatal mortality indicator is a pragmatic convenient measure especially where it is not possible to obtain robust information about the presence of signs of life at birth.

It is recommended that all deaths in babies less than 28 days of age, whether in-utero above a specified threshold, or in the neonatal period, are recorded by gestational age, birthweight and timing (ante-partum, intra-partum, or postnatal age in days).[112] Such reporting of outcomes is of programmatic relevance. For example, the 'Intrapartum Stillbirth and Very Early Neonatal Death Indicator', may be used to monitor improvements of the quality of obstetric and newborn care provided at birth. It excludes most preterm babies and includes only babies ≥2,500g, as these would be expected to survive in all settings, even without inpatient neonatal care. It can be calculated at a facility level as: (intrapartum stillbirths + neonatal deaths within the first 24 hours of life (≥2,500g))/(live births+ fetal deaths (≥2,500 grams)) X 1,000.[113,114]

The fetal death ratio is calculated as the number of fetal deaths/ number of live births occurring during a given period of time, usually a calendar year. In practice this is less-commonly used. Other measures in use include the 'prospective fetal mortality rate': number of fetal deaths at a gestational age per 1,000 ongoing pregnancies (fetal deaths and live births at that gestational age or greater). This is a more accurate denominator for those at risk, and provides an estimate of the risk of fetal death at a given gestational age.[115,116] In high-income settings, this indicator has been used to compare the risk of fetal death with the neonatal mortality rate to determine the optimal gestational age for delivery.[117] It is also useful when studying the impact of gestational age on stillbirth.

2.2.2. Preterm birth indicators

Preterm birth rate is the standard indicator for measurement of preterm birth. It is calculated as:

$$Preterm\ birth\ rate\ (\%) = \left(\frac{Number\ of\ liveborn\ babies < 37\ completed\ weeks\ of\ gestation}{All\ livebirths}\right) X100$$

Multiple gestation pregnancies are at higher risk of preterm birth, and hence traditionally many clinical and epidemiological studies have included only singleton gestations. However, from a public health perspective to understand the population burden of preterm birth, all live births, regardless of multiplicity should be included.[118] If data on multiplicity is also included in the data collected, then desegregations by multiplicity can be undertaken later.

As discussed above, this definition includes only babies who are identified and categorised as live births. Variations in this indicator include the preterm total birth rate which includes both live and stillbirths in the numerator and the denominator.

2.2.3. Low birthweight indicators

Low birthweight rate is calculated as:

$$Low\ birthweight\ rate\ (\%) = \left(\frac{Number\ of\ liveborn\ babies\ born\ with\ birthweight < 2500g}{All\ livebirths}\right) X100$$

Some studies report on mean birthweight instead of overall low birthweight rate. However, from a public health perspective, it is possible to shift the mean birthweight, by shifting the mean of the dominant birthweight distribution of healthy newborns, without impacting on those very small babies in the residual tail.[119] Thus leading to little or no effect on overall mortality and long-term adverse outcome measures that public health interventions are seeking to address. If only birthweight, and not gestational age, is available it has been recommended to estimate the residual distribution as an estimate of babies at highest risk, although this is rarely done as preterm birth rate is increasingly measurable and provides a more useful approximation of this.[101]

For successful implementation of the standardised definitions for all these indicators, there is a real need for frontline healthcare workers, data managers, and policy makers to understand these definitions, and what the resulting indicators mean.[120]

2.3. Measures of burden

To a large extent for general use and communication, as long as the indicators for stillbirth, preterm birth and low birthweight are calculated according to the formulae detailed above, whether this burden measure is called 'birth incidence', 'birth prevalence' or 'rate' could be seen as being an issue of semantics. From a purist epidemiological perspective both prevalence and rate are incorrect as these measures are incidence risks. However, birth prevalence and rate are the terms commonly used in perinatal epidemiology and in the literature and I have therefore, throughout this thesis referred to these as 'rates', without specifying incidence or prevalence.

2.4. Introduction to measurement of stillbirth, preterm birth and low birthweight

Despite the existence of definitions and indicators, measuring outcomes for babies at birth can be problematic. First, all births and deaths need to be identified, and then correctly categorised and counted.

Accurate application of stillbirth, preterm birth and low birthweight definitions is required to correctly categorise these birth outcomes. These require several elements of the baby's status at birth to be measured accurately. These key components are vital status at the time of birth, gestational age, and birthweight. These, and other related parameters such as vital status at onset of labour, day 7 and day 28, are also required for the measurement of related birth outcomes (Table 2-2). These parameters may be difficult to recognize, determine, capture, or remember. If a data system is not able to capture these components accurately, either from a frontline health worker, medical records/ registers or by maternal recall, then the data quality of the given birth outcome indicator will be adversely affected.

Table 2-2 Key data elements used in definitions of birth outcomes

	Gestational age	Birth weight	Vital status at onset of labour	Vital status at birth	Vital status at age 7 days	Vital status at age 28 days
Early Fetal Death	✓	✓		✓		
Late Fetal Death (Stillbirth)	✓	✓		✓		
Antepartum Fetal Death	✓	✓	✓	✓		
Intrapartum Fetal Death	✓	✓	✓	✓		
Live birth				✓		
Neonatal Death				✓		✓
Early Neonatal Death				✓	✓	
Late Neonatal Death				✓	✓	✓
Perinatal Death	✓	✓			✓	
Preterm Birth	✓			✓		
Low Birthweight		✓		✓		
Small-for-gestational age	✓	✓		✓		
Large-for-gestational age	✓	✓		✓		

Comparisons may be difficult because of differences in measurement practices and accuracy, inconsistent definitions used, or where data are not collected at all on a large number of the

population. The requirements for measurement of these important components of the indicator definitions for stillbirth, preterm birth and low birthweight will be discussed below.

2.4.1. Counting every birth - Case ascertainment and omission

The first requisite is for the system to count the baby at all. Omission of individuals and events is a common problem across different data platform and systems.[121,122] This is especially an issue for babies who are stillborn or die shortly after birth, of which preterm and low birthweight babies are at higher risk, as there is no opportunity to capture these children in the data system at later points in their lives e.g. through contact with the health or educational systems. In addition in methods of data collection requiring reporting of these events by families or community members other reasons such as blame or stigma may prevent disclosure of these deaths.[123]

2.4.2. Measuring vital status at birth

Applying the ICD-10[65] definition to distinguish between live and stillbirths requires being able to accurately distinguish between babies with signs of life at birth e.g. breathing, beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles. In cases where the baby is vigorous and crying, there is no doubt of the vital status. However, when the baby is very preterm, under the influence of maternal drugs, or compromised e.g. by fetal hypoxia, detecting signs of life can be more challenging. The delivery attendant, or other person, will be required to assess the baby carefully and institute neonatal resuscitation if required. Attempting neonatal resuscitation is appropriate in most non-macerated babies who are not breathing at birth unless fetal death was confirmed in utero, or a prior decision not to institute active care was made e.g. extremely preterm at the limits of viability such as a baby born at 22 weeks in HIC or with a congenital malformation not compatible with life such as anencephaly. See section 6.4.2 for a fuller discussion of these issues.

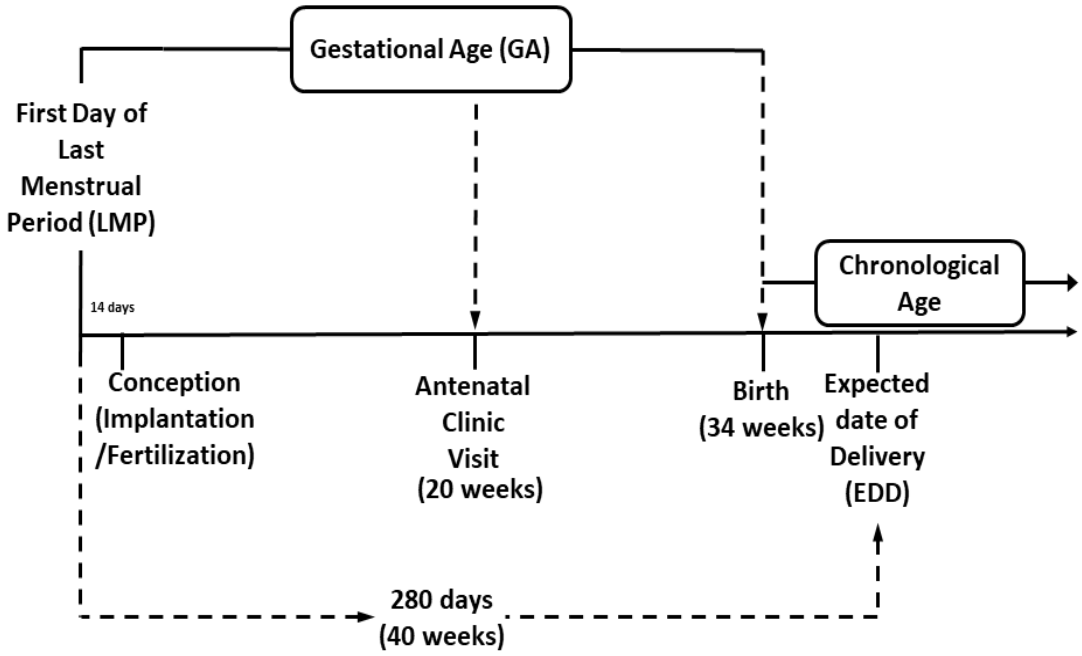
2.4.3. Measuring gestational age

Historically, birthweight was used as a proxy to define 'prematurity'. However, it is a poor proxy, especially in settings with high rates of fetal growth restriction, with many term growth-restricted babies, who have different clinical needs and prognosis, being labelled as premature. The importance of gestational age in predicting outcome has been increasingly recognised and efforts are being currently made to improve its measurement in all settings.

Gestational age is defined as 'The duration measured from the first day of the last normal menstrual period'. Gestational age at birth is therefore the duration measured from the first day of the LMP to the day of birth. Gestational age is expressed in completed days or completed weeks (e.g. events occurring 280 to 286 days after the onset of the last normal menstrual period

are considered to have occurred at 40 weeks of gestation)' (Figure 2-1).[64] As conception typically occurs around 14 days after the last menstrual period, pregnancy duration is in fact around 2 weeks less than the gestational age; however, the exact timing of ovulation, fertilization, implantation is unknown and the actual length of pregnancy may vary at a given gestational age if a woman's cycle differs substantially from this.

Figure 2-1 Gestational and chronological age timelines for a baby born preterm at 34 weeks gestation



Adapted from American Academy of Pediatrics. Committee on Fetus and newborn.[124]

The measurement of gestational age has presented many challenges over the years. Various methods are available to provide an assessment of gestational age which can be used at different stages of pregnancy or after birth. See Table 2-3. There is large variation in the accuracy of these methods, the most accurate being fetal measurements taken at an early (first trimester) ultrasound scan. The WHO definition for stillbirth or preterm birth does not specify a universal reference standard for assessment of gestational age, and the gestational age assessment tools used will affect the classification of these outcomes.

Table 2-3 Comparison of different methods for gestational age assessment

Timing	Method	Accuracy
At any time	Last Menstrual Period	+/- 2 – 3 weeks (accuracy strongly affected by individual woman factors and whether collected prospectively or retrospectively).
Before Birth only	Ultrasound fetal measurements[a]	+/- 5 – 21 days (depending on gestational age when performed. More accurate when measurements taken at earlier gestations).
Before Birth only	Symphysis Fundal Height	+/- 2 - 3 weeks (depending on gestational age when performed. More accurate when measurements taken at earlier gestations).
After Birth only	Newborn Clinical gestational age assessment scores	+/- 2 – 4 weeks (depending on tool used) Assessment not possible in stillborn or very sick babies who die soon after birth.
After Birth only	Newborn anthropometric proxies	Variable depending on cut offs used (see text).
After Birth only	Newborn assessment of anterior capsule of the lens	Variable. Overall correlation with gestational age moderate. More accurate in low birthweight populations, even if growth restricted. Only useful for gestational age assessment up to 35 weeks.

[a] Can be combined with Last Menstrual Period using algorithms to generate a 'Best Obstetric Estimate'
Adapted from Blencowe et al[62]

Last Menstrual Period

This method has the advantage that it can be measured at any point during pregnancy or around the time of birth. It can also potentially be measured later in the weeks, months (or even years) after a birth. However, its accuracy is greatest when measured prospectively.[125]

The accuracy of recalled LMP to assess gestational age is influenced by the accuracy of maternal recall, misinterpretation of bleeding in early pregnancy as a period, and irregularity of menstrual cycles which is more common in undernutrition and after cessation of hormonal contraceptive methods. In some societies closer attention may be given culturally to menstrual cycles, such as Islamic and Hindu societies where women are not permitted to have sex, partake in religious practices such as entering the temple or praying or undertake some household tasks amongst other restrictions while menstruating. However, whilst knowledge of the cycle is necessary for reporting, it is not sufficient, and women may have other reasons for not wanting to disclose a pregnancy.[123,126]

Higher rates of LMP uncertainty are associated with lower levels of literacy, lower socio-economic status, smoking and younger age in HIC.[127] It is likely that similar patterns will be evident in LMICs. Despite this, evidence suggests that LMP can be reasonably accurate, even in LMIC settings when compared to early USS.[125,128-134]

Ultrasound fetal measurements

This method compares fetal size to a reference group of pregnancies of known gestational age. The gestational age is estimated by comparing to the median measurement from the reference population. Accuracy is dependent upon the gestational age at which the ultrasound scan is undertaken. The gold standard is Crown Rump Length measured at <14 weeks, but other measures such as Biparietal Diameter, Femur Length, Abdominal circumference, Head circumference which are used to monitor fetal growth at later gestations can also be used for ultrasound dating.[135] Some limitations of ultrasound scan estimated gestational age include that it assumes that all fetuses grow at the same rate and that size is equal to gestational age. Its validity is hence affected by growth disturbances. These are more common after the middle of the second trimester, hence accuracy at later gestational ages is affected (Table 2-4). At a population level, the accuracy of these methods will depend on the prevalence of abnormal growth patterns.

Table 2-4 Accuracy of currently used ultrasound pregnancy dating at different gestations

Biometric Parameters	**Gestational Age at assessment**	**Accuracy**
1st trimester Crown Rump Length	< 14 weeks	± 5-7 days
2nd trimester Biparietal Diameter, Femur Length	14-20 weeks	± 7-10 days
2nd trimester Biparietal Diameter, Femur Length, Abdominal circumference	20-28 weeks	± 10-14 days
3rd trimester Biparietal Diameter, Femur Length, Abdominal circumference, Head circumference	28+ weeks	± 17-21 days

Adapted from Blencowe et al,[62] American College of Obstetricians and Gynecologists[136], Hadlock et al 1984[137]

Although antenatal care coverage is very high in most settings, in LMICs care is frequently not sought until late 2nd or early 3rd trimester limiting the use of ultrasound dating. In addition to early identification and disclosure of pregnancy, measurement and accuracy of USS dating of pregnancy requires timely access to antenatal care, availability of well-maintained, functioning ultrasound equipment and skilled sonographers with intensive training, and ongoing quality control. These factors currently limit the widespread scale-up of this dating-method in many settings. For example, it is estimated that only around 7% of pregnant women in rural sub-Saharan Africa can access routine ultrasonography in the first and second trimester of pregnancy.[138]

Best obstetric estimate is the "Birth attendant's final estimate of gestation", based on assessment of LMP and ultrasound. This measure is widely used in high income settings, but different algorithms used can affect the gestational age estimate.[139]

Symphysis Fundal Height

Symphysis Fundal Height (SFH) is routinely measured in antenatal clinics as a screening tool for fetal growth restriction – however its utility for assessing gestational age remains limited. For example even in women across 8 geographical sites with low-risk ultrasound dated pregnancies taking part in the INTERGROWTH 21st SFH sub-study (n=4607), at 16 weeks normal (10th – 90th centile) SFH ranged from 14 – 17.5cm.[140] This range widens with increasing gestational age. At 35 weeks the range varies from 31.5 – 36.5 cm. However, when early USS is not available, if measured in the second trimester it can provide an estimate of gestational age +/- 2 weeks,[130] and this may be more accurate than LMP in some settings.[129]

Newborn clinical gestational age assessment scores

A recent systematic review of the literature, for which I was a co-author, identified 18 different newborn exams/scores for gestational age assessment including a range of 4 to 23 signs.[63] These scores combined various signs of physical and neurological maturity associated with gestational age including skin opacity, colour, and texture; nipple/ breast development; presence of lanugo hair, foot creases; development of eyes, ear, genitals; passive flexor tone (posture, popliteal angle, heel-ear); active tone (arm recoil); ankle/wrist flexion; reflexes (including sucking, rooting). Compared to the reference standard of USS or best obstetric estimate Dubowitz (21 signs and complex to administer) was the best performing score, dating 95% of pregnancies +/- 2.6 weeks. Ballard (12 signs) and Parkin (4 signs) scores were accurate only to around +/- 4 weeks. All tests were relatively specific to identify preterm birth (e.g. Dubowitz 99% specificity, Ballard 95%), however sensitivity was much lower (Dubowitz 61% sensitivity, Ballard 64%).

Some of the limitations of postnatal clinical gestational age assessment are that it is not possible to undertake for stillbirths, and its validity is affected by neonatal morbidities, such as asphyxia, sepsis and congenital anomalies, as well as by medication. The full neurological examinations are long, and may not be feasible in busy under-staffed clinical settings. To achieve maximum accuracy, training and standardisation of practices amongst health workers is important. Even when performed optimally, these methods overestimate gestational age in preterm babies and underestimate gestational age in small-for-gestational age babies.[63]

Newborn Anthropometric Proxies

Where accurate measurement of gestational age is not possible, there is a long history of the use of anthropometric proxies. As discussed above birthweight is a poor predictor of gestational age, especially in populations with high levels of fetal growth restriction. In recognition of this, much effort has been invested in identifying improved anthropometric proxies in settings where robust gestational age assessment is not possible. This includes historically in HIC settings before routine early pregnancy ultrasounds, and currently in many LMIC settings. Potential proxies

include symphysis fundal height (discussed above) and newborn measures such as foot length, and mid-upper arm, chest or head circumference. The performance of these tools to predict either preterm birth or mortality risk varies substantially from study to study. In part the evidence base regarding this is limited as many studies used less accurate, non-USS based methods of GA assessment as the reference standards, e.g. LMP. Of the few studies comparing neonatal anthropometry to early USS, the most comprehensive study to date of 710 babies in Bangladesh tested a series of proxies compared to early USS in a setting with a high prevalence of fetal growth restriction. It found that these proxies had relatively poor performance for classifying preterm birth (Table 2-5).[63] In view of this, anthropometric proxy measures are not recommended as a substitute for direct gestational age measurement for the classification of preterm birth.

Table 2-5 Accuracy of neonatal anthropometric measures to detect preterm birth

Anthropometric measure[a]	**AUC**	**Cut-off values used** *(alternative cut-off value)*[b]	**Results**	
Foot length	0.5	≤7.5 cm *(≤7.6 cm)*	sensitivity: 64% *(86%)* specificity: 35% *(28%)*	PPV: 8% *(19%)* NPV: 92% *(92%)*
Head circumference	0.8	≤32cm *(≤33cm)*	sensitivity: 56% *(68%)* specificity: 83% *(65%)*	PPV: 23% *(15%)* NPV: 95% *(96%)*
Birthweight	0.8	≤2500g *(≤2600g)*	Sensitivity: 54% *(75%)* Specificity: 82% *(68%)*	PPV: 22% *(18%)* NPV: 95% *(97%)*
Chest Circumference	0.7	Not shown as poor sensitivity/ specificity		
Mid-upper arm circumference	0.6	Not shown as poor sensitivity/ specificity		
Length	0.6	Not shown as poor sensitivity/ specificity		

[a] Compared to early USS as the reference standard. Data from single study in Bangladesh[63]
[b] Results using the alternative cut-offs used are shown in the table above in brackets
AUC= Area under the curve

The above regarding neonatal clinical examination and neonatal anthropometry relate to gestational age assessment in live born babies only. Limited research has been undertaken on the role of neonatal anthropometry in gestational age assessment in stillbirths, although foot length may be a potential measure.[141-143] Despite this, birthweight proxies are used as part of the ICD-10 definition of stillbirth to distinguish late from early fetal deaths.

Newborn assessment of anterior capsule of the lens

Hittner et al first described in 1977 how the vascularity of the anterior capsule of the lens changes with increasing gestation, from being completely vascularised at 27 – 28 weeks gestation reducing to no vasculature by 35 weeks gestation.[144] This was recognised therefore as a potential tool to be used for postnatal gestational age assessment.[145-147] A recent systematic review found 10 studies, three from LMICs, that had sought to compare assessment of the

anterior vascular capsule of the lens to a reference standard.[63] Overall correlation with gestational age was found to be moderate (-0.64 to -0.45), but it was found to be more accurate in low birthweight populations (median correlation 0.88 (7 studies)), even if they were SGA (median correlation 0.77 (3 studies)). These studies were generally small in size, using non ultrasound-based 'reference standards' and of low quality. A further limitation is that this method is only useful for gestational age assessment up to 35 weeks due to the complete disappearance of the vasculature after this time. Currently this method is not used as a standard method of gestational age assessment.

2.4.4. Measuring birthweight

Accurate measurement of weight measured as soon as possible after birth is an important part of good clinical practice, allowing the early identification of low or high birthweight babies at increased risk, and providing a baseline weight to identify those struggling with establishing feeding, or those unwell.[64] Accurate measures of birthweight are used for classifying stillbirths, and are required to measure low birthweight and small or large for gestational age babies.

Accurate birthweight measurement requires the weighing of the baby (whether live or stillborn) naked as soon as possible after birth (ideally within the first hour), using an electronic scale which is graduated to 10g, calibrated at least once a year (or more often if moved), placed on a level, hard surface and tared to zero.[148] To facilitate accurate weighing for all babies, suitable, well-maintained and calibrated weighing machines should be readily available in labour wards, close to resuscitation areas and in the community for home births. The first weight measured should be recorded as the birthweight on all records and documentation, whether labour ward records, mother's notes or neonatal unit admissions. This weight should be measured as soon as possible in the hours after birth prior to onset of postnatal weight loss. The cut off for timing of the first weight to be classified as a true 'birthweight' is not agreed. A recent systematic review found that post-natal weight loss in term breastfed babies peaked at 2 – 4 days after birth.[149] Despite this, cut offs of 48 hours[148] and 72 hours[150] are commonly in use.

Neonatal Anthropometry Proxys

As for gestational age, when it is not possible to obtain a timely birth weight, anthropometric proxies for low birthweight have been used. These include foot length, and chest, thigh, head and mid-upper arm circumference. A systematic review and meta-analysis undertaken in 2011 to examine the evidence available for the identification of LBW by anthropometric measurements at birth in developing countries found both chest and mid-upper arm circumference to have high predictive power for detecting low birthweight; with estimates of sensitivity around 85% and specificity over 90%.[151] This same study found thigh and foot length to be slightly less accurate. However, the cut offs used in these studies varied, rendering the

interpretation from a clinical perspective challenging. In recent years there has been a resurgence in studies examining these anthropometric surrogates for identification of LBW. These have all shown a positive correlation of the surrogates with birthweight, and whilst other anthropometric measures were shown to be more predictive, many of the studies recommended the use of foot size as it was found to be reasonably predictive and relatively easier to measure without needing to expose the baby.[152,153] Whilst there remains a potential role for these proxies to identify individual clinical risk and need for extra care, for the purposes of low birthweight prevalence data at a population based level, every effort should be made to obtain an accurate birthweight measurement.

2.5. Data Sources and Platforms

An ideal data platform for birth outcomes in a population would capture all pregnancies, ideally in the 1st or early 2nd trimester to allow USS dating, and follow these through to delivery, where all key data elements including vital status at birth, gestational age, and birth weight would be accurately captured. In most settings this ideal is not met, and birth outcome data are collected and collated through overburdened data systems which capture information on many other health outcomes and processes. Table 2-6 highlights some of the most important data platforms for birth outcomes, and these will be discussed further below. Functional Civil Registration and Vital Statistics (CRVS) systems are the preferred data source for information on births and deaths at all ages, including causes of death, which can then be disaggregated to give information at a sub-national level.[47] However, in many settings these do not yield usable data, especially for birth outcomes, and hence interim data solutions are currently required.[154]

Table 2-6 Data platforms for identifying adverse birth outcomes

Data Platform	Data collection methods and tools for birth outcome data	Information on gestational age and birthweight included	Notes
Civil registration	Birth registration Death registration Fetal death/ stillbirth registration where separate	Variable	Works well where there is high coverage, and completeness of birth and death registration. Can be easier to implement in urban areas. Currently low coverage in highest burden areas. Sample vital registration approaches taken initially in some countries when full CRVS not feasible e.g. China, India and Bangladesh. Challenges include differing legal requirements for registration.
Health Information Management Systems	Paper or electronic based Birth outcome information from various labour ward registers collated as input	Birthweight usually GA variable	Widespread in public-sector facilities in many countries. Quality variable, and data captured in registers may not be aggregated into system. Frequently, low coverage of private-sector and home births. Platforms include District Health Information Systems 2 (www.dhis2.org/)
Population-based Household surveys (e.g. RHS, DHS, MICS, Nutrition Surveys)	Differing tools used. DHS and MICS-6 have full birth history allowing any direct information on birth outcomes to be collected.	Birthweight collected in most surveys. Gestational age variable and usually only collected in months.	Surveys are the main source of mortality outcomes on the 45 million births occurring outside facilities. Fetal deaths are frequently omitted, and capture of fetal and early neonatal deaths may be of poor quality. Birthweight is included, but is not available from a large number of respondents in many surveys.

	Data collected retrospectively for births 3 – 5 years prior to the survey		Some DHS survey have a full pregnancy history that collects more details.
Pregnancy and Birth Registries	Paper-based or eRegistries	Yes	Information about antenatal, delivery and immediate neonatal care and outcomes collected prospectively or at the time of birth.
National Perinatal surveys	Medical records, interviews with woman	Yes	Commonly cover all births in a country in a 1-2 week period. Usually facility-based so only suitable for population based estimates in settings with very high facility-birth rates.
Surveillance	Examples includes Demographic and Health Surveillance sites (DHSS), Maternal and Perinatal Death Surveillance and response and Birth Defects surveillance	Variable	Surveillance can be of whole populations, of pregnancies and their outcomes, or of deaths. Surveillance can range from continuous case detection, to surveillance visits up to 1 year apart.
Research studies	Variable	Variable	Many research studies capture information about birth outcomes, frequently using more robust methods than possible in routine systems. However, their usefulness to inform estimates depends upon population representativeness.

RHS=Reproductive Health Surveys (http://ghdx.healthdata.org/series/reproductive-health-survey-rhs)
DHS=Demographic and Health Surveys (http://www.dhsprogram.com/)
MICS=Multiple Indicator Cluster Surveys (http://mics.unicef.org/)

The inclusion of stillbirths in the data platforms above is variable, with only pregnancy and birth registries and national perinatal surveys routinely including this outcome in all settings.

2.5.1. Civil Registration and Vital Statistics

Civil registration and vital statistics (CRVS) should ideally capture every birth and death (including cause-of-death information assigned by a medically-qualified person) in a country. Data collection should be on an ongoing basis, and certificates issued for these vital events. In theory, the national scope and the ongoing effort and investment makes CRVS the "gold standard" for measuring all births and deaths. Unfortunately, CRVS systems remain weak in most areas of highest mortality burden,[47,155,156] missing both births and deaths, and causes of death.

Compulsory registration of live births began in most countries in Europe in the 18th to mid-19th centuries; however currently birth registration remains highly variable across regions, varying from just over 40% in sub-Saharan Africa to 100% in Western Europe and North America. Across all regions there is gender parity in birth registration, however wide socio-economic inequity and gaps between urban and rural remain.[157,158] Identified barriers to registration include accessibility of nearest registration facility, in financial terms as well as distance or terrain, lack of knowledge on how to register a birth, requirement for the father to be present and the cost of registration and obtaining a certificate, even where birth registration is free by law, for example fines for late registration. Those living in urban areas are 1.5 times more likely to be registered.[159]

Death registration systems face further challenges and lag behind birth registration. Only 60 countries worldwide are currently assessed as having good-quality overall child death registration data from vital statistics, with few outside the developed region, and the status for information on neonatal deaths is even worse with fewer than 5% of all neonatal deaths worldwide estimated to receive a death certificate.[58] Information on stillbirth registration is not currently systematically collated, but is likely to be worse than for neonatal deaths.

Timely capture of birth outcomes presents additional challenges for CRVS systems. Despite progress being made overall with birth registration in recent years with 71% of all births globally now registered, many are registered months or even years after birth.[157] Registration of births or deaths with the civil authorities for stillbirths and neonatal deaths lags behind that of other births. Whilst some LMICs include stillbirth in their legal frameworks for birth certification, such as India, Swaziland, Zambia, Zimbabwe, Lesotho and Botswana, this is not universal.[160] In addition, there remains marked variation in terms of the legal deadline for registering a live birth. In Europe this ranges from 3 days in France, The Netherlands and Switzerland, to six weeks in England, Wales and Ireland (Table 2-7).[161] In half of sub-Saharan African countries the deadline is more than 1 month, meaning that many babies who die before this period never get a birth certificate.[162]

Table 2-7 Variations in legal reporting requirements for live and stillbirths across Europe

Country	Netherlands	Switzerland	France	Luxembourg	Austria	Germany	Spain	Greece	Italy	Belgium	Portugal	UK	Turkey
Live birth registration limit	3 days	3 days	3 days	5 days	1 week	1 week	8 days	10 days	10 days	15 days	20 days	21 days (Scotland) 6 weeks (rest)	30 days
Registration of live births who died before birth registration	Issued birth and death certificate	Issued birth and death certificate	Pre 1993, Stillbirth certificate. Since 1993, issued birth and death certificate	Special certificate for a lifeless child (Stillbirth certificate)	Issued birth and death certificate	Issued birth and death certificate	Issued birth and death certificate if >24 hours. <24 hours in 'legajo de abortos'	<10 days issued birth certificate (with death details) only	Issued birth and death certificate	Pre 1984 as Luxembourg. Since 1984 issued birth and death certificate	Issued birth and death certificate	Issued birth and death certificate	Issued birth and death certificate
Legal limit for required stillbirth registration	≥24 weeks	≥7 months	≥180 days	≥180 days	≥500g	≥500g	≥7 months	≥180 days	≥28 weeks	≥180 days	≥22 weeks	≥24 weeks	No civil status instrument
Registration of stillbirths	Entered into register of deaths	Issued birth certificate with reference to the death	Entered into register of deaths	Entered into register of deaths	Entered into register of deaths	Pre 1998, in register of deaths, Post 1998 in birth register	Entered into a special sheet 'legajo de abortos'	Issued birth certificate with reference to the death	Issued birth certificate with reference to the death	Entered into register of deaths	Post 1997 no certificate issued. A registry declaration filed only	Issued a certificate of stillbirth Entered in specific 'Register of Stillbirths'	Not registered
Inclusion of a name in the stillbirth record	Yes if parents request	Yes if parents request	Yes if parents request	First name not allowed	Not permitted	Yes if parents request	Not permitted	Yes if parents request[a]	Under discussion	First name not allowed	Not permitted	Yes if parents request	Not registered
Legal status for burial of stillbirth	No legal framework, but possible in practice	According to local canton practice	No legal framework	At parents request in the family grave	According to local authority practice	At parents request	If present medical certificate	Not permitted	Not permitted	At parents request, but only in special part of cemetery	Not permitted	At parents request	Not permitted

Data source: Civil status and perinatal death in CIEC member states[161]. [a] First name rarely included as naming usually occurs at baptism

Additionally, there are important ethical considerations in the recording of births and deaths around the time of birth. These include controversy around when a baby is considered an individual (personhood), which affects societal perceptions and drives some of the differences in legal frameworks and practice around birth and death certification, especially for stillbirths and very early neonatal deaths. For example, when compulsory registration of stillbirths was added to birth and death certification in HICs in the late 19th and early 20th century (1927 in the UK), its primary aim was to help protect infant life amidst concerns of infanticide, and improve the accuracy of infant mortality statistics as opposed to any perceived benefit for the stillborn child or its family.[163] The right to a name and a nationality is enshrined in the Convention of the Rights of the Child, and the benefits of birth registration for a living child in terms of status and access to services are clear.[164] However, whether a fetus who dies in utero should be afforded the right to registration is not universally agreed.

Much research has been done on the early years of national death registration and cause-of-death statistics from HIC settings showing the complex interaction between the state, the public, and the medical and legal professions. Legal priorities often trump public health ones, leading to the relative neglect of the stillborn baby who has no legal status. As physicians took responsibility for reporting the types and causes of death, they frequently sought to balance public health considerations with the potential stigmatising effect of certain diagnoses on patients and families.[165] The same pattern is being played out in many low and middle income settings today, with some death statistics, for example those of maternal mortality, becoming highly politicised.

Whilst the primary driver behind current pushes to increase the coverage of birth registration may come from a human rights perspective, this provides an important opportunity to capture other important information for perinatal statistics such as information on birthweight and gestational age. Different countries vary over time in the information that they seek to capture. For example, birthweight became part of the US national standard birth certificate in 1950,[166] but is not included in the certificate in all countries. The inclusion of gestational age is even more variable.

Similarly, the information captured on stillbirths is highly variable across settings. WHO have recommended the use of a standard perinatal death certificate which includes key information such as birthweight and gestational age. Uptake has been low, with only nine countries adopting it. As part of ICD-11, WHO now recommends the use of a standard death certificate to be used at all ages, including for stillbirths.[167]

CRVS systems are often difficult and expensive to set up and maintain in LMIC settings, and one option to overcome this to generate useful nationally representative information on births and deaths is to set up a sample registration system. This was the approach taken in several countries in Asia including India, Bangladesh, and China. In India a sample registration system was introduced in 1964 to seek to provide accurate annual data on birth and death rates, infant mortality and fertility indicators. It includes stillbirths, but capture of these events remains low.[168] Bangladesh initiated a birth-death sample registration system in 1980, initially with 15-primary sampling units, increased to 1000 in 2000. Whilst it includes information on live births and neonatal deaths, it does not include stillbirths.[169] In China the sample based National Diseases Surveillance points system was set up in 1990 to collect data on births, causes of death and the incidence of infectious diseases.[170] The completeness of the system is assessed through independent resurveys every 3 years. In 2013 the system was merged with the Ministry of Health's vital registration system and expanded to cover 24% of the population, however concerns have been raised over potential biases due to the sampling methods used in these systems.[171,172]

2.5.2. Health Management Information Systems

Health Management Information Systems (HMIS) are a key building block of a health system.[173] They aim to provide timely data relating to the health system, including health outcomes. In the short-term these can be used for planning and resource allocation, and in the longer term have the potential to improve quality of services, transparency, accountability and governance. They are a source of data on births and deaths that occur in health facilities, although in many settings these exclude private-sector facilities. Traditionally these have excluded home-births, although increasingly efforts are made to use community-based health workers or volunteers to report these births and deaths to the facility.

Whilst the vital event variables collected in HMIS overlap with CRVS, HMIS collect a wider range of variables and these are aggregated at the facility level and are usually designed specifically for statistical and technical health purposes.

In settings with a high proportion of facility births, but weak CRVS, HMIS data on birth outcomes including stillbirth, preterm and low birthweight may provide an interim data source whilst efforts are made to increase the death notification and registration process for all facility births. In countries where birth and death certification excludes stillbirths, HMIS data could be a useful data source, although acknowledging the potential biases, especially where facility birth is not universal.

Despite the great potential of HMIS systems, underfunding, fragmentation and lack of supervision and quality checks have frequently impeded their utility for decision making.[174,175] Concerns have been raised with regard to the quality of birth outcome data collected within these systems, however quality can improve with investment in training and regular supervision.[176] Many countries are now transiting from often fragmented paper-based systems to electronic systems. District Health Information Software 2 (DHIS2), a free and open source platform allowing aggregation, validation, analysis, management, and visualisation of statistical health data, is the most widely used with 67 countries, mainly LMICs, currently using it.[177] DHIS2 has the potential to be used to monitor health at an individual level, improve disease surveillance, map clusters of cases, and allow timely access to health data for health facilities, programs and policy makers.

2.5.3. Household surveys

Cross-sectional, population-based household surveys are an important source of data on health of populations in low and middle income countries without robust CRVS and HMIS data. They are the main source of data to inform neonatal and child mortality and coverage of healthcare estimates in LMIC settings.[58] However, for mortality outcomes such as maternal and neonatal mortality or stillbirths there are frequently small numbers of events in survey samples and hence wide uncertainty intervals around the estimates.[178] Under-reporting of stillbirths in household surveys is common.[70]

Standard Demographic and Health Surveys (DHS) and the later Multiple-Indicator Cluster Surveys (from MICS-5 onwards) include a full live birth history, retrospectively collecting details of all the live births a woman has had in her lifetime, whether they are still alive or not. They also collect further details on recent births, usually in the period 2 to 5 years prior to the survey, including birthweight. Substantial methodological issues are associated with this information in particular related to recall and reporting biases associated with the use of a retrospective survey reporting.[179] The majority of DHS surveys also include a reproductive calendar, where information on pregnancies, including those not resulting in a live birth, and gestational age in months is collected, although its reliability is highly variable.[180] Surveys using full pregnancy history collect data on all pregnancies a woman has had in her lifetime, including those ending in miscarriage, fetal death or stillbirth. Some surveys using a full live birth history have added an additional question regarding stillbirth, including the more recent core DHS modules; however despite this the stillbirth rates reported in many of these surveys remain implausibly low.[25,123]

A few countries have undertaken household surveys explicitly to focus solely on maternal health, including the 2007 and 2017 Ghana Maternal Health Surveys, the 2001 Bangladesh Maternal Mortality and Maternal Health Services survey and the 1993 Philippines National Safe Motherhood Survey. Other special mortality surveys have included maternal health as a key component e.g. Afghanistan 2010 mortality survey. These include a full pregnancy history, detailed information on all birth outcomes and commonly a verbal autopsy for all stillbirths and neonatal deaths.

2.5.4. Pregnancy and birth registries

Traditionally birth registries have collected data on all births at the time of birth and included information about antenatal, delivery and immediate neonatal care and outcomes. They have been scaled nationally in many countries including Norway, Denmark, Sweden, Finland and Iceland. These data can be linked to other electronic data records including civil registers and other health databases to provide further details on other characteristics including maternal age, nationality, ethnicity, maternal conditions and prescriptions.[181]

These can also be linked to vital statistics for example, the Chilean database and register of live births was established by an agreement in 1982 between the Civil Registry of Chile, the National Institute of Statistics (INE) and the Ministry of Health (MINSAL) as part of the process of computerization of vital statistics. It is the official source for all maternal and perinatal statistics and health indicators for all live births, whether home or facility born. However, stillbirths are not included in this data source.

In pregnancy registries all pregnancies are prospectively enrolled and mothers and babies are followed up at least to the time of delivery. Traditionally they have been a useful tool for research purposes, particularly to reduce bias when examining the effect of perinatal exposure on outcomes, for example when monitoring the safety of vaccines in pregnancy.[182] In recent years, with the advent of electronic medical records and the ability to make links between data systems it is now possible to create electronic pregnancy registries in data-rich settings such as Sweden.[183] These have the advantage of capturing all pregnancy outcomes, including stillbirths, but also provide a tool for quality improvement by visualising quality or outcome measures adjusted for case-mix between facilities and over time. As they capture all outcomes they have the potential to improve capture around the threshold of viability.

The most commonly used electronic HMIS platform, DHIS-2, has recently implemented a new ‘tracker’ module that allows the tracking of an individual woman from ANC booking throughout pregnancy to postpartum period.[184]

2.5.5. National perinatal surveys

Historically, perinatal surveys have been used in settings with a large proportion of facility births but lacking routine annual statistics on all births. They typically involve data collected from medical files and by interview with women postpartum over a short period of time, for example 1 week. Although the sample size often precludes robust assessment of rarer outcomes such as stillbirth, they are potentially a useful source of data for other more common birth outcomes such as low birthweight and preterm birth. Historically these have been especially attractive to countries with insufficient infrastructure to capture these events fully in birth registries or civil registration due to political factors, lack of resources or instability. When undertaken periodically, they can provide useful information on changes in perinatal health at a national level.

The method was initially developed in the UK which undertook three surveys capturing all births in the UK in a single week in 1946, 1958 and 1970.[77,185-187] The three surveys had different underlying purposes. The 1946 survey sought to describe the status of maternity services before the introduction of the UK National Health Service in 1948. It aimed to answer key contemporary questions such as whether the medical costs associated with the birth of a baby were deterring couples from parenthood and contributing to the decline in fertility and, what was the national distribution and use of maternity services? These questions were key in the post-war era when potential population decline was a concern due to potential to lead to a loss of political power.[188] The 1958 survey was undertaken to seek to identify social and obstetric factors linked to stillbirth and neonatal deaths as these were not decreasing despite the Midwives Act of 1936 instituting a free midwifery service and the National Health Service Act of 1947 guaranteeing free healthcare for all. In addition to seeking to collect data on all notified births in the survey week, it collected data on all stillbirths and early neonatal deaths notified over the next 3 months. The results were used to inform improvements in maternity services in the UK.[185] The 1970 survey aimed to provide information on the current status of the maternity services in an era of increasing hospital births and early discharge post-delivery, as well as to examine social and biological characteristics of the mother in relation to neonatal morbidity.[189] These surveys were used as the baseline for important longitudinal cohort studies, the MRC National Survey of Health and Development Cohort /1946 Birth Cohort,[190] the 1958 National Child Development Study[191] and the 1970 British Cohort study.[192]

Since that time perinatal surveys have been used by various countries in different ways. France, which until very recently has had no national medical registry for monitoring the main indicators of maternal and perinatal health, has undertaken regular ‘Enquetes nationale perinatale’ in

1995, 1998, 2003, 2010 and 2016 covering all births in private and public maternity units and birth centres in 1 week in France.[193] Other countries have undertaken one-off surveys to address particular questions; for example in Israel over 3 months in 1984 to examine perinatal mortality,[194,195] in Lebanon over 4 weeks 1999-2000 to establish an overview of perinatal health and services post-conflict,[196] in Greece over 1 month in 1983 to examine distribution of, and contributors to, perinatal mortality.[197,198] Other perinatal surveys have focused on a particular geographical region, looking at perinatal mortality,[199-201] or perinatal mortality and preterm birth.[202] In Germany, a Perinatal Survey was introduced in 1975 in Munich in response to concern that the perinatal mortality rate was higher than elsewhere in Germany. It used a 100 item questionnaire relating to pregnancy, antenatal care, delivery and birth outcomes. Despite its voluntary nature it covered over 90% of all births in Munich, and was then extended region-wide and to all West Germany from 1982.[203] The system became the Perinatal Database – functioning in effect more like a detailed birth registry in Germany continuing to collect information to monitor quality of services and undertake scientific analysis of rare maternal and fetal complications.[204]

Other countries have adopted an approach using sentinel sites that are nationally representative, which can then be scaled-up to a national level as resources allow. An example of this are South Africa's Perinatal Care Surveys. The first survey in 2000 covered 73 state-hospitals and aimed to estimate perinatal mortality and its underlying causes, including avoidable factors, missed opportunities and substandard care using The Perinatal Problem Identification Programme (PIPP) approach.[205,206] In view of the identified data challenges faced it sought to reach consensus on a standard dataset for monitoring perinatal care and outcomes in South Africa. This is an ongoing process which now covers 75% of institutional births in the country, and from the outset was designed more as a data collection system than other surveys, and did not include interviews with women in its design.[207]

The World Health Organization has undertaken two multi-country perinatal surveys, however these were for research purposes and were not designed to be nationally representative. The bias towards higher-level facilities limits the generalisability of their data to inform national-level estimates.[208]

2.5.6. Surveillance

Surveillance to capture birth outcomes can be of whole populations, of pregnancies and their outcomes, or of deaths. It can range from continuous case detection, to surveillance visits up to

1 year apart. Active or passive surveillance can be used to supplement standard death registration for stillbirths in settings with weaker CRVS.

Demographic and Health surveillance sites (DHSS) use a cohort approach. Those including pregnancy surveillance seek to identify all pregnancies and the resulting outcome for both mother and baby. In settings without robust CRVS, these can be useful as a step towards full civil and vital registration.[209] DHSS vary in their set up and capture of pregnancies and perinatal events. For example, in Uganda Iganga HDSS capture of stillbirths was higher in a household survey compared to routine HDSS.[210] HDSS also have the potential to collect information on gestational age and birthweight through recall or data linkage with health facilities, although current practices are highly variable with few sites capturing reliable information on these parameters. As HDSS are not nationally representative samples, they are limited in terms of extrapolating birth outcome indicators to the national level, and may be more useful for inferring causal mechanisms and monitoring trends.[211]

Maternal and Perinatal Death Surveillance and response (MPDSR) has the potential to provide important information on maternal and perinatal mortality, as well as providing a detailed review of the causes and contributing factors, and providing an opportunity for a 'response' to address these factors. 86% of all countries worldwide now have policies for notification of all maternal deaths,[212] but full-scale national implementation of the maternal part of MPDSR is limited in many countries by failure to adequately institutionalise MPDSR, or move from facility based to whole population based systems.[213] In most settings the perinatal surveillance part is in early stages, or less well-developed. In these settings the focus for the perinatal component has been on establishing inpatient perinatal audit.[112] Whilst this can potentially be very useful in establishing causes of, and factors contributing to, perinatal deaths, it has less value in providing information on overall population prevalence of these outcomes.[214] In other MPDSR systems a subset of perinatal deaths occurring outside of a health facility may undergo a verbal autopsy to seek to understand causes and contributing factors; this can also be useful to differentiate between stillbirths and live births followed by neonatal death.

Stillbirth specific surveillance can also be undertaken at a facility level. An example of this is WHO South-East Asia region's newborn surveillance network launched in 2014. It uses a smartphone based app or web-form to capture data on birth defects, stillbirths and neonatal deaths in the Newborn and Birth Defects Database (NBBD).[215]

2.5.7. Research studies

Data on stillbirths, preterm births and low birthweight are frequently collected as part of research studies. These studies are rarely national or nationally representative, and in many

cases are not population based, thus limiting their usefulness to inform national estimates. However, due to the large data gaps in the above national systems and substantial concerns with data quality at the national level in many settings with less robust CRVS systems, data from these sources were used as data inputs for both the stillbirth and preterm birth estimates presented in the next chapters. They will be discussed in further detail there.

In summary, this chapter has reviewed the requirements for the measurement of stillbirth, preterm birth and low birthweight including definitions, indicators and measurement issues. It has also provided an overview of the data platforms where these data can be collected. The next three chapters will provide a more detailed overview of the current data availability to estimate these outcomes.

SECTION II. SYSTEMATIC ANALYSIS OF DATA AVAILABLE TO INFORM ESTIMATES OF STILLBIRTH, PRETERM BIRTH AND LOW BIRTHWEIGHT BIRTH RATES

To illustrate some of the issues raised in the previous chapters the first three chapters in the next section present in-depth case studies of data availability worldwide and estimation methods for stillbirth, preterm birth and low birthweight respectively. These chapters provide a review of available prevalence data, and the process for estimation of national, regional and global prevalence rate estimates, including data availability for potential model covariates. The final chapter in this section, Chapter 6, reviews the data gaps, both in terms of data quantity and quality and some of the cross-cutting challenges identified in the data to track these adverse birth outcomes.

Stillbirth, preterm birth and low birthweight are suitable case studies to be able to review in practice how many of the theoretical challenges presented in the previous chapter affect birth outcome data. Accurate preterm birth data require accurate gestational age assessment. Low birthweight requires accurate measurement of birthweight. Defining a stillbirth also requires accurate gestational age assessment or birthweight. These remain a large challenge in many settings. All three outcomes require assessment of vital status at birth, as the preterm birth and low birthweight definition only includes live births, and the stillbirth definition only applies to those with no signs of life at birth. In addition, all are strongly affected by health professionals, women's and societal perceptions of fetal viability and personhood. All of these outcomes have important data gaps currently and rely on estimates in many settings.

The body of work around data availability and use for estimation of preterm birth rates at a national, regional and global level was undertaken in 2011 – 2012; the comparable body of work around stillbirths was undertaken in 2014 – 2015; and for low birthweight from 2014 - 2018. Lessons learnt from the earlier estimation work were used to refine the process for data collection and estimation approaches for the later estimates.

3. Paper A - National, regional, and worldwide estimates of stillbirth rates in 2015

This chapter provides an in-depth analysis of the availability of stillbirth rate data for all countries worldwide (Objective 2). It also provides a description of the development and implementation of methods to produce national, regional and worldwide estimates of stillbirth rate, with time trends (Objective 3).

This chapter was published February 4th 2016 in The Lancet Global Health.[216] The manuscript was published under a creative commons license (CC BY-NC-ND 4.0) and the published manuscript is included in full below. The web appendix referenced in the paper is available at https://ars.els-cdn.com/content/image/1-s2.0-S2214109X15002752-mmc1.pdf. See Annex A.3. for details.

3.1. List of Figures

3.2. List of Tables

3.3. Citation

Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, Hogan D, Shiekh S, Qureshi ZU, You D, Lawn JE; Lancet Stillbirth Epidemiology Investigator Group. **National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis.** *Lancet Glob Health. 2016 Feb;4(2):e98-e108. doi: 10.1016/S2214-109X(15)00275-2.*

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	200160	**Title**	Dr
First Name(s)	Hannah		
Surname/Family Name	Blencowe		
Thesis Title	Counting the smallest: data to estimate global stillbirth, preterm birth and low birthweight rates		
Primary Supervisor	Joy E Lawn		

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

SECTION B – Paper already published

Where was the work published?	The Lancet Global Health as: Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, Hogan D, Shiekh S, Qureshi ZU, You D, Lawn JE; Lancet Stillbirth Epidemiology Investigator Group. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health. 2016 Feb;4(2):e98-e108. doi: 10.1016/S2214-109X(15)00275-2		
When was the work published?	February 2016		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

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

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was jointly responsible with Prof Joy Lawn for the conceptualisation of the paper. I designed and co-ordinated the web-based and systematic literature searches. I undertook the data quality assessment, modelling and analysis with advice from Prof Simon Cousens and Prof Joy Lawn. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors. See Annex A.1. for full details.

SECTION E

Student Signature	Dr Hannah Blencowe
Date	27th April 2019

Supervisor Signature	Professor Joy Lawn
Date	28th April 2019

National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis

Hannah Blencowe, Simon Cousens, Fiorella Bianchi Jassir, Lale Say, Doris Chou, Colin Mathers, Dan Hogan, Suhail Shiekh, Zeshan U Qureshi, Danzhen You, Joy E Lawn, for The Lancet *Stillbirth Epidemiology Investigator Group**

Summary

Background **Previous estimates have highlighted a large global burden of stillbirths, with an absence of reliable data from regions where most stillbirths occur. The Every Newborn Action Plan (ENAP) targets national stillbirth rates (SBRs) of 12 or fewer stillbirths per 1000 births by 2030. We estimate SBRs and numbers for 195 countries, including trends from 2000 to 2015.**

Methods **We collated SBR data meeting prespecified inclusion criteria from national routine or registration systems, nationally representative surveys, and other data sources identified through a systematic review, web-based searches, and consultation with stillbirth experts. We modelled SBR (≥28 weeks' gestation) for 195 countries with restricted maximum likelihood estimation with country-level random effects. Uncertainty ranges were obtained through a bootstrap approach.**

Findings **Data from 157 countries (2207 datapoints) met the inclusion criteria, a 90% increase from 2009 estimates. The estimated average global SBR in 2015 was 18·4 per 1000 births, down from 24·7 in 2000 (25·5% reduction). In 2015, an estimated 2·6 million (uncertainty range 2·4–3·0 million) babies were stillborn, giving a 19% decline in numbers since 2000 with the slowest progress in sub-Saharan Africa. 98% of all stillbirths occur in low-income and middle-income countries; 77% in south Asia and sub-Saharan Africa.**

Interpretation **Progress in reducing the large worldwide stillbirth burden remains slow and insufficient to meet national targets such as for ENAP. Stillbirths are increasingly being counted at a local level, but countries and the global community must further improve the quality and comparability of data, and ensure that this is more clearly linked to accountability processes including the Sustainable Development Goals.**

Funding **Save the Children's Saving Newborn Lives programme to The London School of Hygiene & Tropical Medicine.**

Lancet Glob Health 2016; 4: e98–108

Published Online January 18, 2016 http://dx.doi.org/10.1016/S2214-109X(15)00275-2

This online publication has been corrected. The corrected version first appeared at thelancet.com on Jan 26, 2016

See Comment page e70

*See end of paper for the group list

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Introduction

WHO first published national, regional, and worldwide estimates of stillbirths in 2011, highlighting the large global burden of stillbirths, with an estimated 2·6 million women and families affected in 2009.[1] This process also showed the dearth of reliable data in the regions where most stillbirths occur. In 2014, the Every Newborn Action Plan, a global multipartner movement to end preventable maternal and newborn deaths and stillbirths, set a target for national stillbirth rates (SBRs) of 12 or fewer stillbirths per 1000 births in all countries by 2030, accompanied by action in countries to address disparities.[2] This stillbirth target was included in response to the requests of many countries during the consultation process.[3] To achieve this target, countries will need to act to reduce preventable stillbirths and improve monitoring of SBRs.[4,5]

In this study, our objective was to estimate national, regional, and worldwide stillbirth rates and absolute numbers for 195 countries in both 2000 and 2015, to enable an assessment to be made of the extent to which SBRs have changed over time.

We sought to improve on the 2011 WHO exercise and our work previous to that[6] in terms of both the quantity of SBR data, by undertaking more extensive searches, and the quality of the data, by applying more stringent inclusion and exclusion criteria. Variation in definitions used for stillbirths affects comparability. For this exercise, we examined the effect of different definitions, and sought to adjust all input SBR data to correspond to a standard definition (≥28 weeks' gestation) before modelling.

We present our methods and results using the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) checklist. This is a new reporting checklist for worldwide health estimates that promotes transparency, including the sharing of input data and modelling code.[7]

Methods

Data inputs

For the purposes of these estimates, we defined a stillbirth as a baby born with no signs of life at 28 weeks' gestation or more (third trimester; panel). When

For the **study input data modelling codes** see http://dx.doi.org/10.17037/DATA.25

Research in context

Evidence before this study

Previous global estimates for stillbirths have been undertaken, of which the most recent was for 2009 by WHO.[1] Stillbirths were not tracked under the Millennium Development Goals, and progress in reducing stillbirths is slower than that for maternal or neonatal deaths. In 2014, the Every Newborn Action Plan set a target of a national stillbirth rate of 12 or fewer stillbirths per 1000 births by 2030 and to address within-country disparities in all countries. However, stillbirths are still not included in global burden estimates or global goals.

Added value of this study

Through systematic searches (national statistical office, ministry of health and nationally representative household survey websites, and published literature) and consultation with a group of stillbirth investigators to identify further unpublished stillbirth data, we compiled the largest stillbirth rate dataset so far. The final dataset included 2207 datapoints from 157 countries, almost doubled from 1149 datapoints from 135 countries in the previous estimation exercise. This increase was predominantly due to increased data availability from national routine data sources in middle-income countries. We also improved the consistency of the stillbirth definitions, and strengthened the criteria for quality of data. These national stillbirth rates estimates are for 195 countries for 2015 with time-trends from 2000.

Implications of all the available evidence

We estimate that 2·6 million (uncertainty range 2·4–3·0 million) babies were stillborn in 2015, affecting women and their families in all settings. 98% were in low-income and middle-income countries, of which over two-thirds were in sub-Saharan Africa and southern Asia. Data from 39 countries with complete time series shows slow progress in reducing this burden. Nearly half (45%) of the data available is for the 2% of stillbirths from developed regions, and more must be done to close this data gap and improve data quality and comparability in all settings. Stillbirths are increasingly being counted at a local level; however, absence of global goals and reporting mechanisms continues to restrict their visibility, especially in the countries with the greatest disease burden. Unless this changes, stillbirths are likely to remain invisible beyond 2015.

presenting results by region, we used the Millennium Development Goal (MDG) regions (appendix pp 3–4).

See Online for appendix

For the **DHIS2** see https://www.dhis2.org/

The database for the previous WHO stillbirth estimates[1] included 1149 datapoints covering the period 1995–2009, and this was updated with data covering the whole period from 1990 to 2015. SBR data were identified from multiple sources (figure 1) including national routine data defined as data from national systems such as civil registration and vital statistics (CRVS) systems, national health management information systems (HMIS), and birth registries; nationally representative surveys including demographic and health surveys (DHS) and reproductive health surveys (RHS); and subnational data sources including population-based studies (eg, from demographic surveillance sites or research studies), and facility-based data.

To identify routine national data, we searched the websites of the national statistical office and ministry of health of all countries. For countries where routine CRVS systems are less well developed (those outside the MDG Developed region), we identified additional sources of data for SBRs. These included compiling all DHS and RHS reports from the DHS programme website, and undertaking a systematic search of the published literature (appendix pp 5–7). Searches included terms relating to the following key concepts: "stillbirth", "stillbirth timing", "rate/prevalence", and "low and middle income (LMIC) countries". MESH headings were used where available. Because SBR data can be collected in other programme and study settings, but not reported via the above mechanisms, a Stillbirth Epidemiology Investigator Group was convened to identify further unpublished stillbirth rate data, with calls for data distributed via relevant groups and list serves, and investigators from individual studies approached (appendix p 8). An effort was made to include HMIS data from the District Health Information Systems 2 platform, with emails sent to national contact persons.

For more on the **DHS programme** see http://www.dhsprogram.com

WHO's country consultation process was used to confirm, for every country, the validity of the data from that country included as inputs in the estimation process, and to ask for any additional data. Preliminary estimates were also circulated to WHO member states for review. New or updated country-year observations (282 from 25 countries) were added through the consultation process in July and August, 2015—mainly more recent data, or resubmitted data using the 28 week or more definition.

We assessed all reports that included more than 50 total births with a midpoint of data collection of 1990 or later and in which an SBR was given or could be calculated. Although we aimed to estimate SBRs using the 28 week or more definition, in the input database, we included SBR data using other definitions. Data reports from specialised services such as diabetes, hypertension, or growth restriction clinics or on specific subpopulations or ethnic groups were excluded as non-generalisable. We classified health facility data as likely to have minimum bias, where the facility covered more than 90% of births in the population. We excluded population-based prospective studies with rates of loss to follow-up of more than 20% of pregnant women. Similar to the approach taken for the previous stillbirth estimates, data from health facilities with potential for greater bias were included and identified using a dummy variable.[1]

Premodelling adjustments

Before applying exclusion (implausibility) criteria and modelling, data inputs with a non-standard stillbirth

definition were adjusted to correspond with the 28 week or more definition. For 15 countries in the MDG Developed region with high quality CRVS data, where stillbirth rates based on more than one definition were available for a given year, a pooled estimate of the adjustment factor was calculated using all years with more than one definition from that country, and the stillbirth rates were adjusted for all years reporting only an alternative definition using this adjustment factor. For 34 countries in the MDG Developed region without such data, the rates were adjusted on the basis of meta-analyses of data from countries in the same region. For example, based on a meta-analysis of 139 country-years of data, where the 28 week or more rate was 32% lower than the 22 week or more rate, a data source reporting a stillbirth rate of 6·2 using the 22 week or more definition was adjusted as follows: $6{\cdot}2\times0{\cdot}68=4{\cdot}2$ stillbirths at 28 weeks or more per 1000 total births (panel; appendix pp 72–75). For countries in other regions (n=146), data were adjusted based on a meta-analysis of data from the WHO global survey on maternal and perinatal health and the WHO multicountry survey on maternal and newborn health, which included more than 0·5 million births (appendix pp 75–76).[11,12] Data were not available for gestational age in these facility-based surveys, so the 500 g and 1000 g cutoffs were used to approximate 22 weeks and 28 weeks, respectively. Although our new meta-analysis of routine data from high-income settings shows that use of a 1000 g cutoff instead of a 28-week based one underestimates the gestational age rate by around 15% (panel), this effect could be less in LMICs, where a greater proportion of stillbirths are intrapartum at term without fetal growth restriction, owing to lower access to high quality intrapartum care. However, it was not possible to quantify the degree of underestimation, and currently it is assumed that birthweight and gestational age thresholds are equivalent for stillbirths in these regions; this assumption is likely to underestimate the true burden of stillbirths at 28 weeks or more.

Additionally, for countries with data for several years but small birth cohorts and hence relatively large annual variations in SBRs (coefficients of variation >10%; Cook Islands, Andorra, Iceland, Luxembourg, and Malta), data were smoothed using a moving average (appendix p 72).

Exclusion criteria

Underascertainment of stillbirths is recognised as a common problem across data sources, especially when using definitions with cutoffs close to the threshold of newborn viability. For example, fetal deaths are commonly coded as miscarriages when the health provider assesses the baby to be below the threshold of viability. While in many high-income countries this is most likely to affect fetal deaths at 22 weeks' and 23 weeks' gestation, in lower resource settings, without neonatal intensive care, fetal deaths up to 30 weeks' gestation might not be included in stillbirth figures.

Panel: Definition of stillbirth

A fetal death or stillbirth is defined as a baby born with no signs of life after a given threshold. For international comparison, WHO defines a stillbirth according to the 10th edition of the International Classification of Diseases (ICD-10) definition of late fetal death. ICD-10, which was developed several decades ago when gestational age assessment was not standard, gives birthweight as the first preference in the definition, with gestational age second. ICD-10[8] defines late fetal death as a death at a birthweight of 1000 g or more, if the birthweight is not available, a gestational age of 28 weeks or more or a length of 35 cm or more. The corresponding values are 500 g, 22 weeks, or 25 cm or more for early fetal death, and 500 g, 22 weeks, or 25 cm or more for miscarriage.

However, the birthweight and gestational age thresholds do not give equivalent results. This problem is compounded by the frequent occurrence of fetal growth restriction, associated with an adverse intrauterine environment before fetal death, and hence a birthweight-based cutoff will give a lower stillbirth rate than one based on gestational age. This difference is most marked the earlier the gestational age: in our new meta-analyses, stillbirth rates across high-income countries were 15% (95% CI 13–17) lower using a 1000 g or more definition compared with 28 weeks or more, whereas stillbirth rates in the USA are 40% lower with the 500 g or more definition compared with 22 weeks or more.

A gestational age threshold would be most appropriate because it is a better predictor of maturity and hence viability than is birthweight, with many fetuses at risk of stillbirth or preterm birth having preceding fetal growth restriction.[9] Information about gestational age is also more widely available than for birthweight for many stillbirths, with early ultrasound dating of pregnancies now standard of care in high-income and middle-income countries, and its use is increasing in low-income countries. Hence, most high-income and middle-income national routine data now include robust gestational age data. Even in settings where gestational age is mainly based on last menstrual period, which is less reliable than early ultrasound dating, it is more commonly available than birthweight, especially for those born at home where it is frequently seen as not culturally acceptable to weigh a stillborn baby.[10]

Therefore, we use a 28 week or more definition. Where possible, data were abstracted or requested according to this definition. Data with alternative definitions were adjusted to the 28 week or more definition (appendix pp 72–75).

We excluded datapoints likely to reflect poor case ascertainment based on a conservative implausibility criterion for the ratio SBR:neonatal mortality rate (NMR).[13] The median ratio of SBRs (≥28 weeks) to NMRs from the developed region was 0·9 (IQR 0·65–1·15). Ratios less than 0·33 (first centile) are likely to represent substantial under-recording of stillbirths in comparison with neonatal deaths. Generally, stillbirths are more poorly recorded than deaths of liveborn neonates, which are themselves under-recorded in many settings.[5,13] Because ratios within the normal range will be found where there is under-reporting of both stillbirths and neonatal deaths in a given data source—eg, in some household surveys—we calculated the ratio of the reported SBR (≥28 weeks) relative to the national estimate of NMR for the same year, and excluded datapoints with a ratio of less than 0·33 (n=116). No upper limit for the ratio was set. Although some misclassification of neonatal deaths as stillbirths can occur, especially in lower resource settings, this effect is

For the **UN Child Mortality Estimates** see http://www.childmortality.org/

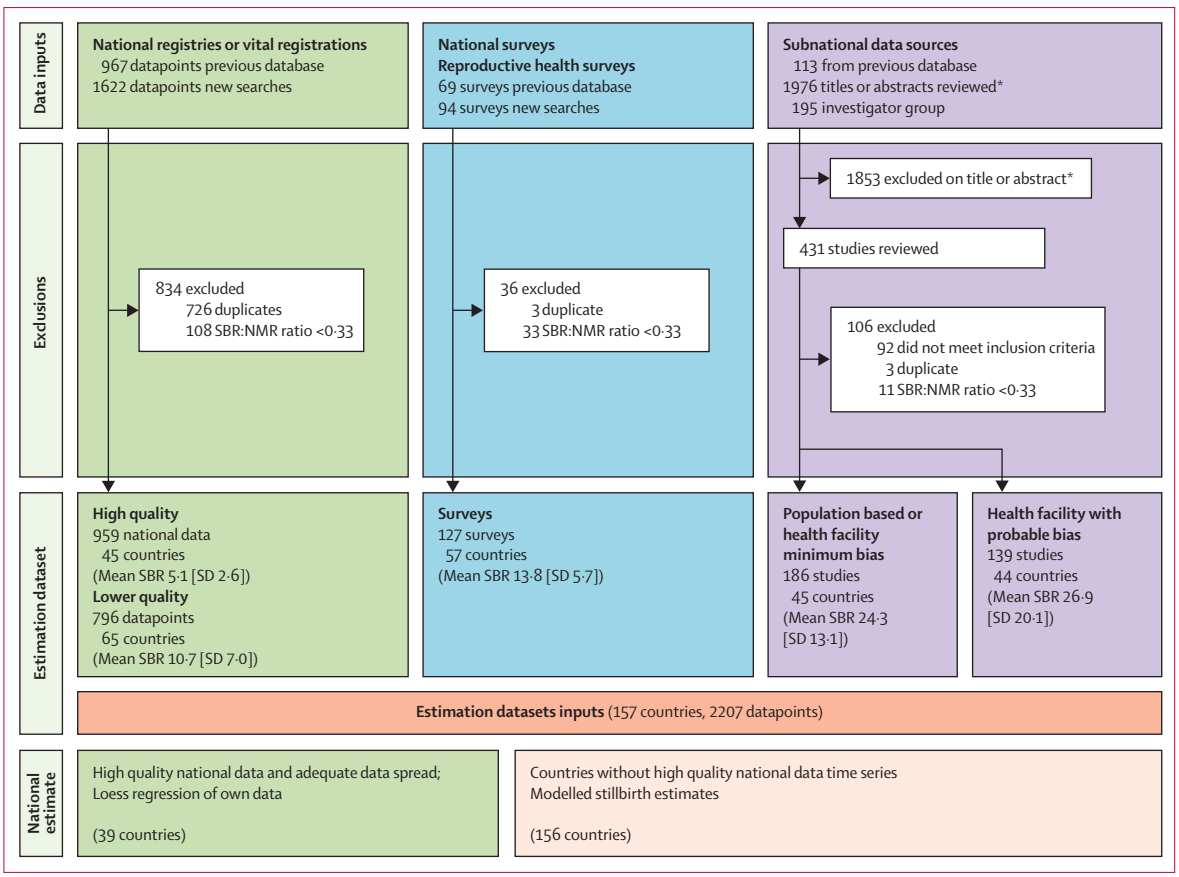

Figure 1: **Flow diagram for input data**
*See appendix p 7 for details. †Includes those with more than one definition for a given country year (n=432).

relatively small on the SBR:NMR ratio,[14] and evidence from high-income countries shows increasing SBR:NMR ratios as NMRs reduce below three per 1000 livebirths (appendix pp 8–9). Six datapoints had a ratio of more than 3·0, but these were small, high-income countries reporting very low NMRs in the given year, and the SBRs from these were in keeping with other years' estimates from these countries.

Classification of stillbirth data type

Included data were categorised into five classes, which were determined a priori, based on data type and quality. A dummy variable was created based on these five types (figure 1): national routine information systems, further categorised as high quality or lower quality; nationally representative retrospective household surveys; subnational population-based data—ie, prospective population-based studies or health-facility-based data with minimum bias (covering >90% of births in the population); and other subnational data—ie, other health-facility-based data with possible sources of bias.

No previously established reliable quality criteria for assessing the capture of stillbirths were identified. Hence, in this exercise, data from national routine information systems were categorised as being of high quality if they met the following criteria. First, if a functioning CRVS system was well established before 2000. Consistent with previous stillbirth estimates,[1] we used good vital registration for purposes of maternal mortality estimation, which included the requirement of a functioning CRVS system from 1996, including the ability to capture high quality information about maternal and perinatal outcomes.[15] Second, if the SBR (adjusted to 28 week definition) to national estimated NMR ratio was greater than 0·5 for all years in the time series. Third, if, for the given year, the country had a greater than 85% female child mortality capture[16] (a marker of CRVS system strength for capture of child outcomes; appendix pp 67–68).

For countries assessed as having high quality CRVS, we assumed that other routinely collected national data—eg, birth registry or HMIS data—would also be of high quality. All other country-years of national routine data not fulfilling all the above criteria were considered to be of lower quality (appendix p 69).

Model fitting

We modelled the natural logarithm of the SBR (≥28 weeks' gestation) as the outcome variable using

restricted maximum likelihood estimation and included a country-level random effect, using the same approach as the previous estimates.[1] We investigated multiple predictor variables with an established association with SBR, and with estimates available for all countries for the period 2000–15.

Potential predictors were selected based on the plausibility of an association with the SBR. These included distal determinants such as socioeconomic factors, and more proximal demographic and biomedical factors, markers of perinatal outcome and access to health care. All potential predictors with time series data or estimates available by country for 2000–15 were included in the model fitting process (appendix pp 76–77). Predictors were retained when the direction of the coefficient was biologically plausible. We sought to maximise the predictive power of the model, while avoiding overfitting. We removed one predictor at a time from the model, commencing with the predictor with the largest Bayesian information criterion (BIC) on univariate analysis, and refitted the model. If the model was improved by removing this predictor (lower BIC compared with the model containing the predictor), the predictor was dropped from the model. If the BIC was higher, the predictor was retained. We cycled through all the predictors once. For the 157 countries contributing data to the input dataset, the best linear prediction of the country-specific random effect was obtained.

The final model included: (natural log) of NMR, (natural log) low birthweight rate, (natural log) gross national income, mean years of female education, coverage of four antenatal care visits, the stillbirth data type (see above), and region (based on condensed Millennium Development Goal regions—Developed, South Asia and sub-Saharan Africa, and Other regions) (appendix p 77). Model performance was assessed with diagnostic plots (appendix pp 78–79).

Uncertainty estimation

Uncertainty estimates were generated with a bootstrap approach. For countries with high quality vital registration data for stillbirths, we assumed that the SE of the reported number of stillbirths was the square root of the reported number—ie, that the number of stillbirths was Poisson distributed (appendix p 99).

Generation of estimated national stillbirth rates and absolute numbers

For all countries the SBR was calculated as the number of stillbirths per 1000 total births, the total births including both livebirths and stillbirths ≥28 weeks.

Of the 45 countries classified as having high quality vital registration data for SBRs, 39 had complete time series data (earliest year of data available was before 2005, the latest year after 2010, and data were available for at least half of all years). For these countries, the country's own reported rates, adjusted where necessary

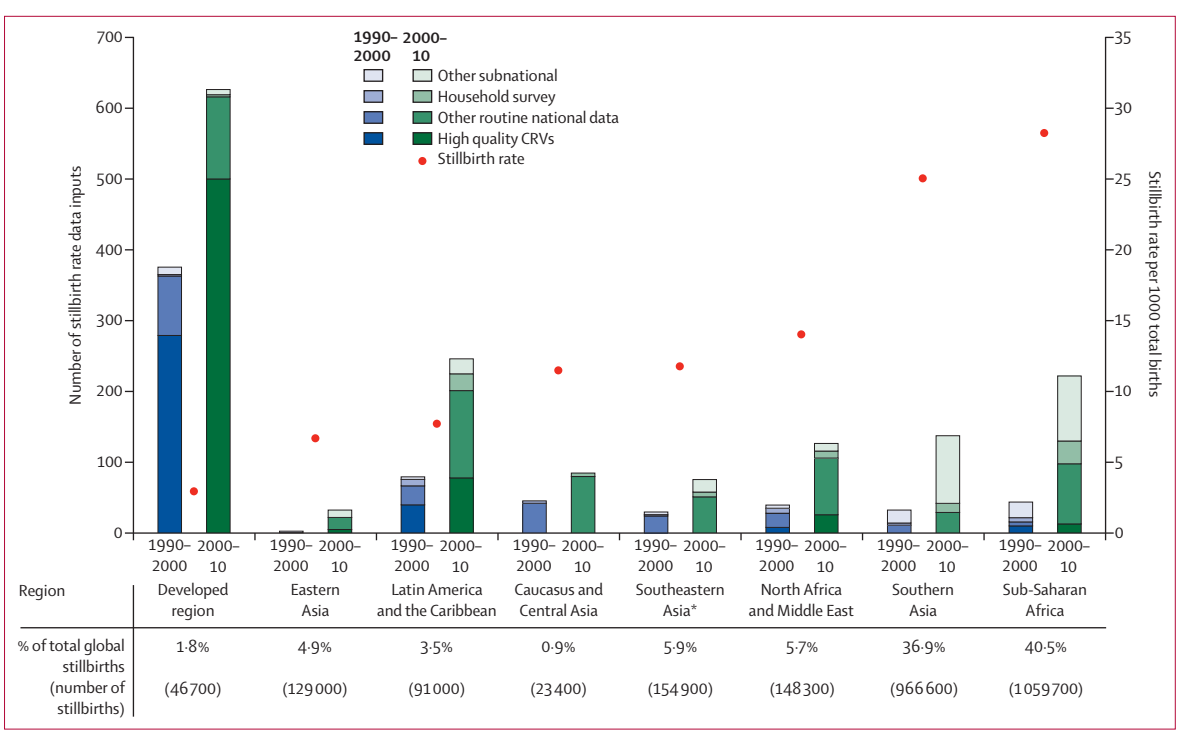

Figure 2: **Availability and type of stillbirth data by region around 1990–2000 and 2000–10**
See appendix p 67 for details. CRVS=civil registration and vital statistics.

(see above), were smoothed with loess regression to produce estimated trends for 2000–15 (figure 1; appendix pp 80–98). For all other countries, estimation and projection of SBRs was undertaken with the regression model as detailed above. For countries with data in the input dataset, the best linear unbiased prediction of the country-specific effect was included in the SBR prediction. For countries with no data, the random effect was assumed to be zero. The high quality national data (CRVS or birth registry) was used as the gold standard for prediction purposes for all countries. Livebirth estimates from the World Population Prospects, 2015 revision,[17] were used to estimate the absolute number of stillbirths using the following formula: number of stillbirths = livebirths × SBR / (1 − SBR).

Role of the funding source

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

	Number of data inputs	Stillbirth rate (≥28 weeks)	SBR:NMR ratio
Good quality CVRS/ birth registry data	959	4·3 (3·3–6·2)	1·03 (0·80–1·30)
Poor quality CVRS/HMIS data	796	8·8 (5·6–13·8)	0·74 (0·52–1·05)
Population based (retrospective survey)	127	13·5 (9·7–16·6)	0·60 (0·47–0·73)
Population based or health facility, minimum bias	186	23·6 (15·9–31·7)	0·77 (0·61–1·00)
Health facility, likely bias	139	21·1 (10·8–36·0)	0·99 (0·68–1·38)

Data are n or median (IQR). See appendix pp 7–12 for details. SBR=stillbirth rate. NMR=neonatal mortality rate. CRVS=civil registration and vital statistics. HMIS=health management information systems.

Table 1: **Stillbirth rate data by type and median rate, showing quality based on ratio of stillbirth rate to neonatal mortality rate**

	Model coefficient (95% CI)
Neonatal mortality rate*	0·33 (0·29 to 0·38)
Low birthweight*	0·01 (0·01 to 0·02)
Gross national income*	−0·13 (−0·07 to −0·19)
Mean years of female education	−0·03 (−0·02 to −0·05)
Antenatal care (4 visits)	−0·004 (−0·001 to −0·006)
Region	
Developed	..
Sub-Saharan Africa/south Asia	0·33 (0·21 to 0·46)
All other regions	0·32 (0·16 to 0·49)
Data type	
High quality CRVS	..
Poor quality CRVS/HMIS data	−0·22 (−0·14 to −0·29)
Population-based (retrospective survey)	−0·36 (−0·27 to −0·46)
Population-based or health-facility, minimum bias	−0·11 (−0·02 to −0·20)
Health facility, likely bias	0·14 (0·04 to 0·23)

See appendix pp 76–77 for details. CRVS=civil registration and vital statistics. HMIS=health management information systems. *Natural log.

Table 2: **Model coefficients for included predictor variables of stillbirth rates**

Results

The final SBR input dataset included 2207 datapoints from 157 countries (figure 1). Overall, we excluded 152 (6%) datapoints with an SBR:NMR less than 0·33. National surveys were more likely to have data excluded for this reason (33/160 [21%]) than were national CRVS or registry data (108/1863 [6%]) or subnational data sources (11/327 [3%]).

80% more datapoints were included from all regions than in previous estimates (appendix pp 67–68). Compared with the previous exercise, the greatest relative increases in datapoints were in sub-Saharan Africa (177%), southern Asia (190%), and eastern Asia (414%). An increase in subnational datapoints is seen; however, from a low baseline, large relative increases in routine national data availability have been seen in both sub-Saharan Africa and southern Asia regions (293% and 233% increase, respectively), with 37% of countries in sub-Saharan Africa and 44% of those in southern Asia now contributing national routine data. Data increases in Latin America and north Africa or west Asia are largely due to increases in data from routine national data sources since 2000 (figure 2). Nevertheless, no data were located for 38 countries, and only subnational data were available for nine sub-Saharan African and south Asian countries.

Important differences in the types of data available from different regions remain. More than 70% of countries in the developed, north Africa, west Asia, and Caucasus and central Asia regions have national data meeting the inclusion criteria for both 2000 and 2010, compared with around a quarter of countries in sub-Saharan Africa and southern and southeastern Asia in 2000. There is some evidence of improvement in these lower-income regions by 2010. However, for many of the large countries in these regions, the national data are from retrospective household surveys, which have major limitations for SBR capture, and further research is required to address these (figure 2; table 1).[5]

Table 2 shows the estimated coefficients for the predictors retained in the final model. Each unit increase in natural log NMR is associated with a 0·33 unit increase in natural log SBR. Unit increases in natural log low birthweight are associated with a 0·014 unit increase in natural log SBR, whereas a unit increase in natural log gross national income, coverage of four antenatal care visits, and female education are associated with decreases in natural log SBR (by 0·13, 0·004, and 0·03 units, respectively). Compared with high quality vital registration, facility-based data that are subject to bias are estimated to overestimate the SBR, whereas all other data sources tend to underestimate the SBR. The model seems to fit the data well overall (R^2=0·81), and both the estimates of the country-specific random effects

	2000		2015		Annual rate of reduction in stillbirth rate 2000–15
	Stillbirth rate per 1000 total births (uncertainty range)	Number of stillbirths (uncertainty range)	Stillbirth rate per 1000 total births (uncertainty range)	Number of stillbirths (uncertainty range)	
Developed region	4·5 (4·4–4·6)	59 000 (58 000–61 000)	3·4 (3·4–3·5)	47 000 (46 000–48 000)	1·8
Southern Asia	35·5 (31·3–41·2)	1 443 000 (1 266 000–1 684 000)	25·5 (22·5–29·1)	967 000 (847 000–1 104 000)	2·2
Caucasus and Central Asia	16·8 (13·9–23·6)	23 000 (19 000–33 000)	11·9 (9·8–15·6)	23 000 (19 000–31 000)	2·3
Eastern Asia	14·3 (10·6–19·6)	240 000 (177 000–331 000)	7·2 (5·6–9·7)	129 000 (100 000–175 000)	4·5
Latin America	11·3 (10·3–12·8)	135 000 (123 000–153 000)	8·2 (7·5–9·2)	91 000 (83 000–103 000)	2·1
North Africa and Middle East	19·9 (17·7–23·6)	156 000 (139 000–185 000)	14·5 (12·9–17·5)	148 000 (131 000–180 000)	2·1
Southeastern Asia	17·0 (14·6–21·5)	194 000 (166 000–246 000)	12·2 (10·7–14·6)	155 000 (135 000–186 000)	2·2
Sub-Saharan Africa	35·6 (31·4–42·2)	1 000 000 (879 000–1 194 000)	28·7 (25·1–34·2)	1 060 000 (923 000–1 271 000)	1·4
Worldwide	24·7 (22·4–28·4)	3 250 000 (2 931 000–3 740 000)	18·4 (16·6–21·0)	2 620 000 (2 359 000–2 984 000)	2·0

See appendix p 3 for details.

Table 3: **Estimated stillbirth rates and number of stillbirths for 2000 and 2015, by Millennium Development Goal region**

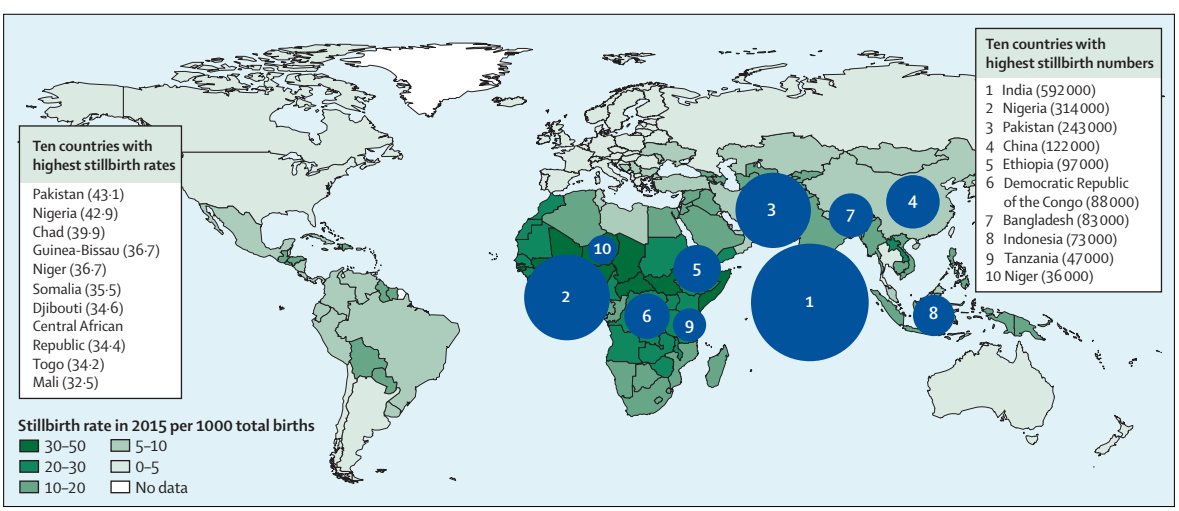

Figure 3: **Variation between countries in stillbirth rates in 2015 showing the ten countries with the highest rates, and those with the largest numbers**
See appendix pp 100–04 for details.

(SD 0·29) and the residuals for the individual datapoints included (SD 0·23) seem to be approximately normally distributed (appendix pp 78–79).

We estimate that the global SBR in 2015 was 18·4 per 1000 births (uncertainty range 16·6–21·0), down from 24·7 in 2000 (22·4–28·4; table 3). This represents an estimated 25·5% decline in the global SBR over this period. Although the uncertainty around this estimated reduction is sizeable (uncertainty range 6·6–41·5%), some decline in stillbirth rate over this time period is likely. The absolute number of stillbirths is estimated to have declined from 3·25 million in 2000 (uncertainty range 2·93–3·74 million) to 2·62 million in 2015 (2·36–2·98 million), a 19·4% decline (–1·8 to 36·9%). The highest burden, both in terms of stillbirth rates and numbers of stillbirths, continues to be found in sub-Saharan Africa and southern Asian regions: 98% of all stillbirths occur in low-income and middle-income countries; 77% in south Asia and sub-Saharan Africa (table 3; figure 3). The estimated rate of reduction in stillbirth rates remains slowest in sub-Saharan Africa (1·4%), despite high baseline stillbirth rates. At a national level for 2015, six countries in western Europe were predicted to have SBRs of less than two per 1000 total births, whereas Pakistan and 13 countries in sub-Saharan Africa had estimated stillbirth rates of more than 30 per 1000 total births, with relatively slow progress since 2000 (appendix pp 100–05).

Our global and regional stillbirth rate estimates are within the uncertainty bounds of those from the last estimation round. Our current estimate of the global

stillbirth rate in 2009 is 20·3 (uncertainty range 18·4–23·0), compared with 18·9 (15·2–27·3) in the previous estimates. Of note, these two sets of estimates are not directly comparable. In this study, we attempted to estimate stillbirth rates using the 28 week or more definition, which would be expected to result in higher rates than in estimates based mainly on birthweight from the previous exercise. Changes for individual countries are mainly those for which new data have become available (appendix pp 8–67).

Discussion

Our estimates suggest that 2·6 million (2·4–3·0 million) babies were stillborn at 28 weeks or more in 2015. This represents a large burden for women, families, communities, and health-care providers.[18] Progress in reducing stillbirth rates is slower than that required to meet targets set to end preventable stillbirths,[3] and considerably slower than for maternal mortality reduction and for child mortality reduction, especially after the first month of life.[19] Despite this large burden, stillbirths remain barely visible on the global policy agenda.[20]

These new estimates are based on 80% more national datapoints than our previous estimates, with more such datapoints in all regions—notably from south and east Asia and sub-Saharan Africa (appendix pp 67–68). National-level data, from routine national data sources or nationally representative surveys, were available for more than three-quarters of countries in most regions, apart from sub-Saharan Africa (61% countries with national data) and southeastern Asia (32% of countries). However, there still remains huge variation in data availability and quality, especially over time, to enable improved tracking of stillbirth rate trends. Despite some progress, almost half (45%) of all datapoints are from the developed region, which accounts for fewer than 2% of the world's stillbirths, with only 17% from sub-Saharan Africa and south Asia, which account for 77% of stillbirths and where the stillbirth rate is ten-fold higher (figure 2).

Although we tested a wider range of potential predictors of stillbirth in this exercise, the final model was broadly similar to that used in the last exercise. Of the predictors retained in the model, low birthweight can be secondary to both fetal growth restriction and to preterm birth. Both fetal growth restriction and preterm birth are strongly associated with placental dysfunction and subsequent poor fetal health, which carry increased risk of both antepartum stillbirth, and, for a compromised fetus who handles the labour process poorly, intrapartum stillbirth. Of the other predictors, antenatal care coverage, neonatal mortality, and gross national income are associated with access to health-care services during pregnancy and at the time of birth. Stillbirth rates are highly sensitive to access to timely high quality antenatal and intrapartum monitoring and care;[19] however, the available indicators for these capture only coverage, and not effective coverage or the quality of these interventions. Women's empowerment plays an important part in reducing stillbirths, because women are able to maximise their prepregnancy health, access family planning enabling them to plan the timing of their pregnancies when desired, and demand and engage in high-quality antenatal and intrapartum care.[21] Our model includes mean years of maternal education, which might capture some of the variation in women's empowerment across settings.

Our estimates represent third trimester stillbirths and hence undercount the true burden if earlier fetal deaths were included. In high-income settings around half of fetal deaths at 20 weeks or more occur before 28 weeks' gestational age.[22,23] Further research is required to quantify the effect of including all fetal deaths of 20 weeks or more across low-income and middle-income settings. Stillbirth capture is lower around the threshold of viability. It is plausible therefore that in settings without neonatal intensive care, with near-universal neonatal mortality among babies born at less than 28 weeks, that these babies would be under-captured in statistics.

We sought to identify national routine data of the highest quality and use this as the gold standard for prediction purposes. No guidelines exist on the optimum classification of quality of stillbirth rate data from national routine sources. We sought to apply criteria consistent with previous estimation exercises; however, we were constrained by the availability of routine data sources to assess quality—notably reporting by gestational age—and further research is required to optimise these parameters. As in previous exercises, the results of our model suggest that population-based data sources outside of the developed regions consistently under-report SBRs compared with high quality routine national data systems, and have much wider uncertainty (table 1). For countries without high quality CRVS time series data, the estimated trends are mainly driven by covariate data, which might not fully capture any changes in stillbirth rates over the same time period.

A major limitation is the low quality of some of the data available. We excluded 152 so-called implausible datapoints based on a simple assessment of the SBR:NMR ratio. Of included datapoints, the median ratio of SBR:NMR in DHS/RHS was 0·6 (IQR 0·47–0·73) compared with 1·03 (0·80–1·30) for higher quality CRVS (table 1)]. More research regarding the SBR:NMR ratio, and other markers of quality—eg, markers of birth outcome capture measured around the threshold of viability where under-reporting is more common,[24] the use of intrapartum or antepartum stillbirth ratios and birthweight, or gestational age distributions in stillbirths—will be important to ensure that increases in data quantity can also be better assessed for quality.

Progress has recently been made in estimation of neonatal mortality rate, which shifted from intermittent estimates up to a decade apart to annual UN national estimates, with improvements in modelling and high visibility in UNICEF reports alongside child mortality, in

	High-income countries	Middle- income countries	Low-income countries (mainly sub-Saharan Africa and South Asia)
Data platforms	Vital registration—full coverage National perinatal and maternal mortality audit and strong Health Information Systems	Vital registration and HMIS—high coverage, quality may be variable Audit may not be full coverage	Limited vital registration 5 yearly national household surveys HMIS—variable coverage and quality 84% of global neonatal deaths and 81% of stillbirths
Counting all livebirths	Consistent counting of all livebirths regardless of gestation, noting if singleton or multiple birth		
Comparable definitions to count stillbirths	All countries to report stillbirths ≥28 weeks' gestation definition for international comparison and intrapartum stillbirth rate for same stillbirth definition (we propose a shift to gestational age as basis for stillbirth definition)		
	Record all stillbirths from 22 weeks and 28 weeks and birthweight (whilst collecting by other national definition for stillbirth if required—eg, 20 weeks in USA, Australia, New Zealand)		Prioritise collection of representative data for ≥28 week stillbirths and intrapartum stillbirths Promote standardised clinical records in facilities and strengthen facility recording and reporting mechanisms
Categorising small babies (weight and gestational age)	All babies (live and stillbirths) to be weighed at birth and recorded on birth and death certificates, whilst also improving and recording gestational age		
	Gestational age to be assessed using routine high-quality early pregnancy ultrasound and recorded on birth and death certificates Track the % of births that are reported <28 weeks (noting that if under 3% of preterm births are <28 weeks the system may be underrecording preterm births)		Gestational age to be assessed in all babies using simplified clinical examination or last menstrual period where early pregnancy ultrasound is not available Improved technology and low-cost assessment tools required to increase reliability
Collecting more detailed data on equity and improve linkage of data to action	Vital registration using death certificates which include birthweight and gestational age and maternal conditions Health facility surveillance with detailed dataset Cross-link vital registration and health facility databases to maximise capture Analyse to track and target disparities		Ensure that large-scale retrospective household surveys include more reliable measure of stillbirth (eg, pregnancy history as opposed to livebirth history) Consider including stillbirth data in middle-income countries surveys Consider developing or enhancing sentinel surveillance sites for pregnancy, child, and other health outcomes (prospective), with a focus on enhancing national representativeness and coverage of the poorest Improve vital registration systems and include stillbirths Use death certificates which include birthweight and gestational age and associated maternal conditions Track urban/rural and other key disparities
	Invest in making the data accessible (eg, online) and in communication approaches (eg, score cards and infographics)		
Comparable cause of death categories and linked to risks including maternal	Consensus on a minimum dataset to be collected on all stillbirths, neonatal deaths with a limited number of programmatically relevant, causal categories which are linked to ICD codes and that can be assigned using verbal autopsy, but can be further expanded in settings where detailed clinical data and diagnostics are available Include a direct fetal or neonatal causal group and cross-tabulate with associated maternal conditions[28]		

Adapted from the *Lancet* Every Newborn series analysis (appendix p 76),[3] following WHO technical consultation on newborn health indicators and the findings of the *Lancet* Ending preventable stillbirths Series.[19-21,29]

Table 4: **Potential considerations in improving the measurement of stillbirths**

part driven by the MDG 4 target (appendix p 208).[25,26] This should also be possible for stillbirths, but will require increased leadership and accountability for the data.

Improving measurement of stillbirths must occur alongside improvements in recording of all birth outcomes for mothers and their babies. The limitations of global estimates have been highlighted,[27] and efforts to support systems working towards high-quality reported data are sorely needed. Table 4 highlights some of the factors to be considered when seeking to improve the quality and availability of SBR data. Further recommendations regarding other aspects of stillbirth data, such as classification systems, are outlined in the *Lancet* Ending preventable stillbirths Series.[19] SBR data are collected and collated through death certificate data or routine hospital data—eg, birth registries, perinatal death surveillance, or hospital management information systems, linked to CRVS systems—in most high-income and many middle-income countries; however, inconsistent stillbirth definition makes comparisons of SBR data between countries and over time challenging. This could be rapidly remedied by consistent use of a gestational age threshold (≥22 and ≥28 weeks).

However, most stillbirths occur in settings without strong CRVS and routine data systems. As these systems develop, priorities should include ensuring that all facility births, including stillbirths, are recorded and collated in routine health information systems, linked to CRVS and made available in the public domain. The current expansion of DHIS2 provides a platform for this, and could rapidly increase the quantity of SBR data available. Integration of perinatal deaths into maternal death surveillance and response where available is another potential source of improving data availability and of facilitating data-based action at a local level. All facility births should also be registered, including details on vital status, gestational age, and birthweight. To achieve this, further work is required to improve both

For the **WHO indicators** see http://www.who.int/maternal_child_adolescent/documents/newborn-health-indicators/en/

birthweight measurement and the accuracy of gestational age assessment. Assessment of gestational age is a crucial metric to enable improved capture of birth outcomes. Currently, assessments are restricted by the methods used, especially in settings where routine first trimester ultrasound dating is not widespread.[30–32] Possible approaches to improve gestational age could include improving recall of last menstrual period, biomarkers, ultrasound assessment of gestational age after the first trimester, and improved algorithms to enable a best gestational age estimate.[30,33] At a minimum, death records should include the time of death (antepartum, intrapartum, or age at neonatal death). Currently, time of death is poorly assessed and recorded, but should be possible for all facility births.[3,13,34,35]

For the 45 million births occurring outside facilities, most without a skilled attendant, household surveys are the largest source of population-based SBR data. However, the capture of stillbirths in these surveys remains mainly low quality. Recent evidence has highlighted the stigma and taboos around stillbirths that persist in many cultures, which might affect a woman's or family member's response to a survey question.[18,36,37] Despite being listed as a top priority to improve the SBR data inputs in 2011,[5] no research has yet been undertaken to compare pregnancy and livebirth history modules in terms of accuracy, time load, and relative costs, or to investigate the process of stillbirth data collection in surveys, including standard operating procedures for interviewers for this potentially sensitive information, especially where interviewers are male. Such research is urgently needed.[38]

Our estimates, even given the uncertainty in high-burden countries, indicate a large number of stillbirths, and little progress in reducing them. As the Sustainable Development Goal (SDG) era begins, stillbirths have gained some visibility. Despite no SDG target,[21] the Every Newborn Action Plan included a national target[2] and the WHO Global Reference List of 100 Core Health Indicators lists SBR.[39] Increasingly, stillbirths are routinely reported in national data and, especially in low-income and middle-income countries, there is an increase in population-based SBR data.

We welcome these changes. However, to ensure continued and increased momentum, as well as more and better data, leadership is required.[1,35] The high burden alone has been insufficient to drive appropriate action. More voice must be given to affected families, especially women. The leadership gap must also be addressed to ensure the gains in women's and children's health are accompanied by comparable reductions in stillbirths, especially in high-burden countries where most stillbirths could be prevented with known, low-cost, and effective interventions.

Contributors

JEL contributed to overall coordination. HB contributed to overall coordination, collating of data sources, and model fitting and analysis. SC provided overall statistical advice. ZUQ undertook the systematic review of published studies searches and abstraction. SS contributed to registry data review. FBJ contributed to data analysis and figures. CM, DH, and DY provided input into the overall estimation process. CM and DH coordinated the WHO country consultation. All the authors reviewed and provided input to the manuscript. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

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Declarations of interests

We declare no competing interests.

Acknowledgments

HB and JEL were funded by the Save the Children's Saving Newborn Lives programme. We are grateful to the staff of the General Bureau of Statistics of Suriname, Malaysian National Statistical Office, Central Informatics Organisation of Bahrain, Turkisk Statistical Institute, National Statistical Committee Belarus, INEGI (Mexico), INEC (Costa Rica), and INE (Chile) for their assistance in responding to queries in their country's stillbirth rate data. We would like to thank Rayko Kalenderove, Chris Counts, Alexander Zamaev, Tung On Yau, Joanna Osmanska, Silvia Moens-Lecumberri, Takashi Doyama, and Clarissa Rodrigues for their assistance with translation and data abstraction. We are grateful to Josh Vogel and the WHO Multi-Country Survey on Maternal and Newborn Health Research Network for their assistance in reanalysing the stillbirth rate data from the WHO Global Survey on Maternal and Perinatal Health and WHO Multi-country Survey on Maternal and Newborn Health.

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4. Paper B - National, regional, and worldwide estimates of preterm birth rates in 2010

This chapter provides an in-depth analysis of the availability of preterm birth rate data for all countries worldwide (Objective 2). It also provides a description of the development and implementation of methods to produce national, regional and worldwide estimates of preterm birth rate, with time trends where possible (Objective 3).

This chapter was published June 9th 2012 in The Lancet.[56] The published manuscript is included in full below. The copyright is held by Elsevier and permission to reproduce the contents is included in Annex A.4. The web appendix referenced in the paper is available at https://ars.els-cdn.com/content/image/1-s2.0-S0140673612608204-mmc1.pdf . See Annex A.4. for details.

4.1. List of Figures

4.2. List of Tables

4.3. Citation

Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE. **National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications.** *Lancet. 2012 Jun 9;379(9832):2162-72. doi: 10.1016/S0140-6736(12)60820-4.*

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	200160	**Title**	Dr
First Name(s)	Hannah		
Surname/Family Name	Blencowe		
Thesis Title	Counting the smallest: data to estimate global stillbirth, preterm birth and low birthweight rates		
Primary Supervisor	Joy E Lawn		

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

SECTION B – Paper already published

Where was the work published?	The Lancet as: Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012 Jun 9;379(9832):2162-72. doi: 10.1016/S0140-6736(12)60820-4.		
When was the work published?	June 2012		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	This work was undertaken prior to the registration for my research degree however it is included in this thesis as the topic is very closely linked to the two later analyses on stillbirth and low birthweight data which form the body of the work in this PhD. The skills that I learned as I undertook these preterm birth rate estimates formed the foundation for the stillbirth and low birthweight work during the PhD registration period.		
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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was responsible with Prof Joy Lawn and Dr Lale Say for the conceptualisation of the paper. I designed and co-ordinated the web-based and systematic literature searches. I undertook the data quality assessment, modelling and analysis with advice from Prof Simon Cousens, Prof Joy Lawn and Mikkel Ostergaard. I wrote the first draft of the manuscript with Prof Joy Lawn and prepared the subsequent revisions with consideration of comments from co-authors. See Annex A.1. for full details.

SECTION E

Student Signature	Dr Hannah Blencowe
Date	27th April 2019

Supervisor Signature	Professor Joy Lawn
Date	28th April 2019

National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications

Hannah Blencowe, Simon Cousens, Mikkel Z Oestergaard, Doris Chou, Ann-Beth Moller, Rajesh Narwal, Alma Adler, Claudia Vera Garcia, Sarah Rohde, Lale Say, Joy E Lawn

Lancet 2012; 379: 2162–72

See Comment page 2128

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Summary

Background Preterm birth is the second largest direct cause of child deaths in children younger than 5 years. Yet, data regarding preterm birth (<37 completed weeks of gestation) are not routinely collected by UN agencies, and no systematic country estimates nor time trend analyses have been done. We report worldwide, regional, and national estimates of preterm birth rates for 184 countries in 2010 with time trends for selected countries, and provide a quantitative assessment of the uncertainty surrounding these estimates.

Methods We assessed various data sources according to prespecified inclusion criteria. National Registries (563 datapoints, 51 countries), Reproductive Health Surveys (13 datapoints, eight countries), and studies identified through systematic searches and unpublished data (162 datapoints, 40 countries) were included. 55 countries submitted additional data during WHO's country consultation process. For 13 countries with adequate quality and quantity of data, we estimated preterm birth rates using country-level loess regression for 2010. For 171 countries, two regional multilevel statistical models were developed to estimate preterm birth rates for 2010. We estimated time trends from 1990 to 2010 for 65 countries with reliable time trend data and more than 10 000 livebirths per year. We calculated uncertainty ranges for all countries.

Findings In 2010, an estimated 14·9 million babies (uncertainty range 12·3–18·1 million) were born preterm, 11·1% of all livebirths worldwide, ranging from about 5% in several European countries to 18% in some African countries. More than 60% of preterm babies were born in south Asia and sub-Saharan Africa, where 52% of the global livebirths occur. Preterm birth also affects rich countries, for example, USA has high rates and is one of the ten countries with the highest numbers of preterm births. Of the 65 countries with estimated time trends, only three (Croatia, Ecuador, and Estonia), had reduced preterm birth rates 1990–2010.

Interpretation The burden of preterm birth is substantial and is increasing in those regions with reliable data. Improved recording of all pregnancy outcomes and standard application of preterm definitions is important. We recommend the addition of a data-quality indicator of the per cent of all live preterm births that are under 28 weeks' gestation. Distinguishing preterm births that are spontaneous from those that are provider-initiated is important to monitor trends associated with increased caesarean sections. Rapid scale up of basic interventions could accelerate progress towards Millennium Development Goal 4 for child survival and beyond.

Funding Bill & Melinda Gates Foundation through grants to Child Health Epidemiology Reference Group (CHERG) and Save the Children's Saving Newborn Lives programme; March of Dimes; the Partnership for Maternal Newborn and Childe Health; and WHO, Department of Reproductive Health and Research.

Introduction

Preterm birth complications are estimated to be responsible for 35% of the world's 3·1 million annual neonatal deaths, and are now the second most common cause of death after pneumonia in children under 5 years old.[1] Preterm birth also increases the risk of death due to other causes, especially from neonatal infections,[2,3] and in almost all high-income and middle-income countries, preterm birth is the leading cause of child deaths.[1] Additional to its contribution to mortality, preterm birth has lifelong effects on neurodevelopmental functioning such as increased risk of cerebral palsy, impaired learning and visual disorders, and an increased risk of chronic disease in adulthood.[4] The economic cost of preterm birth is high in terms of neonatal intensive care and ongoing health-care and educational needs. The social cost is also high, with many families experiencing the sudden loss of a preterm baby or a stressful hospital stay, sometimes for months.[5]

The WHO defines preterm birth as any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the women's last menstrual period (LMP)[6] and this can be further subdivided on the basis of gestational age: extremely preterm (<28 weeks), very preterm (28–<32 weeks), and moderate or late preterm (32–<37 completed weeks of gestation; figure 1). These subdivisions are important since decreasing gestational age is associated with increasing mortality, disability, intensity of neonatal care required, and hence increasing costs.

Preterm birth is a syndrome with a variety of causes which can be broadly classified into two groups: (1) spontaneous preterm birth and (2) provider-initiated preterm birth (defined as induction of labour or elective caesarean section before 37 completed weeks of gestation for maternal or fetal indications or other non-medical reasons, and sometimes previously called "iatrogenic").[7] Globally, the highest burden countries have very low levels of provider-initiated preterm births, with most African countries having caesarean sections rates lower than 5%.[8] However, many high-income and middle-income countries have increasingly high numbers of provider-initiated preterm births and a recent assessment of 872 provider-initiated preterm births at 34–36 weeks' gestation in the USA suggested that more than half were done in the absence of a well defined medical indication.[9]

Spontaneous preterm birth is a multifactorial process, resulting from the interplay of factors causing the uterus to change from quiescence to active contractions and to birth before 37 completed weeks of gestation. The precursors vary by gestational age,[10] with the precise cause of spontaneous preterm labour being unidentified in up to half of all cases.[11] Individual or family history of preterm birth is a strong risk factor.[12] Many other maternal factors have been associated with an increased risk of spontaneous preterm birth, including young or advanced maternal age, short interpregnancy intervals, low maternal body-mass index (BMI), multiple pregnancy, pre-existing non-communicable disease, hypertensive disease of pregnancy, and infections.[13,14]

The number of liveborn preterm babies, whether singleton or multiple births, is the numerator for preterm birth rates. Liveborn preterm babies drive the need for neonatal care, and in high-income countries half of babies under 25 weeks now survive, but with increasing evidence of major disability.[15] By contrast, in low-income and many middle-income settings, moderate and late preterm babies do not have even basic care and account for most preterm babies dying. However, from a public health perspective for policy and planning, and from a family loss perspective, both liveborn and stillborn babies born before term are important (figure 1).

The International Classification of Diseases: tenth revision (ICD-10) recommends recording all newborns with any signs of life at birth as livebirths.[16] However, for extremely preterm babies, practice is variable and is closely linked to perceptions of viability and stillbirth registration thresholds. Classifications vary between countries and over time, complicating the comparison of reported rates and interpretation of time trends (figure 1).[17,18] Furthermore, some reports exclude babies with congenital abnormalities, and others include only singleton births. Additionally, methods for assessing gestational age have improved over time, at least in high-income countries, and variations in methods for measurement of gestational age further complicate the interpretation of preterm birth rates both within and between countries.

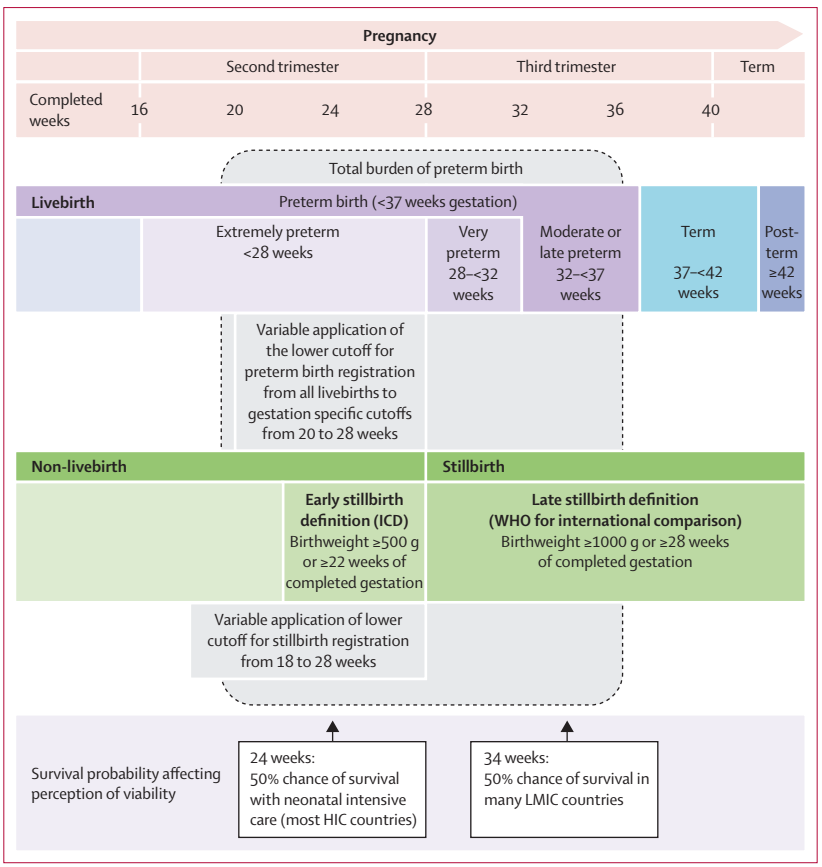

Figure 1: **Overview of definitions and variable cutoffs applied for pregnancy outcomes related to preterm birth and stillbirths**

Figure adapted from Lawn and colleagues.[17] HIC=high-income countries. LMIC=low-income and middle-income countries. *Very preterm group in this analysis includes babies 28–<32 weeks and extremely preterm births are defined as <28 weeks.

These differences and the absence of routinely collected data on preterm birth rates in many countries have limited the understanding of the size of the burden of preterm birth globally. A previous exercise estimated that 9·6% of livebirths worldwide in 2005 were preterm (12·9 million preterm births).[19] No national systematic estimates of preterm birth rates have been published,[20] and no multicountry time trend analysis is available.

In this study, we report worldwide, regional, and national estimates of preterm birth rates for 184 countries in 2010, and provide a quantitative assessment of the uncertainty surrounding these estimates. We have based the regional estimates on the Millennium Development Goal (MDG) regions (appendix p 1).[21] We also present trend estimates for the period 1990–2010, where sufficient data exist. In the interests of public health planning, we also estimate preterm birth by three subgroups—namely, extremely preterm, very preterm, and moderate or late preterm (figure 1).

For the purpose of these estimates, the definition of the preterm birth rate used is "all livebirths before 37 completed weeks, whether singleton, twin, or higher order multiples, divided by all livebirths in the population".

See Online for appendix

Methods

Data inputs

We assessed preterm birth data for inclusion from four sources: national registries or statistical offices, Reproductive Health Surveys,[22] unpublished data from principal investigators collaborating with the Child Health Epidemiology Reference Group, and published papers identified through a systematic review (figure 2).

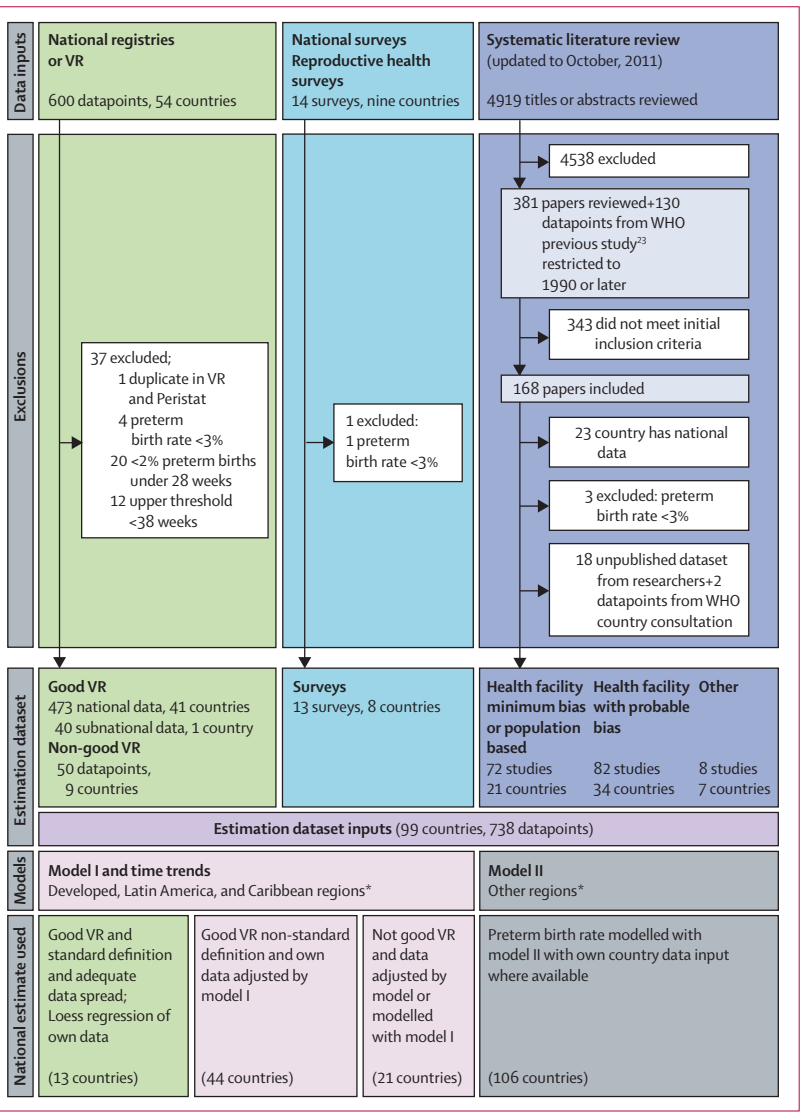

Figure 2: **Preterm birth rate data search strategy, selection progress showing the methods, and models used for estimation**

VR=vital registration. Good VR= national VR with high-quality reporting for maternal deaths.[25] *Millennium Development Goal regions.

	Gestational age	Proportion of all <37 weeks (%, 95% CI)
Extremely preterm	<28 weeks	5·2% (5·1–5·3)
Very preterm	28–<32 weeks	10·4% (10·3–10·5)
Moderate or late preterm	32–<37 weeks	84·3% (84·1–84·5)

Table 1: **Distribution of preterm birth according to gestational age subgroup based on meta-analysis of 345 datapoints from 41 countries (*n*= 131 296 785 live births)**

We systematically searched all the National Statistical Offices websites,[24] and Ministry of Health websites. For countries without National Statistical Office or Ministry of Health data, we searched for data from nationally representative household Health Surveys.[22] For countries with less robust national health registration systems (those classified as not having national vital registration with high-quality reporting for maternal deaths),[25] we did a systematic review of all the main online literature databases. Search terms used included multiple variants of terms covering the following areas "preterm or premature" and "birth or labour" or "newborn or infant" and we used Medical Subject Headings terms when available (appendix pp 3–4 lists the databases that were searched and the full set of search terms used). Unpublished data from principle investigators collaborating with the Child Health Epidemiology Reference Group, and data from the WHO Global Health Survey were requested.

Data inclusion and exclusion criteria

We assessed all reports that included more than 50 births with a midpoint of data collection of 1990 or later and in which a preterm birth rate was given or could be calculated. Although we aimed to estimate the preterm rate using a standard definition, we included data using other definitions and sought to account for the different definitions in the modelling. Data from specialised services reports were excluded as non-generalisable for example diabetes, hypertension, intrauterine growth restriction, or specific subpopulations or ethnic groups. Data from health facilities with potential for selection bias were included and identified using a dummy variable similar to a previous estimation exercise for stillbirth rates.[26]

Data were excluded if obtained over a period of less than 12 months unless the source stated no seasonality, or data from the same source for another year showed no seasonality. We excluded datapoints likely to reflect poor case ascertainment on the basis of two conservative criteria: (1) less than 3% of all births reported to be preterm, since the lowest reliable national reported rates identified in our database were about 5% and less than 3% was deemed biologically implausible on the basis of this distribution; (2) less than 2% of all preterm births at less than 28 weeks' gestation, as based on our meta-analysis of the distribution of gestational age subgroups, which showed that the proportion of births at less than 28 weeks' gestation was very consistent at about 5% (table 1).

A country consultation process was carried out by WHO involving circulation to Member States of WHO of the national input data, together with estimation methods and the preliminary preterm birth estimates. Countries were asked to review and provide feedback and any relevant additional data. 55 countries provided

additional data, and if criteria were met, these were included in the final dataset and the estimates remodelled based on this dataset (figure 2).

Final dataset used as input for statistical models

The final dataset used included 738 datapoints (figure 2). Most datapoints (539 of 738, 73%) were from National Statistical Offices, Ministry of Health databases, or nationally representative surveys;[22] 103 (14%) were derived from subnational, population-based sources or hospital-based studies in settings with institutional birth rates higher than 90% (assumed to provide unbiased estimates of the population preterm birth rate), and 11% were from hospital-based studies in settings with institutional birth rates lower than 90% where preterm birth rates might not be representative of the population rates. 547 (74%) datapoints were from countries in MDG regions Developed, Latin America, and the Caribbean (median year 2002). 191 datapoints (26%; median year 2002), were from countries in other regions; these regions had few high-quality datapoints. The preterm birth rate based on the standard definition was available for 612 datapoints, with most (101) of the remaining datapoints including only singleton livebirths. For 85 countries, no data were available (appendix pp 5–54).

Statistical models

For 13 countries classified as having good vital registration for maternal deaths,[25] using the standard definition for preterm birth, and with data for more than 50% of the years 1990–2010 including at least one year before 1995 and one year after 2005, we used country-level loess regression to estimate preterm birth rates for all years (appendix pp 55–56).

For all other countries, preterm birth rates were modelled using preterm birth data from the country itself, when available, along with other countries' preterm birth data. Since regional variation existed in the quality of data available and the underlying causes and predictors of preterm birth between high-income settings and the rest of the world, two regional models were developed. Model I included 65 countries in the MDG regions "Developed region", and "Latin America" and "the Caribbean", including 547 data inputs from 52 countries. Model II provided estimates of preterm birth rates in all other world regions (for 106 countries, including 191 data inputs from 47 countries). Table 2 shows covariates investigated as potential predictors.

Where data for continuous predictors were not available for all years 1990–2010 for all the countries, the missing years were interpolated using loess regression or linear interpolation (appendix pp 57–59 for details of sources, methodology and univariate analysis). We examined both restricted cubic splines and linear trends when assessing the relationship between the outcome and these potential continuous predictors. The final modelling approach was determined by the best fit to the data.

The models were fitted with a forward step-wise approach, retaining variables if there was evidence of predictive value existed after taking account of the other variables in the model ($p<0·10$) or, for variables relating to the methodology used, if the coefficients were of the expected sign and of plausible magnitude. Both models included a country-level random effect. For countries contributing data to the input dataset, the best linear unbiased prediction of the country-specific random effect was obtained and used in predicting that country's preterm birth rate. If no national data were available the random effect was assumed to be zero. Variables retained in Model I included: linear log (low birthweight rate) ($p<0·0001$), mean adult female BMI ($p=0·09$), year ($p<0·0001$), data source ($p<0·0001$), method of gestational age assessment ($p<0·0001$), and denominator (singleton or all births) ($p=0·004$; table 2, appendix p 60 for full model equation). The preterm birth rate increased with increasing low birthweight rate and mean adult female BMI (appendix p 61). Regression diagnostic plots

	Retained in Model I	Risk ratio (95% CI)	Retained in Model II	Risk ratio (95% CI)
Neonatal mortality rate	No	..	No	..
Low birthweight rate	Yes	1·40 (1·26–1·56)	Yes	1·34 (1·17–1·53)
Caesarean section rate	No	..	No	..
Adolescent pregnancy rate	No	..	No	..
HIV prevalence	No	..	No	..
Malaria endemicity	No	..	Yes	1·17 (0·99–1·37)
Mean adult female BMI	Yes	1·03 (1·00–1·06)	No	..
Gross National Income	No	..	No	..
General fertility rate	No	..	No	..
Female literacy rate	No	..	Yes	1·01 (1·00–1·01)
MDG region	No	..	No	..
Preterm definition	No	..	No	..
Upper and lower cutoff	..	..	No	..
Method of gestational age assessment	Yes	..	Yes	..
Ultrasound, best obstetric estimate	..	1·00	..	1·00
Last menstrual period	..	1·15 (1·04–1·26)	..	1·12 (0·93–1·36)
Other	..	0·75 (0·66–0·84)	..	0·87(0·75–1·01)
Singleton/all births	Yes	..	Yes	..
Singleton	..	1·00	..	1·00
All births	..	1·12(1·05–1·20)	..	1·06 (0·93–1·21)
Not known	..	1·15 (0·94–1·42)	..	1·31 (0·82–2·11)
Livebirths/total births	No	..	No	..
Year of study	Yes	1·01 (1·00–1·01)	No	..
Type of data source	Yes	..	Yes	..
National	..	1·00	..	1·00
Subnational	..	1·36 (1·06–1·75)	..	1·47 (1·10–1·97)
Facility–possible bias/other	..	1·40 (1·26–1·56)	..	1·24 (0·96–1·61)

BMI=body-mass index. MDG=Millennium Development Goal.

Table 2: **Variables tested for prediction of preterm birth rates in statistical models showing risk ratio estimates**

suggest that the model fits the data well (overall R^2=0·4; appendix p 62).

Variables retained in Model II included: linear log (low birthweight rate) (p<0·0001), malaria endemicity (p=0·06), female literacy rate (p=0·04), data source (p=0·02), method of gestational age assessment (p=0·01), and denominator (singleton or all births; p=0·40; table 2, see appendix p 60 for full model equation). Preterm birth rates increased with increasing low birthweight rate, malaria, and female literacy (table 2; appendix p 61). Regression diagnostic plots show the fit of the model to the data (overall R^2=0·29; appendix p 63).

The numbers of preterm births by country were derived by applying our preterm birth rate estimations to the UN estimate of livebirths for that country and the relevant year, taking account of demographic trends.[27]

	Number of livebirths	Estimated mean preterm birth rate (%) (uncertainty range*)	Number of preterm births (uncertainty range*)
Developed regions	14 300 000	8·6% (8·3–9·4)	1 233 200 (1 188 500–1 345 100)
Eastern Asia	17 400 000	7·2% (5·4–9·0)	1 262 200 (943 100–1 564 100)
Latin America	10 200 000	8·4% (6·8–11·4)	852 800 (695 500–1 164 000)
Northern Africa	3 543 100	7·3% (4·8–10·9)	259 200 (168 700–387 900)
Oceania	263 200	7·4% (4·5–15·6)	19 500 (11 800–41 000)
Southeastern Asia	11 000 000	13·6% (9·3–18·6)	1 497 500 (1 019 400–2 044 700)
Southern Asia	38 700 000	13·3% (10·1–16·8)	5 159 300 (3 900 100–6 504 200)
Sub-Saharan Africa	32 100 000	12·3% (9·5–15·8)	3 936 800 (3 039 500–5 068 000)
Western Asia	4 855 300	10·1% (6·9–14·3)	488 200 (334 000–693 700)
Caribbean	682 800	11·2% (7·8–20·8)	76 500 (53 300–142 000)
Caucasus and Central Asia	1 643 000	9·2% (6·0–13·0)	151 300 (99 100–212 800)
Total worldwide	135 000 000	11·1% (9·1–13·4)	14 936 700 (12 268 200–18 089 700)

*Uncertainty ranges derived using a bootstrap approach see appendix p 64.

Table 3: **Estimated preterm birth rates and total number of preterm births for 2010, by Millennium Development Goal region**

Statistical analysis

To estimate the distribution of preterm births by gestational age subgroup, we did a meta-analysis of all 345 datapoints in our input database which presented data by our agreed gestational age subgroups (N=131 296 765; table 1). The median year of these data was 2004 (range 1990–2010). A random effects model was used as some evidence of heterogeneity, assessed using I^2 and the χ^2 test, was present (p<0·10). The proportions were remarkably similar across these datasets suggesting a biological basis for the distribution. Given this consistency, we applied these proportions to our estimates of preterm births for all countries for 2010. However, only 13% (44 datapoints) were from outside the Developed region, with only seven datapoints from southern Asia, or sub-Saharan Africa. There was some evidence of a difference in the distributions of the subgroups for all other regions, compared with Developed region, reported on average slightly lower proportions of preterm births at less than 28 weeks (4·8% *vs* 5·3%; p=0·02); similar proportions of preterm births for 28 to less than 32 weeks (10·2% *vs* 10·6%; p=0·13); and higher proportions for births at 32 weeks to less than 37 weeks (85·1% *vs* 84·1%; p=0·03)). These differences are likely to represent differences in case ascertainment in the group of less than 28 weeks' gestation between regions. We did not estimate trends for the gestational age subgroups.

We estimated the uncertainty around the gestational age subgroups as 95% CIs using a probabilistic method (table 1) since there were large and consistent datasets. However a probabilistic approach would be misleading for country estimates with limited or no input data since

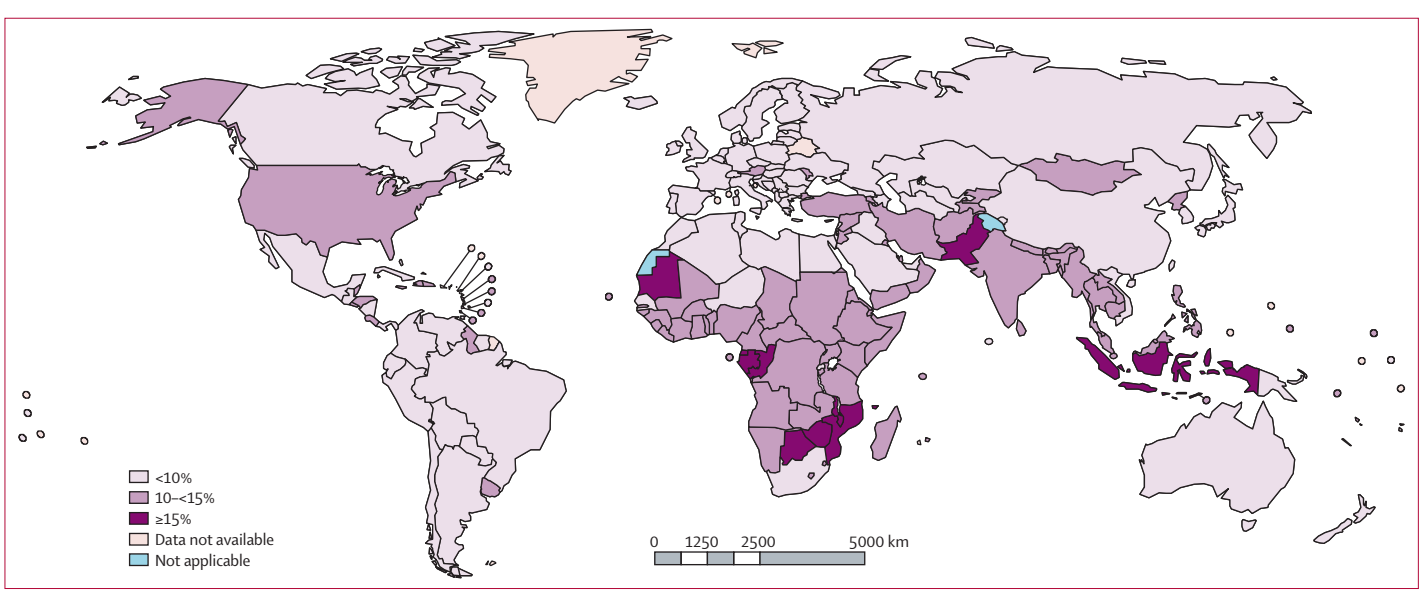

Figure 3: **Estimated preterm birth rates by country for the year 2010**

fewer data might result in the appearance of narrower uncertainty, or no data is taken to be no uncertainty when such estimates would be expected to have the widest uncertainty. We used a statistical approach based on the model to estimate uncertainty ranges for national preterm birth rates for Model I, Model II, and loess countries separately using a bootstrap approach (appendix p 64).

We estimated trends for the 65 countries in Developed, Latin America, and the Caribbean regions with over 10 000 livebirths in 2010, using loess regression (12 countries, excluding Luxembourg <10 000 births) or Model I estimates (53 countries) as described above. We did not estimate trends in other regions because of the absence of consistent data over the 21 year period.

Funding

The funding source had no role in study design, data collection, data analysis, data interpretation, or writing of the report. HB, DC, ABM, LS, SC, and JEL had full access to all the data. HB, SC, and JEL had final responsibility to submit for publication.

Results

Based on 184 countries, the global average preterm birth rate in 2010 was 11·1% (uncertainty range 9·1–13·4%), giving a worldwide total of 14·9 million (12·3–18·1 million; table 3). Preterm birth rates varied widely between countries (figure 3; appendix pp 65–72 and country plots for individual country data). At a national level, the estimated preterm birth rate ranged from about 5% in several northern European countries to 18% in Malawi. In 88 countries, this rate was lower than 10%. Of the 11 countries with estimated rates of 15% or more in 2010, all but two were in sub-Saharan Africa (figure 3). Rates are highest for low-income countries (11·8%), followed by lower middle-income countries (11·3%), and lowest for upper middle-countries (9·4%) and high-income countries (9·3%). High preterm birth rates were also noted in many high-income countries (eg, USA at 12·0% and Austria at 10·9%), making a major contribution to child mortality and morbidity.

The regions with the highest preterm birth rates in 2010 were Southeastern Asia, South Asia, and sub-Saharan Africa (figure 4). More than 60% of all preterm births are estimated to have occurred in sub-Saharan Africa and South Asia where 9·1 million livebirths (12·8% of livebirths) were estimated to be preterm in 2010. Table 4 lists the ten countries with the highest numbers of estimated preterm births, accounting for 60% of all preterm births. USA alone accounts for 42% of all preterm births in the Developed region (>0·5 million), but only 30% of the region's livebirths.

No evidence of a systematic difference existed between the estimated preterm birth rates for 2010 and the nationally reported rate in the 26 countries with available data for 2009 or 2010 using the standard definition and of acceptable quality (paired *t* test p=0·84).[24] The median difference between estimated and reported rates was –0·3% (IQR –1·3 to 2·3%; appendix pp 73–74).

Applying the estimated distribution of gestational age subgroups to every country (table 1), in 2010, an estimated 0·78 million (uncertainty range 0·76–0·87 million) preterm babies were extremely preterm, 1·6 million (1·5–1·7 million) were very preterm, and most (12·6 million, 12·3–14·1 million; 84%) were moderate and late preterm (figure 4, appendix p 75).

Time trends for preterm birth rates were estimated for 65 countries in Developed and Latin America and the Caribbean regions with more than 10 000 births in the year 2010. The mean estimated rate in these countries for 1990 was 7·5% (total preterm births in these countries 2·0 million, uncertainty range 1·8–2·5 million preterm births) compared with 8·6% (total preterm births 2·2 million, 2·0–2·6 million preterm births) in 2010 (table 5). Only three countries, Croatia, Ecuador, and

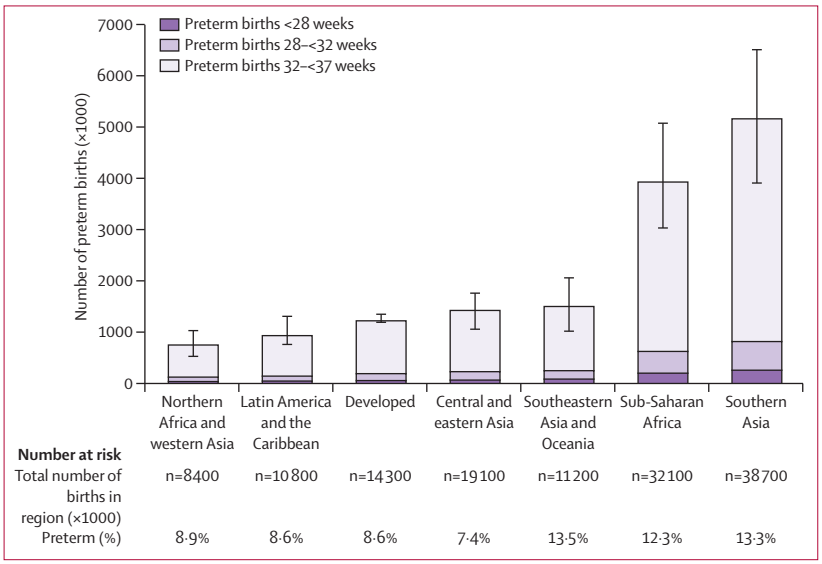

Figure 4: **Estimated preterm births by region and by gestational age grouping for the year 2010**

	Rank for number of preterm births	Number of preterm births (% of global total)	Preterm birth rate (% of livebirths)	Number of livebirths (% of global total)
India	1	3 519 118 (23·6%)	13·0%	27 200 000 (20·1%)
China	2	1 172 259 (7·8%)	7·1%	16 600 000 (12·3%)
Nigeria	3	773 597 (5·2%)	12·2%	6 332 251 (4·7%)
Pakistan	4	748 142 (5·0%)	15·8%	4 741 460 (3·5%)
Indonesia	5	675 744 (4·5%)	15·5%	4 371 818 (3·2%)
USA	6	517 443 (3·5%)	12·0%	4 300 620 (3·2%)
Bangladesh	7	424 144 (2·8%)	14·0%	3 037 652 (2·3%)
Philippines	8	348 871 (2·3%)	14·9%	2 344 154 (1·7%)
Democratic Republic of Congo	9	341 421 (2·3%)	11·9%	2 872 606 (2·1%)
Brazil	10	279 256 (1·9%)	9·2%	3 022 823 (2·2%)
Total	..	8·8 million (59%)	..	74·8 million (55%)

Table 4: **The ten countries with the highest numbers of preterm births in 2010**

	1990			2010			1990–2010	
	Number of livebirths	Preterm birth rate (%)	Number of preterm births (uncertainty range*)	Number of livebirths	Preterm birth rate (%)	Number of preterm births (uncertainty range*)	Increase in preterm rate (%)	Average annual % increase in preterm birth rate
Developed regions	15 100 000	7·2%	1 090 000 (1035 000 –1179 000)	14 300 000	8·6%	1 233 000 (1 189 000–1 345 000)	19·4%	1·1%
Latin America	10 900 000	7·7%	845 000 (707 000–1217 000)	10 200 000	8·4%	853 000 (696 000–1 164 000)	9·1%	0·5%
Caribbean	769 000	8·9%	68 000 (48 000–125 000)	683 000	11·2%	77 000 (53 000–142 000)	25·8%	1·5%
Total	26 769 000	7·5%	2 004 000 (1839 000–2468 000)	25 183 000	8·6%	2 163 000 (1 987 000–2 593 000)	14·7%	0·8%

*Uncertainty ranges derived with a bootstrap approach (appendix p 64).

Table 5: **Preterm birth rates and totals for 1990 and 2010 for Developed and Latin America and Caribbean Millennium Development Goal regions**

Estonia, had reductions in estimated preterm birth rates from 1990 to 2010. 14 countries had stable preterm birth rates (<0·5% annual change in preterm birth rates). In all other countries, the preterm birth rate was estimated to be greater in 2010 than in 1990. Comparison of the estimated trends with reported trends by country suggested that the model predicted trends close to reported data (appendix pp 76–81 for individual country rates).

Discussion

We estimated national preterm birth rates for 184 countries in the year 2010 suggesting a worldwide total of 14·9 million preterm births (uncertainty range 12·3–18·1 million), more than one in ten of all babies (panel). Most preterm births (84%, 12·5 million) occur after 32 completed weeks of gestation. Most of these newborns would survive with supportive care, and without neonatal intensive care.[28] Yet, a huge survival and equity gap remains between the richest and poorest countries.[28] Currently, more than 90% of babies born before 28 weeks of gestation survive in high-income countries, but in low-income settings, only 10% of these babies or less survive, a 90:10 survival gap. At the start of the 20th century, the UK and USA had neonatal mortality rates of 40 per 1000 livebirths—similar to Africa in 2000—but these were reduced to 15 per 1000 livebirths before neonatal intensive care was widely available. Over the decade 2000–2010, seven low-income and middle-income countries have halved their numbers of deaths due to preterm birth.[29] Rapid reductions in deaths among preterm babies are possible and given the increasing proportion of deaths that are neonatal in children younger than 5 years, this could alter the trajectory of many countries towards MDG 4 for child survival.[30] Strategies for maternal mortality reduction to meet the MDG 5, such as family planning and obstetric care, can also improve pregnancy outcomes including preterm birth.[31]

We have highlighted the differences in preterm birth rates between countries, but substantial disparities exist within countries. For example, in the USA, reported preterm birth rates were as high as 17·5% in black Americans in 2009, compared with 10·9% in white Americans, with rates varying from about 11–12% in those 20–35 years of age, to more than 15% in those younger than 17 years or older than 40 years.[32]

Preterm birth is more common in boys than girls, with about 55% of all preterm births being boys,[33] and is associated with a higher risk of fetal and neonatal mortality[34–37] and of long-term impairments[37,38] in boys than in girls born at a similar gestation. For both boys and girls, preterm birth has a major effect on child development and adult economic productivity. Recent studies show that even babies born at 34–37 weeks have an increased risk of immediate complications,[39–41] neonatal and infant death, cerebral palsy, and worse neurodevelopmental and school performance outcomes when compared with those born at term.[42,43]

Rates of preterm birth increased or were stable in all but three of the 65 countries with consistent data. This rise is partly due to increases in registration of extremely preterm births, which reflect improved case ascertainment rather than a genuine change in rate.[44] An increase in the proportion of preterm births occurring at 32–<37 weeks, linked to increased provider-initiated preterm births secondary to changes in obstetric practices, has been reported over the past decades in some countries.[45] However, for countries with available data in this study, we found no evidence of a change in the proportion of all preterm births that were 32–<37 weeks from 1990 to 2010 (p=0·9).

Low birthweight is a strong predictor in both statistical models. Although birthweight is closely linked with gestational age, it cannot be used interchangeably since there is a range of "normal" birthweight for a given gestational age and sex. In some settings, especially in South Asia, a high proportion of low birthweight babies are term babies who are small for gestational age.[46] Distinguishing between the two is important as a baby born preterm has a higher risk of death than a baby of the same birthweight born small for gestational age at term. Babies who are both preterm and small for gestational age are at even higher risk than babies with one of the conditions.[47]

Maternal BMI is an important risk factor for preterm birth, and is of public health importance in its own right. BMI was retained as a predictor in the Model I; in developed and Latin American and the Caribbean regions where increasing mean female BMI was associated with increasing preterm birth rates. Whereas some studies

have shown an increase in preterm birth with low BMI (<18·5 kg/m²),[48–51] others support an increase in provider-initiated preterm birth with increasing BMI.[49,52,53] The effect of high BMI is greater in primigravidae, and might be mediated by an increase in pre-eclampsia in this subgroup and potentially mediated by provider-initiated preterm births.[49] A recent systematic review[53] showed both increased induced preterm birth and overall preterm birth rates in overweight and obese women after accounting for publication bias.

Predictors of preterm birth retained in model II covering regions other than Developed or Latin America and the Caribbean included malaria and female literacy. Malaria is associated with an increased risk of preterm birth, especially in areas of unstable transmission.[10,54,55] Somewhat counter-intuitively, female literacy is associated with increasing preterm birth rates. It may be that increased literacy is a marker of a "Western" lifestyle which Chinese immigrant cohort studies suggests may confer an increased risk of preterm birth.[56]

For 85 of the 184 countries included (17% of livebirths worldwide), no data were available, whereas for a further 40 countries (54% of livebirths worldwide), the available data are unlikely to be nationally representative (appendix p 53). This limitation is shown by the wide uncertainty ranges, especially for countries with no nationally representative data. This data gap is most marked for the 48 countries in the sub-Saharan African region—where no available data exist for 28 countries, and the available data from the other 20 countries are unlikely to be nationally representative. A paucity of high quality data on the distribution of the subgroups of preterm birth was available from some regions, notably south Asia and sub-Saharan Africa. The quality of data on preterm birth depends on the extent to which births are correctly classified as preterm or not. This is highly dependent upon both the method of gestational age assessment used and the skill of the user. The method used can affect substantially the number of preterm births reported. For example, results from a large study[57] from a Canadian teaching hospital showed a preterm birth rate of 9·1% when assessed with ultrasound alone, compared with 7·8% in the same cohort when using LMP and ultrasound. LMP alone, although more feasible to record, is relatively imprecise (uncertainty range of about 3 weeks) because of variation in the length of menstrual cycle between women, conception occurring up to several days after ovulation and recall of the date of LMP being subject to errors.[58]

Data quality is particularly affected by under-registration of extremely preterm births, or their misclassification to stillbirths near the thresholds of perceived viability and stillbirth registration.[59] Countries using preterm birth definitions that include births from 20 weeks onwards report a higher proportion of preterm births under 28 weeks, possibly reflecting increased data capture of livebirths around the margins of viability (figure 5). Other countries with no specified lower cutoff have variable capture of extremely preterm babies. When reporting thresholds are changed it might take some time before recording of cases near the new threshold improves. For example, Denmark changed their lower threshold for registering preterm births from 28 to 22 weeks in 1997, but it was several years later that the proportion of all preterm births under 28 weeks increased from 4% to 7% (figure 6).We excluded 20 datapoints from our input dataset based on the implausibility criteria of less than 2% of preterm births being at less than 28 weeks' gestation (figure 2). We did a sensitivity analysis regarding these exclusions and found no evidence of a systematic difference between the estimated preterm birth rates at country level with and without these data included (paired *t* test p=0·44).

We applied statistical modelling to try to correct for definition variation, data limitations, and to estimate for countries for which no or poor data were available. The use of statistical models can never be a substitute for improved empirical data. Prediction of the prevalence of preterm birth, in essence a syndrome and with varying risk factors around the world, has presented modelling challenges. The predictor variables available as time series are poor when compared with the complex interplay of different factors leading to preterm birth. Particularly, it was not possible to distinguish between spontaneous and provider-initiated preterm births, since even in high-income countries, this distinction is not readily available

***Panel:* Research in context**

Systematic review

Preterm birth is the largest cause of neonatal death worldwide and second leading cause of child deaths—1·1 million deaths a year. Yet, data on preterm birth rates is not routinely collected in many countries. We did a systematic search of online databases, National Statistical Offices, and Ministry of Health sources, and assessed reports according to pre-specified inclusion criteria. Search terms used included multiple variants of terms covering the following areas "preterm or premature" and "birth or labour" or "newborn or infant", and Medical Subject Headings terms when available. Additional data were collected through a WHO country consultation process. A total of 738 datapoints from 99 countries met inclusion criteria and were used to model estimates of preterm birth rates for 184 countries, with time trends for 65 countries in regions with reliable data

Interpretation

These are the first national estimates of preterm birth rates suggesting that in 2010, 11·1% of all livebirths worldwide were born preterm, ranging from around 5% in several northern European countries to 18·1% (Malawi), and that the rates of preterm birth are increasing in those regions with reliable data. Over 60% of the 14·9 million babies born preterm in 2010 were born in south Asia and sub-Saharan Africa. However preterm birth affects rich and poor countries, with Brazil and USA featuring in the 10 countries with the highest numbers of preterm births. Boys are at higher risk of preterm birth and of adverse outcomes than girls. The high and rising incidence of preterm birth, associated with death and disability, represents a significant public health impact in all countries. Preventive approaches have had poor national impact so far, and innovative solutions are urgently needed. However, major progress has been made in mortality for preterm babies in high income countries. Rapid scale up of basic interventions in low-income and middle-income countries could accelerate progress towards Millennium Development Goal 4 for child survival in 2015 and beyond.

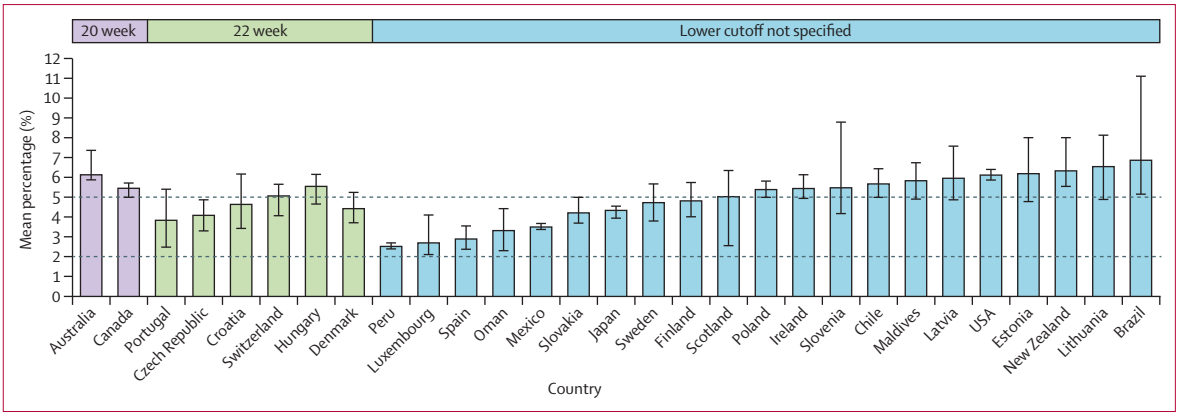

Figure 5: **Percentage of reported preterm births that are less than 28 weeks by country showing variation with different lower gestational age thresholds**
Data from 29 countries with more than one reported datapoint providing information on the proportion of preterm births that are <28 weeks from 1990 to 2010. Error bars show range of reported proportions. All these countries report using livebirths as numerator or denominator. The 5% standard is based on meta-analysis shown in table 1. For estimation input dataset <2% was considered implausible and the data were excluded.

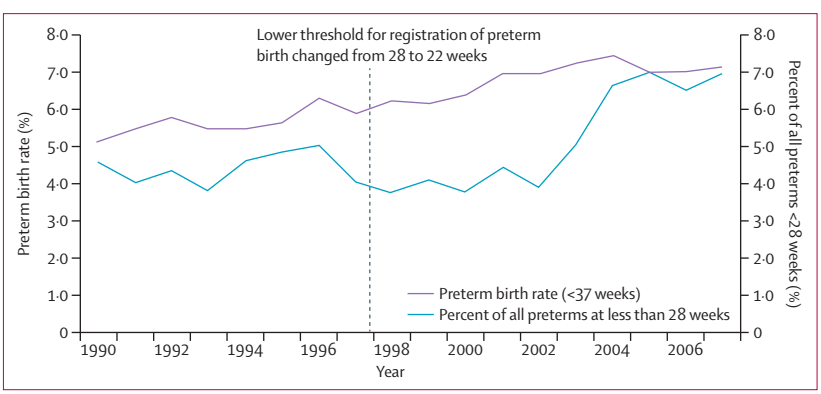

Figure 6: **Variation in preterm birth rate and proportion of preterm births at less than 28 weeks with a reduction in the lower threshold for registration of preterm births from 28 to 22 weeks' gestation in Denmark**
Analysis of 1 191 000 livebirths 1990 to 2007 Data source: National Board of Health.[60]

at national level or consistently over time. Tracking "medically-indicated" versus "non-indicated" provider-initiated preterm births would be crucial for accountability in reduction of unnecessary caesareans, but definitions and data are missing.

Improved quality and quantity of preterm birth data are needed in every country, but especially in low-income countries. Efforts in every country should be directed to the increase of coverage and systematic recording of all births, whether live or stillborn in a standard reporting format, which includes both birthweight and estimated gestational age. Application of a standard definition for preterm birth in terms of both the numerator and the denominator is essential. We have used the standard ICD 10 definition focusing on all livebirths at less than 37 weeks' gestation. A 28 week threshold was mentioned in ICD 10, but since the last edition, increased viability at lower gestational ages calls for this threshold to be reviewed, and consequently, very few countries are now applying this as a threshold for reporting (figure 5).[18] We recommend the use of an additional data quality marker regarding the percent of liveborn preterm babies under 1000 g or 28 weeks of gestation because of highly variable reporting of this group of babies and variable practices in resuscitation of the "micro preemie" group under 26 weeks' gestation.[61] The ICD 11 process provides an opportunity to give clear guidelines regarding this and other perinatal birth and death certificate issues, relevant to both high-income and low-income contexts.

Our estimates indicate a large burden among liveborn babies. Although focusing on livebirths is important to monitor neonatal and longer term outcomes, data on stillbirths are required to measure the full burden and to assist in the interpretation of trends in the preterm birth rate in liveborns, given potential misclassification between stillbith and livebirth in preterm babies and changing trends which might relate to obstetric care. In developed countries, between 5% and 10% of all preterm births are stillbirths, most of which constitute antepartum preterm stillbirths.[62] Advanced fetal medicine and obstetric and neonatal intensive care are routinely available, so babies not growing well in utero can be delivered early, reducing stillbirths, especially late stillbirths, but increasing preterm birth rates. In some countries, including the USA, this trend is reported to be at least partly responsible for the overall increase in the preterm birth rate from 1990 to 2007 and the decline in perinatal mortality.[63] This number contrasts with the large burden of 1·2 estimated million intrapartum stillbirths in low-income settings, which are mostly term babies and could be prevented with obstetric care.[17]

One option for increasing the amount of population-based data available in high-burden countries is to develop and test survey-based modules for consideration in nationally representative surveys such as the Demographic and Health Surveys (DHS) and demographic surveillance sites. These surveys are the major source of data for mortality and coverage tracking in most low-income countries. Innovation of locally appropriate, simpler, low-cost, methods for assessing birthweight and gestational age could improve both the coverage and quality of gestational

age assessment, for example, based on simplified clinical assessment for example of foot size.[64] Data from hospital-based information systems would also be helpful, but potential selection and other biases must be taken into account. Additionally, achieving consensus around comparable case definitions and improving the recording of the different categories of preterm birth (eg, spontaneous *vs* provider-initiated), although challenging, is needed to monitor changes with increased caesarean sections.[7] Improved standardised methods to assess acute and long-term morbidities associated with preterm birth are essential to track the proportion of impaired survivors.

Strengthened data systems are needed to record all pregnancy outcomes including maternal, stillbirth, preterm birth, low birthweight, and neonatal mortality. Consistent with ICD, we recommend adding a data quality indicator of the percent of all live preterm births that are under 28 weeks. Preterm birth is a syndrome and distinguishing important subgroupings is important to inform programmatic interventions.

Preterm birth prevention currently has few high impact solutions. Recent investments in discovery research show increasing recognition of this important knowledge gap.[65] However, new preterm prevention solutions will take years to develop and deliver. In the meantime, urgent action is required to increase survival and reduce disability in those born preterm, especially in the lowest income settings in which even moderate and late preterm babies die needlessly. Parent groups in high-income countries have been a powerful mobilising force yet, in low-income settings, these preventable deaths are accepted as inevitable by parents and often by health-care workers. About 84% of all preterm babies are moderate and late preterm, most of whom should survive with supportive care and feasible interventions such as antenatal steroids[66] and kangaroo mother care,[67] which would accelerate progress towards MDG 4 for child survival.[28] Preterm birth will be increasingly important beyond 2015 as an unfinished agenda for child survival and an important approach to improve health and sustainable development. Many countries cannot afford to rapidly scale up neonatal intensive care. Yet, no country can afford to miss simple care for every baby and investing extra attention in survival and health of newborns that are born too soon.

Contributors

HB coordinated the literature searches, undertook the modelling with SC, JL, and MO and drafted the report with JL, SC, and MO. DC, ABM, and LS undertook the identification and data abstraction of the national registry data. RN, AA, and GVG undertook the literature searches and abstraction. SR compiled the covariate time series. JL and LS initiated the process. JL oversaw the process and drafted the manuscript with HB. All authors reviewed the manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

This analysis was funded by the Bill & Melinda Gates Foundation through grants to US Fund for UNICEF for the Child Health Epidemiology Reference Group and to Save the Children's Saving Newborn Lives programme, with additional funding from March of Dimes, the World Health Organization, Department of Reproductive Health and Research, and the Partnership for Maternal Newborn and Child Health. We thank Mary Kinney and Erica Corbett for help with covariate time series data, and Florence Rusciano for generating the maps. We thank Colin Mathers and Mie Inoue for reviewing data and supporting the county consultation process, and Alexandre Peregoudov for their assistance with translation. We thank Joanne Katz and Anne CC Lee, Louise Day, and LAMB MIS-Research Department, Aroonsri Mongkolchati, Jean Humphrey, Gordon Smith, Nanbert Zhong, and James Tielsch and colleagues who provided preterm birth rate data and reanalysed data according to the standard definition when necessary. We also thank WHO Member States, country and regional offices for their participation and collaboration during country consultation.

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5. Paper C - National, regional, and worldwide estimates of low birthweight in 2015

This chapter provides an in-depth analysis of the availability of low birthweight rate data for all countries worldwide (Objective 2). It also provides a description of the development and implementation of methods to produce national, regional and worldwide estimates of low birthweight rate, with time trends (Objective 3).

This chapter was published May 15th 2019 in The Lancet Global Health.[217] The manuscript was published under a creative commons license (WHO/ UNICEF-CC BY) and the published manuscript is included in full below. The web appendix referenced in the paper is available at https://www.thelancet.com/cms/10.1016/S2214-109X(18)30565-5/attachment/7950f057-2932-4eaf-9270-d47ecc7462e1/mmc1.pdf. See Annex A.5. for details.

5.1. List of Figures

5.2. List of Tables

5.3. Citation

Blencowe H, Krasevec J, de Onis M, Black RE, An X, Stevens GA, Borghi E, Hayashi C, Estevez D, Cegolon L, Shiekh, Ponce Hardy V, Lawn JE, Cousens S. **National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis.** *Lancet Glob Health. 2019 Jul 1; 7(7):e849-e860*

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	200160	**Title**	Dr
First Name(s)	Hannah		
Surname/Family Name	Blencowe		
Thesis Title	Counting the smallest: data to estimate global stillbirth, preterm birth and low birthweight rates		
Primary Supervisor	Joy E Lawn		

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

SECTION B – Paper already published

Where was the work published?	The Lancet Global Health as: Blencowe H, Krasevec J, de Onis M, Black RE, An X, Stevens GA, Borghi E, Hayashi C, Estevez D, Cegolon L, Shiekh, Ponce Hardy V, Lawn JE, Cousens S. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health. 2019		
When was the work published?	May 2019 (In press at time of submission)		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	

Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was jointly responsible with Prof Joy Lawn for the conceptualisation of the paper. I designed and co-ordinated the web-based and systematic literature searches. I contributed to the household survey data collation and adjustment through supervision of a research assistant (Suhail Sheikh). I undertook the data quality assessment, modelling and analysis with support from Suhail Sheikh and advice from Prof Simon Cousens and Gretchen Stevens. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors. See Annex A.1. for full details.

SECTION E

Student Signature	Dr Hannah Blencowe
Date	27th April 2019

Supervisor Signature	Professor Joy Lawn
Date	28th April 2019

National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis

Hannah Blencowe, Julia Krasevec, Mercedes de Onis, Robert E Black, Xiaoyi An, Gretchen A Stevens, Elaine Borghi, Chika Hayashi, Diana Estevez, Luca Cegolon, Suhail Shiekh, Victoria Ponce Hardy, Joy E Lawn, Simon Cousens**

Summary

Background Low birthweight (LBW) of less than 2500 g is an important marker of maternal and fetal health, predicting mortality, stunting, and adult-onset chronic conditions. Global nutrition targets set at the World Health Assembly in 2012 include an ambitious 30% reduction in LBW prevalence between 2012 and 2025. Estimates to track progress towards this target are lacking; with this analysis, we aim to assist in setting a baseline against which to assess progress towards the achievement of the World Health Assembly targets.

Methods We sought to identify all available LBW input data for livebirths for the years 2000–16. We considered population-based national or nationally representative datasets for inclusion if they contained information on birthweight or LBW prevalence for livebirths. A new method for survey adjustment was developed and used. For 57 countries with higher quality time-series data, we smoothed country-reported trends in birthweight data by use of B-spline regression. For all other countries, we estimated LBW prevalence and trends by use of a restricted maximum likelihood approach with country-level random effects. Uncertainty ranges were obtained through bootstrapping. Results were summed at the regional and worldwide level.

Findings We collated 1447 country-years of birthweight data (281 million births) for 148 countries of 195 UN member states (47 countries had no data meeting inclusion criteria). The estimated worldwide LBW prevalence in 2015 was 14·6% (uncertainty range [UR] 12·4–17·1) compared with 17·5% (14·1–21·3) in 2000 (average annual reduction rate [AARR] 1·23%). In 2015, an estimated 20·5 million (UR 17·4–24·0 million) livebirths were LBW, 91% from low-and-middle income countries, mainly southern Asia (48%) and sub-Saharan Africa (24%).

Interpretation Although these estimates suggest some progress in reducing LBW between 2000 and 2015, achieving the 2·74% AARR required between 2012 and 2025 to meet the global nutrition target will require more than doubling progress, involving both improved measurement and programme investments to address the causes of LBW throughout the lifecycle.

Funding Bill & Melinda Gates Foundation, The Children's Investment Fund Foundation, United Nations Children's Fund (UNICEF), and WHO.

Introduction

Low birthweight (LBW) is defined as a birthweight below 2500 g regardless of gestational age[1] and is usually applied to livebirths only. LBW includes both appropriately grown preterm neonates (<37 completed weeks of gestation) and term and preterm growth-restricted neonates (<10th centile of weight for gestational age and sex) but remains an important public health indicator, especially in settings where accurate gestational age assessment is not possible.[2] LBW is a substantial public health problem in every country, associated with a range of both short-term and long-term consequences affecting human capital.[3] More than 80% of neonatal deaths are in LBW newborns, of which two thirds are preterm and one third are term small-for-gestational-age.[3–6] LBW newborns also have a higher risk of morbidity, stunting in childhood, and long-term developmental and physical ill health including adult-onset chronic conditions such as cardiovascular disease.[7–10] Factors influencing LBW include extremes of maternal age (especially younger than 16 years of age or older than 40 years), multiple pregnancy, obstetric complications, chronic maternal conditions (eg, hypertensive disorders of pregnancy), infections (eg, malaria), and nutritional status.[11–14] Other contributors include exposure to environmental factors, such as indoor air pollution, and tobacco and drug use.[15]

In 2012, the World Health Assembly (WHA) endorsed a Comprehensive Implementation Plan on Maternal, Infant and Young Child Nutrition, which specified six global nutrition targets, including a 30% reduction in the number of LBW livebirths between 2012 and 2025.[16] LBW is thus a key indicator of progress towards the achievement

Lancet Glob Health 2019; 7: e849–60

Published Online May 15, 2019 http://dx.doi.org/10.1016/S2214-109X(18)30565-5

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Research in context

Evidence before this study

Low birthweight (LBW; <2500 g), a composite measure of fetal growth and gestational length, is an important indicator of maternal and perinatal health and a predictor of adverse short-term and long-term health outcomes. LBW is a key outcome in global nutrition targets. However, LBW data from administrative data sources have not been systematically collated, existing methods for adjusting survey LBW data are recognised to have several limitations, and no standardised, systematic estimates for LBW prevalence have been produced.

Added value of this study

Through systematic searches (eg, of national statistical offices, ministry of health websites, and websites of the major household survey programmes of Multiple Indicator Cluster Surveys and Demographic and Health surveys), we compiled a global LBW dataset (1447 datapoints from 148 countries). New methods to adjust survey data were developed with UNICEF. We estimate that 20·5 million (uncertainty range 17·4–24·0) livebirths had a birthweight of less than 2500 g in 2015. Most (91%) were in low-income and middle-income countries, with nearly three-quarters in sub-Saharan Africa and southern Asia. Reported data from 57 mostly high-income countries with relatively low baseline suggests almost no change in LBW prevalence. For the remaining countries, we estimate a 17% reduction in LBW prevalence over the years 2000–15, most notably in the countries with the highest LBW prevalence in 2000. Globally, the annual rate of reduction in LBW from 2000 to 2015 was 1·23%.

Implications of all the available evidence

Data meeting inclusion criteria were available for three quarters of all UN member states, with survey data remaining the primary source in low-income and middle-income countries and administrative data the major source in high-income countries. Data adhering to the inclusion criteria were not available for 47 countries. Closing this data gap is an important priority. Data quality remains a concern, with evidence of missing birthweights and heaping. Our methods attempt to correct for heaping in survey data, but correction was not possible for administrative data. To increase data quality and availability, every newborn, whether live or stillborn, must be weighed, and data systems improved to capture the birthweight of every newborn, including those at home or in private facilities. Rates of LBW reduction worldwide will need to more than double to reach the annual rate of reduction of 2·74% required to meet the ambitious global nutrition target of 30% reduction of LBW by 2025. Action is required both to tackle the underlying causes of LBW and to improve the data.

of the global nutrition targets and monitoring LBW trends is an essential component of the Global Nutrition Monitoring Framework approved by member states at the WHA in May, 2015.[17] These targets are reiterated in the Sustainable Development Goals (SDGs).

Previously, it was estimated that there were 20·6 million LBW livebirths in the year 2000;[18] however, there are no contemporary standardised worldwide, regional, and national estimates or systematic trend estimates for LBW, which are essential for tracking progress towards the global nutrition target. The LBW prevalence and trends presented here aim to fill this gap and assist in setting the baseline against which to assess progress towards the achievement of the WHA targets.

See Online for appendix

Methods

Overview

Our study was a systematic analysis of livebirth LBW input data from national administrative sources and nationally representative surveys. We sought to identify all available LBW input data for livebirths. We accessed data that met preset inclusion criteria, and implemented data preprocessing steps, including adjustments to raw data where applicable, to calculate an LBW prevalence from each datapoint—ie, the number of livebirths (regardless of the gestational age) with a birthweight of less than 2500 g divided by the total number of liveborn babies who are weighed or for whom a birthweight could be imputed. Finally, we estimated the LBW prevalence for 195 countries for the years 2000–15 and summed the results to obtain regional and global estimates. We report national-level estimates for 148 countries with data meeting our inclusion criteria. We present our methods in a manner that follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) checklist, which promotes transparency, including the sharing of input data and modelling code (appendix).[16]

Input data

Figure 1 summarises the administrative and survey data inputs and estimation methods. We considered population-based national or nationally representative datasets for inclusion if they contained information on birthweight or LBW prevalence for livebirths (appendix). Nationally representative estimates of LBW prevalence can be derived from a range of sources, broadly defined as administrative data or representative household surveys. National administrative data are defined as data from national systems including Civil Registration and Vital Statistics (CRVS) systems, national Health Management Information Systems (HMISs), and birth registries. Nationally representative household surveys include Demographic and Health Surveys (DHSs), Multiple Indicator Cluster Surveys (MICSs), and other national surveys.

The optimal data source is a CRVS system that records details on all births, including their birthweight, on a continuous basis.[19] Where all newborns are weighed accurately at birth, birthweight is recorded, registration is complete, and the system functions efficiently, the

resulting LBW prevalence will be accurate and timely. However, existing administrative data systems might not cover all births, or might not collect birthweight data at all. In these settings, household surveys, such as the UNICEF-supported MICS and the USAID-supported DHS are important data sources for estimates of child health, including LBW, but are recognised to have biases. These data systems rely on accurate birthweight measurement, but despite increasing prevalence of facility births, many newborns are not weighed, and when weighed, so-called heaping at specific birthweights (eg, multiples of 100 g or 500 g) is common. We excluded subnational or other non-population-based data such as those from demographic surveillance sites and individual hospital data from the LBW data searches as they are rarely nationally representative.

To identify national administrative data, we searched the websites of the national statistical offices (NSOs) and ministries of health of all countries. Data from years 2000–16 were included. For countries with more than one source of national administrative data available for a given year, we gave preference to NSO website data where available. Where NSO data were unavailable, we used data obtained from the Ministry of Health website. We used WHO regional databases and a UNICEF database (TRANSOMNEE)[20] to identify countries with national administrative data not retrieved through initial searches. These data were only included if they contained a reference to their source or could be verified as national administrative data from the NSO or Ministry of Health. Where necessary we contacted WHO and UNICEF regional and country offices to request further details of data sources.

We obtained datasets for all DHSs and MICSs with a midpoint of data collection of 1998 or later, and for which raw datasets were publicly available and contained birthweight data.[21–23] A national team from the China Health Information and Statistics Center of the National Health Commission reanalysed data from the Chinese National Health Services Surveys. If data were available from both national administrative or nationally representative surveys for a given country, all data meeting the inclusion criteria were included in the database and subsequent modelling process.

Where no national administrative or nationally representative survey data were readily available through web-based searches, we contacted UNICEF and WHO regional and country offices in September–December, 2014, and again in autumn 2015 and invited them to provide details of any available national LBW data.

From October, 2017, to January, 2018, we did a joint WHO–UNICEF country consultation process to enable each country to provide feedback on the LBW input data used, modelling methods, and preliminary estimates for their country. We received further data from 55 countries through the consultation process, resulting in 341 new or updated country-year observations.

Exclusions based on population representativeness at a national level

We excluded national administrative data covering less than 80% of the population, or from countries with less than 80% facility births in the data source year or less than 80% of the UN estimated livebirths in a given year. We also excluded survey data that were not nationally representative, as well as those with less than 30% weighed at birth. We applied a lower threshold for coverage of livebirths weighed to surveys (≥30%) compared with administrative data sources (≥80%) because raw data are available for surveys, allowing multiple imputation of missing birthweights by use of other covariates from the survey. This was not possible for data from administrative sources.

Data quality assessment

We identified several potential sources of bias in LBW data sources (table 1). These include errors in birthweight measurement and recording (including heaping of recorded birthweights on 2500 g), misclassification between livebirths and stillbirths, missing birthweight data, and, for administrative data, non-representativeness at national level of births captured in the data system. Overall, these biases are likely to result in an underestimate of LBW prevalence. We took a two-step approach to seek to adjust for possible biases. First, we

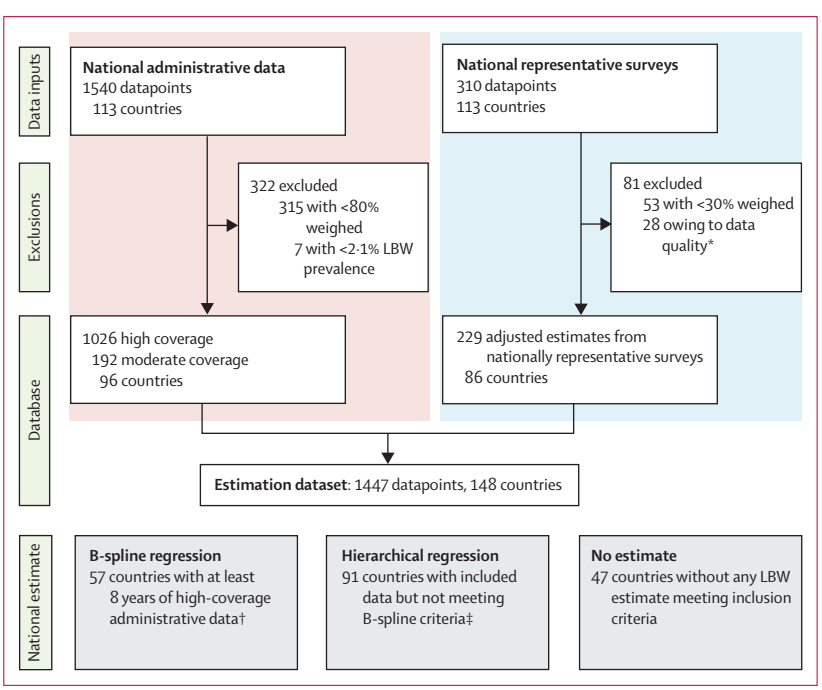

Figure 1: **Administrative and survey data inputs and estimation methods**
LBW=low birthweight. *28 survey datasets were excluded on quality criteria: seven datasets were excluded because of extreme heaping around three values, nine because more than 10% of births weighed at least 4500 g, one because of excessive heaping on the tail end of the birthweight distribution, seven because of an inability to obtain results from adjustment procedures, and four because very low numbers of livebirths were weighed. †8 years of data between 2000 and 2015, with at least one datapoint before 2005 and one after 2010. ‡The estimate for India was based on partial data for the most recent survey; therefore, modelled estimates are not shown for individual country.

	Likely effect on LBW prevalence estimates*
Coverage of weighing: bias in newborns weighed at birth	
Many newborns in LMICs are not weighed at birth, especially if born at home. These are more likely to be socioeconomically disadvantaged and at higher risk of LBW.	↓
Extremely preterm or sick babies, those stillborn or dying soon after birth and those born around threshold of viability are the most likely to not be weighed. These babies are at high risk of being LBW.	↓
Coverage of data system: bias in newborns included in data source	
Low coverage of administrative data systems in many LMICs (eg, lower coverage of birth registration for those who die shortly after birth, missing home births, and births in private facilities even if weighed). Births in private facilities are more likely to be socioeconomically advantaged and at lower biological risk of LBW; however, high prevalence of medical interventions (eg, caesarean sections both indicated and elective before 37 weeks, may increase risk of LBW).	↓ or ↑
Loss of birthweight data: biases in missing birthweight data†	
In surveys, biases in card retention (eg, birthweight not available for babies who died who are more likely to have been LBW).	↓
Missing administrative birthweight data on sickest babies (frequently LBW) who are transferred immediately to (and weighed in) a newborn ward.	↓
Measurement errors: individual measurement or recording error	
Heaping of recording of birthweight on 2500 g. As definition excludes babies with birthweight exactly 2500 g, those LBW newborns with birthweight near the threshold frequently heaped at 2500 g.	↓
Errors in birthweight measurement (eg, poorly calibrated scales, inappropriate devices), suboptimal weighing practices (eg, clothed or delayed weighing until days after birth).	↓ or ↑
Extremely preterm or sick babies and those born around threshold of viability who die soon after birth are more likely to be misclassified as stillbirth. These babies are at high risk of being LBW.	↓
Measurement units error	
Confusion in surveys collecting data in both lbs and grams (eg, LBW baby weighing 4·0 lb recorded as 4·0 kg).	↓
Denominator calculation errors in LBW prevalence calculation	
LBW prevalence calculated as: number with birthweight <2500 per all livebirths (whether weighed or not).	↓

LBW=low birthweight. *↓=the potential bias is likely to lead to a decreased LBW prevalence. ↑=the potential bias is likely to lead to an increased LBW prevalence. †For newborns who are both included in the data source and weighed at birth.

Table 1: **Potential sources of bias in low birthweight data**

did a quality assessment of all the available data. Second, where possible, we adjusted included data.

Raw individual-level data were available from household surveys as the datasets are in the public domain, allowing analysis of data quality and recording errors. We excluded surveys with inadequate data quality in three areas as follows. First, implausible birthweight distribution defined as extreme heaping whereby more than 55% of all birthweights in the dataset fall on only three values (eg, >55% of birthweights in the dataset were 2500 g, 3000 g, or 3500 g); more than 10% of births weighed at least 4500 g; or excessive heaping on the tail end of the birthweight distribution with more than 5% of birthweights at 250–500 g and 5500 g. Second, inability to obtain from adjustment procedures of multiple imputation or fitting of a mixture of two normal curves, or both. Third, data from surveys with very low numbers of livebirths weighed (<200) and hence high stochastic variation.

We made no further categorisation of data quality among included surveys. We made adjustments to the data from nationally representative household surveys by use of a revised methodology to seek to overcome the limitations of the previously used approach to address missing birthweights and heaping. We implemented a modelling approach that comprised multiple imputation with individually linked variables for all surveys (appendix). We replicated multiple imputations five times per survey and used several variables related to birthweight available in the survey datasets, including maternal factors (height, body-mass index [BMI], and parity), and newborn factors (sex, singleton–multiple status, and perceived size at birth).

To address heaping, we fitted a mixture of two normal distributions to each survey dataset. Whereas previous studies have found that, under ideal conditions such as low-risk full-term singleton livebirths included in the WHO child growth standards, birthweight is approximately normally distributed,[24] this assumption might not apply to all national populations. We tested this assumption in an analysis of high-quality administrative data from the USA.[25] Fitting a single normal distribution to this data from which the proportion of LBW could be estimated resulted in an overestimate of the proportion of livebirths with LBW compared with the raw data. This might indicate that the population of all births comprises two or more subpopulations with different distributions. Fitting a mixture of two normal distributions resulted in an estimated proportion of LBW very close to that seen in the raw data. We also investigated fitting a mixture of three normal distributions. However, this did not substantially improve the estimate of the proportion of LBW.

In summary, we estimated the proportion of LBW livebirths from each survey by the use of five steps. First, we developed five datasets that had a birthweight for each livebirth (reported where available or imputed). Second, we fitted two normal distributions to the datasets. Third, we calculated the LBW Z score for each of the two normal distributions:

$$Z_{2500} = \frac{2500\text{ g} - \text{mean birthweight}}{\text{SD}_{\text{birthweight}}}$$

Fourth, we estimated the percentage of LBW (LBW[%]) for each of the two distribution curves:

$$\text{LBW}(\%) = \text{P}\ (x < Z_{2500})$$

(ie, the percentage of the area under the curve $<Z_{2500}$). Finally, we estimated the overall LBW prevalence by calculating the LBW(%) of the full dataset, which was a weighted average of the LBW(%) from both curves. The weights used were based on the proportion of the population estimated to belong to each subpopulation.

Since data from administrative data sources in the public domain usually only provide an aggregate number

of LBW livebirths—ie, total livebirths or the reported LBW prevalence without individual-level data, or both—it was not possible to adjust LBW estimates to account for missing data and heaping in these data. To our knowledge, there are no previously used markers of data quality specifically for reported aggregated LBW prevalence. To assess and categorise the quality of available national level routine data, we reviewed previously used data quality criteria from other related maternal and perinatal global estimation exercises.[6,26,27] Of these, only population representativeness, assessed by completeness of birthweight data, was feasible to apply (appendix). Datapoints from countries with less than 80% facility births or reporting a birthweight for less than 80% of the UN estimated livebirths in a given year were excluded. We further categorised included data into higher quality administrative data (data from countries with a facility birth prevalence ≥90% and with the data source covering ≥90% of UN estimated livebirths in the given year) and moderate quality administrative data (data from countries with a facility birth prevalence of at least 80% and with the data source covering at least 80% of UN estimated livebirths in the given year, not fulfilling higher quality criteria).

Exclusions based on implausibility

We used conservative cutoffs to identify implausible LBW data. We excluded datapoints with an LBW prevalence of less than 2·1%, on the basis of the lowest population-based LBW prevalence in any country from the INTERGROWTH study.[28] Since the INTERGROWTH study only included healthy women at low risk of pregnancy complications, including preterm birth and fetal growth restriction, the national LBW prevalence for all countries would be expected to be substantially higher than this cutoff. For example, the lowest national LBW prevalences from countries with strong national reporting systems are around 4%. The highest population-based LBW prevalence from any data source was 37%.[29] We therefore decided to exclude datapoints with LBW prevalence greater than 40%; however, no datapoints were excluded on the basis of LBW prevalence of more than 40% (figure 1).

Estimation of LBW prevalence by year and country

We defined higher quality time series administrative data for LBW prevalence as data from countries with the earliest year of data available before 2005, the latest year after 2010 with data available for at least half of all years, and no evidence of large year-on-year variability in LBW prevalence (coefficient of variation <15%). We estimated LBW prevalence for all other countries by means of a regression model. We modelled the logarithm of LBW prevalence as the outcome variable by use of restricted maximum likelihood estimation and including a country-level random effect.

We investigated multiple predictor variables associated with LBW, including distal determinants such as geographical and socioeconomic factors, more proximal demographic and biomedical factors, and markers of perinatal outcome (appendix). We included dummy variables in the model to account for systematic bias in different data types (higher quality national administrative data, moderate quality national administrative data, and nationally representative survey). We included all potential predictors with time series data or estimates available by country for 2000–15 in the model selection process (appendix).

We assessed correlations between predictors by use of the variance inflation factor. We dropped predictors with a variance inflation factor of greater than 10 as this is likely to indicate high correlation with other predictors. We retained predictors when the direction of the coefficient was biologically plausible. We sought to maximise the predictive power of the model, while avoiding overfitting. We removed one predictor at a time from the model, commencing with the predictor with the largest value of the Bayesian information criterion (BIC) on univariate analysis, and refitted the model. If removing this predictor improved the model (lower BIC compared with the model containing the predictor), we dropped the predictor from the model. If the BIC was higher, we retained the predictor. We cycled through all the predictors once.

The final model included the logarithm of neonatal mortality rate, the proportion of children underweight (below –2SDs from median weight for age of reference population), data type (higher quality administrative data, lower quality administrative data, household survey), UN region (southern Asia, sub-Saharan Africa or other region), and a country-specific random effect (table 2). We assessed model performance by use of diagnostic plots. The model seemed to fit the data reasonably well overall (R^2=0·48), and both the estimates of the country-specific random effects (SD 0·31) and the residuals for the individual datapoints included (SD 0·11) appeared to be approximately normally distributed (appendix).

For the 91 countries with data in the input dataset, we included the best linear unbiased prediction of the

	Coefficient (95% CI)
Neonatal mortality prevalence	0·009 (0·005 to 0·012)
Child underweight	0·615 (–0·031 to 1·260)
Region	
Other regions	..
Sub-Saharan Africa	0·300 (0·169 to 0·4)
Southern Asia	0·6 (0·355 to 0·915)
Data type	
High-quality administration data	..
Moderate-quality administration data	–0·008 (–0·0 to 0·002)
Nationally representative survey	0·165 (0·132 to 0·198)

..=baseline category.

Table 2: **Model coefficients for included predictor variables of low birthweight prevalence**

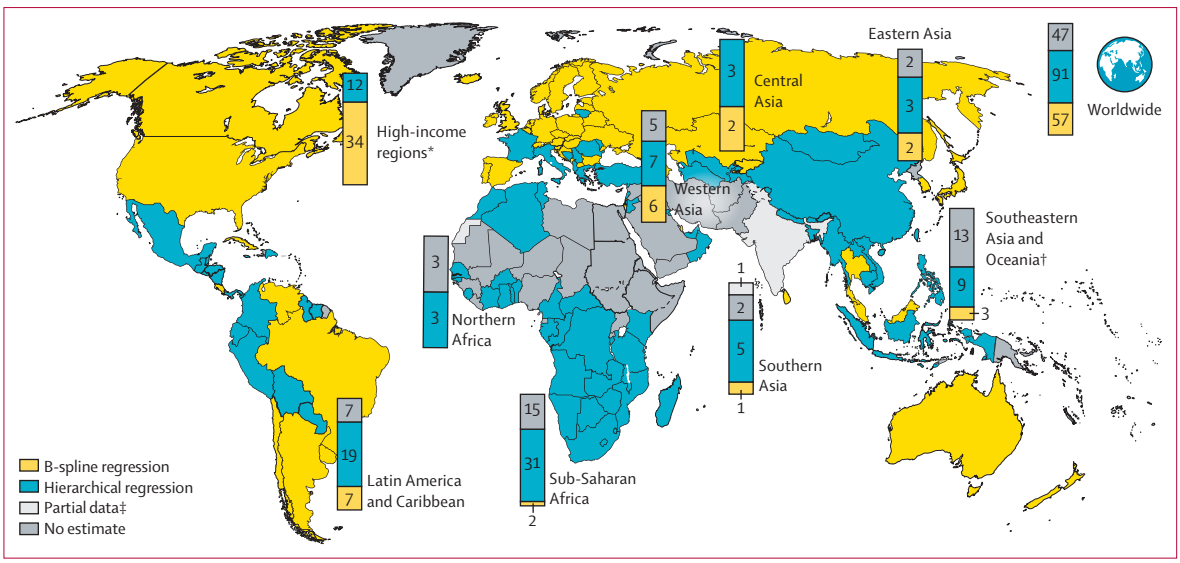

Figure 2: **Low birthweight estimate methodology, by country (map) and region (bars), 2000–15**
B-spline regression countries met criteria for minimum number of years of highly representative administrative estimates, hierarchical regression countries did not meet B-spline criteria but had at least one estimate meeting inclusion criteria; no estimate countries did not have any LBW estimate which met the inclusion criteria. See appendix for details. *High-income regions include North America, Europe, and Australia and New Zealand. †Southeast Asia and Oceania excluding Australia and New Zealand. ‡Estimate based on partial data for most recent survey; therefore, modelled estimates are not shown for the individual country.

	Number of data inputs	Number of livebirths included	Low birthweight prevalence		
			Mean (SD)	Minimum	Maximum
Overall	1447	281 418 400	8·1% (3·9)	2·2%	32·9%
High-quality administrative data	1026	235 500 000	7·1% (2·5)	2·2%	17·6%
Moderate-quality administrative data	192	44 631 000	7·9% (3·1)	2·4%	15·7%
Nationally representative surveys	229	1 287 000	12·9% (5·6)	3·1%	32·9%

Table 3: **Low birthweight prevalence input data by type**

country-specific effect in the LBW prediction. For countries with no data, contributing only to the regional and global levels, we assumed the country random effect to be zero. We used high-quality national administrative data as the reference standard for prediction purposes for all countries in the higher-income regions (North America, Europe, and Australia and New Zealand). We used nationally representative household surveys as the reference for prediction purposes for countries from all other regions. We generated uncertainty ranges (URs) for modelled estimates by use of a bootstrap approach. When presenting by region we used an aggregate grouping of the United Nations regional subgroups (appendix). To obtain worldwide and regional estimates of uncertainty we summed the country LBW estimate at worldwide or regional level for each of the 1000 samples obtained from the bootstrap or B-spline approach and used the 2·5th and 97·5th centiles of the resulting distributions (appendix). Analyses were done with Stata 14.

We used livebirth estimates from the World Population Prospects: the 2017 revision[30] to estimate the absolute number of LBW livebirths (livebirths × low birthweight rate) in a given year. LBW estimates generated from all 195 countries contributed to the regional and global estimates. National-level estimates are presented for the 57 countries with higher quality time series data and 91 other countries with at least one LBW prevalence datapoint since 2000 meeting the inclusion criteria (total 148 countries; figure 2; appendix). The modelled national-level estimate generated is not shown for 47 countries without any input data.

Role of the funding source
The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. HB had full access to all the data in the study and all authors had final responsibility for the decision to submit for publication.

Results
Our final dataset was 1447 country-years of birthweight data (281 million births), comprised of 1026 high-coverage and 192 moderate-coverage datapoints from administrative data sources and data from 229 surveys (figure 1; table 3; appendix). Although data were available for 148 countries, most datapoints were categorised as national administrative data, predominantly from high (65%) or upper middle-income (28%) settings. The majority (54%) of LBW datapoints meeting inclusion criteria from low-income and lower middle-income settings were from household surveys. Countries from high-income regions had an average of 13 datapoints

	2000		2015		Annual rate of reduction in low birthweight prevalence 2000–15
	Low birthweight prevalence per 100 livebirths	Number of low birthweight newborns (UR)	Low birthweight prevalence per 100 livebirths	Number of low birthweight newborns (UR)	
North America, Europe, Australia, and New Zealand	7·0 (6·8–7·2)	832 900 (813 800–856 600)	7·0 (6·8–7·1)	884 400 (866 900–905 600)	0·01%
Northern Africa	13·7 (10·4–19·3)	602 400 (458 800–846 700)	12·2 (9·4–17·9)	712 600 (546 300–1 043 500)	0·77%
Sub-Saharan Africa	16·4 (13·8–20·4)	4 436 000 (3 729 700–5 499 000)	14·0 (12·2–17·2)	5 000 100 (4 349 600–6 146 300)	1·09%
Central Asia	6·0 (5·1–6·9)	71 700 (62 000–83 500)	5·4 (4·8–6·1)	85 500 (76 200–96 700)	0·71%
Southern Asia	32·3 (22·4–44·0)	12 694 600 (8 800 300–17 292 700)	26·4 (18·6–35·2)	9 807 400 (6 913 700–13 104 600)	1·37%
Eastern Asia	6·0 (4·9–7·4)	1 111 000 (900 100–1 364 100)	5·3 (4·3–6·6)	1 010 600 (822 600–1 264 800)	0·83%
Western Asia	10·9 (9·0–13·7)	532 300 (437 400–667 200)	9·9 (8·1–12·5)	560 200 (456 400–703 000)	0·63%
Southeast Asia and Oceania*	13·6 (10·1–16·6)	1 598 600 (1 190 300–1 947 200)	12·2 (9·5–14.6)	1 471 000 (1 151 700–1 763 800)	0·75%
Latin America and Caribbean	8·8 (8·1–9·6)	1 023 300 (945 800–1 113 500)	8·7 (8·1–9·6)	938 300 (871 500–1 032 100)	0·07%
Global	17·5 (14·1–21·3)	22 902 400 (18 405 800–27 798 400)	14·6 (12·4–17·1)	20 469 700 (17 375 000–24 017 900)	1·23%

*Excluding Australia and New Zealand.

Table 4: **Estimated low birthweight prevalence and number of low birthweight babies for 2000 and 2015, by region**

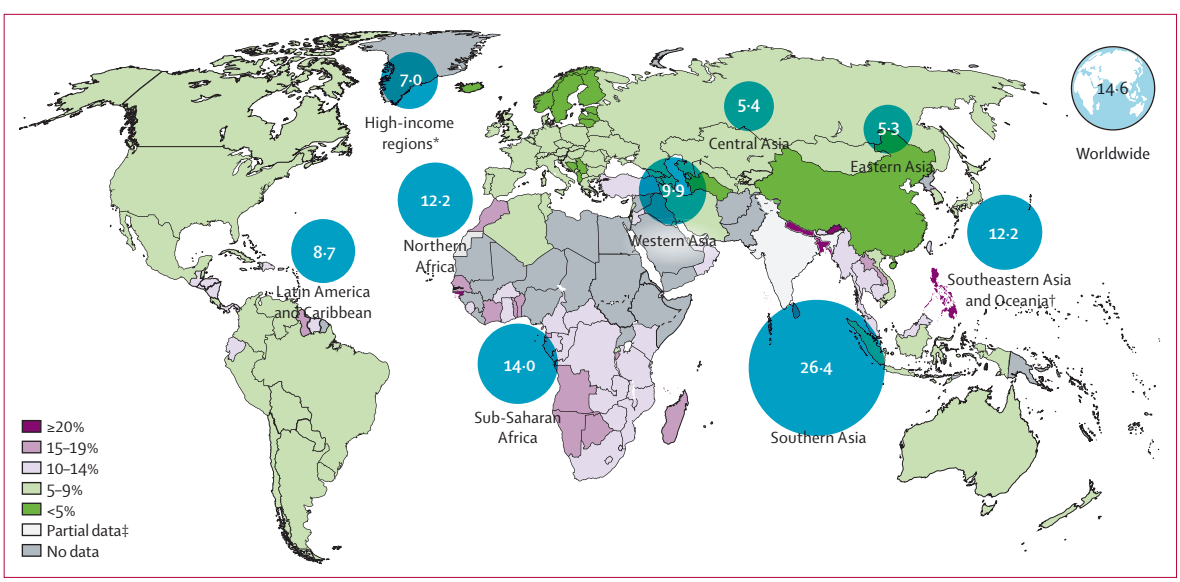

Figure 3: **National and regional low birthweight prevalence, 2015**
*High-income regions include North America, Europe and Australia and New Zealand. †Southeastern Asia and Oceania does not include Australia or New Zealand. ‡Estimate based on partial data for most recent survey; therefore, modelled estimates are not shown for the individual country.

included compared with eight for upper-middle-income, four for lower-middle-income, and two for low-income regions (appendix). For 47 countries, no data fulfilling the inclusion criteria were located.

We estimate that the global LBW prevalence in 2015 was 14·6% (UR 12·4–17·1), compared with 17·5% (14·1–21·3) in 2000 (table 4). This represents an estimated 16·6% decline in the LBW prevalence over this period (average annual rate of reduction [AARR] 1·23%). Although the uncertainty around these estimates is sizeable, they suggest some reduction in LBW prevalence over this time period. The highest burden of LBW is in the southern Asian, southeastern Asian, and sub-Saharan African regions (table 4; figure 3). The estimated rate of reduction in LBW prevalence is fastest in the regions with the highest baseline LBW prevalence and

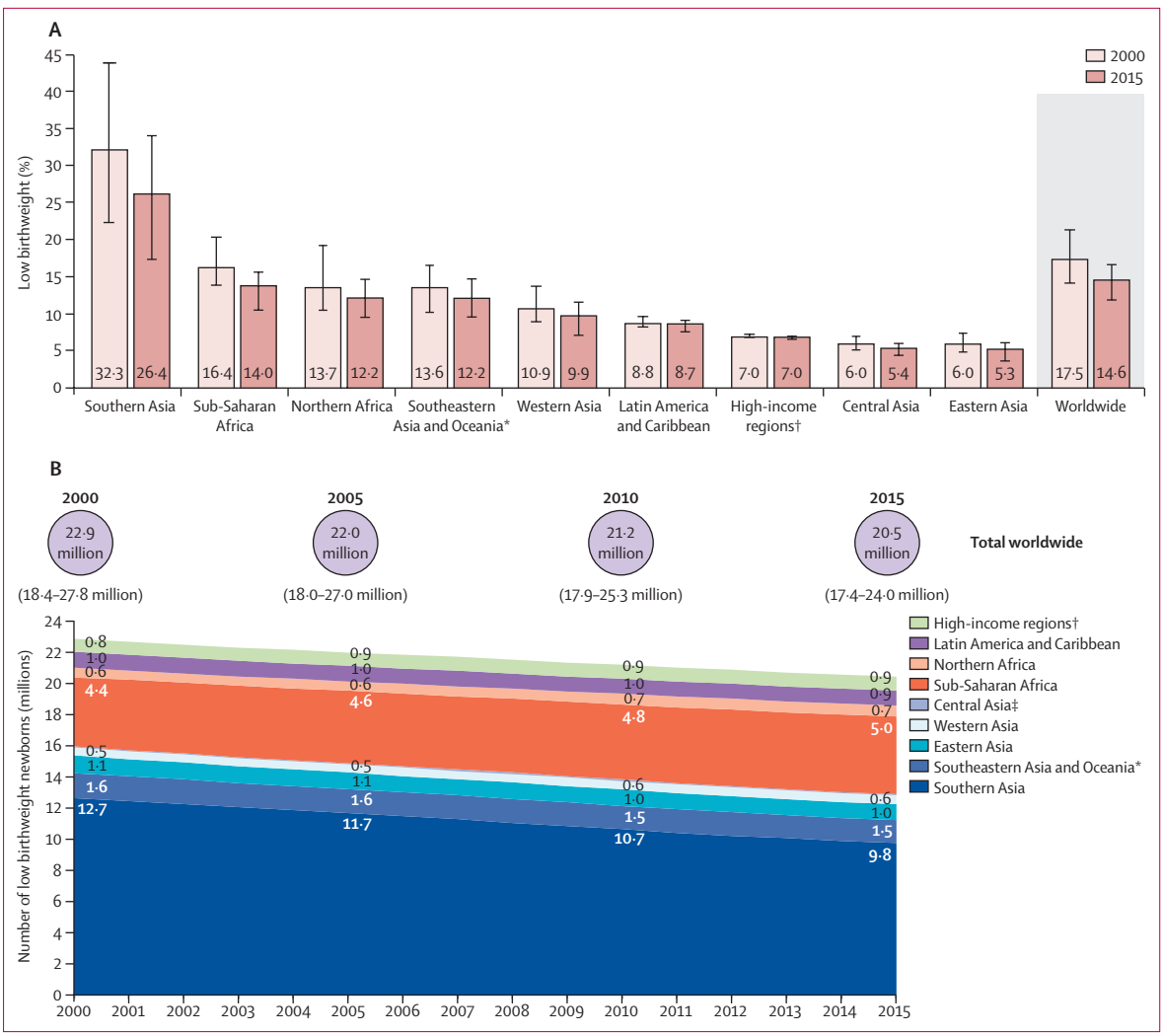

Figure 4: **Regional and worldwide change in low birthweight between 2000 and 2015**
(A) Changes in low birthweight rates. (B) Changes in absolute numbers of low birthweight newborns. *Southeastern Asia and Oceania does not include Australia or New Zealand. †High-income regions include North America, Europe, and Australia and New Zealand. ‡Central Asia labels not on graph due to space limitations, the number LBW is 0·1 million in all years.

slowest in high-income regions and Latin America and the Caribbean (table 4; figure 4). In 2015, 85 of the 148 countries with data had an estimated LBW prevalence of less than 10%, whereas six countries were estimated to have LBW prevalence of at least 20% (appendix).

The absolute number of livebirths with LBW globally is estimated at 20·5 million (UR 17·4–24·0) in 2015 compared with 22·9 million (18·4–27·8) in 2000 (figure 4). This represents a 10·6% decline in the point estimate against a 7·7% increase in the number of livebirths overall during this period. However, in some regions, despite reducing LBW prevalence, the overall estimated number of LBW livebirths has increased owing to demographic trends. In sub-Saharan Africa, the number of LBW livebirths is estimated to have increased from 4·4 million in 2000 to 5·0 million in 2015 (table 4). Southern Asia remains the region with the largest burden in terms of numbers, despite progress in reducing LBW prevalence (AARR 1·37%). An estimated 9·8 million LBW livebirths were born in this region in 2015—nearly half (48%) of the worldwide total.

Discussion

We present global, regional, and national estimates for LBW with trend estimates, which are essential for tracking progress towards the Global Nutrition World Health Assembly target regarding LBW. Our estimates suggest that 20·5 million (UR 17·4–24·0) livebirths had a birthweight of less than 2500 g in 2015. Estimated progress in reducing LBW prevalence is slower than that required to meet the global nutrition target[16]—with an AARR of 1·23% between 2000 and 2015 compared with the required 2·74% between 2012 and 2025 to reach the target of a 30% reduction.

A strength of this work is that this LBW dataset is the largest compilation to date, including data from 148 countries and a more than 281 million births. In addition to the increased data quantity, we have applied new methods to adjust estimates on the basis of survey data that are more able to account for both data heaping and missing data. However, an important challenge is that almost half (48%) of all datapoints are from the high-income regions of North America, Europe, and Australia and New Zealand, which account for 4% of the world's LBW livebirths. By contrast, only 13% of data are from sub-Saharan Africa and southern Asia, the regions with the highest LBW prevalence, accounting for nearly three quarters of all LBW livebirths in 2015. 47 countries—the majority (87%) low-income or middle-income—that account for 23% of all births worldwide had no data meeting inclusion criteria. This is a classic example of the inverse data law—the least data for the highest burden settings.[31] In addition, when available, these data tend to be lower quality with more heaping and other challenges, which probably lead to underestimates of LBW (table 1).

Regarding trends, no high-quality LBW trend data were available for 138 countries (91 with some LBW data meeting inclusion criteria and 47 without such data), and we therefore predicted LBW prevalence by use of a statistical model. The regions with the highest estimated change in LBW prevalence (and numbers) are sub-Saharan Africa and southern Asia, where the data are most uncertain and the estimated trends are driven by changes in predictors, which might not accurately reflect true changes in LBW prevalence over the same time period. Hence, it is plausible that the true change in prevalence for LBW worldwide is lower than our estimation of 1·23%, and the gap to reach the target is even greater.

The LBW data available from the highest burden settings are predominantly from household surveys and are susceptible to bias owing to missing birthweights and heaping. From 2004 to 2017, UNICEF used a simple cross tabulation to adjust for missing birthweight by use of data from a single variable (perceived size at birth), and a crude standard adjustment for heaping that assumed that 25% of birthweights reported as 2500 g were actually below 2500 g in every survey.[18,32] This previously used method had a number of important limitations.[33] Hence, we used multiple imputation to impute missing birthweights. We used several variables including perceived size. We sought to address heaping throughout the birthweight distribution by fitting a mixture of two normal distributions to the observed data to obtain an estimate of the proportion of livebirths with a birthweight of less than 2500 g. Although we believe our approach represents an advance on the previous method, it does require assumptions—namely, that missing birthweights are missing at random and that the true distribution of birthweights in a population can be well approximated by a mixture of two normal distributions.

Although we were able to adjust for heaping in the survey data for which we had individual birthweight data, we were unable to do so for national administrative data sources for which such data were unavailable. This might lead to an underestimate of the LBW prevalence from these sources when LBW livebirths with birthweights of less than 2500 g are recorded as (heaped on) 2500 g and categorised as normal birthweight.

Global estimates have well recognised limitations,[34] and investments in data systems are needed to improve multicountry tracking of progress towards global targets. Large countries, such as India, are taking steps to improve the data. However, ongoing efforts are required to support countries in strengthening their routine reporting systems to decrease missing and erroneous birthweight measurements as part of their commitment to report on the Global Nutrition Monitoring Framework and SDGs.[17] Improving measurement of birthweight must occur alongside improvements in recording and reporting of all birth outcomes for mothers and their newborns, whether live or stillborn.[35,36] Challenges arising from the low quality of some data are compounded by absence of clear, internationally harmonised guidelines on how to assess LBW data quality.

More than 80% of all births worldwide are now in health facilities, yet despite this, most of the included datapoints from the highest burden regions are from household surveys, often with relatively low proportions having a reported birthweight. Improving the coverage

	Potential approaches
Ensure accurate birthweight for all births	
Equipment	Improve availability and maintenance of suitable devices for birthweight measurement in all locations where births occur (facility or community). Establish minimum standards for equipment, including precision and scale type.
Training–human resources	Develop and disseminate protocols and guidelines. Preservice and in-service birthweight measurement training. Promote culture of weighing all babies (including the smallest and sickest). Identify and address barriers to weighing (eg, layout, staffing, etc). Improve awareness of clinical and public health importance of birthweight (eg, local data use in birthweight specific mortality).
Ensure all birthweights captured in data systems	
Data management	Standardise and streamline recording process for clinical staff, reduce repetitive recording.
Data coverage	Improve coverage of routine data systems in all facilities (including private) and timeliness of reporting. In settings with high rates of home birth, strengthen weighing in the community (eg, by CHW or TBA and link to health data system). Improve coverage of birth certificates and health cards including birthweight and motivate for birthweight to be included on all birth certificates.
Maximise data quality	
Data quality	Ensure minimum data collated (including number LBW, number weighed, number missing birthweight). Data quality checks and feedback as required. Correct data for heaping where required. Promote data literacy so that poor data are recognised and improved.
Use data to inform policy	
Data use	Improve timely data availability and use at local, district, and national level for policy, programming, and practice.

CHW=community health worker. TBA=traditional birth attendant.

Table 5: **Recommendations for improving birthweight data**

and quality of birthweight data is crucial to drive actions to reduce LBW and will require action at many levels of the health system (table 5). Closing the gap between facility births and accurate birthweight recording should be feasible and would transform data availability. At the individual clinical level, appropriate equipment and trained staff are needed in both the public and private sectors. Weighing devices have been available since antiquity and routine birthweight measurement has been standard practice in Europe since the late 19th century; however, accurate information on birthweight is absent for most births worldwide. For example, heaping has been shown to be worse when analogue scales are used rather than digital ones and where scales with low precision are used.[37,38] There is a pressing need to develop affordable, robust, portable, and accurate weighing devices for use in both facility and community settings.

Recording of birthweight data on health cards, which can be used as a data source at the time of the survey, could substantially improve the quality of survey birthweight data and reduce the need for adjustments (table 5).

The sickest and smallest newborns are often missing from the data systems, including those who die soon after birth, or are admitted to another ward. Data system improvements and linkages are required to capture information on these most vulnerable newborns.

Misclassification of early neonatal deaths as stillbirths remains an issue. Since these babies are more likely to be LBW, this can lead to an underestimate of LBW prevalence if stillbirths are excluded.[39] Therefore, it is important that every newborn, whether live or stillborn, is weighed at birth and that core information including birthweight and gestational age is captured within the data system.

Societal and family demand for birthweight data is an understudied issue. Little is known about family and community perceptions and demand for birthweight measurement, including cultural barriers to birthweight measurement, especially in some community settings, and for stillbirths. Innovations that increase the value parents attach to birthweight data might help recall, and lead to improved recording on handheld health cards and birth certificates.

Birthweight reflects both intrauterine fetal growth and length of gestation. Assessing measures of weight for gestational age, for example small-for-gestational age, enables these two components to be distinguished. However, challenges in assessing gestational age accurately in many low-income and middle-income countries limit its use as a routine public health measure.[40,41] Debate has focused on the appropriateness of a single birthweight-for-gestational age cutoff for defining fetal growth restriction, with ethnic-specific standards associated with more accurate prediction of neonatal mortality and morbidity.[42–44] Clear guidance on appropriate standards will be required as more data on gestational age become available at a national level worldwide, enabling tracking of fetal growth.

Reducing LBW requires a multifaceted approach.[46] Even in the absence of accurate gestational age data at a national level, an understanding of the underlying pathways to LBW in a given setting is required to reduce the burden. For example, in southern Asia around half of LBW newborns are phenotypically term but small-for-gestational age, which is driven by underlying maternal undernutrition including maternal stunting.[4] Conversely preterm birth is the major contributor to LBW in settings with many adolescent pregnancies or with high prevalence of infection (eg, in east and southern Africa) or where pregnancy is highly medicalised with high levels of fertility treatment and intensive obstetric management including high prevalence of caesarean sections (eg, the USA and Brazil).[47] Improved birthweight data, coupled with high-quality data on gestational age, will be needed to target interventions appropriately and to track progress. Ongoing initiatives to improve CRVS and HMISs should be designed to ensure that this information is captured for all births.

We estimate that there were 20·5 million LBW livebirths in 2015 worldwide, nearly three quarters of them in southern Asia and sub-Saharan Africa. Progress in reducing LBW prevalence (AARR 1·23%) is insufficient to reach the global nutrition targets, which will require an AARR of 2·74%. Accurate birthweight data are needed for all births to improve both individual clinical care and public health action. There are large data gaps for the countries with the highest burden. In addition to better birthweight data, better gestational age assessment would help to identify the most appropriate interventions in a given setting. Targeted action to address the underlying causes of LBW (preterm birth and fetal growth restriction) and improved care for those born with LBW is needed to ensure that all realise their full potential to survive and thrive. In the SDG era, these most vulnerable babies must not be left behind.

Contributors

MdO, EB, CH, REB, and JEL contributed to overall co-ordination and overseeing of the process, and the idea was proposed by JEL. JK contributed to overall co-ordination and led the survey analysis work. HB contributed to overall coordination, collating of data sources, model fitting, and analysis. SC and GAS contributed overall statistical advice. LC contributed to administrative data collection and review, and initial data analysis. SS contributed to administrative data collection and review, model fitting, administrative data analysis, and preliminary survey analysis. XA contributed to survey analysis. VPH contributed to the data analysis and figures. MdO, DE, and CH contributed to co-ordination of the country consultation. The authors alone are responsible for the views expressed in this Article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

Declaration of interests

We declare no competing interests.

Acknowledgments

This work was funded through the Bill & Melinda Gates Foundation via a grant to the Johns Hopkins Bloomberg School of Public Health (Maternal and Child Epidemiology Estimation) and via UNICEF (Strengthening Data for Accountability in the Areas of Child Survival, Health and Nutrition grant). Also funded by the Children's Investment Fund Foundation as part of a grant to the London School of Hygiene & Tropical

Medicine for Every Newborn measurement improvement. WHO and UNICEF also provided resources. WHO and UNICEF participated in the analyses. We thank the China Low Birthweight Epidemiology Analysis group from the China Health Information and Statistics Center of National Health Commission: Zhang Yao Guang, Deputy Division Director. We are deeply grateful to UNICEF and WHO regional and country offices for their support during the country consultation process and to all Member States who provided updated birthweight data and validated their country LBW estimates. Special thanks to Brazil, Ecuador, Jamaica, Macedonia, and the Philippines, for their valuable feedback on the methodology. We acknowledge Nona Reuter from UNICEF for production of the maps and figures and Ivana Bjelic and Yadigar Coskun from UNICEF for support with analysis of the survey data.

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6. Where are we now? Where are we going? Lessons learnt from national estimates of stillbirth, preterm birth and low birthweight rates

In the preceding chapters data collation and estimation exercises for stillbirth, preterm birth and low birthweight have shown that while many countries have data to inform these estimates, the quality of such data varies between settings and within settings over time. In addition, there are still some countries with no empirical data to inform estimates.

6.1. Summary of current data availability

There were 41 countries with national CRVS data classified as 'higher quality' across all three outcomes (Table 6-1). An additional four countries had higher quality national CRVS data for stillbirth and low birthweight, and a further 27 countries had such data for low birthweight along. Whilst acknowledging that these data are not perfect, with some limitations that will be discussed later in this chapter, they provide a good starting point for further data improvements to increase data comparability. In contrast there are 47 countries with no national data meeting inclusion criteria for any of the outcomes.

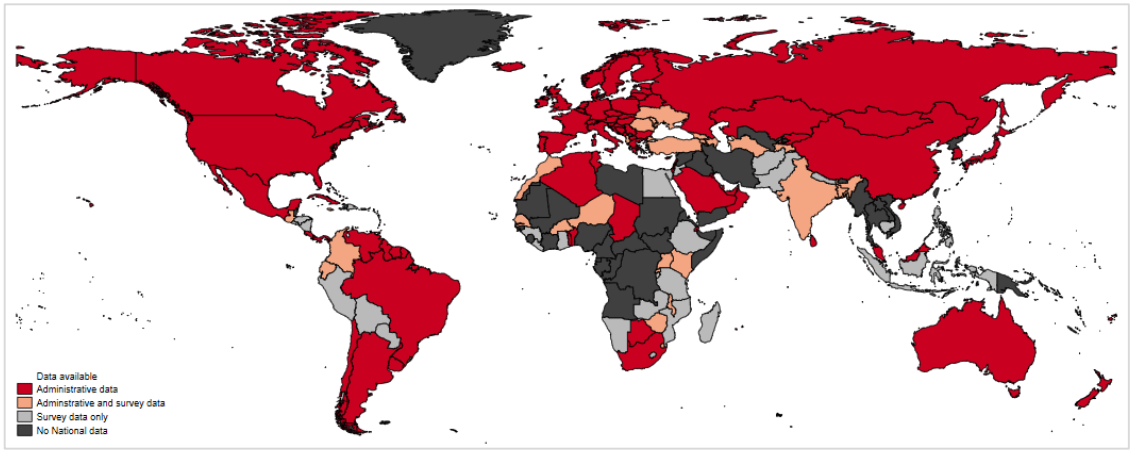
Table 6-1 Data availability for stillbirth, preterm birth and low birthweight estimates

Data type	Stillbirth Data	Preterm Birth	Low birthweight
National CRVS: higher quality	45 countries (23%)	41 countries (22%)	72 countries (37%)
National CRVS: lower quality	65 countries (33%)	9 countries (5%)	15 countries (8%)
Nationally representative survey	57 countries (29%)	8 countries (4%)	61 countries (31%)
No national data	51 countries (26%)	126 countries (68%)	47 countries (24%)
Subnational data only	*13 countries (7%)*	*41 countries (22%)*	*Not applicable*[a]

For low birthweight and stillbirth estimates data were collated for 195 countries. For preterm birth outcome data were collated for 184 countries; 11 countries small nations with fewer than 1,000 births in 2010 were excluded.
[a]Subnational data were not considered as part of the estimation process for low birthweight

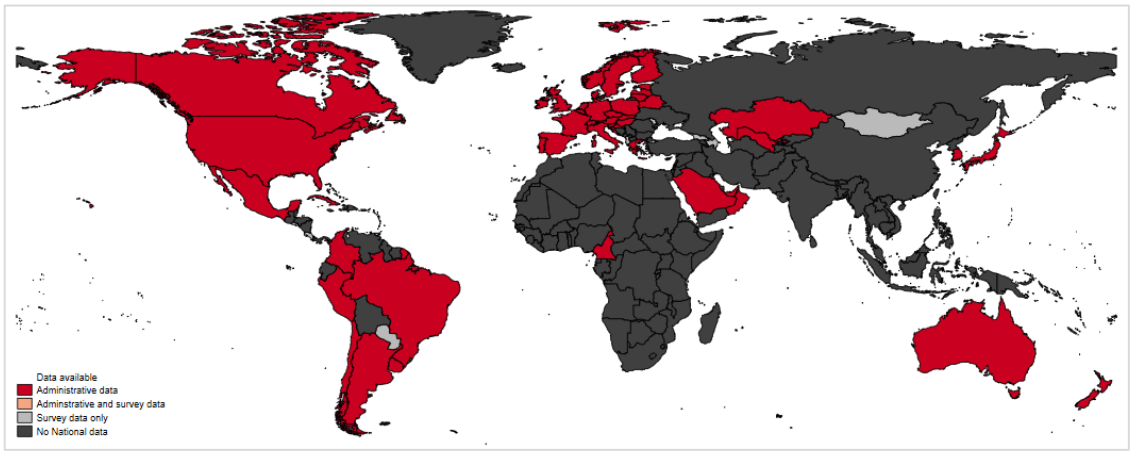
Figure 6-1, Figure 6-2 and Figure 6-3 show the geographical distribution of national data availability. These figures need to be interpreted in light of the different inclusion criteria used for administrative type national routine data (CRVS, HMIS, national birth registry or other routine administrative data source) between the estimates. The LBW estimates have the most stringent criteria, by including only those data sources capturing data on >80% of all estimated live births in the country in any given year. However, similar patterns are seen across the three outcomes, with widespread availability of administrative data across Europe, the Americas and Australia and New Zealand, and large data gaps in sub-Saharan African, and North African and Eastern Mediterranean regions. In many countries in sub-Saharan Africa and South Asia these data gaps for stillbirth and LBW are filled by household survey data. Eastern Mediterranean region countries have fewer surveys and frequently weaker administrative data sources, coupled with recent and ongoing conflict and weaker accountability structures, contributing to data gaps in the region. Data gaps are largest for data on preterm birth, as these data are not reliably collected within standard household surveys such as DHS.

Figure 6-1 Empirically-measured data available as input to stillbirth estimates



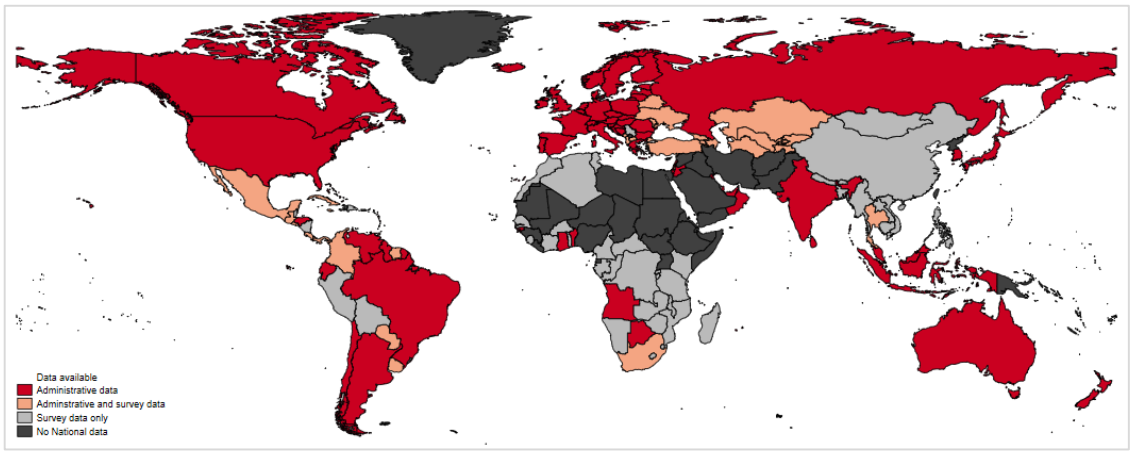
Administrative data refer to CRVS (higher and lower quality) and HMIS combined

Figure 6-2 Empirically-measured data available as input to preterm birth estimates



Administrative data refer to CRVS (higher and lower quality) and HMIS combined

Figure 6-3 Empirically-measured data available as input to low birthweight estimates

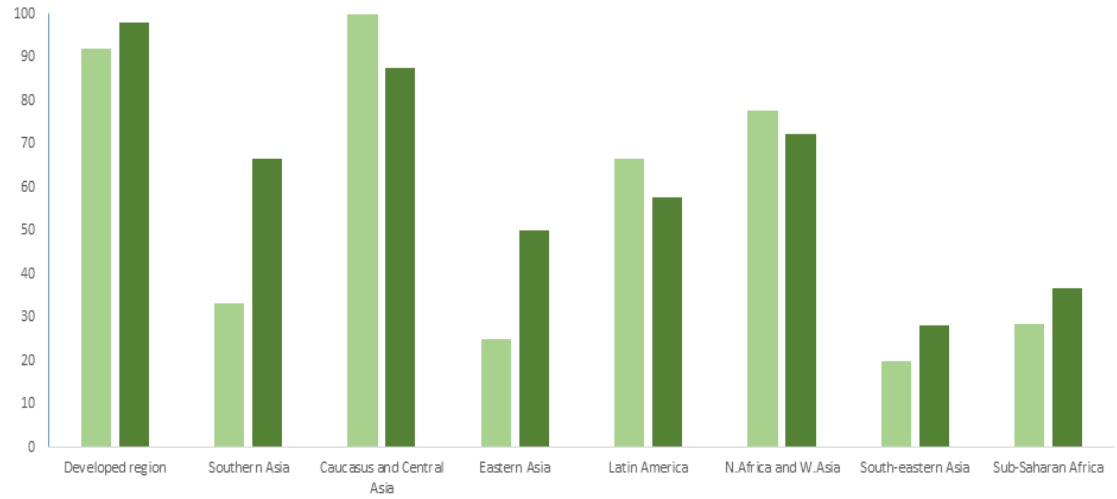


Administrative data refer to CRVS (higher and lower quality) and HMIS combined

Sub-national data are very useful for planning purposes for an individual country, especially in large and heterogeneous countries such as India, Brazil and China. Moreover, subnational data from one region in a country may provide useful information to inform estimates for another country with similar demographic, health and economic profiles. However, as discussed before, ideally, high quality national or nationally representative data would be used to generate estimated national rates for a given country. Overall fewer than a quarter of all countries globally have higher quality administrative data for all three outcomes. In the highest-burden settings, much of the national data available comes from household surveys where the quality of the data captured is variable.

Some improvement in coverage of national data in high mortality burden regions has been seen in recent years. In the case of stillbirths, a larger proportion of countries in the high burden regions of South Asia, East Asia, sub-Saharan Africa and South-East Asia have at least one national data point, from survey or administrative sources, around the year 2010 compared to 2000 (Figure 6-4). Some predominantly middle-income regions show a slight decrease in coverage over time, this is in part due to a reduction in nationally representative surveys over this time period, and whilst administrative data systems are improving in some countries in these regions, they are not yet nationally representative.

Figure 6-4 National data availability for stillbirth rate data 2000 and 2010 by MDG region



Light green bars show % of countries in region with at least one national data point around the year 2000. Dark green bars show for the year 2010.

Changes in stillbirth rate data availability over time are shown in Figure 2 in Chapter 3. Outside of HIC regions, much of the increase in data availability is due to an increase in routine administrative national data from the predominantly middle income regions of Latin America, North Africa and West Asia and Caucasus and Central Asia. Much of the increase is due to increased availability of HMIS data, with some increase in CRVS data. Notable increases are also

observed in South-eastern Asia, predominantly due to an increase in data availability from studies and sub-Saharan Africa where both the contribution of study data and HMIS data have been important. Similar patterns are seen for preterm and low birthweight data.

6.2. Standardisation of definitions

6.2.1. Challenges with standard definitions

The challenges of adhering to standard definitions for perinatal outcomes are not new.[64] Currently there is much debate in high income countries about the role of variations in definition, and in particular the application of these definitions in explaining variations seen in stillbirth, preterm birth rate and infant mortality across these regions.[94,218,219] This is particularly marked for stillbirth where an ICD-10 definition which prioritises birthweight over gestational age is recommended for international comparisons. This means that for stillbirths or 'late fetal deaths', data are captured on birthweight of ≥1000g as a proxy for third trimester deaths. Analysis in Chapter 3 has shown that this is a poor proxy. Consequently in settings where reliable gestational age assessment is possible, many countries prefer the use of gestational age thresholds for health planning and statistical purposes and hence use gestational age cut offs as the basis for their legal thresholds and for reporting.[220]

There is much variation in the legal requirements for reporting of stillbirths across countries (Table 6-2), particularly varying birthweight and gestational age requirements for reporting and whether terminations of pregnancy meeting the birthweight or gestational age registration requirements are included. These, alongside variation in the aggressiveness of obstetric practices for extremely preterm labour or severe congenital anomalies, complicate interpretation of international comparisons of overall stillbirth rates.[218] Despite wide variation in these thresholds, if both birthweight and gestational age are recorded for every birth in the system as I recommend, data from all these countries could be processed to produce reported rates compliant with the WHO ≥1000g or ≥28 weeks definition.

Whether a system includes or excludes terminations of pregnancy can also have an impact on overall stillbirth rates, especially in high income settings where stillbirth rates are low. In these settings fetal congenital disorders are frequently detected at 12 - 20 weeks with routine ultrasound scans to detect major structural abnormalities, and targeted prenatal diagnosis. In the majority of high-income countries termination of pregnancy for fetal abnormality is legal, and many women and partners opt to terminate an affected pregnancy. As most defects are detected during the 20-week scan, these terminations frequently occur after the legal limit for stillbirth or fetal death registration. There is large variation in how terminations of pregnancy after the legal gestational age threshold for reporting of stillbirths are recorded in official statistics. In countries with a low stillbirth rate, a greater proportion of these deaths will be terminations of pregnancy that would have otherwise resulted in a live birth.[221,222]

Table 6-2 Definitions used for legal reporting of stillbirths

Country	Gestational age +/or Birthweight criteria	Terminations of pregnancy included?[a]
Australia	≥20/40 or ≥400g	Yes
Canada - Quebec	≥500g	Yes
Canada - rest of country	≥20/40 or ≥500g	Yes
Denmark	≥22/40	No
England and Wales	≥24/40	Yes
Finland	≥20/40 or ≥500g	No
Iceland	≥20/40 or ≥500g	Yes
Italy	≥180 days	No
Netherlands	≥24/40	Yes
New Zealand	≥20/40 or ≥400g	Yes
Norway	≥16/40	No
Poland	≥500g	No
Spain - Valencia	≥22/40	No
Spain - rest of country	≥26/40	No
Sweden	≥22/40	No
US - 25 states	≥20/40	No
US -14 states	≥20/40 or ≥350g	No
US - 8 states	All gestational ages	No
US - Pennsylvania	≥16/40	No
US - Puerto Rico	≥5 months	No
US - Michigan	≥20/40 or ≥400g	No
US - District of Columbia	≥20/40 or ≥500g	No
US - Kansas	≥350g	No
US - Delaware/ Montana	≥350g or if not known ≥20/40	No
US - South Dakota	≥500g	No
US - Tennessee	≥500g or if not known ≥22/40	No

[a] Denotes whether terminations of pregnancy meeting the gestational age and/or birthweight criteria are included in the routine statistical reporting of stillbirths in a given country i.e. a termination of pregnancy weighing 750g would be included as a stillbirth in Quebec in Canada, but not in Poland

In addition, for those choosing to continue with the pregnancy, maternal-focused obstetric care (aimed at the wellbeing of the mother rather than at the baby's survival) is often prioritised. This will increase the number of these pregnancies ending in an intrapartum stillbirth, compared to cases where a fetal-orientated approach is used, which may result in a neonatal or infant death instead.[223] To overcome this challenge it is recommended that delivery type, including elective termination of pregnancy is included in the stillbirth or fetal death record to allow these to be disaggregated. This information is most easily collected within medical based systems such as HMIS or medical birth registries, which can then be linked to fetal death certificates and registers and ultimately to vital statistics. This linkage can be achieved through an individual unique identifier, such as a national personal identification number where available. Where no national identification system is available record linkage can be done based on other identifiers such as

date of birth, mother's name, child's name and address, but is more time intensive and errors can be introduced.

A more challenging problem for stillbirth is when the competing needs of bereaved families and statistical and public health monitoring are at odds with each other. For example, in 2008 France made registration of a stillbirth from 15 weeks onwards voluntary and at the parent's discretion. This had the advantage that parents could register their 15 week fetal death in their 'livret de famille' and could arrange a burial. However, from an epidemiological perspective, as neither birthweight nor gestational age are captured in the fetal death certificate in France, this 15 week fetal loss would be included in the stillbirth numerator, but a stillbirth at full term might be omitted if the parents chose not to register it.[224,225] This particular case led to the setting up of the NéMoSI project in 2011 to link civil registration data, including the fetal death register, to hospital discharge data to obtain a fuller picture of stillbirth epidemiology in France.

In the main, most countries report on preterm birth and low birthweight outcomes using the standard WHO definitions. Limitations in comparability across settings for these outcomes arise primarily due to differences in legal or practical applications of the live birth classification. In terms of legal requirements, countries such as France and the former United Socialist Soviet Republics (USSR) used alternative definitions of live birth until recently, which limited the comparability of their data.[68,226] In China births before 28 weeks, whether live or stillbirths, are still excluded from vital statistics registration and analysis by China's family planning system.[227]

Even where standard definitions are used for birth and fetal death registration for health information system purposes, the quality of the data is still dependent on the actual application of these standard definitions in practice. Differences in birth registration practices have been suggested to be responsible in part for differences in perinatal and infant mortality rates, and preterm birth rates seen in high income countries.[79,94,218,219,228]

EUROPERISTAT has been an important initiative to bring together perinatal data from across Europe to work towards producing a comparable outcome dataset.[229] This initiative has been very useful in advancing the field of perinatal epidemiology and has led to a number of recent publications, which reflect the lessons learnt across Europe, many of which are applicable to other data-rich settings.[220,222,230-232] In addition, work from perinatal epidemiology colleagues in North America has sought to further advance understanding in this area.[81,228]

With regards to standardisation of definitions for the purposes of vaccine studies, the Brighton Collaborative have produced a standard set of case definitions to capture perinatal outcomes in a standard method for use in vaccine research studies.[148,233,234] Whilst these are useful for

research settings, ideally these should also be designed to allow reporting according to the normative global standards.

Ultimately, data on these outcomes must be useful to the individual country. Different countries have different priorities, and these are rightly reflected in the data that they collect. However, to enable valid international comparisons, it is important that data are collected in such a way as to enable disaggregation of data to facilitate comparable reporting using WHO ICD definitions.

6.2.2. Compliance with the WHO ICD-10 definitions for international comparison in stillbirth, preterm birth and low birthweight rate datasets

Both legal thresholds and registration practices were reflected in the data available to include in the input datasets for stillbirth, preterm birth and low birthweight. The table below shows a high level of concordance with the definition used for reporting for low birthweight, some variation for preterm birth, and substantial variation for stillbirth (Table 6-3).

Table 6-3 Definitions used for stillbirth, preterm birth and low birthweight rates in input datasets

Birth Outcome	Used Standard ICD-10 definition (%)[1]	Other definition 1 (%)[1]	Other definition 2 (%)[1]	Other definition 3 (%)[1]	Other definition 4 (%)[1]	Other definition 5 (%)[1]	No definition specified (%)[1]
Stillbirth rate dataset (Chapt 3)	n=547 (25%)	≥28 weeks n=686 (31%)	≥7 months n=123 (6%)	≥24 or ≥26 weeks n=59 (3%)	≥22 weeks or weight equivalent n=412 (19%)	≥20 weeks or weight equivalent n=28 (1%)	'All fetal deaths' or not specified n=352 (16%)
Preterm Birth dataset (Chapt 4)	n=612 (83%)	Only including singleton live births <37 weeks n=104 (14%)	All live births <38 weeks n=22 (3%)	-	-	-	-
LBW dataset (Chapt 5)	n=1447 (100%)[2]	-	-	-	-	-	-

[1] Number and percentage of all included data points using given definition

[2] Using either 2500g or 5 pounds 5 ounces (2494g)

For the input data for low birthweight estimates, the finding of universal compliance with the WHO definition (<2500g) or the widely accepted imperial unit proxy 5 pounds 5 ounces (2494g), is similar to other recent studies.[148]

For the preterm birth data, although 14% of the available data included only singleton births, the majority of these data were from research studies, which may not have had an aim of estimating population prevalence. Almost all data sources complied with the <37 completed weeks definition.

In contrast for stillbirths, definitions used for reporting varied widely (Table 6-3). The estimates presented in this work did not adhere strictly to the ICD-10 definition of stillbirth for international comparison. At the recommendation of the expert perinatal community, these were generated for stillbirths ≥28 weeks rather than ≥1000g. This recommendation was based on the premise that if the notion of a 'stillbirth' is around the perception of viability of a fetus, then the length of in-utero development is more predictive of survival and longer term outcomes and hence would be a more logical measure than how well the fetus managed to grow during this gestation. However, there is a balance to be sought in terms of weighing up the benefit of including gestational age on better defining risk of mortality or other adverse outcomes, versus the feasibility of its accurate measurement.[235] In the dataset used in Chapter 3, 39% of included data points either did not state the definition used for stillbirths or relied on an alternative gestational age or birthweight criterion. The WHO estimates for 2000 used the country's own definition of stillbirth with no attempt to standardise these,[236] the 2008 estimates used a dummy variable in the model to adjust for differing definitions,[237] the 2016 WHO estimates sought to adjust the input data prior to modelling (see Chapter 3).

The increase in data availability over time is encouraging. However, this work has identified several common problems with the available perinatal data. These include omission, misclassification, including misreporting of events, and denominator challenges. These are consistent with the key challenges associated with death recording in vital statistics overall which also include omission or misreporting age at death and result in misclassification of deaths.[121]

6.3. Counting every birth

As shown in chapter 2, the first step required to collect accurate data on birth outcomes in every data system is to capture the birth event. Until now CRVS has been used rarely in most LMICs for monitoring and improving health outcomes due to low coverage and data quality. However, the capture of overall deaths in CRVS systems when compared to other sources e.g. surveys and census has improved for the last 40 years in many settings. This has led to the call that it is time to view CRVS as the standard for data on deaths in these settings.[47] However, the use of CRVS as the standard for data on deaths is problematic for stillbirths and early neonatal deaths because they are frequently poorly captured, or missed entirely, in surveys and censuses, and as such there is no 'gold standard' benchmark to compare performance of CRVS to. Studies have shown that obtaining high quality fetal death register data as part of CRVS in high income settings is possible, but not without financial investment, technical assistance and local ownership.[238]

Large improvements in coverage of birth registration have been seen over the past few years.[239] Latest data suggest that 71% of all births globally (excluding China) were registered, although wide disparities exist with over 90% coverage in high income regions, Latin America, the Middle East and Central Asia, compared to just 40% in LICs.[240] In addition, there remain large disparities in coverage by wealth quintile and between urban and rural populations, especially in LICs.[158] However, in all regions babies that were stillborn, or died shortly after birth before the time of registration are less likely to be captured in the data system. Even for birth events that are captured by the CRVS system, missing data on gestational age or birthweight can prevent their classification into stillbirth, preterm birth or low birthweight if appropriate. For countries with a large amount of missing data on gestational age or birthweight, inappropriate use of whole population denominators can further bias the prevalence estimates produced. This was particularly noted during the data collection for the LBW estimates. These challenges of low quality and incomplete data currently limit the use of CRVS data to inform national level estimates of these outcomes in most LMICs. The main alternative data platforms in use, HMIS and nationally representative household surveys, also face similar issues in ensuring that every birth event is captured with sufficient details to allow correct classification. The following sub-sections will review these challenges of omission of events, missing-ness of associated birthweight or gestational age details, and denominator issues which are common to all these data platforms.

6.3.1. Omission – who is missing and why?

This sub-section looks in more detail at a few key groups that are commonly missing completely from these data platforms: stillbirths, live born babies who die before birth registration, and births in marginalised populations.

Stillbirths

Stillbirths may be missing from a data system completely, for instance in CRVS where there is no legislation around the collection of data on fetal deaths, or in other data sources, for example MICS household surveys, where no attempt is made to capture this information. In data systems that seek to capture information on all births, both live- and stillborn, births can still be missed for various reasons. Understanding these is essential to make recommendations for data improvements.

Capture of stillbirths in CRVS systems

In CRVS systems, the tension between 'civil registration' and 'vital statistics' is very apparent in the case of stillbirths. As it is stated (although arguably not very tactfully) in The United Nations Handbook on Civil Registration and Vital Statistics Systems: Preparation of a Legal Framework: *"The expulsion of a dead foetus from the mother is not a matter for civil registration since it does not in any sense affect civil status; it does not lead to the acquisition of personality and therefore lacks relevance as a depository of rights in terms of the legal function performed by civil registration. However, registering all miscarriages or foetal deaths as physical events is certainly important statistically for public health purposes."*[241] So where does that leave stillbirths within the current large global effort to increase registration of births and deaths? As much of birth registration is being driven from a 'civil rights' perspective, little weight is given to the importance of collecting accurate data on fetal deaths for the purposes of vital statistics, either in their own right or in view of the substantial misclassification issues they pose which hinder the improvement of neonatal and under-five mortality reporting.

In many LMIC settings, capture of stillbirths within data platforms remains low despite them being included in the CRVS legal and data collection frameworks. It has been estimated that fewer than 5% of stillbirths and neonatal deaths globally have either a birth or a death certificate.[25] Introduced in 1964, the Sample Registration System in India provides one example of persisting low capture of stillbirths. The system is designed to be representative at the State and national levels, and sampling units are replaced every 10 years. It involves first a baseline survey of sampling units, then continuous enumeration of births and deaths in the area by the 'volunteer' enumerator from within the community, with 6-monthly house-to-house surveys to confirm events from the preceding 6 months by a supervisor. Matching of events is used to

eliminate errors from duplicate or missing vital events. The system is used to provide accurate annual data on birth and death rates, infant mortality and fertility indicators, however its capture of stillbirths has remained very low. For example, in 2015 the Sample Registration System reported a national early neonatal mortality rate of 19 per 1,000 live births, but a stillbirth rate of just 4 per 1,000 total births, with stillbirth rates of 0 in some of the highest mortality areas such as rural Bihar and Jharkhand.[168] Whilst the report recognises that *"stillbirths are extremely difficult to capture"*, it does not discuss any potential steps to take to improve capture.

Little information is available in the published literature regarding completeness and omission of stillbirths, or early neonatal deaths in CRVS in LMICs. No studies were found from LICs, but studies from Jamaica and Thailand,[242-244] coupled with historical information from HICs highlight some of the important factors to consider. These can be used in the development of recommendations to other countries seeking to avoid these pitfalls as they strengthen their CRVS systems. Under-capture of perinatal deaths was common in CRVS systems. One district of Thailand reported no stillbirths in 1986, giving an official stillbirth rate of 0 per 1,000, whereas a survey of the same district for the same time period identified 17 unregistered stillbirths (SBR 13.3 per 1,000). A similar pattern is noted for neonatal deaths, for example a study in Quang Ninh province of Vietnam found an NMR of 16 per 1,000 live births (95%CI: 14 – 18) compared to the 4.2 reported in official statistics.[245]

These studies, and an increasing body of literature, describe some of the important factors contributing to omission of stillbirth in CRVS systems. These include: a failure to include stillbirths in the legal framework for CRVS; low understanding and engagement in stillbirth registration process by the public, including bereaved parents; and the failure of systems to cover births events among the most marginalised

Failure to include stillbirths in the legal framework for CRVS

Failure to include stillbirths within the CRVS legislation currently limits this as a source of data in many settings. Even where they are included, standard definitions to allow operationalisation are frequently missing. In recognition of their importance for monitoring pregnancy outcomes and maternal health, WHO has recommended that provision be made for collecting stillbirth data in CRVS, even where this might not yet be possible to implement.[246] Despite this, stillbirths are not routinely being included in CRVS strengthening efforts. For example, the legal framework for CRVS in Albania did not include stillbirth reporting or define a 'live birth', and despite recent technical assistance to modernise the system provided by Statistics Norway, the upgraded system did not seek to include stillbirths. This is a real missed opportunity to substantially

improve the information available on stillbirths in a country with a very high percentage of facility births.[247] In contrast the Northern Marianas provide a good recent example of how stillbirths can be fully incorporated into the system, with clear and explicit guidance on definitions to be used, methods for gestational age assessment and whose responsibility it is to register the death.[248]

Much work is underway to strengthen CRVS in general.[246,249] Guidance for inclusion of stillbirths in this process has been provided by UN agencies (Table 6-4). However, birthweight and recording timing of stillbirth (antepartum or intrapartum) are excluded from the priority items for information despite being collected on the death certificate. In addition, various inconsistencies can be seen across the different documents in terms of compliance with standard categorisations, who the informant should be, and which information should be recorded for each death. Efforts should be made to standardise normative advice given and provide support to countries seeking to improve the reporting of birth outcomes in their CRVS systems, recognising however that implementation of any proposed changes in vital registration is often challenging and time-consuming. For example, it took 12 years for the changes to the Certificate of Live Birth recommended by the Centers for Disease Control and Prevention (CDC) in 2003 to be implemented in all US states.[250]

Table 6-4 Summary of existing UN recommendations regarding stillbirths in CRVS

Document	Notes
Handbook on Civil Registration and Vital Statistics Systems: Preparation of a Legal Framework[241]	Para. 46: "*Recording information on fetal deaths should be given a lower priority…than live births, deaths, marriages and divorces*" Para. 49: Uses non-standard categorisation of fetal deaths (early <20 weeks; intermediate 20 - <28 weeks; late ≥28 weeks) Para. 64: Encourages reporting of all fetal deaths, regardless of GA, as part of vital statistics; but separately from civil registration Para. 123: States only doctor should certify fetal deaths (not nurse or midwives) Para. 127: States physicians to report fetal death to registrar including time of death (AP/IP). Unrealistic to expect parents to play a role in fetal death reporting "*because their expectations have been dashed and they usually leave the remains at the hospital*" Para. 165: A statistical report to be prepared for every fetal death. 11 priority items for fetal death reporting for the compilation of vital statistics given including: date and place of occurrence, date of registration, type of birth (single or multiple issue), gestational age, legitimacy, sex, age of the mother, duration of marriage (for legitimate pregnancies), number of children born alive to the mother, and number of previous foetal deaths to the mother. Para. 208: The right to register a fetal death is included in article 12(2) (a) of the International Covenant on Economic, Social and Cultural Rights'

Handbook on Civil Registration and Vital Statistics Systems: Management, Operation and Maintenance[251]	Para. 106: Definitions should be consistent with international standards. Para. 180: "*if management makes a policy decision to include… fetal death reports in a system that did not previously include them. Then it must provide for the necessary increase in staff*" Para. 610: Strongly recommended that countries adopt international standard definitions. Para. 611: Strongly encourages all states to use the same definition. Para. 612: Need to distinguish between live birth with early neonatal death and fetal deaths. Para. 613: To avoid misclassification between fetal deaths and abortions use standard definitions and ensure effective training and monitoring system in place. Annex 1 p105: Suggests that the informant for fetal death should be in order of preference: 1) mother, 2) father 3) the nearest relative of the mother. Annex 1 p110: Provides full list of potential items to collect in fetal death registration. In addition to 11 priority items (Para.165 above) includes 15 further optional indicators (one of these is birthweight). Annex 1 p111: Repeats fetal death definitions as above. "*The term stillbirth should be used only if it is essential for national purposes, and it should be regarded as synonymous with late fetal death.*"
Model State Vital Statistics Act and Regulations[252]	Fully incorporates fetal deaths. Distinguishes between 'vital record' for a legally certifiable event such as a live birth, death, marriage or divorce and a 'vital record' for fetal deaths. Both contributing to vital statistics but having different legal standing.
Principles and Recommendations for a Vital Statistics System[253]	Highlights the importance of standard ICD-10 definitions. Emphasises the importance of classifying stillbirths by birthweight, GA, age of mother and place of occurrence to maximise use of these data for planning, operate and evaluating maternal health services. Recommends that "*first priority should be given to setting up procedures for the registration of live births and deaths including causes of deaths, followed closely by foetal deaths*". The designated person at the institution is recommended as the first option for the informant, with parents, birth attendants, nearest relative of the mother or any other adult person having knowledge of the facts as other options.

Low understanding and engagement in stillbirth registration process by the public, including bereaved parents

Since death and stillbirth certification were introduced, those involved at each stage of the process have played an important role in ensuring that these deaths are reported. Reliability of information depends on the perceived value of the information and the benefits and risks of reporting it for the informant, whether a mother, a healthcare worker or other person. For example, in medieval Europe, parish priests had a vested interest in maintaining registers to

record the sacraments of infant baptism and burial, as these provided them with part of their income.[165] In a recent Lancet series on the vital role of CRVS to health policy formation, the importance of requiring both the trust and willing participation of citizens and ongoing political will was highlighted.[254] Both of these require the relevant parties to perceive a benefit of the system and of reporting this information. In systems where the reporting of stillbirths is not well established, it can be expected that substantial resistance will be faced unless those playing a part in the successful functioning of the system understand and buy into its importance, either to themselves or to the wider society. In all settings it is likely that cultural barriers will be encountered, which could compromise the quality of the data unless effort is taken to address these in a culturally sensitive manner.[255] Understanding perceived benefits of stillbirth registration in a given context, for example allowing parents the opportunity to have their child officially acknowledged and to give him or her a name where this is permitted (See Section 2.5.1.), or issuance of a burial permit could allow CRVS systems to be more tailored to the needs of bereaved families.

The public, and even health professionals, in many countries are generally unaware of the requirement to register all births and deaths, even stillbirths or early neonatal deaths, which could account for registration failures.[242] In addition, there is a lack of clear benefit visible to the mother of registering her baby in terms of civil rights, healthcare or other societal advantage that can serve as an incentive for registration of a live birth; and frequently no legal sanctions for non-registration of these events.[242] For example, only 12 out of 170 countries with maternity benefit policies in the International Labour Organization database include specific provision for stillbirths and the provision was generally very short, averaging just 11 days of paid leave.[23] In many cases, there can be financial disadvantages due to cost of registration, burial or other associated costs such as for transport. Even for women and families aware of requirement and willing to register their stillborn child, the registration systems are logistically complex for grieving parents to navigate, and often include having to attend a separate venue or make multiple visits to register their baby.[245] To date, there has been little community stakeholder participation in the design of the registration process or use of the data for stillbirths which could be an important next step to improve these data.[242]

In addition, negative perceptions around stillbirth may affect willingness to publicly declare the event by registering it. An international survey asked healthcare workers to report on their understanding of lay perceptions around stillbirths in their setting and found that around 1/5th of respondents globally thought that mothers and their spouses felt a sense of failure if their child was stillborn. In Latin America and sub-Saharan Africa, around half of respondents reported that stillbirth was commonly perceived to be due to a mother's sins or witchcraft.[255]

Perceptions of viability and personhood vary across contexts and may affect parents' stillbirth registration behaviours. A study from South Africa found that from 6 months of gestation onwards, fetuses were referred to as 'baby', with potential to survive or to be stillborn. It reported that term or near-term stillbirths were usually buried, whilst 'smaller' stillbirths were frequently left at the hospital for disposal as they were perceived as not really being human as only the mother had seen them.[256] Frequently these babies were not mourned as it is not the role of the community to mourn someone that they had not known; so in this context, personhood depended on your participation in society. Even in HICs, non-registration of live born infants considered non-viable is common in practice unless they satisfy the minimum gestational duration used for stillbirth reporting.[68]

Perceptions of personhood are changing, however. Widespread use of antenatal USS, in many settings now, coupled with sharing of ultrasound images of babies in utero on social media, means wanted pregnancies are regarded as babies who can be 'seen' and bonded with from early pregnancy. In the US this has affected birth registration legislation, with a lobby to allow both birth and death registration for stillborn babies which has complicated legal repercussions, and clashes with options for legal termination of pregnancy.[4]

Streamlining the process of registration, and moving responsibility for registration to health facilities, could remove the large barriers currently faced by placing the responsibility on parents and increase capture of events occurring within the health system. In several Latin American countries, including Argentina, Bolivia, Uruguay, Brazil and Colombia, setting up of civil registration offices in health facilities increased birth registration rates.[246] This may be a potentially useful strategy to increase coverage, especially in settings with high rates of facility births, and could also be extended to include death registration for stillbirths and early pre-discharge neonatal deaths. However, this approach may be inequitable, and may therefore underestimate mortality, which is likely to be higher in lower socio-economic status groups who also have lower rates of facility births.

Where little or no effective implementation of stillbirth registration exists, this can be an opportunity to design a system that is user-friendly. In many countries with a longer history of stillbirth registration, registration procedures were modelled on those for live births and are complex, burdensome and distressing for grieving families (See Box 6.1);[81] removing the onus of stillbirth registration from the parents or family to the health care provider could reduce distress and improve this process for the family.[81]

Box 6.1: Who can legally register a stillbirth in the UK?

- If parents were married to each other at the time of the stillbirth or conception, either the mother or father can register by taking along the medical certificate of stillbirth issued by the doctor.
- If they were not married and the mother can attend the registration, father's details will only be included if he also attends or makes a statutory declaration acknowledging his paternity.
- If mother cannot attend, the father can register only if he brings a statutory declaration acknowledging his paternity.
- If neither parent can attend the occupier of the house or manager of the hospital where the birth took place, someone who was present at the stillbirth, someone who is responsible for the stillborn child or the person who found the stillborn child (where the date and place of the stillbirth are unknown) can register the stillbirth.

Capture of stillbirths in HMIS

Many of the important underlying factors affecting the omission of births and perinatal deaths within the CRVS system are also applicable to the other main sources of data: HMIS and household surveys.

HMIS systems are in many ways potentially better placed than CRVS systems in the near-term to provide data at a national level on births. Previously they were usually limited to birth events occurring within the health system, and hence, even with rapidly increasing facility birth rates did not provide any information on a substantial minority of births in LICs which occur outside of facilities. Now, using new technology such as DHIS-2 Tracker, individual-level data can be used to produce prospective pregnancy registers from ANC booking to birth outcome, combined with active follow-up of those without a birth outcome recorded. With 86% of all women attending at least one ANC contact,[257] even if they don't deliver in a facility, this has potential to reduce omission of birth events, particularly stillbirth and early neonatal deaths from the system. This can be supplemented by community-based systems to seek and reach those with no access to the formal healthcare system at all during their pregnancy.

To realise this potential will require further investment and action. Health care workers who enter the events in registers from which data are extracted for inclusion in the HMIS should be trained in the importance of recording all birth outcomes, including stillbirth. A no blame culture for perinatal audit should also be fostered to reduce potential omission of adverse events, such as a stillbirth or early neonatal death; this will help ensure health workers and parents are

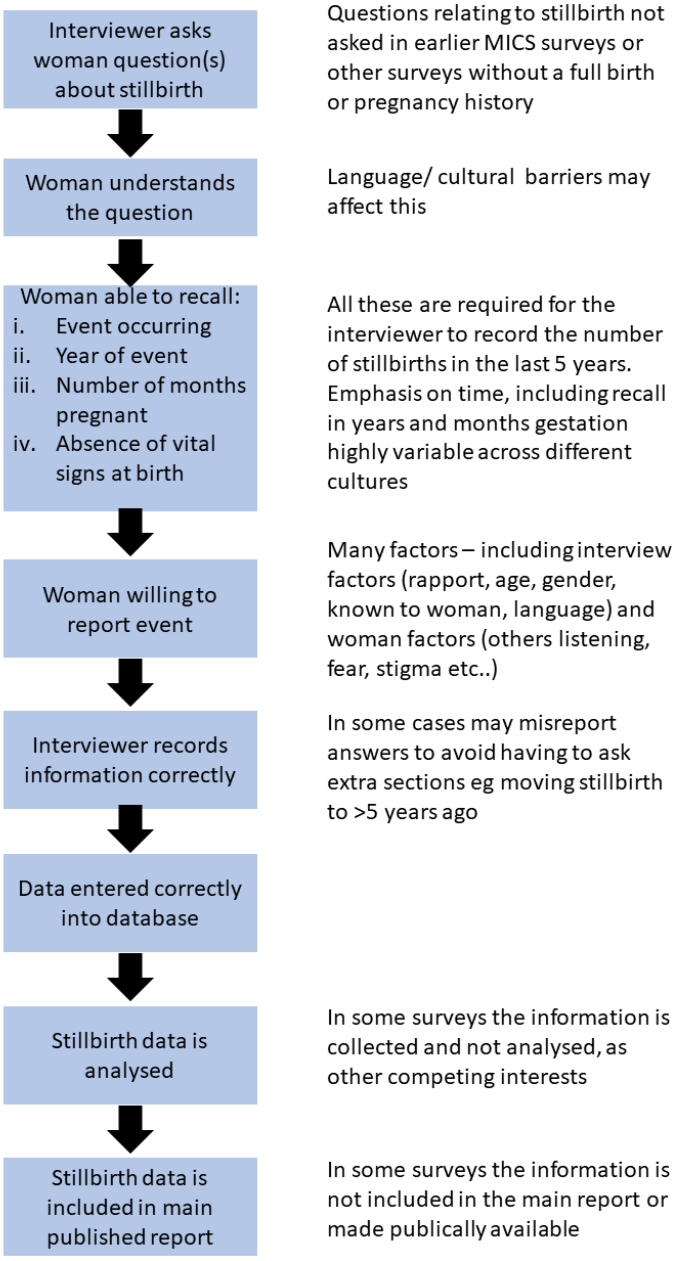
protected from litigation, disciplinary action, distress, cost or other factors (see section 6.4 on misreporting of events for further details).

Capture of stillbirths in household surveys

Capture of accurate data on stillbirths in household surveys is complex, and involves several important steps (Figure 6-5). Firstly, relevant questions must be included in the survey, and the women and interviewers must understand the wording of these questions. In view of differing cultural variations in understanding of stillbirth, these questions may be interpreted differently by the interviewer and respondents. Then the mother must both recall and report the birth event, including accurately reporting the number of months pregnant at the time of the event, and whether vital signs of life were present at birth. Perceptions of personhood, viability and underlying causes of stillbirth detailed above are all likely to impact a woman's willingness to disclose a previous stillbirth to an interviewer. Interviewer factors such as age, gender, previous relationship, trust and language may also be important.[258-260]

In addition to these potential barriers, there are two further considerations in population estimates of perinatal outcomes based on data from household surveys. Firstly, as these surveys collect data retrospectively, omission of birth events could be related to the time elapsed since the birth; although evidence to suggest that women forget their births, stillbirths or early neonatal deaths is lacking.[261] Secondly, adverse perinatal outcomes are more common in the case of a maternal death.[29,262] As data from household surveys on perinatal outcomes are obtained from the women's questionnaire, adverse perinatal outcomes in a population will be missing from mothers who have died, and hence may underestimate the overall population rates.

Figure 6-5 Data flow for stillbirth outcome reporting in household surveys



Early neonatal deaths (prior to birth registration)

Another group of babies commonly missing from data sources are live born babies who die in the early neonatal period before birth registration. As over 75% of all neonatal deaths are estimated to occur in preterm or SGA babies, this can lead to a large underestimate of not only neonatal deaths, but also preterm birth and low birthweight. For example, in a study in Thailand only 7% of neonatal deaths occurring before 15 days of life were registered, compared to 93% of those after day 15.[242] These babies may not be recorded by healthcare workers within HMIS systems, and also not be reported by their mothers in household surveys. In particular, as discussed above, when a baby is very preterm or very small, this may plausibly impact the

maternal and community perception of the personhood of the child and hence may adversely affect reporting of these births and deaths.

A brief review undertaken for this thesis found that little is known globally about community perceptions of preterm (and therefore very small) births. Limited evidence, all from Malawi, suggests that, similarly to stillbirth, preterm birth has often been viewed at a community level as a very negative outcome, associated with witchcraft.[263] Although there is some evidence that this may be improving due to changing perceptions around preterm birth, with increased emphasis on care provision to improve outcomes,[264,265] this may still affect willingness to report a preterm birth followed by an early neonatal death in a household survey if these perceptions are common to other settings.

Marginalised populations

Most CRVS systems, especially in LMICs, currently have low coverage of births and deaths in the most marginalised populations e.g. events occurring outside health facilities,[266] those of lowest socio-economic status, very rural populations, refugees, displaced persons, or those living in conflict or fragile states. HMIS systems also frequently only capture information on births in facilities, and thus similarly exclude those most marginalised. Household surveys, whilst they seek to be nationally-representative, for logistical reasons rarely include those living in fragile states, fragile regions of countries, or refugee and displaced populations. Failure to include these populations, who have a higher risk of adverse birth outcomes, will underestimate the overall burden.

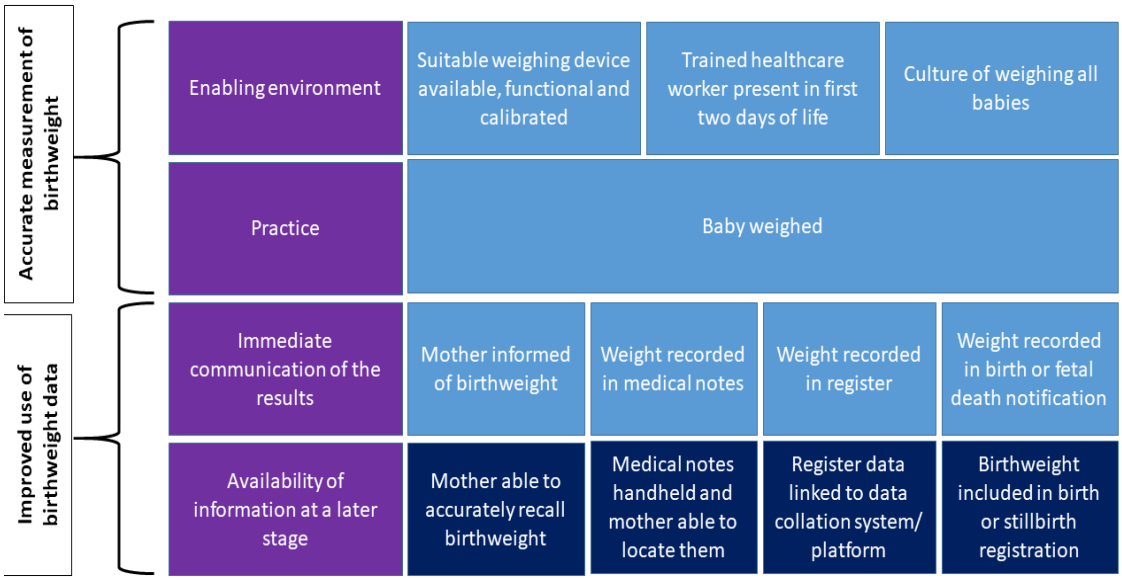
6.3.2. Capture of data on birthweight and gestational age

The birth, whether live- or stillborn, needs to be captured as an event, but also to be correctly classified to enable international comparisons. This also requires accurate classification of the baby's vital status at birth and information on gestational age and/or birthweight. This requires firstly that birthweight and gestational age are measured accurately and recorded for all births, whether in facility or community. Secondly, this data needs to be integrated into relevant data platforms including national routine platforms such as CRVS, HMIS and nationally representative household surveys.

Birthweight

Figure 6-6 depicts a conceptual framework for the flow of information on capturing birthweight through the healthcare and information systems to the data platforms where we sourced the information for low birthweight estimates.

Figure 6-6 Conceptual framework for capturing birthweight in data systems



As described in detail in Chapter 5, there are many potential barriers to this flow of data, which can result in biases in those included within the data system. Evidence of incomplete reporting of birthweight within data collection system was found in the work undertaken in Chapter 5. In some national routine or nationally representative data sources, a substantial number of reported live births do not have birthweight data available. For example, across available DHS surveys, 0% to 100% of did not have a reported birthweight in the survey. This may be due to many infants not being weighed at birth, however as availability of birthweight in surveys relies on maternal retrospective recall of events over the last 3 to 5 years, it is likely that even when weighed, birthweight information will be missing or inaccurate for births several years ago as information may have been forgotten and health cards may have been lost. In addition, many birth events captured in CRVS and HMIS systems do not have birthweight data available, either because a birthweight was not measured, or it was not recorded in the system. Those without birthweight information are more likely to be around the threshold of viability, or rural, home births, and lower socio-economic class, and hence at higher risk of low birthweight, thus potentially biasing any LBW estimate derived from these sources.

Stillbirth estimates may also be biased by missing birthweight information if gestational age data are also not available as it is therefore impossible to assess if the fetal death met the reporting threshold, and hence may be excluded from the stillbirth count. This work also confirmed that even amongst those with a recorded birthweight, measurement and recording errors are common, including heaping at specific weights, poorly calibrated scales, inappropriate weighing devices, weighing clothed, and errors in reading the birthweight from the device. In theory, heaping of birthweights on 1000g could lead to an overestimate of the stillbirth rate due to misclassification of miscarriages as stillbirths. In practice, this is unlikely to have a big effect as

gestational age is usually used in preference to birthweight in HIC settings where stillbirth rates are low, and in LIC settings with higher stillbirth rates, a greater proportion are at or near term due to lack of quality intrapartum monitoring and care.

When an accurate birthweight has been measured, this information can be captured in CRVS systems by:

- recording these parameters on the birth or stillbirth notification form,
- including this in the registration documentation, and then using record linkage to link to death certification, or
- by requiring these parameters to also be recorded on the death certificate in the case of a perinatal death.

However, in many countries neither birthweight nor gestational age are included on the birth registration form and record linkage remains weak or non-existent.

WHO had recommended the use of a perinatal death certificate, including vital status, gestational age and weight at birth, for all stillbirths and live born infants dying within 1 week of birth.[65] However, uptake of this was low, and WHO have recently revised a death certificate for all deaths, regardless of age to include an additional part for fetal or infant deaths which has space to record both birthweight and gestational age.[67,265]

In terms of HMIS data, evidence from Chapter 5 suggests that despite the increasing proportion of births now occurring in facilities, and the availability of a weighing device in most of these, an accurate birthweight for facility births is not universally recorded. When recorded, birthweight recording in the medical notes and registers is not always accurate and timely, limiting the availability of such data for action. In addition, these data are not always collated or made available to inform local, regional or national program tracking for birthweight.

Gestational Age

Accurate data on GA are most likely to be missing for those of lower educational or socio-economic status in all settings, as they may be less likely to access an early pregnancy dating USS or to be able to recall LMP.[267] Similar to birthweight, availability of accurate data within any given data system requires firstly accurate measurement (see section 2.4.2), but then communication of the GA assessment to the mother, the handheld notes, the register and the birth or death notification. Currently, even when measured, GA information is not always communicated through these channels and therefore not available for use to inform stillbirth or preterm birth population estimates.

In most settings, information on gestational age is not included in the birth certificate, or captured within the CRVS system. Where it is not possible to include gestational age on the birth certificate increasing availability and potential for linking data, mean other methods can be put into place to ensure that this information is available to allow adequate classification of birth outcomes. For example, in the UK, gestational age, whilst included in the birth notification, is not included in the registration data on the birth certificate, but these data can be obtained from the National Health Service 'numbers for babies' database and linked to birth and death registration data.[268] Whilst information on gestational age is frequently captured in facility registers, it is rarely aggregated up the data system.

Birthweight and gestational age data for stillbirths

Availability of these data elements is frequently worse for stillbirths than live births. Stillbirths have fewer options for gestational age assessment, as they can't utilise clinical gestational age assessment, and anthropometric proxies are not validated in a stillborn population. Additionally, cultural practices may prohibit their use (see section 2.4.3). Similarly, in view of cultural rituals and practices around burial or disposal of a stillborn baby, even if there is perceived value in weighing a stillborn baby, the time window for weighing is very limited, and frequently they are not weighed at birth at all. This affects the ability to classify a fetal death as a stillbirth. As noted above despite WHO recommendations, birthweight and gestational age are not routinely included in fetal death certificates in all settings.

6.3.3. Denominator challenges

Similar to other health estimates, denominators for these outcomes present challenges. In all data systems, the denominator population should be comparable to the numerator. For example, in the case of low birthweight, if not all babies are weighed, only those with a birthweight recorded should be used in both the numerator and denominator, and the potential bias of the weighed population should be acknowledged. Failure to consider this explained some of the implausibly low LBW rates reported in some data systems (see Chapter 5). This is likely to be similar for preterm birth, where omission of the birth event from the data system is more likely for those with the lowest gestational ages around the threshold of viability.

For the stillbirth denominator of total births, it is not necessary to distinguish between live and stillbirths, but it is required for the numerator. For preterm birth and low birthweight rates, stillbirths should be excluded from the denominator, therefore it is important to assess the vital status at birth for all births; although as stillbirth is much less common than live birth any misclassification error will have a minimal effect on overall rates.

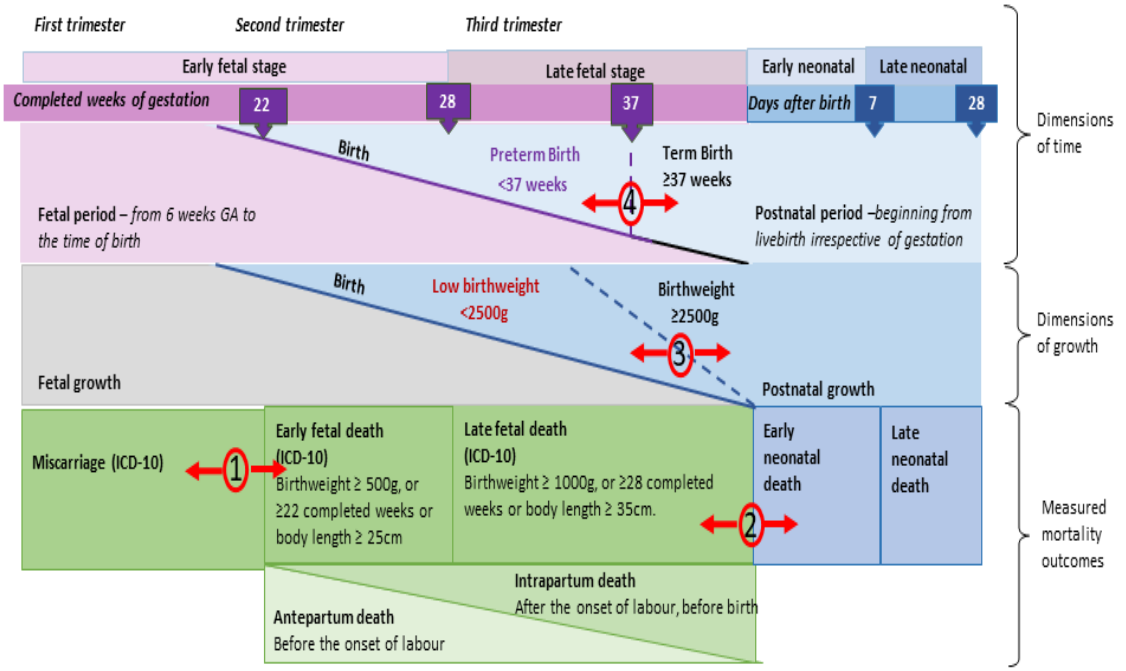
6.4. Misclassification

Figure 6-7 presents the birth outcomes considered in this thesis by dimensions of time and growth. The time dimension includes two separate components:

A) Those measured in completed weeks of gestational age, which includes the current gestational age of a fetus in-utero during the fetal period from 6 weeks to birth and the timing of birth in completed weeks of gestational age and;

B) Those measured in days of postnatal age, such as day of death for a neonatal death. As we have seen previously, definitions vary for live- and stillbirths. For example, a live birth at <37 weeks should be recorded as a preterm birth regardless of gestational age. However, if the baby shows no signs of life at birth and is <22 weeks of gestational age then it should be recorded as a 'miscarriage', if between 22 and <28 weeks an 'early fetal death', and if after 28 completed weeks a 'late fetal death'.

Figure 6-7 Schematic representation of birth outcomes in relation to dimensions of time and growth



Source: Adapted from Lawn et al, 2011[70]. The numbers in the red circles denote different types of misclassification 1. Between early fetal death and miscarriage. 2. Between stillbirth and early neonatal death. 3. Between low birthweight and non-low birthweight. 4. Between preterm and term births.

Concerning birth outcomes, misclassification can occur based on errors in the measurement, recording or reporting of any of the component data elements required for defining stillbirth, preterm birth or low birthweight: vital status at birth, birthweight or gestational age. These errors may be inadvertent, or due to deliberate misreporting. This misclassification can occur across any of the boundaries of definitions including: 1) miscarriage and fetal death/stillbirth; 2) stillbirth and neonatal death; 3) low birthweight and non-low birthweight; and 4) preterm and term. The following sub-sections will discuss each of the threshold-points for potential

misclassification in turn, considering first inadvertent misclassification from measurement or recording errors, and then misclassification due to misreporting of individual data elements or the overall birth outcome.

6.4.1. Misclassification between stillbirth and miscarriage

Measurement at the time of birth

As discussed previously, accurate measurement of birthweight or gestational age is required to allow the application of the standard ICD-10 definition to distinguish between a stillbirth and a miscarriage in a baby assessed to have no signs of life at birth. In many high burden settings 'miscarriage' includes early fetal deaths together with ICD-10 defined miscarriages. In these cases, the misclassification comes at the 28-week boundary (or 1000g if birthweight is being used preferentially). Where birthweight is being used preferentially to gestational age (as currently recommended by ICD), this will lead to a systematic misclassification of growth restricted stillbirths around or just above the threshold as miscarriages and an underestimate of true stillbirth rates as impaired fetal growth is a common underlying factor in stillbirth. For example, the data presented in Chapter 3 from 7 million births in 23 HICs found that the stillbirth rate was 15% (95%CI: 13 – 17%) lower when using a birthweight ≥1000g definition when compared to a ≥28 week one. In the USA the stillbirth rate is 40% lower using a ≥500g definition when compared to a ≥22 week one.[216]

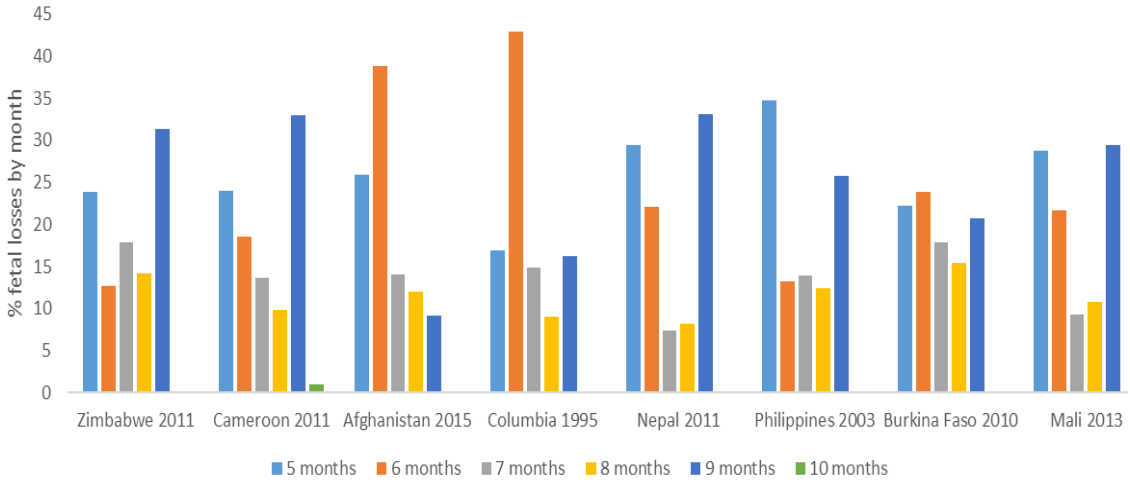
Issues related to the communication of the outcome to women and families

In view of the sensitivity around pregnancy loss in many contexts, information on the classification of the pregnancy loss may not be provided to women and families, particularly in settings where there is no legal framework for registering stillbirths. If at a later stage a woman is asked about this pregnancy outcome, for example in a household survey, she may not be able to correctly classify her loss as a stillbirth versus a miscarriage. For this reason, more recent DHS surveys ask women how many months pregnant she was at the time of pregnancy loss rather than requiring the woman to characterise her spontaneous pregnancy loss as a miscarriage or a stillbirth. As previously discussed, this is an imprecise marker of gestational age.

Some variation in gestational age of stillbirths is to be expected across different settings, in view of the differences in underlying causes. A greater proportion of intrapartum stillbirths at term is expected in settings with weak health systems, and a lower proportion of third trimester stillbirths in settings with high quality obstetric care, fetal medicine and the potential for both obstetric intervention and neonatal intensive care. However, patterns of gestational age distributions amongst pregnancy losses suggest that errors in gestational age assessment and

heaping at certain gestational ages is not uncommon. Figure 6-8 shows the gestational age distribution of fetal deaths in eight recent DHS surveys, all undertaken in LMICs with relatively weak health systems. This figure shows that many, but not all, show the expected peak in the number of stillbirths at term. The relatively low proportion at term in Colombia might be expected in view of its relatively strong health system, whereas the low proportion in Afghanistan is unexpected and may relate to omission of these term stillbirths or their misclassification as early neonatal deaths. Both Afghanistan and Colombia have high proportion of fetal losses at 6 months of age, which may represent misclassification of some ≥7 month stillbirths as miscarriages. A similar pattern is seen to a lesser extent in the case of Nepal and Ethiopia surveys. Potential heaping is seen at 7 months in Zimbabwe which may reflect misclassification of miscarriages at 6 months as stillbirths at 7 months, or under capture of miscarriages. In the Philippines a high proportion of reported fetal losses are reported to be at 5 months, compared to 6 months, although this is unlikely to impact on misclassification around the 7-month threshold.

Figure 6-8 Proportion of fetal loss by gestational age in 8 recent DHS surveys



Misreporting by healthcare workers, women or informants

In settings where stillbirth legislation is in place and adhered to, stillbirths may be reported as miscarriages to avoid costs potentially associated with registration, funeral and burial of a stillborn baby which are not required for a miscarriage. There are other potential social and cultural situations in which a stillbirth may be reported as a miscarriage, for example in the case of an adverse outcome in an unmarried teenager in settings where this is not culturally well-accepted these births may be misreported to avoid official registration. In household surveys, where more detailed questions are asked for stillbirths than miscarriages, interviewers may misreport stillbirths as miscarriages.

Whilst less common than other misreporting, in some circumstances birth attendants may overestimate the gestational age of a baby to enable its registration as a stillbirth, which may facilitate the parents' grieving process.[68]

6.4.2. Misclassification between stillbirth and early neonatal death

Misclassification between stillbirths and early neonatal deaths is thought to be common, even in data from HICs.[269] Some of the potential contributing factors to this are described below.

Measurement at the time of birth

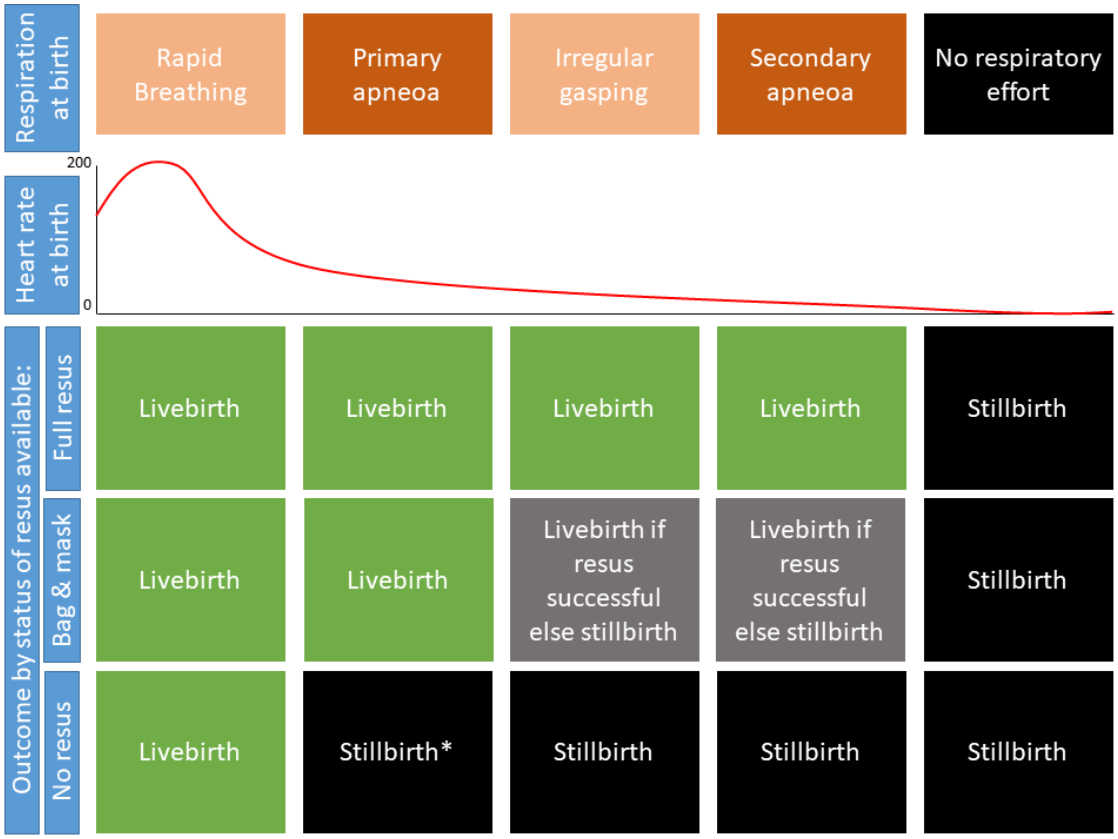
Capturing vital status at birth is critical to enable distinction between stillbirth and early neonatal death. This is dependent on the delivery attendant's ability to accurately assess for signs of life. Assessing breathing, crying or movement is usually clear to most observers, regardless of their level of training; however, assessing for the presence of a heart rate is more challenging and hence is often poorly done. If no action is taken to resuscitate a live born baby with a heartbeat but no other signs of life, unless the baby gasps and revives itself, this baby, though live born, becomes an early neonatal death. If no heartbeat was recognised it will be misclassified as a stillbirth.

Several recent studies have reported on the effect of training in neonatal resuscitation on stillbirth rates. Recent pre-post studies have shown reductions of 24 – 54% in intrapartum stillbirths after instituting Helping Babies Breathe (HBB) training in various settings.[270,271,272] Conversely, Bellad et al found no difference in stillbirth rate after HBB training in three Global Network research sites.[273] However, as this study was conducted in 2011-2013, it is possible that the classification of live and stillbirths had benefited from previous research in these sites, and greater emphasis on the quality of the outcome data reported.[270] These findings are consistent with other studies from low income settings where training in resuscitation led to a reduction in reported stillbirth rates.[274-276]

As highlighted above, the vital status recorded at birth in a compromised baby can vary depending on the delivery attendant or delivery team. In a well-resourced setting with multiple trained personnel assisting the birth, at least one person (often more) can be dedicated to care of the newborn. In such situations (labelled 'full resus' on Figure 6-9) the heart rate will be monitored closely by auscultation and pulse oximetry, allowing the detection of a regular heart beat and a diagnosis of a live birth, regardless of whether or not the resuscitation efforts are successful. In the second scenario (labelled 'bag & mask' on Figure 6-9), where frequently there is a single birth attendant responsible for both mother and baby, it is critical that urgent clinical need takes preference over correct classification and many simplified resuscitation guidelines therefore emphasise stimulation then bag and mask ventilation for non-breathing babies at

birth. In these scenarios, as long as resuscitation with this approach is successful, the baby will be recorded correctly as a live birth. In a small minority of cases a baby may have been live born but not possible to resuscitate with the simple algorithm, and may be misclassified as a stillbirth. In addition a very small number of babies with no heartbeat, nor respiratory effort at birth (Apgar 0) who would be defined as stillbirths by the ICD-10 definition, could potentially be resuscitated with access to 'full resus'.[274] However, as the number of these cases is likely to be small, this is unlikely to have a large effect at a population level. In addition, as the babies are very severely compromised, interventions to reduce these deaths, as for the intrapartum stillbirths they could be misclassified as, would need to be directed at intrapartum care, so the misclassification would not result in any different programmatic implications.

Figure 6-9 Possible outcomes recorded by birth attendant in a baby compromised at birth



*If no stimulation of the baby is undertaken.

In practice, many high-income countries use a definition of stillbirth, which whilst consistent with that of ICD-10, is more specific and objective. The most commonly used definition is 'a newborn with no heartbeat, respiratory effort, or movement, and with a 1- and 5- minute Apgar score of 0'.[277]

Some settings have presented specific challenges with stillbirth to neonatal death misclassification. For example in China, babies successfully resuscitated during the early post-

partum period, but who then have their treatment withdrawn due to parent's inability to pay or concerns over longer-term prognosis are frequently recorded as stillbirths rather than live births.[172]

Standard DHS survey questionnaires require a woman to be able to distinguish between a live birth, followed by a neonatal death (which would be captured as part of a live birth history), and a stillbirth, which would be captured as part of the additional questions on pregnancies not resulting in a live birth in the last 5 years. In the case of a homebirth, in view of the challenges of assessing vital status at birth even for healthcare workers in LMICs, it is likely that substantial misclassification will occur. It is likely that social, cultural, education and religious factors play a role in how a woman, family member or healthcare worker may interpret and report 'signs of life at birth'.[278]

Evidence from a study in Malawi reported that 20.5% of neonatal deaths captured in a household survey using a full birth history were re-classified as stillbirths following a verbal autopsy.[279] This study did not capture stillbirths in the household survey, so it is not possible to look at potential misclassification of neonatal deaths as stillbirths. The Afghanistan 2010 mortality survey included a full pregnancy history and verbal autopsy for all neonatal deaths and stillbirths. Whilst some caution is required in the interpretation as the overall rate of stillbirth is relatively low (23 per 1,000), only 2.7% (n=11) of early newborn deaths captured in the pregnancy history were re-classified as stillbirths following a verbal autopsy and 6.4% (n=35) of stillbirths captured in the pregnancy history were reclassified as early neonatal deaths.[280]

As a result of the difficulties in distinguishing between a stillbirth and a live birth resulting in an early neonatal death and potential misclassification, perinatal mortality rate has frequently been used as a pragmatic way to capture all these deaths.[281] Recently, in settings where this is still an issue, it has been recommended that for the purposes of research studies only a composite outcome, including both stillbirth and perinatal deaths is used.[282] This is reasonable in clinical studies with the survival of the baby as an outcome, however from a public health perspective, as we have seen above, it remains important to collect and present the results separately as different policy and programme responses may be required to tackle different types of death.

Issues related to the communication of birth outcome to women and families

In most HIC settings, the birth outcome is usually communicated clearly to the woman and her birth partner in a timely manner where appropriate. In most cases the diagnosis of fetal death has been made prior to the stillbirth. In LMICs, the diagnosis of fetal death may only be made at the time of birth and communication is more varied. Only a minority of settings practice high

levels of communication at each stage of process, including at the time of diagnosis of fetal death or during any medical procedures such as induction of labour, fetal destructive surgery or failed neonatal resuscitation. Barriers to effective communications are likely to include time pressures, lack of privacy, seeking to protect the mother, and fear of blame. These may result in absence of communication, leaving the woman to piece together her own narrative based on her experience, and consequent potential for misreporting of the outcome.

Misreporting by healthcare workers, women or informants

Misreporting of neonatal deaths as stillbirths by healthcare workers may occur in an attempt to protect the mother and family. Neonatal deaths are frequently associated with higher economic costs compared with stillbirths, especially in settings that legislate for registration and burial of neonatal deaths, but not stillbirths. Neonatal deaths also may be associated with increased paperwork for the healthcare workers and parents alike. It is also plausible that frontline healthcare workers may misreport neonatal deaths as stillbirths to protect themselves from blame, for example in the case of a failed neonatal resuscitation; or from additional work e.g. if there is increased administrative paperwork, requirement for auditing with a neonatal death that is not present for a death classified as a stillbirth.

At a political level, with global goals and targets set for perinatal outcomes, league tables facilitating international comparison, and great media interest in reporting on these, there can be potential political gain from the misreporting of these deaths. This may be more of an issue for misclassification from neonatal death to stillbirth. Neonatal mortality has an SDG target and is being closely tracked with intense political pressure to reduce it. On the other hand, stillbirth, although it has an ENAP target and is included in the core indicators for monitoring women, adolescent and children's health as part of the Global Strategy, does not have the same level of political buy-in. Historically such misreporting has been seen in Cuba in some recent years, where it has been estimated that up to 50% of all recorded fetal deaths were actually neonatal deaths.[283]

The misreporting of a stillbirth as a neonatal death by health workers is thought to be less common. However, this could be plausible if benefits associated with a live birth resulting in a neonatal death are not given following a stillbirth, for example maternity benefits, bonus payments or other benefits.

No information could be found on the potential misreporting of stillbirths and neonatal deaths by women, but it is plausible that in certain cultures the reporting of either stillbirth or neonatal death may be more culturally acceptable, or desirable to the individual woman.

6.4.3. Misclassification between extremely preterm neonatal deaths and miscarriages

In the case of extremely preterm babies, if signs of life are not accurately assessed at the time of birth, they may not fulfil the gestational age or birthweight requirements for registration, and therefore will be misclassified as a miscarriage. In most settings, these babies will be omitted from vital statistics.[68] The underlying factors contributing to issues with assessment of vital status at birth, communication of the outcome to women and misreporting by women, healthcare workers and informants are similar to those presented above for the misclassification for neonatal deaths and stillbirths.

6.4.4. Misclassification between preterm and term neonates

If the presence of signs of life are correctly identified at the time of birth, the baby will be recorded as a live birth, and potentially characterised as preterm or term depending on gestational age.

Measurement at the time of birth

The challenges of gestational age assessment have been discussed in detail previously (see Sections 2.4.3, 6.3.2 and Chapter 4). Accuracy of gestational age assessment will influence this classification, if the method used results in an underestimate of gestational age, particularly amongst those 37 – 38 weeks, this will result in an overestimation of the preterm birth rate.

Heaping of gestational ages is also a potential factor in the classification of preterm birth.[284] Heaping on exact gestational age e.g. 37+0 completed weeks, would potentially lead to an underestimation of preterm birth.

Issues related to the communication of the outcome to the woman and family

In the case of a very preterm baby who is admitted to a neonatal inpatient care facility, it is likely that the diagnosis of preterm birth will be communicated to the parents in all settings. In case of a mildly preterm baby at 35 or 36 weeks, especially if not low birthweight and not admitted to a neonatal ward or Kangaroo Mother Care Unit, it is plausible that the diagnosis of preterm birth may be less likely to be communicated to the mother, particularly in LMICs; although no evidence was found to support this.

Misreporting by healthcare workers, women or informants

This is less likely to be a factor in the misclassification of preterm births. However, in specific circumstances, if there are real or perceived benefits of having a preterm baby, these births may be misclassified. For example, in view of the increased interest by donors in preterm birth some programs may give benefits only to mothers of preterm infants e.g. food, blankets for Kangaroo Mother Care, soap, hats or cash there may be an incentive to report a term birth as preterm.

Misreporting of gestational age is one of the important limitations to capturing information about preterm birth from household surveys. Unlike for stillbirths, information on gestational age is not routinely collected in most large household surveys such as DHS for live births. In Brazil, higher preterm birth rates than the official national statistics were obtained by DHS using reported gestational length of less than 9 months to define preterm birth.[285] However, it is not clear whether this finding was attributable to misreporting of gestational age in the survey, or deficiencies in the official statistics.

In a study from Nepal mothers were asked to classify their babies using reported birth timing using the question 'When your child was born, was he/she born very early, early, on time, late, or very late?'. Preterm birth data derived from this were found to have poor accuracy when compared to prospective pregnancy surveillance using urinary pregnancy testing: sensitivity (14.8% (95%CI: 10.6 – 19.9) respectively), specificity (96.1% (95%CI: 94.9 – 97.1)) and AUC (0.56 (95%CI: 0.53 – 0.58)).[286] In addition, as these women were all enrolled in a trial setting and had early pregnancy testing, it is possible that their knowledge and classification of timing of birth may be different from women in the general population. A further study from Colombia of maternal recall of pregnancy duration <9 months had sensitivity 0.67 specificity 0.86 for identification of preterm birth.[287]

Despite the relatively low accuracy of women's reporting of gestational age in surveys, as information on pregnancy duration is collected for pregnancy losses, including stillbirths, in DHS surveys it would be consistent to collect this information also for live births. This could provide important information in the understanding of prevalence of preterm birth amongst neonatal deaths in surveys. These data are likely to improve over time with increased coverage of ANC, and increasing access to early USS, coupled with improving coverage of handheld records.

6.4.5. Misclassification between low birthweight and non-low-birthweight newborns

Measurement at the time of birth

The challenges of birthweight assessment have been discussed in detail previously (see Sections 2.4.4, 6.3.2 and Chapter 5). Accuracy of birthweight assessment will have an effect on classification into low or non-low birthweight. Heaping of birthweights on 2500g is likely to be an important factor in the misclassification of low birthweight infants. As discussed in Chapter 5, heaping is common in all data platforms. Heaping usually occurs on multiples of 100g or 500g. As the low birthweight definition is less than 2500g and a proportion of low birthweight infants

will have their birthweight rounded up and hence recorded as exactly 2500g, heaping may underestimate the true low birthweight prevalence.

Issues related to the communication of the outcome to the woman and family

Information about birthweight is communicated verbally to the woman and her family soon after the baby is weighed in many settings. However, high workload and time pressures on healthcare workers, and the healthcare worker's perceptions of woman's desire or need for this information may influence the effectiveness of this communication, or even whether this information is communicated at all.

In addition, the birthweight is usually recorded in the mother's and baby's handheld records, also called home based records, if these are available. Handheld health cards are a potentially effective way of communicating information from one health provider to another, or to an interviewer in a household survey.[288] Coverage of these is very varied across LMICs. Even in settings where there is a policy for handheld records, lack of government funding to maintain implementation, regular stock outs, low quality of completion of various elements, including missing data and illegible entries limit their practical utility.[289,290] For example, in 228 DHS surveys reviewed for potential inclusion in the LBW estimates presented in Chapter 5, of the 1.7 million births in the 5 years preceding the survey, nearly half (48%) of women reported that their baby was weighed at birth, but just 14% had a birthweight available from handheld record data at the time of the survey.

Currently, the extent to which mothers value and use information on birthweight included in these records is not well researched.

Misreporting by healthcare workers, women or informants

Within household surveys, misreporting of birthweight is thought to be common. Findings regarding the reliability of birthweight data collected during routine surveys to adequately classify low birthweight babies has been varied (

Table 6-5). Overall, evidence suggests some errors in precision of recalled birthweight at an individual level. In the studies that provided disaggregated data, these were found to be worse in those with lower educational or socio-economic status. These lead to some loss of accuracy in LBW estimates from these sources when compared to birthweight records, which are more marked in populations with higher LBW rates where a larger number of babies have a birthweight around the 2500g cut off.

Table 6-5 Summary of studies assessing the validity of maternal reports of LBW status

Study setting (year of birth)	Recall period	Reference standard used (LBW prevalence %)	Summary of results
Kenya[291] (2013)	Exit interview	Direct observations of births (7.8%)	Sensitivity 71.1% (55.7 – 83.6) Specificity 98.7% (97.3 – 99.5) AUC 0.85 (0.82 – 0.88) Inflation Factor ≥0.75 and <1.25 Survey estimated LBW rate 6.7%
Kenya[292] (2013)	13 – 15 months	Direct observations of births (9.6%)	Sensitivity 68.1% (52.9 – 80.9) Specificity 95.0% (92.6 – 96.9) AUC 0.82 (0.78 – 0.85) Inflation Factor 1.15 Survey estimated LBW rate 11.0%
Nepal[286] (2016)	1 – 24 months (Median 10.6 months)	Birthweight recorded within 72 hours of birth by study staff (27.3% (25.0 – 30.0))	Sensitivity 45.0% (40.0 -51.0) Specificity 93.5% (91.8 – 94.9) AUC 0.69 (0.67 – 0.72) Inflation Factor 0.62 (0.52 – 0.72) Survey estimated LBW rate 17.0% (15.1 -19.1) *Recalled size at birth:* *Sensitivity 19.1% (15.4 – 23.2)* *Specificity 96.7% (95.4 – 97.7)* *AUC 0.58 (0.56 – 0.60)*
Colombia[287] (1994-2001)	5 – 12 years	Hospital records (12.5%) (Mean birthweight 2977g)	Sensitivity 66% Specificity 95% Mothers overestimated birthweight on average by 129g (55 – 203g) Survey estimated LBW rate 12.9%
Uganda[293] (2003 – 2005)	4 – 7 years	Birthweight recorded at delivery (Mean birthweight 3.21kg (sd-0.5))	Mothers overestimated birthweight on average by 0.06kg (0.0 – 0.13kg) *Recalled size at birth:* *Sensitivity 76% (50 – 93%)* *Specificity 70% (65 – 75%)*
Brazil[294] (1993)	11 years	Birthweight measured by research team for 1993 Pelotas Cohort (9.0%) (Mean 3.18kg (sd-0.52))	Sensitivity 82.1% Specificity 96.5% Positive Predictive Value 70.2% Negative Predictive Value 98.2% Survey estimated LBW rate 10.6%

AUC= Area under the curve.

Where data for recalled size at birth were also available in a given study these are included in italics.

6.5. Detecting data quality issues in reported stillbirth, preterm and low birthweight rate data

Data to inform stillbirth, preterm and low birthweight rate estimates are now being increasingly captured across many platforms in various settings (see Chapter 3, 4 and 5). However, a large challenge in estimating these rates relates to the low quality of data being generated in some data systems, and the low capacity at a local level in some settings to be able to critically assess the perinatal aggregate data being produced, and to take action where data quality is found to be sub-standard. Reasons identified for poor data quality in a given system include excessive amounts of information being collected, perceived duplication, unclear definitions, lack of data use, and absence of routine data quality checks.[295] Strong routine health data systems will have well-trained frontline staff reporting on a limited number of data elements, and data managers who regularly monitor and use the data to drive action. They will be able to detect any changes in reported outcomes, and when detected to investigate these.

As described above, omission and misclassification of birth events are not uncommon and data quality assessments should be targeted to detect these as well as monitoring overall rates. This will require monitoring overall outcome data, in addition to also specific data elements required for the classification of these outcomes including vital status, birthweight and gestational age. These quality checks could be completed internal to the data source, or via comparison to or benchmarking against external data sources or standards. Table 6-6 below provides a general overview of potential data quality checks for perinatal data that could be undertaken in most data systems.

Table 6-6 Examples of potential data elements for monitoring of quality of perinatal data

Data element or outcome	% births in system with missing or non-valid entries	Heaping, data distribution, outliers	Comparison to previous trends	Benchmarking against an external source
Vital Status at birth	✓	-	-	-
Date of birth	✓	✓	-	-
Sex of the baby	✓	✓	✓	-
Birthweight	✓	✓	-	-
Gestational age	✓	✓	-	-
LBW rate	-	-	✓	✓
Preterm Birth rate	-	-	✓	✓
Stillbirth rate	-	-	✓	✓
Stillbirth to early neonatal mortality rate	-	-	✓	✓
Sex ratio	-	-	✓	✓

At the individual data level, measures of completeness or its counterpart missing-ness and non-valid entry of data elements are useful internal checks. In addition, reviewing the distribution of the data can identify common issues such as heaping, unexpected skewness of the distribution and the number of outliers.

At the aggregate level, comparison to trends in previous months, quarters or years (depending on the rarity of the outcome) can provide a red flag to investigate further potential underlying data issues in the case of an outlier data point. Funnel plots, for example of the number of total births plotted against stillbirth or pre-discharge neonatal mortality, can also be used to identify potential outliers. Benchmarking against an external source, such as a "gold" or reference standard if one exists, or against reported rates from similar settings, preferably ones with robust data quality procedures in place, can also be useful to assess the plausibility rate calculated from the aggregate data.[296]

In addition, these quality checks should be undertaken disaggregated by birthweight, gestational age or by groups which may experience higher data quality issues, for example by stillbirth or live birth, caesarean section or vaginal birth, and potentially male or female where appropriate. Ratios can also be used to monitor data quality and two examples are given below.

As an example of this, in the U.S. clear guidance for hospitals on reporting live births, infant and fetal deaths and terminations of pregnancy is provided to ensure that data reported to the U.S. birth/infant death data set are comparable. Trend data in this system are routinely monitored and an increase in infant deaths between 2001 and 2002 led to a detailed investigation which found the increase to be due to an increase in number of births <750g recorded in the system. As babies born at <750g have a very high risk of death in the first year of life, this was found to explain the overall increase in infant mortality rate. Possible contributing factors for further investigation include: 1) changes in the reporting of births or fetal deaths between these two years, 2) a true increase in these births due to a change in the risk profile of births, or change in medical management of pregnancy.[297]

Additional aspects to data quality such as timeliness and accuracy and validity are beyond the scope of this work. Combining these potential data quality checks with normal or acceptable limits can provide a suite of performance metrics, which can be used to provide feedback on data quality at an individual or aggregate level.[270] Where data systems are electronically based the user can be alerted to the red alert status of any data element in real-time.

In chapters 4 and 5, I have included details of potential approaches to assessing data quality in preterm birth (see Chapter 4) and low birthweight data (see Chapter 5). Further details on

potential considerations for assessing data quality specifically for stillbirth data are discussed below.

6.5.1. Exploring potential quality criteria – the example of stillbirths

In order to assess the quality of data specifically relating to perinatal outcomes, including stillbirths, various approaches have been used. Different quality assessment tools will be required for local data quality assurance checks for stillbirth rate data, when compared to data quality assessments required on aggregate population-based stillbirth rate data collated for the purposes of stillbirth rate estimation generation. A brief overview of some examples of the potential approaches to assessing the quality of stillbirth rate data is provided below, with some examples of possible challenges associated with these.

Stillbirth to early and overall neonatal mortality ratios

The ratio of stillbirth to overall neonatal mortality rates was used as a quality criterion in the estimates presented in Chapter 3.[216] This method seeks to detect where stillbirths are under-reported compared to neonatal deaths or where substantial misclassification between stillbirths and neonatal deaths is present. One advantage of this method is that neonatal mortality rates are commonly collected together with stillbirth rates in many data collection systems, and data quality assessment can be done using aggregate data. Where overall neonatal mortality rate is not captured in a data system e.g. HMIS systems which usually capture details of the birth and very early neonatal deaths before discharge, but do not capture details following discharge from the facility, it is usual to count 'inpatient neonatal deaths prior to discharge' as a proxy for all early neonatal deaths. However, as inpatient stays for uncomplicated deliveries are often only a matter of hours if no complications are recognised in the mother or baby,[298] the inpatient pre-discharge neonatal mortality may substantially under-estimate the overall early neonatal mortality. Where NMR is disaggregated by day of death into early and late neonatal mortality, a ratio of SBR: ENMR may be preferable.[236,237,283] For hospital-based databases with poor capture of neonatal deaths after discharge, a SBR to day 1 NMR ratio is another possible metric. This indicator may be of greater use in this case as the day 1 neonatal deaths are the most likely to be misclassified, and capture of these deaths in facility births in HMIS systems is likely better than that of deaths occurring after day 1 when the majority of babies will have been discharged.

Review of historical data from high income settings

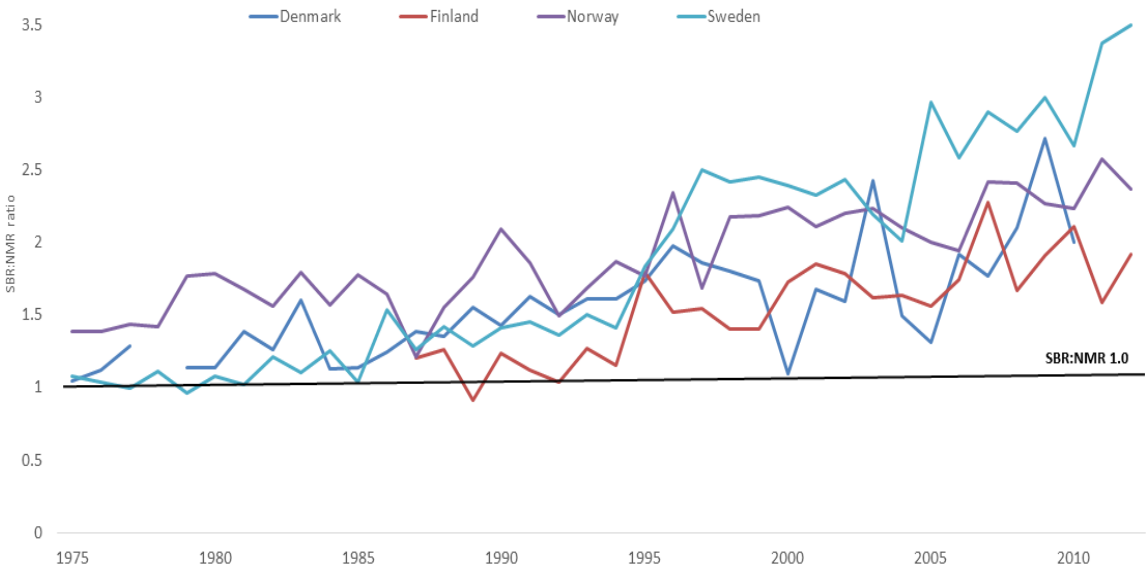
The SBR:NMR quality criterion was further reviewed using historical data located during the searches undertaken as part of the work detailed in Chapter 3. Ability to track the ratio over time is hampered by several factors, including:

(1) gestational age was not routinely assessed in most settings until around 30 years ago, and reporting was therefore based on birthweight.

(2) neonatal mortality was rarely separated out from infant mortality before the 1970s-1980s, when the relative importance of the contribution of neonatal mortality to infant mortality was recognised. This corresponded also with the development of neonatal medicine as a sub-specialty. The reporting of early neonatal deaths separately is a recent development.

Figure 6-10 SBR:NMR ratio in four Nordic countries from 1975 to 2012 shows the relationship between SBR (measured as ≥1000g) and NMR from 1975 to 2012. The SBR:NMR ratio remains around 1 – 1.5 until the NMR reaches very low levels of around 3 per 1,000 live births, and after this a gradual increase in the ratio is seen as neonatal mortality is reduced at a more rapid rate than stillbirth rates.[299] These data do not therefore support the addition of an upper ratio limit for the SBR:NMR ratio in HIC low mortality settings. Data using the 28-week definition were not available for the full time series, however based on our analysis, it would be expected that the SBR: NMR ratio would follow a similar trend using ≥28-week definition, with slightly higher ratios.

Figure 6-10 SBR:NMR ratio in four Nordic countries from 1975 to 2012



Source: Nordic perinatal statistics (Using ≥1000g definition)

National population based high quality stillbirth rate data are lacking from most high mortality settings. To seek to better understand the relationship between stillbirth rates and neonatal mortality from these settings, historical data from England and Wales where stillbirth rate and neonatal rate data are available annually from 1927-1991, during the transition from a high neonatal mortality to low neonatal mortality setting, was used.[186] Over this period, despite a

reduction in the NMR from around 35 per 1,000 to around 5 per 1,000, very little variation in SBR:NMR ratio was seen, with ratios remaining between 1 and 1.4.

These findings are consistent with those previously reported between 1900 and 1950 in 6 European countries for the relationship between SBR:ENMR shown in Table 6-7.[236]

Table 6-7 SBR: ENMR in Denmark, England, Netherlands, Norway, Scotland, Sweden 1900 – 1950

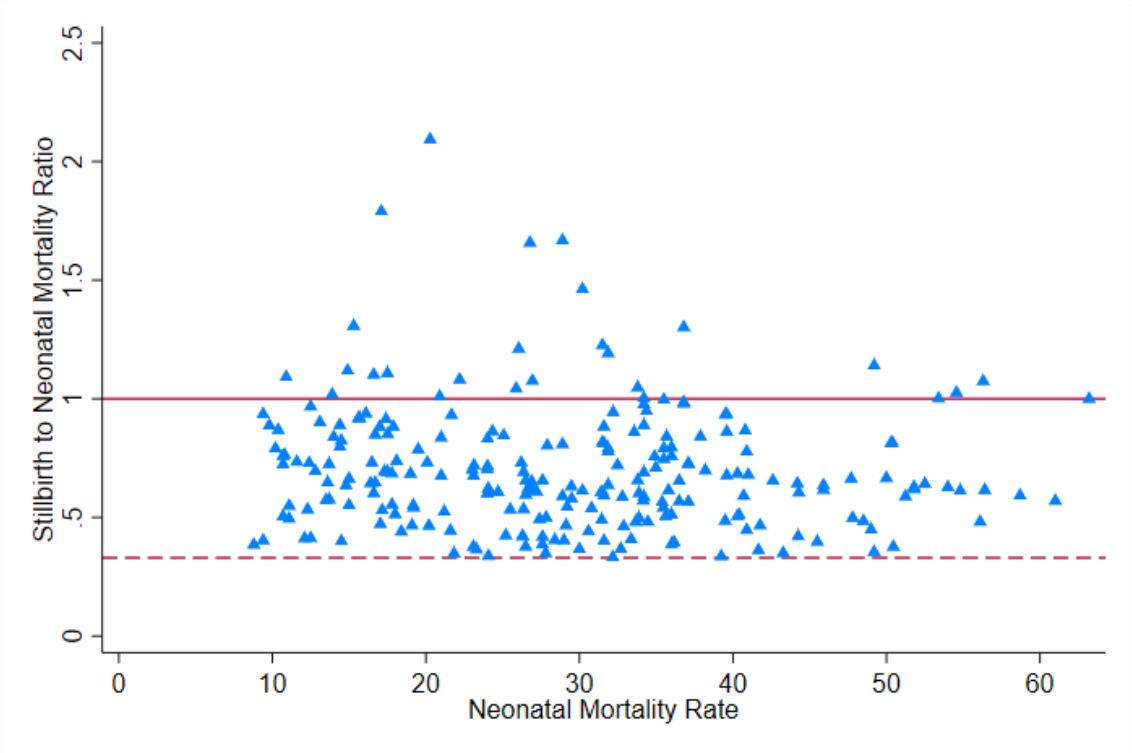
Early neonatal mortality rate	SBR:ENMR in Denmark, England, Netherlands, Norway, Scotland, Sweden 1900 - 1950
20 – 24	1.5 (1.2 – 1.9)
15 - 19	1.4 (1.0- 1.6)
10 - 14	1.4 (1.2 – 1.6)

Data source: World Health Organization [236]

Examples from recent low and middle income country data

In the preparation of the input data from LMICs for the stillbirth estimates presented in Chapter 3, 45% (n=141) of population data points from LMIC were excluded due to a SBR:NMR of less than 0.3. Figure 6-11 shows the remaining population-based data (1990 - 2013) n=173.

Figure 6-11 Ratio of stillbirth to neonatal mortality rate in stillbirth estimate data inputs from LMICs



It is seen that, contrary to the recent and historical data from HIC shown above, the majority of identified population based data from LMIC settings have a SBR:NMR ratio lower than 1.0. Whilst it is plausible that there is some variation in these ratios across settings and over time – even at similar neonatal mortality rates, such low ratios are likely to represent substantial under-capture of stillbirths.

Challenges

Despite the strengths of using ratios of stillbirth to neonatal mortality as a potential quality indicator, there are also concerns associated with its use. These include that there are potentially multiple explanations for an abnormal ratio, and that a normal ratio does not necessarily indicate high quality stillbirth data (Table 6-8).

Ongoing work is required both to further investigate the SBR:NMR ratio as a quality criterion and to review potential thresholds. For example, would a fixed threshold as currently used or a relative threshold based on any predictable relationship found with other variables, for example NMR be more appropriate? Recommendations for thresholds would need to take into account both the variation of ratios at different neonatal mortality rates, and allow provision for assessing trends in small countries.

Table 6-8 Challenges associated with the use of SBR: NMR ratio as a quality criteria

Scenario	**Effect on SBR: NMR ratio**
Low capture of neonatal deaths or better stillbirth capture e.g. weaker HMIS, CRVS, facility studies	Increased
Small population with large year on year variation of both SBR and NMR – reporting large number of stillbirths in given year	
Misclassification or misreporting of neonatal deaths as stillbirths	
Low capture of both neonatal deaths and stillbirths cancelling out various opposing scenarios that otherwise would have led to an increased or decreased ratio	Within normal range
Under-capture of stillbirths is greater than the under-capture of neonatal deaths	Decreased
Small population with large year on year variation of both SBR and NMR – reporting large number of neonatal deaths in given year	
Misclassification or misreporting of stillbirths as neonatal deaths	

Birthweight specific fetal mortality

Birthweight specific mortality was introduced as a concept and researched by populations geneticists during the 1950s – 1970s to seek to better describe the process of natural selection.[300,301] It has been used since the 1980s as a clinical tool to detect risk of perinatal outcomes and to check the quality of perinatal statistics.[11] Whilst it is rarely reported, data on birthweight are collected in most systems so it would be possible to generate this indicator with re-analysis of raw individual level data when available. Norms and standards would need developing as it would be expected to vary by context, but mortality would be expected to be

higher with lower birthweights in any one setting. Its potential for use at a global level is limited as it requires individual level data.

Gestational age specific fetal mortality

Conventionally gestational age specific mortality is defined as:

$$\text{Conventional SBR}_{week=I} = \frac{\text{Number of Stillbirths}_{week=i}}{\text{Number of Total Births}_{week=i}}$$

There has been much debate in the literature over the appropriateness of this conventional indicator, in terms of both its consistency with commonly used epidemiological terms, and its utility for clinical and public health practice. Many advocate instead to use a 'fetuses-at-risk approach' and estimate a cumulative incidence.[120,302,303] Ultimately the indicator used depends on the focus of the question it is seeking to answer.[304] Yudkin's initial or revised indicator gives an indication of imminent risk of death in the next 1-2 weeks, which was designed as a potential decision-making tool for obstetricians.[120]

$$\text{Yudkin SBR}_{week=I} = \frac{\text{Number of Stillbirths}_{week=i} + \text{Number of Stillbirths}_{week=i+1}}{\text{Number of Total Births}_{week\geq i}}$$

It shows an increasing stillbirth rate with each week of gestation, the correct interpretation of which is that in the preterm period death is less imminent. However, it received much criticism in terms of it being misinterpreted by many, potentially leading to an increasing number of labour inductions pre-term especially in the US.[120,305,306] Joseph states: "just as rising age-specific cancer rates do not imply the need for routine chemotherapy and radiation for all middle aged people" so increasing gestational-age specific stillbirth rates shouldn't lead to indiscriminate practice of iatrogenic preterm delivery.[120] Feldman proposed an alternative indicator 'prospective risk of stillbirth', including in the numerator all stillbirths occurring at week$_i$ or later:[302]

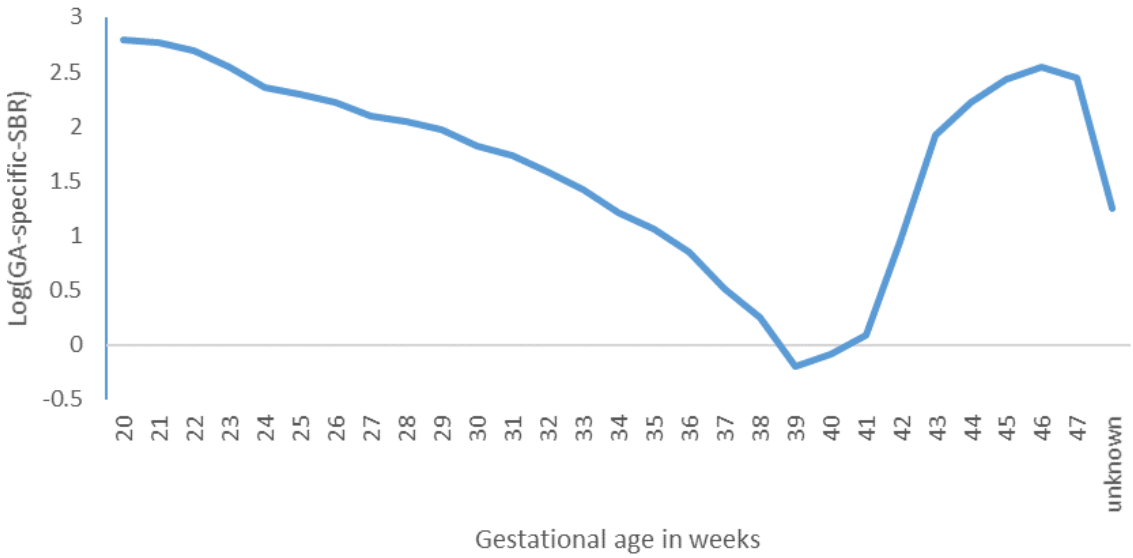
$$\text{Feldman SBR}_{week=I} = \frac{\text{Number of Stillbirths}_{week\geq i}}{\text{Number of Total Births}_{week\geq i}}$$

Since women are usually more concerned with the final outcome of their pregnancy, this indicator could therefore potentially be used to provide a woman of a given gestational age with a given condition, for example anencephaly, information on the overall risk of stillbirth in her continuing pregnancy.

Therefore, a 'fetuses-at-risk' approach may be useful especially for guiding individual clinical decision making, and for giving prognostic information on risk to families, for example the risk of stillbirth, neonatal death or cerebral palsy at a given gestation.[303]

However, for the purposes of population level overall stillbirth rate comparisons, we are more interested in a cross-sectional snapshot of the number of deaths occurring at each gestational age and have therefore used the conventional definition of gestation specific stillbirth rates below. The concept of gestation-specific-mortality in this case is more of an extension of the 'time of death' concept of early fetal death, late fetal death, early neonatal death, and later neonatal death, but providing higher resolution information on stillbirths. As with the proposed late fetal death (SBR) to neonatal mortality ratio proposed quality criteria, standards could be drawn up to indicate red flags in terms of potential missing or misclassified stillbirths. Using the 2013 data from U.S., and plotting on a log-scale, the relationship of GA-specific-SBR to gestational age is shown in Figure 6-12.

Figure 6-12 Gestation specific stillbirth rates from USA (2013)



Gestation specific stillbirth rates calculated using the conventional formula.
U.S. National Vital Statistics System, Birth Data (2013) https://www.cdc.gov/nchs/nvss/births.htm

It would be expected that in view of active fetal monitoring and planned early delivery of a baby once the risk-benefit balance between remaining in-utero to delivering swings in favour of delivery, that many babies who would be stillbirths at gestation=g in a setting with no interventions would, with timely obstetric intervention be live born at gestation=g-x. Hence, the GA-specific SBR would be expected to be lower in the US than in a setting without intensive obstetric monitoring. Therefore, data from a lower resourced-setting reporting lower gestation-specific SBR at any given gestation than the US may be evidence of data quality concerns. When

capturing data on stillbirths ≥28 weeks, the largest number of deaths occur around term, although the risk is lowest at these gestations, although in settings with poor intrapartum care the SBR is likely to be substantially higher than high income settings such as the US.

Whilst in theory this could be used as a quality criterion, and may have a role, for instance in research studies where much attention is paid to ensuring maximal completeness of the dataset, in practical terms, even in middle-income settings with reasonably strong data systems that present data by gestational age groups, the level of missing information for stillbirths is such that gestation-specific stillbirth rate is unlikely to be a useful metric at present. In such settings, a more useful quality marker may be the completeness of gestational age reporting for stillbirths. Countries should also be encouraged to report by individual week of gestation, or if this is not possible, by more granular gestational age groups. For example, Colombia collects GA data in weeks for its live and stillbirths, but groups the data into very large categories, with a large number of missing values, hence limiting its use (Table 6-9).

Table 6-9 Gestation-specific SBR USA (2013) and Colombia (2015)

	USA			Colombia		
Gestational Age group	**number of fetal deaths**	**% of all fetal deaths**	**GA-SBR**	**number of fetal deaths**	**% of all fetal deaths**	**GA-SBR**
22 - 27	7373	38	241.8	2569	15	514.4
28 - 36	7150	37	20.0	2141	12	16.5
≥37	4504	24	1.3	1225	7	2.3
Missing	134	1		11280	66	
Total	19161	100	4.9	17215	100	25.4

GA-SBR= Gestation-specific SBR Data Sources: U.S. National Vital Statistics System, Birth Data (2013) https://www.cdc.gov/nchs/nvss/births.htm Colombia: Departamento Administrativo Nacional de Estadística DANE (2015) http://formularios.dane.gov.co/Anda_4_1/index.php/catalog/475/get_microdata

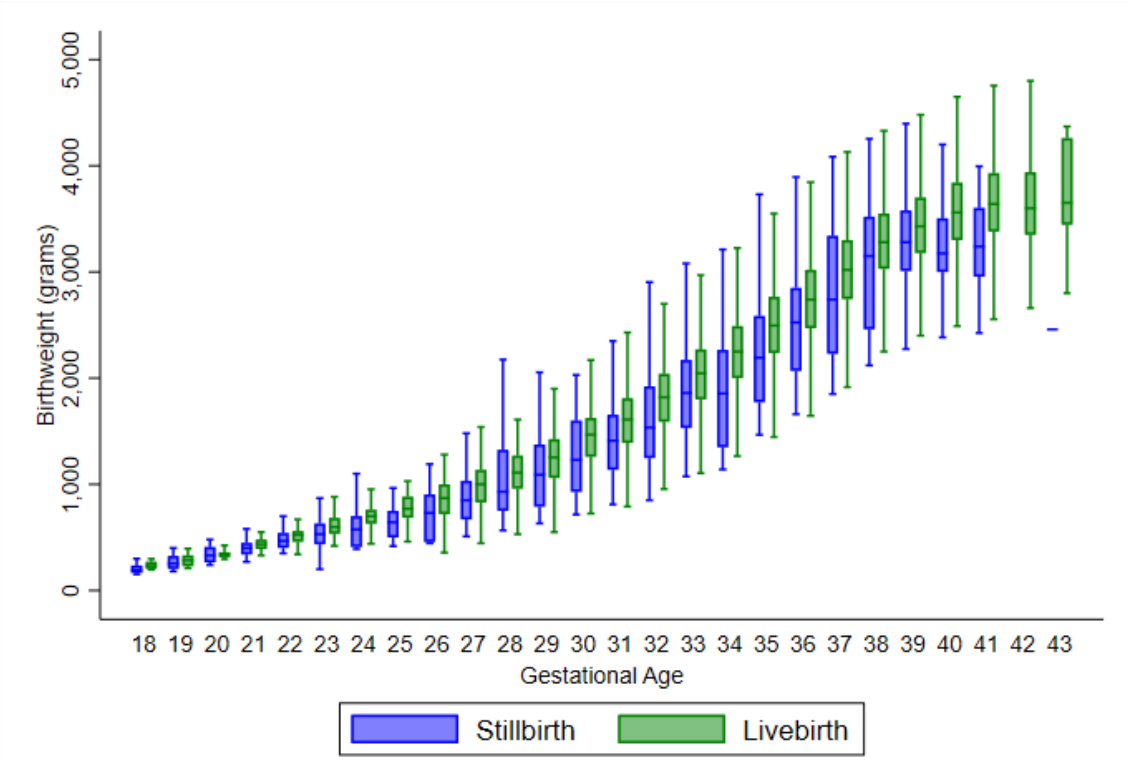
As can be seen from this table, two thirds of stillbirths in Colombia were missing GA information, which limits the value of the GA-specific mortality approach. For those with information, although the overall Colombian SBR is five times that of the US, for those with GA information the Colombian rates were less than twice the US ones, and for the 28 – 36-week category, the GA-specific mortality was actually higher in the US. Thus raising concerns about data quality in the Colombian data.

Other potential criteria

The distribution of stillbirths and live births by gestational age, and the distribution of birthweights by gestational age for live birth and stillbirths may also provide potential insights

into data quality. The following graphs show data on 245,808 live and stillbirths at ≥18 weeks in Chile 2015. Figure 6-13 shows the distribution of birthweights by gestation at birth is similar for live and stillbirths (fetal deaths), with a slightly lower birthweight for stillbirths compared to live births, which is expected in view of fetal growth restriction being a not uncommon final pathway to stillbirth.

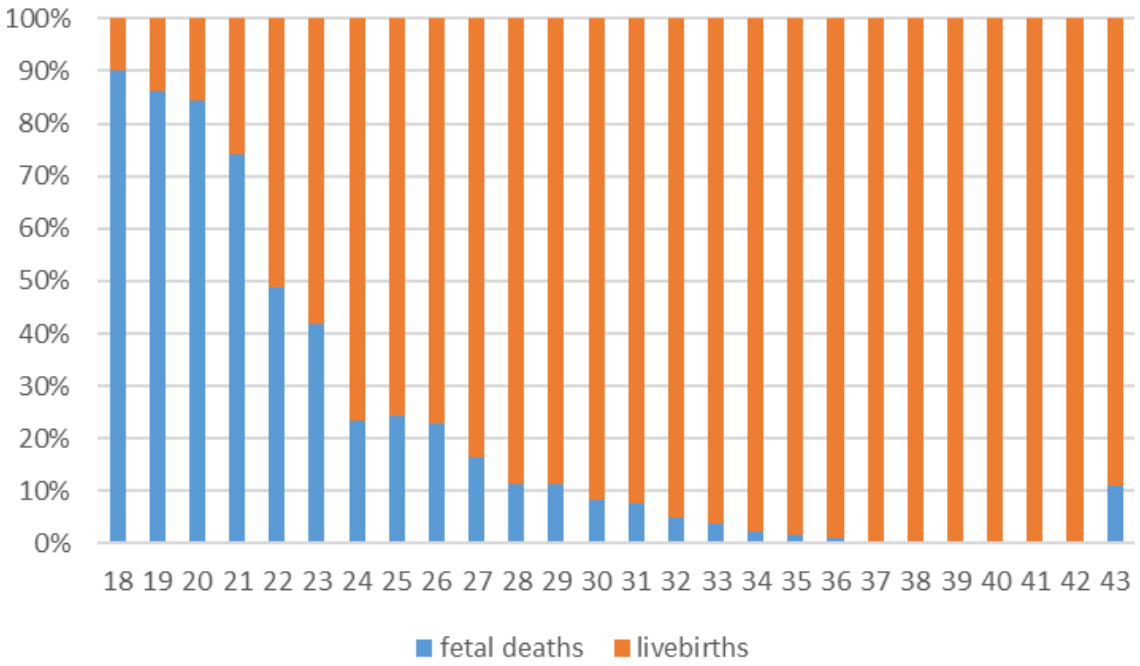
Figure 6-13 Birthweight distribution in live and stillbirths by gestational age in Chile (2015)



Source: Instituto Nacional de Estadisticas, Chile. https://www.ine.cl/estadisticas/demograficas-y-vitales Data for 245,808 total births.

Figure 6-14 shows this distribution of live to stillbirths at each gestational age. This follows the expected pattern with a high proportion of births being fetal deaths at the earliest gestations. It may be possible, using data from higher quality data systems, to define a plausible range of stillbirth to live birth ratio at any given gestational age. However, for such a quality criterion to be useful, it would need to take into account the varying contextual factors that could influence such a ratio, such as intensive obstetric monitoring and intervention.

Figure 6-14 Percentage live births and fetal deaths by gestational age in Chile (2015)



Source: Instituto Nacional de Estadisticas, Chile. https://www.ine.cl/estadisticas/demograficas-y-vitales Data for 245,808 total births.

The proportion of live births, or total births, <28-week gestation is another potential marker of perinatal data quality. This was used as a quality marker for assessing data on preterm births assuming that the capture of live birth outcomes around the threshold of viability is a marker of the strength of perinatal data capture.[56]. A worked example of these is shown below using the 2015 data from Chile (Table 6-10). Preterm birth rates were 8.1% amongst live births and 83.2% for stillbirths, this is consistent with what may be expected with a higher proportion of stillbirths being born before 37 weeks. 5.7% of all preterm live births recorded were born before 28 weeks. This is consistent with the work undertaken in Chapter 4, and suggests reasonable capture of preterm births in the Colombian routine system. In view of misclassification of live births to stillbirths around the threshold of viability, the proportion of all preterm stillbirths that are born at <28 weeks may be less valid as a quality marker for stillbirths. However, it could be adapted to include the proportion of total births that are <28-weeks gestational age to assess the quality of overall capture, but would not capture potential misclassification of outcomes between stillbirth and early neonatal death. No current standards exist for this. Overall 0.5% of live births, 0.8% of total births and 50.6% of stillbirths were extremely preterm (<28 weeks) (Table 6-10).

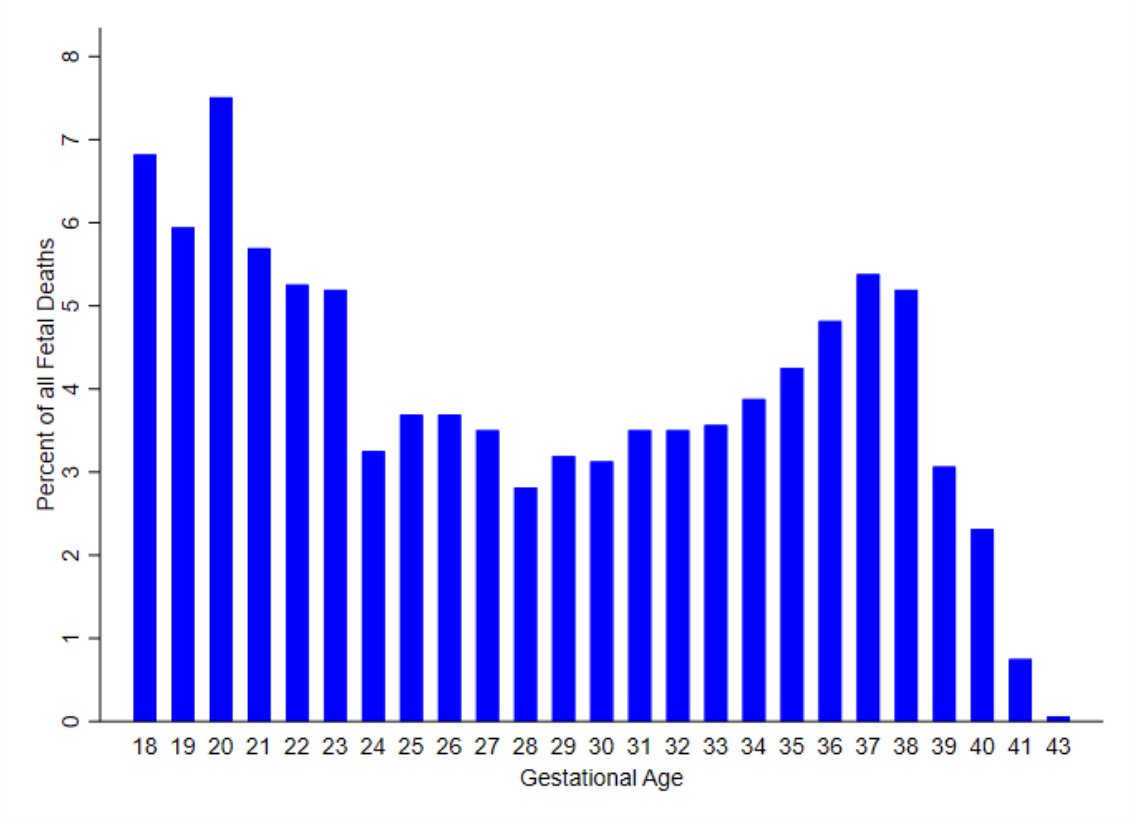
Table 6-10 Percentage live births and fetal deaths <28 and <37 weeks of gestation in Chile (2015)

	Fetal Deaths % (n)	Live births % (n)	Total Births % (n)
Total births (All gestational ages)	100% (1,598)	100% (244,210)	100% (245,808)
Overall % preterm <37 weeks gestation	83.2% (1,330)	8.1% (19,815)	8.6% (21,145)
% extremely preterm <28 weeks gestation	50.6% (808)	0.5% (1,120))	0.8% (1,928)
% of all preterm <28 weeks gestation	60.8%	5.7%	9.1%

Source: Instituto Nacional de Estadisticas, Chile. https://www.ine.cl/estadisticas/demograficas-y-vitales

A variation on this is examining the distribution of stillbirths and live births by gestational age, e.g. a very large number of fetal deaths reported at 27 weeks compared to 28 weeks, with few live births at 27 weeks could suggest potential misclassification. The data from Chile shows a relatively smaller number of events at 24 and 28 weeks, corresponding to the thresholds for reporting of fetal deaths, which may warrant further investigation (Figure 6-15).

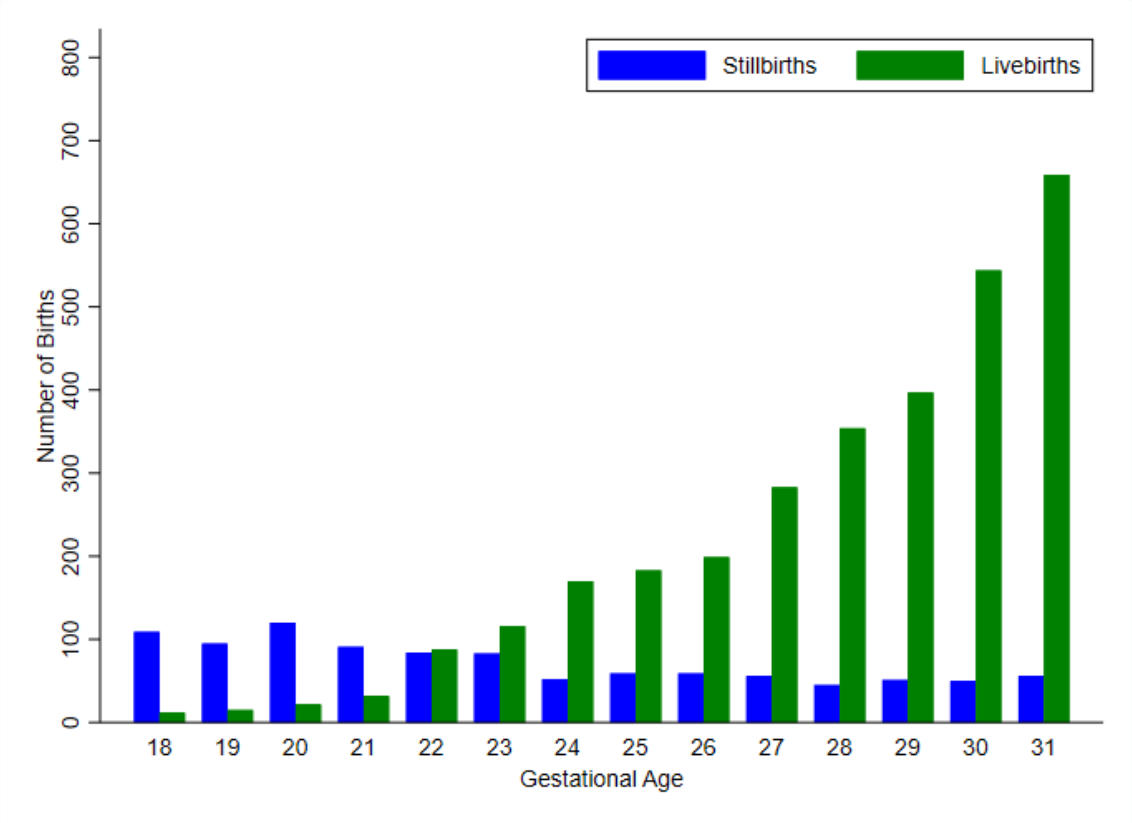
Figure 6-15 Distribution of the number of fetal deaths by gestational age in Chile (2015)



Source: Instituto Nacional de Estadisticas, Chile. https://www.ine.cl/estadisticas/demograficas-y-vitales

Figure 6-15 of vital status by gestational age for birth outcomes at <32 in Chile shows a smooth gradual increase in the number of live births from 22 to 31 weeks as expected, with no evidence of substantial misclassification between live births and fetal deaths in this dataset.

Figure 6-16 Number of live and stillbirths at 18 to 31 weeks in Chile (2015)



Source: Instituto Nacional de Estadisticas, Chile. https://www.ine.cl/estadisticas/demograficas-y-vitales Data for 245,808 total births.

Completeness of birth outcome information is another potential marker of data quality. In the Chile dataset detailed above 461 records (0.19% of the total) were excluded due to missing birthweight and gestational age. Stillbirths had a slightly lower rate of missing information (0.13% compared to live births). This is a criterion frequently used to monitor data quality in pregnancy surveillance and labour ward registers.[270,307]

The proportion of cause of death codes that are ill-defined or 'garbage codes' is used by WHO for neonatal and child cause of death estimates as a marker of quality.[8] However, it is unlikely to be useful to inform the assessment of the quality of stillbirth rate data as many systems do not collect information on cause of death for stillbirths, and death classification is more complex, particularly for stillbirths where many different classification systems are used.[308] Completeness of birth and death registration has been used as a marker of the quality of CRVS systems. UN-IGME child mortality estimates use coverage of child death registration as a quality criterion.[58] Whilst fetal death registration coverage could potentially be used as a marker of quality, these data are not currently available in most settings.

Finally, triangulation of reported rates with other external data sources could be used to assess data quality in one data source in a country compared to another. Data could be excluded where

capture is less than a given % threshold of events reported in the data source with higher capture. However, it does not provide information on the quality of data in the reference source, and for the purpose of deriving estimates in practice the 'higher quality' data source would be used. External data sources could be used to identify potential non-plausible outlying data-points which may indicate data quality issues for further investigation.

In summary this chapter aimed to summarise data lessons learnt through estimation exercises for stillbirth, preterm birth and low birthweight. Data gaps were evident for all outcomes. It found that omission and misclassification were common problems affecting data for all three outcomes. In addition, further condition-specific challenges were identified notably for stillbirth variation in definitions used and application of these definitions; for preterm birth data were sparse from LMICs as this outcome is not captured in household surveys; and for low birthweight missing birthweight and heaping. It also discussed potential approaches to assessing data quality for these outcomes, and provided a more detailed exploration of the potential to apply these for stillbirth data.

6.6. Strengths and limitations of this work

The strengths of the work presented in this thesis include that it undertook a systematic analysis of data considering three linked birth outcomes, stillbirth, preterm birth and low birthweight and used these data to generate national, regional and global estimates for each of these outcomes. In considering these three outcomes together it found substantial overlap in the measurement challenges in accurately capturing these events in commonly used data platforms, and in the resultant data gaps. In addition, as this work looked at data from all countries globally, it was able to identify many similarities in the challenges faced across diverse geographical settings and over time. This information potentially enables the sharing of learning across different settings and data platforms for these, and potentially other, birth outcomes. The estimates generated from this work for preterm birth and stillbirth have played an important role in advocacy for these issues since their publication.

Several limitations were also identified. No standard data quality criteria for aggregate data are in existence currently, and hence the assessment of data quality was undertaken on a case by case basis. Only for household survey data for low birthweight were individual level micro-data analysed enabling more detailed quality assessment and data adjustment. Whilst focusing the work on three outcomes gave breadth to the work and highlighted synergies in learning across these outcomes, it was not possible to go into great depth on each of the individual birth outcomes. This work has proposed possible methods to improve measurement, assess quality of data, and close data gaps across key data platforms; however, no primary data have been collected to test these approaches. Some of these could be considered as a next phase, including work on improving the measurement of these outcomes in household surveys which I am currently involved in.[309] However, many will require national level systems changes, and are not within the scope of this thesis. Finally, this thesis focused only on the data for measuring these outcomes and did not examine modelling improvements. Whilst modelling improvement may improve the estimation processes, data quantity and quality for these birth outcomes remain the greatest challenges at present.

SECTION III. DISCUSSION AND RECOMMENDATIONS TO IMPROVE DATA TO INFORM STILLBIRTH, PRETERM BIRTH AND LOW BIRTHWEIGHT ESTIMATES

This section builds on the lessons learnt through collating input data to inform national estimates of stillbirth, preterm birth and low birthweight, and the cross-cutting data challenges identified in Section II. These exercises have highlighted that high quality, comparable input data are critical for credible estimates and for tracking of progress towards national and global targets for stillbirth, preterm birth and low birthweight. In chapter 7, an overview of measurement and usage gaps for birth outcome data is provided and solutions to close these gaps are proposed. An overall summary and recommendations for policy and areas for future research is presented in Chapter 8.

7. Implications and proposed solutions for data improvement

The previous chapter discussed common challenges associated with the capture of stillbirth, preterm birth and low birthweight outcomes across all data platforms, and proposed some methods for detecting data quality issues associated with these. In this chapter the overall gaps in measurement and data usage for stillbirth, preterm birth and low birthweight will be summarised and solutions proposed to close these gaps. This chapter will focus on the three main data platforms collecting national-level population based data on birth outcomes, Civil Registration and Vital Statistics (CRVS), Health Management Information Systems (HMIS) and large-scale household surveys from which the body of the data used in this thesis came. Whilst the other data platforms discussed in Chapter 2 have played, and in some cases will continue to play, an important role in providing information on the prevalence of these birth outcomes, especially in LMICs. Going forward high quality, standardised data in routine data platforms with equitable coverage are needed. Ultimately, the goal should be systematic population based-recording of all births, everywhere. This could use a variety of approaches, for example by combining CRVS with a medical birth registry approach as taken in many Nordic countries, or using prospective pregnancy registers through the DHIS-2 platform. However, whatever approach is used will require targeted investment to improve data quality specifically for these outcomes.

7.1. Overview of measurement and usage gaps for birth outcome data

7.1.1. Why data on stillbirth, preterm birth and low birthweight are important

Accurate data on stillbirth, preterm birth and low birthweight are important on many different levels. Firstly, on an individual level these data enable every woman her right to have her baby counted, and for live-born children, the child's right to an identity and to be counted.[310] As detailed in previous chapters, mothers of stillbirths are at increased risk of maternity mortality and morbidity and babies born preterm and/ or low birthweight are at higher risk of short and longer term mortality and morbidity.[14,23,57,311] Accurate recording of these outcomes in clinical records can facilitate provision of optimal tailored care to the woman and the child, both around the time of birth, but also for the child throughout childhood and for the woman to manage risk and improve care in subsequent pregnancies.[312,313]

Secondly, data on stillbirth, preterm birth and low birthweight are important for frontline health workers in supporting decision making in clinical care on an individual level as highlighted above, but also in guiding reviews of facility-level outcomes.[311] For example, through perinatal audits to review and monitor trends in levels and underlying causes of stillbirth to develop locally-informed solutions and to monitor these at a facility-level.[112] To improve perinatal outcomes these data on stillbirth, preterm birth and low birthweight should be analysed specifically for hospital use, and not only for routine reporting to the next level of the health information system.[314]

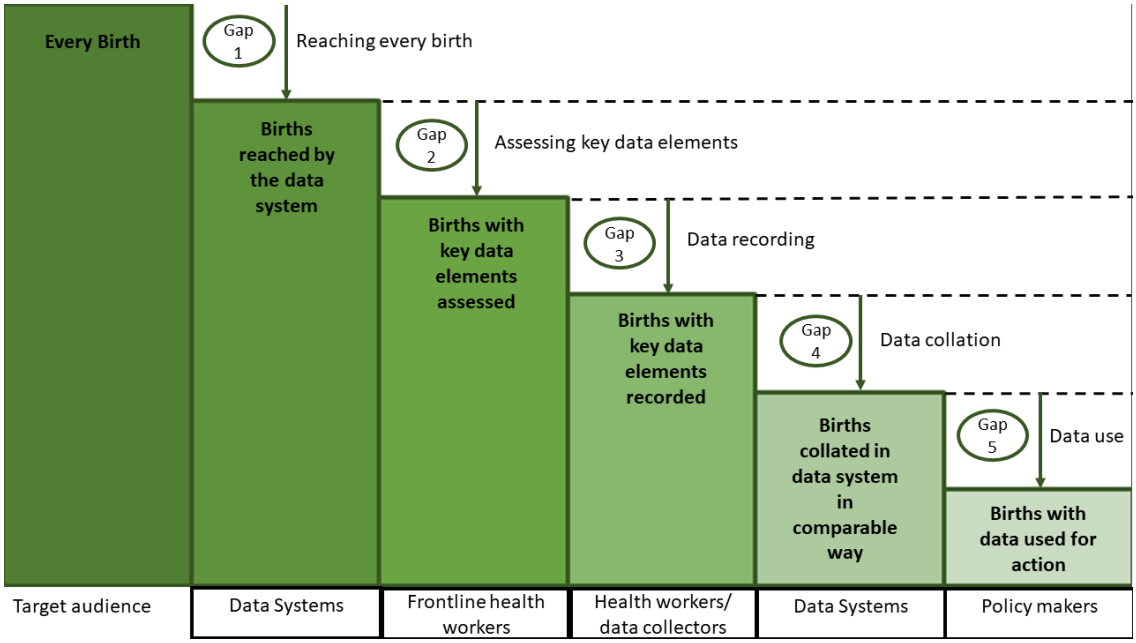
Thirdly, data on these indicators can be used at a subnational or national level both for public health planning and accountability. Accurate data on stillbirth rates can be a useful barometer of women's health in general, and health system strength for public health planners. Stillbirth rates are very sensitive to the quality of antenatal and intrapartum care. LMICs with the highest stillbirth rates have a high proportion of deaths occurring during labour, improving access and quality of 24-hour obstetric care is critical in reducing these largely preventable deaths.[25,315] Accurate data on stillbirths can be used to prioritise investments in strengthening access to and quality of care for highest burden regions in a country. Despite the challenges in the measurement of stillbirth, these are potentially more amenable to data improvements than other related maternal health morbidity outcomes whose measurement is very challenging.[316] Similarly data on preterm and low birthweight rate can be used to guide investment in resources to provide access to high quality care for these vulnerable infants with their increased health needs, both around the time of birth and in the immediate postnatal period, but also throughout childhood.[311]

Finally, these indicators can be used by national and international policy makers to compare health between populations and monitor progress towards global goals as shown in Chapter 1.

7.1.2. Summary of measurement and data usage gaps

Data gaps impeding accurate population-level stillbirth, preterm birth and low birthweight data identified through this work can be summarised in 5 steps (Figure 7-1). The first gap is that in too many cases neither babies nor their mothers are reached by the data system at all. Closing this gap will require understanding the barriers to access and addressing these to improve coverage of the data system for every birth. The second gap is in the accurate assessment and measurement of the key data elements required for correct categorisation of stillbirth, preterm birth and low birthweight babies. The third gap is in the recording of the key data elements within the data system, for example in electronic patient records, registers or survey collection tools. Addressing the second and third gap will require working together with frontline healthcare workers, data clerks and civil registrars, or in the case of surveys, data collectors.

Figure 7-1 Five gaps for population-level data regarding stillbirth, preterm birth and low birthweight

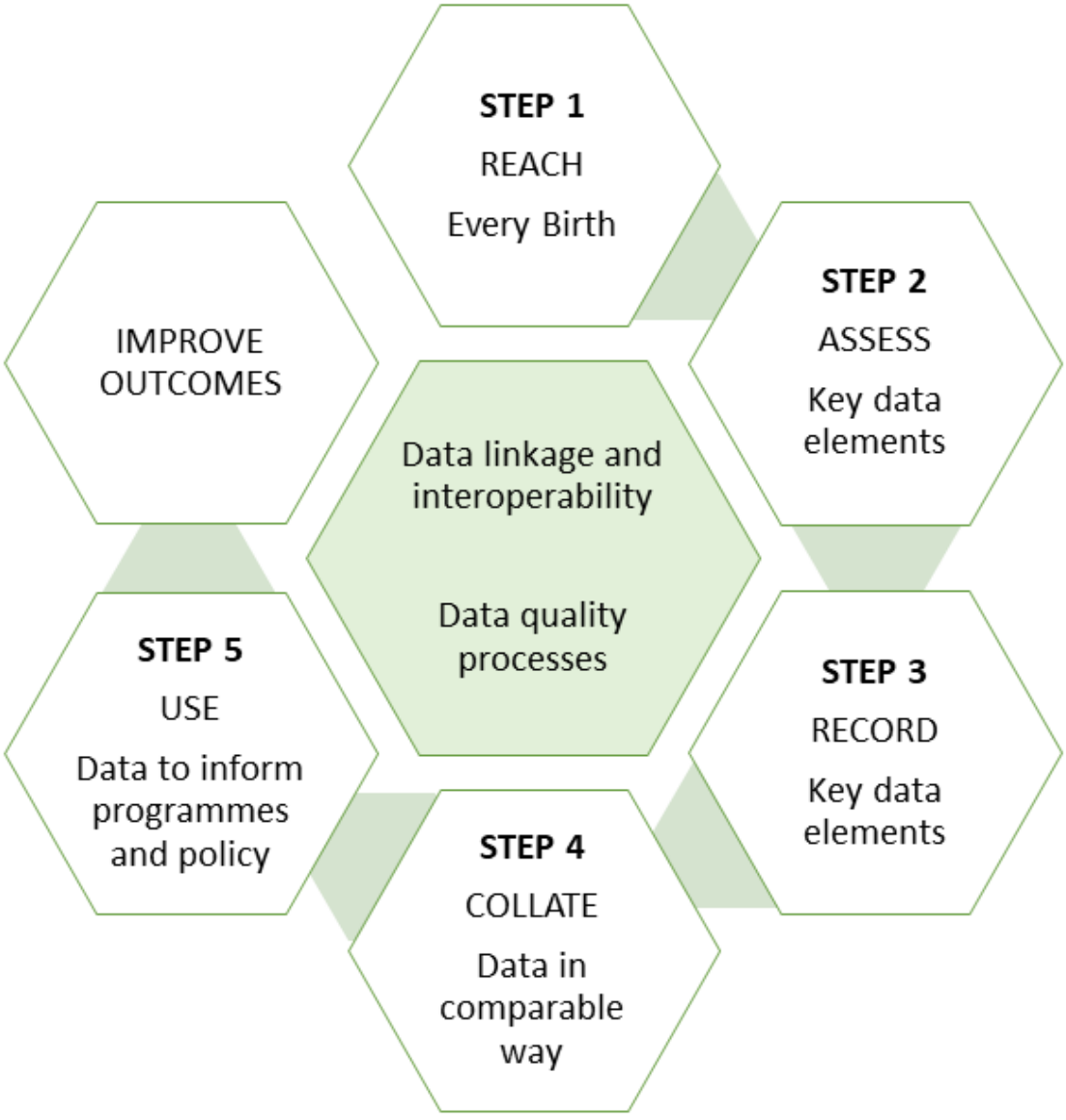


The fourth gap identified is in the collation of the data. Even if all details are correctly measured and recorded for a birth, if these data are not collated up the data system or are collated in a non-comparable way, these data will be limited in their use for action. The final gap identified is in data use. Closing the first four gaps could provide accurate data for every birth in a population, but does not necessarily lead to action unless these data are readily accessible to and valued by potential users. Potential users include both national and sub-national policy makers, international organisations, advocates including civil society and also frontline health workers.

7.2. Proposed solutions to close gaps for birth outcome data

Five steps are required to close the five gaps described in the section above and to improve stillbirth, preterm birth and low birthweight data for action (Figure 7-2). In addition, two cross-cutting components, data linkage and interoperability, and data quality processes are required to achieve these steps.

Figure 7-2 Five steps to close the five gaps to improve stillbirth, preterm birth and low birthweight data for action



Key data elements include vital status at birth, gestational age and birthweight

An overview of these five steps is presented below and in Annex A.6. A synthesis of the cross-cutting principles for closing these gaps is presented for each of the five steps. For Step 1 (REACH) and Step 3 (RECORD) platform specific issues must be addressed to close the data gaps, and for these, the approaches required are discussed separately for the three main platforms CRVS, HMIS and household surveys. For Step 2 (ASSESS), as assessing the key data elements vital

status at birth, gestational age and birthweight have specific challenges, approaches to address these are discussed separately.

7.2.1. STEP 1: REACH every birth

As a general principle, efforts should be made in all data systems to reach every birth, with particular attention to those most likely to be missing from the data system including stillbirths, early neonatal deaths especially those around the thresholds of viability, births in marginalised populations, home births and births in the private sector. Data on preterm and low birthweight babies who are live born are necessary for programming and budgeting purposes in view of the increased healthcare needs in these at-risk-infants. However, from an epidemiological perspective including every birth whether live or stillborn is more appropriate in view of the substantial misclassification highlighted in the previous chapter, but also as the underlying risk factors, cause of death and public health interventions to address these are similar and stillbirth is associated with increased maternal morbidity and healthcare needs.

Closing this gap requires that the data system reaches every birth and that it is designed to capture every birth, including stillbirths, in its legal framework, data collection tools, registers or questionnaires. As platform specific issues are required to be addressed to close the gap in reaching every birth, potential approaches are discussed separately for the three main platforms CRVS, HMIS and household surveys with further details in Annex A.6.1.

Improving coverage of the data system to reach every birth

In both CRVS and HMIS data systems population-based surveillance has the potential to improve the coverage to reach every birth, especially those occurring outside a health facility. Real-time mortality monitoring systems in Ghana, Mali, Ethiopia and Malawi, where community based health workers or volunteers capture pregnancies, births and deaths and report vital events to the overall birth and death registration system have shown promising short-term results for neonatal mortality. This is attributed in part to data collectors being trusted members of the community.[317-320] However, high levels of monitoring and supervision may be required to achieve sustained, adequate results at scale as other studies with less supervision had lower capture of neonatal deaths.[317] This approach has not yet been tested for stillbirth.

The use of community health extension workers or community volunteers to collect information on births occurring outside of the health system, using pregnancy registers and mhealth innovations where available could improve HMIS coverage.[266,321,322] A study in four districts in Bangladesh found stillbirth surveillance at a community level using grassroots level health and family planning workers, Health Assistants and Family welfare Officers was feasible.[321] However, the long-term sustainability of using community health volunteers to capture events in

communities should be considered. Whilst in view of shortage of trained health workers they are an increasingly used group to both deliver health interventions and record outcomes, concerns have raised around sustainability of these approaches in general.[323-325]

Linking to other surveillance programmes can improve coverage, even in high income settings. For example, in the US data from active birth defects surveillance programs were used to improve quantity and quality of stillbirth data.[326,327] In Haryana state India, the population-based Maternal Infant Death Review System launched in 2013 led to a large increase in capture for stillbirth rates from <5 per 1,000 to 20 per 1,000 births.[322] MPDSR has the potential to provide information on overall population prevalence of these outcomes where the perinatal surveillance component is well developed, for example parts of Ethiopia.[328] However, in most cases the perinatal focus has been on facility-based perinatal audit, rather than surveillance, and hence limited population level data are available. Lack of funding for these surveillance initiatives has frequently presented a barrier. Some examples of novel financing strategies are available, although their long-term costs and sustainability are yet to be seen.[329]

CRVS systems

A large number of CRVS improvement initiatives are currently underway to increase birth registration driven predominantly by a Child Protection agenda to provide the child with official recognition by the state, and the associated benefits linked to this. Associated benefits include: access to health care, education, social assistance, employment in formal sector, the right to vote, obtain a passport, or to own property; and safeguarding against entry into marriage, the labour market, or armed forces before the legal age. These are clearly important and necessary motives. However, failure to include key information such as birthweight and gestational age and the registration of stillbirths into efforts to strengthen CRVS is a missed opportunity to improve the available information for stillbirths, preterm births and low birthweight babies.[159] Including these is possible, for example focussed efforts to improve coverage of CRVS in Jamaica, including 'bedside' facility birth registration and improved procedures to facilitate the registration of facility stillbirths and early neonatal deaths led to an increase in capture of stillbirths from 12.8% in 1986 to 69% in 2008.[243,244] Innovations are being used to seek to increase the coverage of CRVS. These include conditional cash transfers, the use of mobile communication devices and SMS services and including the birth notification process as part of a combined maternal child health card.[330-332] However, the current evidence base for these is not strong.

HMIS systems

Efforts have also been made to improve the capture of birth outcomes within the HMIS systems. For example, in Brazil proactive searching for live births and deaths not reported to the Ministry of Health has been undertaken using probabilistic sampling, and the results used to correct the vital statistics.[333] Capture–recapture (CR) methods uses matching of two or more independent data sources to assess the degree of underestimation, and to thus estimate of the total number of cases (unreported and reported) in a population when data sources overlap but are potentially incomplete.[334] Recently it has been used across a number of settings for capture of stillbirths.[327,335,336] On a smaller scale, a study in Pakistan used all potential health information sources to create an enhanced data system to capture information on births and maternal and perinatal deaths using information from Lady Health Workers, Community Health Workers, Community midwives, Maternal Child Health cards and facility information from both public and private health facilities.[336] However, whilst neonatal mortality capture was improved, there was no difference in stillbirth rates compared to those obtained from the basic system, which may in part be due to the inclusion of verbal autopsy leading to a reduction in misclassification of early neonatal deaths as stillbirths.

Failure of HMIS systems to include births outside public health facilities remains a large challenge. Extending the reach of HMIS systems to capture births occurring in private facilities could improve population based coverage. One potential approach to achieving this is through the development of formal data sharing structures and incentivising data sharing.[337]

Household surveys

Information on births from household surveys is collected through interviews with the mother. Many household surveys miss the most vulnerable women and their babies, for example by excluding women <15 years, never married women or women residing in difficult to access areas of the country. Ensuring a good sampling frame is critical for reaching a representative population. Whilst large-scale household surveys seek to be nationally representative, for logistical reasons they are rarely undertaken in the most vulnerable settings e.g. fragile states or less stable areas of countries, which are areas where robust CRVS and HMIS data systems are also frequently lacking. The inclusion of a perinatal outcome component to rapid assessment survey tools used in humanitarian settings could increase the coverage of information on birth outcomes amongst this most vulnerable group.

Designing data systems with potential to reach every birth

Achieving this will require ensuring that all services, forms and questionnaires are available in all local languages. It is also important that they are flexible to local culture and traditions which

might otherwise impact on capture. For example, allowing a name to be added later to a birth registration enabling the timely registration of an unnamed or not yet named baby, or using culturally appropriate and respectful language in a survey questionnaire to increase the likelihood of a mother mentioning a specific birth.

CRVS systems

In CRVS currently the lack of legal framework prevents inclusion of stillbirths in some settings. Going forward, all counties should follow WHO recommendations to provide for the collection of fetal death (stillbirth) data within CRVS, even if it is not yet viable to do so.[253]

Household surveys

Even amongst women who are reached by household surveys, failure to include a full maternity history or including only a live birth history is an important barrier to identifying each of her births. Existing evidence suggests that using a full pregnancy history improves stillbirth estimates from surveys. In a review of 168 DHS and RHS surveys the stillbirth data quality was higher in surveys using a pregnancy history (early neonatal mortality ratio 0.9, compared to 0.6 for birth history). For higher mortality settings (early neonatal mortality rate>20 per 1,000) the stillbirth rate was 50% higher using a pregnancy history compared to a birth history (26 vs 16 per 1,000).[180] However, most birth histories in this analysis used reproductive calendars and did not include additional questions on non-live births as in the more recent DHS surveys.

A randomised comparison of the DHS-7 full birth history plus additional questions on non-live births to a full pregnancy history approach has recently been undertaken in approximately 70,000 women in 5 Health and Demographic Surveillance Sites in Africa and Asia.[309] Preliminary results from this study have shown that a pregnancy history approach took a median of 1 minute longer, but the stillbirth rate was 21% higher (95%CI -10 – 62%) compared to the birth history approach. On the basis of this evidence, a full pregnancy history approach is recommended over a full birth history. However, consistent with DHS surveys, in this randomised comparison although the capture of stillbirths was better with a full pregnancy history, stillbirth rates remained lower than would be expected in these populations, with stillbirth to neonatal death ratios of around 0.8 compared to expected ratios of around 1.2 (see section 6.5.1), suggesting that these births are still under-captured. Addressing this will require further work to understand the barriers and enablers to reaching these stillbirths in surveys. This could include a review of the wording of the standard questions and their translation to ensure that they are understood by women who may use different local terminology.[338] Literature from a given context about pregnancy disclosure and the perceptions of stillbirth could be used to inform

culturally-sensitive training materials for interviewers which could inform strategies to overcome barriers to reporting stillbirths such as stigma, fatalism or fear.[338,339]

7.2.2. STEP 2: ASSESS key data elements

Accurate assessment of key data elements in births reached by the data system, including vital status at birth, gestational age and birthweight, is required for their accurate categorisation. Currently, many births that are reached by the data system do not have these key data items assessed accurately. Closing this measurement gap will require improvements in knowledge, understanding, and technical ability to assess these amongst frontline healthcare workers. For births captured outside the health sector, data collectors such as community scouts and survey interviewers are responsible for assessing these data elements. Assessment of these births will depend on the mother or informant's knowledge about the baby's vital status at birth, gestational age and birthweight, their understanding of the questions (which will depend in part on the interviewer's skill in asking these questions) and their ability to accurately recall these. As assessments of these key data elements have specific challenges, approaches to address each key data element are discussed separately below with further details in Annex A.6.2.

Improving assessment of vital status at birth

For births occurring with a skilled attendant, providing training for healthcare workers in neonatal resuscitation is an effective way of both improving survival, and reducing the misclassification between fresh stillbirths and early neonatal deaths in the delivery room; hence reducing measurement error of vital status at birth.[272] This is especially important in LMIC settings where over half of all stillbirths are recorded as 'fresh' in appearance.[25,340] This training should be coupled with an enabling environment, including non-blame perinatal audit, to reduce misreporting.

Births occurring outside the health sector and with no skilled attendant may be captured later through community informants such as 'scouts' used by many Health and Demographic Surveillance sites, community health workers, or by survey interviewers. In such cases, substantial misclassification between stillbirth and neonatal death remains common.[279] The use of a verbal autopsy may assist in the differentiation between stillbirth and live birth followed by early neonatal death. Where this is not possible adding additional questions to survey or data collection tools to seek to establish if the baby showed any signs of life and birth such as "Did

that baby cry, move, or breathe when it was born?" could potentially improve retrospective assessment at the time of data collection. Further work is underway to assess these.[309]

Improving assessment of gestational age

Early USS remains the gold standard for measuring gestational age, but coverage in LMICs is low.[341] New technologies bring potential to extend its use across LMIC settings including lower-cost, increasingly portable machines,[342] with the option of telemedicine to monitor the quality of measurement in the field and provide guidance and support.[343,344] Routine early USS can improve gestational age assessment. This has the potential to improve preterm birth and stillbirth categorisation and data, reduce erroneous 'post-term inductions', and improve outcomes in placenta praevia and multiple pregnancy through early detection allowing for increased monitoring and timely intervention to reduce risks for the mother and her baby.[345,346] Traditional methods require a 'dating scan' scan by a skilled sonographer prior to 18 weeks of gestation. In some settings availability of USS may increase early antenatal clinic attendance,[347,348] but this association is not universal.[349] However, concerns have also been raised about potential unintended consequences of routine early pregnancy USS, including sex-selective termination of pregnancy in cultures where the male child is more highly valued,[350] excessive costs to the women from repeated, non-medically indicated USS,[351] and the potential for increased unnecessary obstetric intervention.[138] In addition to the costs associated with routine USS, a certain amount of infrastructure including electricity, ongoing training and buy-in from clinical, technical and maintenance staff, feasibility of referral if high-risk conditions diagnosed and political will are required. These may act as barriers to USS scale-up.[352,353] In view of these systems challenges, it is unlikely that universal routine early pregnancy ultrasound assessment of gestational age will be feasible in the short-term in many settings.

Innovations are being developed to seek to overcome these barriers. Recent research has also focused on improving the accuracy of late (third trimester) ultrasound dating. The INTER-GROWTH-21st Fetal Growth Longitudinal Study developed equations for estimating GA from USS in late pregnancy using fetal head circumference and fetal length biometric data from 4,229 singleton pregnancies (compared to 361 used in the development of the previous standards). The estimates were associated with uncertainty of $\pm$13.2, 14.3, 15.4 and 16.5 days at 28, 30, 32 and 34 weeks respectively.[354] The Alliance for Maternal and Newborn Health Improvement (AMANHI) has also undertaken methodological work in this area in three of their sites, Pakistan, Tanzania and Bangladesh investigating the potential of using trans cerebellar diameter on USS to date pregnancies in the third trimester as the cerebellum is relatively spared with fetal growth restriction.[355] Amongst 1319 singleton pregnancies the trans cerebellar diameter predicted GA at 24 – 36 weeks with an accuracy of ±13.3 days. Automated devices such as TraCer, which

includes an ultrasound probe coupled to an Android app to automatically recognise and measure the cerebellum, could enable health workers with minimal or no training in sonography to undertake more accurate gestational age assessment from 15 to around 34 weeks of gestation.[356]

Where there is no USS, LMP is routinely used alone for gestational age assessment. Data on LMP can be of variable quality; however, measures can be put in place to improve this. For example, the quality of LMP data was improved in rural Bangladesh through prospective collection of LMP data together with the use of a home calendar, resulting in a high sensitivity (86%) and specificity (96%) for classifying preterm birth.[125] This may be a potential method to improve reliability of preterm birth classification in settings without access to early USS.

Other potential tools to improve assessment of gestational age after birth include the use of simplified newborn gestational age algorithms, such as that being developed in the AMANHI project across 5 countries in S. Asia and sub-Saharan Africa.[355] The potential of newborn skin assessment to estimate gestational age is currently under investigation including skin reflection,[357] and skin thickness.[358,359] The vascularity of the anterior lens capsule has long been recognised as a marker of gestational age.[144] New technology has led to the development of a Smartphone Ophthalmoscope, which if successful could allow bedside or community gestational age assessment.[360] There is also interest in using smartphone technology and machine learning to assess gestational age using facial, foot and ear appearance.[361] However, most of the newborn assessment tools currently under development are only possible for live births, and not stillbirths.

Recent interest is also being directed towards the development of neonatal dry blood sample metabolic profile analyses to predict gestational age, with some encouraging early results.[362,363] However, as these methods involve tandem mass spectrometry, high costs and feasibility considerations would currently prohibit their widespread use in LMICs. In addition, these methods have the disadvantage of a 24 – 72-hour time lag for results, compared to real time information for driving clinical decision making for other methods.

In household surveys, as detailed above, a standard birth history is most commonly used. This only includes questions attempting to assess gestational age from maternal report for pregnancy losses to be able to define stillbirths. Such information is not collected on live births in view of concerns regarding the reliability of gestational age assessments based on maternal reports. Work is currently underway to assess the feasibility of revised questions to assess gestational age retrospectively at the time of the survey.[309] In line with the principle of collecting the same information on every birth whether live or stillborn, questions on gestational age

should be included in these surveys also for live births. This is already standard in the minority of surveys that have used a pregnancy history approach.[180] However, ultimately improving the quality of gestational age data in surveys is likely to require improvements in coverage and quality of gestational age assessments by healthcare workers and linking these to survey data systems through handheld or facility paper or electronic records.

Improving the assessment of birthweight

Methods to overcome the specific challenges of recording an accurate birthweight will vary depending on the place of birth. Substantial challenges remain for capturing birthweight for home births; however accurate birthweight measurement and recording should be feasible for all facility births. This would assist both with recognition of individual risk e.g. need for extra care for small or exceptionally large infants, but also in monitoring population low birthweight rates, and providing disaggregated data on neonatal outcomes including morbidity and mortality.

There is limited literature on potential innovations to improve the measurement of birthweight, although the provision of weighing scales, training and community engagement have been shown to increase coverage of weighing at birth for homebirths.[364-366] In sub-populations where coverage of weighing at birth remains low, for example stillbirths or rural Ethiopian populations, specific cultural behavioural interventions will need to be designed and implemented to close the gap.

Ensuring that a functional, suitable weighing device is available for every birth is challenging. Weighing machines are frequently not calibrated.[367] Most digital scales are expensive, require batteries and lack the robustness required for heavy use in facility or community settings. As highlighted in Chapter 5 developing affordable, robust, portable and accurate devices is a priority. Despite this, little research is evident in this area.[368,369]

Where suitable devices are available, improving the accuracy of birthweight in babies who are weighed at birth could be achieved through training, standards, guidelines and support. Whilst multiple sources of standard guidance, best practice protocols and job aides are available for weighing older infants or children in a variety of settings, few include specific guidance around weighing at birth.[370,371] WHO has produced guidance for weighing of newborns at home visits which have been adapted for use in many community health worker training packages, however these recommend weighing the baby whilst dressed, which is contrary to best practice.[372] WHO has not produced standard guidance on the weighing of newborns at birth, but guidance, such as produced by All India Institute of Medical Sciences (AIIMS) could be adapted for more widespread use.[373]

Ideally an accurate birthweight would be measured for all babies. However, where this is not possible, prediction models based on anthropometric surrogates such as head circumference and chest circumference are a potential promising innovation to estimate birthweight which could, after further validation, be included in a paper-based or mobile phone app-based tool in community settings with high levels of homebirths in LMIC settings.[374]

In household surveys, for births occurring outside the health sector, perceived size at birth was previously used to estimate whether an individual birth was low birthweight or not. This approach is no longer recommended as mother's recollection of size at birth has been shown not to be accurate at an individual level.[375] Efforts should be focused on weighing babies, or using anthropometric surrogates where weighing is not feasible, and use methods such as handheld cards to link this information to the survey data system (see 7.3.1.). Most household surveys include birthweight only for live births in the 2 – 5 years preceding the survey. In line with the principle of collecting the same information on every birth, whether live or stillborn, questions on birthweight should be included in these surveys also for stillbirths.

7.2.3. STEP 3: RECORD key data elements

For babies reached by the data system with their key data elements accurately assessed, the next challenge is to ensure that these data are recorded within the measurement system such as in a hospital or civil registrar register, electronic data record, or in a survey questionnaire. Closing this gap will require that data systems are designed to facilitate accurate recording of key data elements and also improved understanding of current recording practice, and barriers and enablers to recording. As platform specific issues are required to be addressed to close the gap in recording key data elements for every birth, potential approaches are discussed separately for the three main platforms CRVS, HMIS and household surveys below with further details in Annex A.6.3.

Designing data systems to record key data elements for every birth

CRVS systems

Within CRVS, birth and death certificates commonly do not include information on gestational age or birthweight as this is not required for the legal purpose of civil registration. However, streamlined notification systems for every birth, including all relevant data elements collected within the health data system, can facilitate the availability of this information for the purposes of vital statistics. This could include direct electronic notification, or by providing this information to the families at the time of birth e.g. in a sealed envelope or as a birth notification page within the mother or child's handheld health card.[332] Where possible following a stillbirth

or early neonatal death the responsibility to register these events should be placed on the health facility as these systems can be costly and hard to navigate, and bereaved parents have little incentive to overcome these barriers to report these events.

HMIS systems

Not all HMIS and health-based data systems are designed to record key data items for every birth reached and assessed within the health system. Work on a standardised set of minimal perinatal indicators to be collected for all births began in the 1980s with the work of the International collaborative effort on Perinatal and Infant Mortality which was accepted across many HICs.[376] This work has culminated with the recent publication by WHO of a standard minimum perinatal dataset recommended to be recorded by the health system for each birth as part of the 'Making Every Baby Count – Audit Guide'[112] and 'The WHO application of ICD-10 to deaths during the perinatal period: ICD-PM'[67] (see Annex A.6.3). This dataset contains the recommended data elements that should be recorded for every birth at the point of care for local purposes as well as for aggregating up the data system. Accurate recording of these data elements in a data system, including vital status at birth (collected under details of death), gestational age and birthweight will allow correct classification of birth outcomes. Collecting all these data elements on every birth will allow potential disaggregation of data e.g. gestational age or birthweight specific mortality indicators. In addition to these, especially where TOP is legal – an additional category could be added to type of delivery 'TOP' to enable differentiation between stillbirth and TOP as these have different underlying causes, and will require different public health approaches to address. For example, most late TOPs are associated with congenital anomalies, compared to fewer than 10% of spontaneous fetal deaths.[25]

Despite the plethora of registers and records that frontline workers complete, and the agreed definition of a standard minimum perinatal dataset, facility-based data systems do not always record key information. It is recommended that all countries review the standard registers used in their facilities to capture information on birth outcomes, whether paper-based or electronic, to ensure that all elements of the minimum perinatal dataset are included and that standard harmonised data collection forms are used to improve the quality of these data.[295]

Births around the threshold of viability are more likely to be missing from HMIS systems, even if the mother attends a facility for the delivery. For example, in many settings when a woman presents in labour, if her pregnancy is assessed to be less than the threshold of viability, she will

usually be directed to deliver on a gynaecology ward rather than the labour ward. In LMIC where gestational age assessment can be very unreliable, and where perceived thresholds of viability are around 28 weeks or even later, these babies delivered on the gynaecology ward, even if they show signs of life or are potentially resuscitable, are not usually included in the standard delivery registers, or aggregated in HMIS. Whilst this may be appropriate from a clinical perspective where there are limited neonatal care facilities as long as care is delivered in a respectful manner, this presents a barrier to recording data on these births and efforts should be made to design processes to record the minimum perinatal dataset regardless of where in the facility the baby was born.

As the collection of these data within health systems depends on time-pressured frontline health workers it is important that the data system be tailored to the needs of healthcare workers. Therefore, reviewing and understanding current practices and data flow will be required to improve the efficiency of the data system and to improve these data. For example, one study in Indonesia found that community midwives used notebooks instead of bulky registers and recorded births later in the register, but that this was prone to errors in transcription due to shorthand, misspellings and illegibility and errors due to inaccurate recall.[266]

Duplication of recording is also likely an important factor in reducing efficiency and adding to healthcare worker burden. In some labour wards, frontline staff are required to complete up to seven different registers, in addition to patient hospital and handheld notes.[377] Work is currently underway to look in general at improving health information systems functionality and the quality of data produced by these systems.[296,378,379] Much redundancy is found in data systems. Data systems could be streamlined by reviewing currently collected data, including who is it for and how is it used, to prioritise key data to retain, enabling efforts to improve data quality to be focused on a limited number of indicators. This could be an important first step to maximise the utility of information collected by any data system and reduce costs by cutting redundant information. This can be coupled with triangulation of data sources and data linkage to improve the completeness of reporting, and reduce reporting burden on frontline health workers.[266]

Involving healthcare workers in the design of changes to be made to the data system could enable data collection to be tailored both to the needs for clinical decision-making and the reporting needs for data that will be aggregated up the data system.

Household surveys

As detailed in section 7.2.2. above, surveys should seek to assess and record information on vital status at birth, gestational age and birthweight for every birth. Careful review of the wording of the questions in each context to check understanding of potential respondents, with special

attention and pilot testing of translations coupled with improved training for DHS interviewers in capture of adverse pregnancy outcomes including stillbirth could improve recording of these outcomes.

Improving the understanding of the importance of accurate recording

Lack of awareness of the public health importance of recording information on every baby, including those born around the threshold of viability or stillborn, remains a potential barrier. Improving awareness in communities and amongst women, for example through media outlets and ANC clinics, could potentially improve understanding and reduce misreporting, although no published studies assessing these were located.

In some settings, those responsible for recording these outcomes have a low understanding of the data being collected. For example, in one study in Pakistan, two thirds of Lady Health Workers responsible for completing community pregnancy and child health registers did not know the difference between a miscarriage, stillbirth and a neonatal death. It is therefore unlikely that they recorded these correctly in the register. Understanding the definition of each outcome and accurate completion of registers was limited even in health facilities.[338] In this study, many respondents, both in facility and community, did not perceive the benefit of completing the registers or sending monthly tallies to the HMIS officer.

These issues are likely to be common across data platforms. One potential method to improve awareness amongst the healthcare workers, civil registrars and data collectors recording these outcomes could be through pre- and in-service training. For example, in Tanzania a study found that following refresher training frontline workers recorded all relevant data elements in the register and perinatal outcomes could be correctly classified by vital status into antepartum, intrapartum stillbirths and neonatal deaths based on register data alone.[380] In community-based data platforms including household surveys understanding of pregnancy and child health outcomes amongst interviewers, and empathy for those experiencing a loss can be improved through training.[381,382]

Reduce incentives to misreport

Another important area is to understand the incentives that women, interviewers or healthcare workers may have to misreport these birth events, specifically stillbirths and neonatal deaths, and address these directly. For example, incentives for healthcare workers may include fear of blame, reduction in paperwork or to protect the woman (see Section 6.4). Ensuring that the same requirements are in place for both stillbirths and neonatal deaths including reporting of all events, avoiding duplication of reporting, and no-blame auditing accompanied with adequate

training, supervision and support for the health care worker may reduce incentives to misreport.[214]

Incentives for survey interviewers to misreport may be seen if more detailed questions are required for some kind of birth events, e.g. live births compared to stillbirths.[121] Therefore, the same reporting requirements should be required for every birth.

For women and families incentives may be different for example in China in the 1990s under the one-child policy, women had an incentive to report miscarriages, stillbirths and neonatal deaths to the family planning system as they were then authorised to have a new pregnancy.[383] Women may misreport vital status at birth, gestational age or birthweight when it may be more culturally acceptable or desirable or because of feared stigma. For example, if preterm birth or stillbirth are perceived to be attributed to witchcraft or failings as a woman, she may report her baby as being born full-term or as an early neonatal death instead, or may not report the baby's existence at all.

7.2.4. STEP 4: COLLATE data in a comparable way

Once a birth is reached by a data system, the key data elements are assessed and recorded, for the data to be available for wider public health use, it must be collated within the data system. Closing this gap will require improved understanding of current practice and barriers and enablers to data collation. Common approaches across data systems are discussed below with further details in Annex A.6.4.

Currently even when recorded, data collected around the time of birth are not always reported in aggregated data. For example, CRVS systems infrequently report fetal death data even when collected, and many DHS surveys in West African region collect data on stillbirths, but do not analyse and report these in their aggregate data. A similar pattern is seen for HMIS where a recent review of HMIS systems in 24 countries found that, whilst all systems recorded stillbirths, only 71% of countries use registers which capture information on timing (antepartum/ intrapartum) and all of these use fresh or macerated stillbirth as proxies, and in only 42% of countries could this information be obtained from the current summary form.[384] The diagnosis of preterm birth was only recorded in the registers of nine countries, and summary forms of six countries. Registers in 19 countries (79%) had a designated place to record birthweight. Birthweight information is aggregated up the HMIS system as birthweight<2500g in the summary form in 18 countries (75%), and in 4 countries as birthweight<2000g (17%).

Whilst every birth should be reached, assessed and recorded, not all will meet the requirements for collation for local, regional, national or international comparisons. Normative standards for data collation and reporting are required to ensure comparability.

Normative standards for data collation and reporting

Accurately assessing and recording the key data elements in a standard way, as detailed above, will allow for aggregation and collation of these data in a comparable way up the system to the facility, district, national and then global level. Whilst all countries have their specific requirements for data to use at a local, regional and national level – these data should be collated in a way that enables disaggregation for reporting using standard definitions.

The body of work in this PhD has demonstrated good adherence to the relatively simple definitions for numerator for preterm birth and low birthweight. However, adherence to the ICD stillbirth definition is poor, with many different non-standard definitions currently in use. With regard to denominator issues, low birthweight data had the most substantial issues due to a large number of babies without a birthweight recorded in some data systems, with stillbirth and preterm birth collated data affected to a lesser extent. It is recommended that the denominator reflect the total number of births with the relevant key data element measured for example in the case of low birthweight rate, the denominator should include only babies who are weighed. The proportion with missing birthweight should also be reported alongside the low birthweight rate, with details of how this may impact the generalisability of the result to assist with interpretation of the data and comparisons over time and with other settings. Efforts should be made to improve awareness, guidance, training and supervision for all those involved in the collection and aggregation of data to improve practical adherence to the standard definitions and correct classification of every birth and correct use of denominators.

Proposed updates to normative guidance

Whilst normative guidance is available from WHO's ICD, in the case of stillbirth, the field of perinatal epidemiology is changing more rapidly than the guidance, and classification guidance based on birthweight threshold is no longer considered appropriate in view of new perceptions around viability and new, increasingly accessible and more accurate methods of gestational age assessment. The increasing quantities of high quality perinatal data collected and analysed in Europe and North America have improved our overall understanding in this field, and are driving both clinical care and societal and programmatic priorities.[218,229,385] In addition, the understanding of the current ICD-10 criteria of 'birthweight or if not available, gestational age or length at birth' are poorly understood; with many countries adopting a 'birthweight or gestational age' approach instead which is difficult to interpret in view of the fact that the

birthweight and gestational age thresholds are not equivalent, and in the aggregate data there is no method of knowing what proportion used which method. Whilst most health facilities could measure birthweight at the time of delivery, in reality despite three quarters of all births occurring in a health facility, less than half of the world's births are weighed, and even fewer stillbirths are weighed. In practice, gestational age is used rather than birthweight to define a stillbirth in household surveys, most middle and high income countries, and increasingly in low income settings.

An additional challenge with the current ICD stillbirth definition is that it does not allow differentiation between terminations of pregnancy and spontaneous fetal deaths. As discussed above, in settings with low rates of spontaneous fetal deaths, but widespread fetal anomaly screening and where termination of pregnancy for fetal anomalies is legal, this can account for an important proportion of all early fetal deaths.[94,222]

WHO recommends collecting data on all fetal deaths ≥22 weeks, collating information only on late fetal deaths (≥28 weeks) for international comparisons. However, early fetal deaths account for 1/3rd of all stillbirths in data rich settings.[386] Including these babies in international comparisons across data rich MICs and HICs could make international comparisons more informative for clinical practice and policy in HIC and many MIC settings and would allow consistency with reporting of neonatal deaths which are reported regardless of gestational age, but in practice are uncommon prior to 22 weeks.[386] It could also play a role in acknowledging the burden of these deaths on affected families. However, attention will need to be paid to those around the threshold of viability as even in HIC capture of these babies in data systems is variable.

In summary, it is recommended that ICD-11 guidance be changed to reflect the changing public health needs to include gestational age threshold in preference to the existing birthweight one, and to make clearer the importance of collecting the minimum perinatal data for each birth and death to allow disaggregation by different gestational age groups and TOP. It is recommended that the revised ICD definitions be followed by all UN normative guidance for both CRVS and HMIS systems.

7.2.5. STEP 5: USE data to inform programmes and policy

The final gap is in the use of data for action. Once data are collated in an accurate and comparable manner for every birth, ensuring that data are used for action will require the that they are accessible to both frontline health workers and policy makers and that they are understood, valued and perceived as useful. Closing this gap will require improved understanding of how data are currently used, and current barriers and enablers to more

widespread use. Common approaches across data systems are discussed below with further details in Annex A.6.5.

The first step in facilitating data use for action is to promote data ownership and use at a local level. Many routine health systems rely on healthcare workers for the collection of data. Increasing demands on healthcare workers, both in terms of clinical and administrative workloads, can affect the data quality as seen above, but also how data are perceived.[387] Current data collection systems, even the newly emerging electronic based ones, are commonly designed with the needs of stakeholders higher up the system rather than those recording the data, with data systems frequently not adapted to actual workflow or healthcare worker's clinical decision-making requirements.[388] Use of local data is critical for improving quality of care. The generation of actionable data, such as through DHIS-2 dashboards, could provide timely information to clinical and local level health staff to improve care, and linked to perinatal audit could be used as a tool to facilitate facility level quality improvement.[112] Involving healthcare workers in the design of dashboards and linking to tools to make clinical data available in real-time could increase data availability for clinical decision-making and improve ownership and use of such data to improve outcomes at a local level.

The next step is to make data accessible and understandable to policy makers to enable it to influence public health policy and programmes and to guide decision making at local, district and national level. This may include a variety of formats such as data dashboards, monthly reporting and annual reports. Data should be presented disaggregated by subnational, equity and other relevant grouping to track progress and enable targeted interventions to those groups at greatest risk. When available, information on stillbirth timing (antepartum or intrapartum) and cause of death can be used to further refine areas to target. High quality tracking in a comparable way, across all data platforms including CRVS, HMIS and surveys, could enable data to be used to monitor investments in programmes, identify areas of concern and set priorities for maternal newborn health or wider health sector 5 year plans. Barriers to including data on stillbirth, preterm birth and low birthweight in formats accessible to policy makers include failure of those responsible for data collating to appreciate the potential of these indicators as markers of health of women and children in their populations, and of indicators of strength of their health systems. The technical maternal–newborn health community, frontline health workers, affected families and communities could all potentially play an important role in raising the profile of the large preventable burden associated with stillbirth, preterm birth and low birthweight on women, families and communities.[5] This could include knowledge translation to communicate the issue more clearly to programmes and policy makers using varying mediums such as reports, policy briefs and infographics and individual and group advocacy efforts. The

increasing attention given to these outcomes in global institutions with mandates for establishing and maintaining administrative and technical services, such as epidemiological and statistical services, including the setting of normative guidance (WHO) and advocating for the protection of children's rights, to help meet their basic needs and to expand their opportunities to reach their full potential (UNICEF) is increasing the visibility of these health issues in many countries.[35] Many countries are now reporting on these outcomes as part of sharpened newborn plans towards ending preventable stillbirths and newborn deaths.[389]

Including data in all relevant publicly available reports that include maternal and child health will also allow parent groups and other interested parties the opportunity to advocate and increase political pressure by highlighting these issues and thus further increasing visibility, for example, in the media. One example of this resulting from this work was the Born Too Soon Report published in 2012 alongside the estimates in chapter 4 which received major media coverage with an estimated reach of 1 billion, including 72 million Twitter "impressions". Parent groups had an important role in raising awareness with activities in over 60 countries, including national events with government and other stakeholders in Bangladesh, India, Malawi, and Uganda and a Facebook page.[6,390] Data were key to many of the messaging strategies used, and provided evidence to show the size of the burden, preventability and to use as inputs to models to estimate how many lives could be saved using different intervention approaches.[6,391]

However, ultimately data use will depend on how data are perceived and their social robustness, both are linked to data quality and coverage. For example, in CRVS, birth registration data are used for population and health planning purposes. Perinatal mortality data in contrast, whilst collected in most settings, are rarely used. This in part is due to low confidence in and perceived low quality of much of the data collected. As such, the preceding steps to reach every birth, assess, record and collate the data elements will be critical to improve the quality of such data, and facilitate a change in perception about the data, increasing the likeliness of data use. In HMIS, as healthcare data systems are complex the completeness and quality of routinely collected HMIS data remains a challenge for data use. A recent study found that completeness of DHIS-2 data in Kenya was a challenge to data use for decision making.[392] Improving the quality of data will involve investment to close each of the data gaps.

7.3. Data linkage, interoperability and quality assessment

7.3.1. Data linkage and interoperability

The ability of data systems to be able to communicate and share information is critical to increase efficiency and reduce duplication. In recent years the importance of data linkage or interoperability has been highlighted. Data interoperability is defined as "the ability of two or more systems or components to exchange information and to use the information that has been exchanged".[393] Going forward the interoperability of data between CRVS and HMIS will be important to improve coverage, accuracy and detail of the data.

Data linkage between different data sources is increasingly feasible, especially where electronic data systems have been designed with in-built data interoperability such as through the use of a common individual identifier (ID). This has the potential to improve the quality of birth outcome data, however, capturing the full range of these outcomes requires careful planning. The ability to link the mother's and child's unique ID can improve both the availability of birth outcome data, but also enables future inter-generational studies. Ideally assignment of a child's ID could be done through antenatal clinic, thus allowing the tracking of all pregnancy outcomes including stillbirth.[394] Where this is not possible, the child IDs should be assigned immediately at birth as part of the birth notification process. The child ID could be assigned for both live and stillbirths, allowing comparable information to be collect as part of vital statistics.

It is important to acknowledge that data linkage adds another level of complexity to the data. Both a clear understanding of the data and guidance at each step of the data linkage are required to ensure that the data generated are reproducible, accurate and valid.[395] Although the practice of data linkage is common in Nordic countries, it is currently under-utilised, even in settings with high coverage of CRVS and electronic health information systems.[396] However, recently several Latin American countries have fully integrated their HMIS into CRVS with benefits in terms of enumeration of the population, but also to support care provision, health monitoring, identify service delivery gaps and inequities, and improve accountability. In Peru this has been achieved through the development of an on-line free system that registers newborns in the labour ward, providing them with a unique identifier which can be used in both the health and CRVS systems.[397]

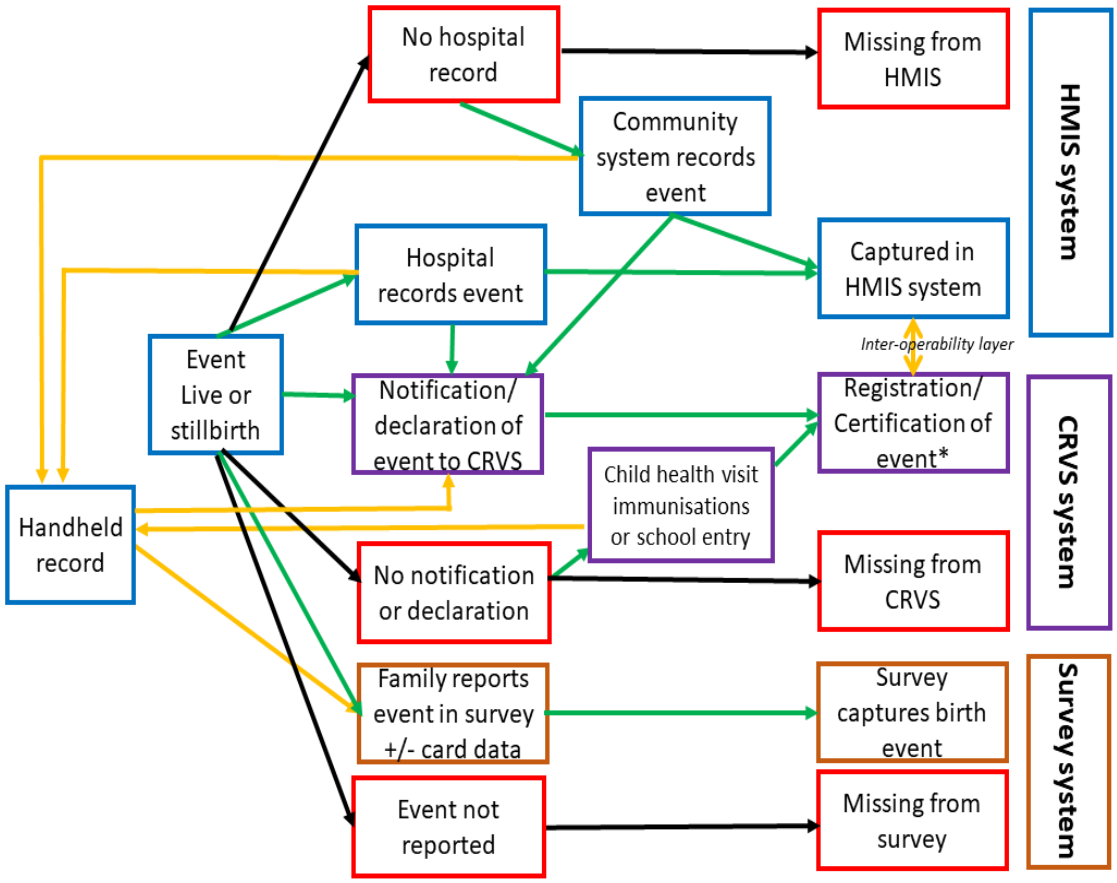
New initiatives, such as OpenHIE which aims to improve health outcomes, especially in LMICs, through supporting pragmatic implementation of health data sharing architectures could play an important role in facilitating data availability for the user.[398] However, impact will only be seen if data users at a local level value and are able to access the data that they require in a timely manner.

eRegistries can also play a role in improving data utility. eRegistries are "systems using information and communication technologies for the systematic longitudinal collection, storage, retrieval, analysis and dissemination, of uniform information on health determinants and outcomes of individual persons, to serve healthcare services, health surveillance, health education, knowledge, and research".[394] The potential for eRegistries to act as a backbone to health information systems, increasing the interoperability within the system has been proposed. eRegistries can be used to identify and follow up all women accessing antenatal care without a birth outcome recorded in the system. However, to maximise this potential all stakeholders should be involved in this process including the community, women and families; healthcare providers: facility and community-based, Traditional Birth Attendants, private sector; and other systems collecting data on vital events: including village administration units and community volunteers.

In all cases data interoperability will be critical to ensure capture of every birth event and reduce duplication. Figure 7-3 shows the three main platforms, CRVS, HMIS and household surveys where outcome data to inform stillbirth, preterm and low birthweight estimates are collected. The orange arrows show the potential routes of communication between the three data platforms – through direct interoperability between HMIS and CRVS or via handheld health records for communication between the health system and household surveys, and the health system and CRVS.

Going forward it will be important to build interoperability into data systems. DHIS-2 tracker is one example where interoperability between registers is used to create an individual patient level 'pregnancy e-registry' where data are entered once and 'tracked' through the system at each visit from antenatal care, through delivery and postnatal care to child health services and immunisations. Interoperability between health data systems for example between HMIS and Logistics Management Information Systems, MPDSR and data from the private sector could increase the coverage and quality of data. In some cases, additional benefits can be achieved by building interoperability with external non health data systems, for example with CRVS systems.

Figure 7-3 Data linkage and interoperability in birth outcome data



*registration and certification are two separate steps in most CRVS systems but are included here together to simplify as the focus here is on registration.

7.3.2. Data quality processes

The importance of data quality in ensuring social robustness of data and to improve use of data for action has been highlighted above. Data quality is an important function of any data collection system. The importance of routine data quality assurance systems for birth outcome data has been discussed above (Section 6.5). Such systems should be tailored to birth outcome data and developed alongside, and integrated into all data systems using the principles expanded in Section 6.5.[399] Attention is required to prevent sub-optimal data quality during the set up and organisation of the data collection system, alongside data quality assurance checks throughout data collection and actions to identified problems to facilitate data quality improvements.

Clear guidance should be developed on data quality checks and actions to be taken to address potential issues. These should include measures internal to the data system, such as the percentage of births with missing or non-valid entries, examining the data distributions/outlier analysis, and comparison to previous trends. Where feasible, data can be benchmarked against

an external source. Implementation of data quality processes will require clear guidance to be drawn up, and these processes included in both pre-service and refresher trainings for all data platforms. The development of a short set of birth outcome specific data quality indicators could be a useful tool to facilitate data improvement. These indicators should include both coverage of data and measures internal to the data system such as the proportion of births with missing or non-valid entries, data distributions and comparison to previous trends, and where feasible benchmarking against an external source (Section 6.5). These indicators could be included in a data quality report which could be communicated to data systems to facilitate action to address quality concerns, and also to data users to increase the social robustness of the data e.g. withhold specific data from final reports where data concerns are present.

Implementation of data quality processes will vary across data platforms. For HMIS mortality data investment in building local analytical capacity, regular national audits of perinatal mortality data, development of improved pre- and in-service perinatal data training and strengthening Maternal and Perinatal Death Surveillance and Response, where possible linked to pregnancy registries, could be important first steps to improved data quality.[296]

A good understanding of data flow through a data system is required to identify potential bottlenecks and develop tailored data quality guidance.[400] Frameworks have been a useful tool to improve this understanding. For example, within the health system, the Performance of Routine Information System Management (PRISM) framework developed by MEASURE evaluation seeks to promote continuous evaluation and data improvement through the development of performance targets, tracking progress, and knowledge management.[379] These frameworks could be refined to specifically address the challenges of perinatal data.

The increasingly widespread use of electronic data systems has the potential to simplify the running of routine data quality checks, as these can be easily integrated into the system. They can be programmed to allow validation of the data entry for each data element e.g. that the entry is in the correct format, and within a plausible pre-defined range. Data validation rules can be used to ensure internal consistency of data elements in an individual record e.g. an individual entry cannot be both a stillbirth and a neonatal death. Data checks on aggregated data detailed above such as missing values, examining the data distributions and benchmarking/ triangulating against external data sources can be undertaken in a more time-sensitive manner, to enable timely investigation and clinical action or correction of data where required. DHIS2's quality tool is an example of such an inbuilt system, with easily generated dashboards to facilitate the communication of the information to the user,[401,402] and there is some evidence that mhealth interventions have the potential to improve data quality in community settings.[403]

8. Transforming the future for stillbirth, preterm birth and low birthweight data

8.1. Overall summary

A systematic analysis of available data for stillbirth, preterm birth and low birthweight was undertaken for this PhD. Based on the estimates generated from this systematic analysis, the burden of these adverse birth outcomes is large, with an estimated 2.6 million stillbirths, 14.9 million preterm and 20.5 million low birthweight births. Overall an estimated 11.1% of live births were preterm, 14.6% were low birthweight and 1.84% of total births were stillbirths. 4,392 data-points from 148 countries were included in these estimates; the majority were from Civil Registration and Vital Statistics (CRVS), Health Management Information Systems (HMIS) or nationally representative household surveys. Whilst data are available for stillbirth, preterm birth and low birthweight, substantial gaps in the data have been identified. These data gaps have been summarised as gaps in reaching every birth, in assessing and recording key data elements, in collating data in a comparable manner and in using data for action. These data gaps necessitate most LMICs to rely on modelled estimates for these outcomes currently.

Estimates of birth outcomes generated as an academic exercise alone are unlikely to have much utility at a local, national or international level.[404] As this work was undertaken as part of official WHO or WHO-UNICEF estimates this increases the likely uptake and use of the estimates, including by donors, international organisations and media. The estimates presented in the papers in Chapters 3 and 4 have been published in peer-reviewed journals for a period of time, and the resulting estimates have contributed to wider work, both in terms of academic publications,[25,62] but also in policy documents and advocacy efforts.[6] The low birthweight estimates paper is currently in press and will be published around the time of submission of this PhD. It will be used as a baseline for the Global Nutrition Target goals, and the methods developed used to generate ongoing monitoring to track progress.

However, the reliability of stillbirth, preterm birth and low birthweight rate estimates depends on the quality and comparability of the input data. In addition, as these estimates were derived from covariate based models, the estimated trends are driven by trends in the covariates, which may not reflect trends in the outcome of interest. Whilst improvements in modelling techniques can play a role in strengthening the estimates available, this is not a long-term solution. Ultimately improved measurement and reporting of these outcomes is needed as every mother's baby should have the right to be counted, this information should be used to improve frontline clinical care, then aggregated at local, sub-national and national level to guide public

health priority setting and contribute to accountability, before finally contributing to global health tracking of stillbirth, preterm birth and low birthweight (Figure 8-1).

Figure 8-1 Need for improved data throughout the data system

There have been calls recently for every baby to count, including those who are stillborn,[14,25,112] and work is underway in many countries to strengthen routine data systems including CRVS, HMIS and perinatal audit to improve their capture of events especially around the time of birth, including stillbirths.[405] However, it is clear from this body of work that many babies still are not counted, or not counted well enough to enable them to truly count and contribute to robust data to drive appropriate policy, programmes and investment in maternal and newborn health to improve these outcomes. Although data collection for these estimates was undertaken in some cases more than five years ago, a recent update of the WHO preterm birth estimates and ongoing work to update the global stillbirth database suggests that although data availability is increasing, the ongoing data quality challenges identified in this PhD continue to limit the utility of these data.[406]

To have an impact on local and national policymakers, local empirical data are imperative. Achieving this will require local and national political will to take steps to close the five data gaps identified in Chapter 7. Existing estimates and lessons learnt through these by academics and UN agencies have the potential to be used as a tool to inform improvements in data collection to strengthen the coverage and accuracy of such data. This potential will only be realised if this

learning can be communicated as a resource for a grass-roots, bottom up, locally driven drive to improve empirical data as part of a wider data improvement.[407] Improvement in measurement of the data elements required to classify stillbirths, preterm births and low birthweights, including gestational age and birthweight, also has the potential to improve data for other key perinatal outcomes which can be used to inform health policy makers on priorities e.g. gestational and birthweight specific neonatal mortality, small-for-gestational age and large-for-gestational age.

As this work has shown, the main data sources for stillbirth, preterm birth and low birthweight outcome data currently are CRVS, HMIS and large scale, population based, nationally representative surveys such as DHS. They all have the potential to capture the key data elements to enable classification of stillbirth, preterm birth and low birthweight; although their current and future role for these is varied (Table 8-1).

Table 8-1 Summary of data collection platforms for birth outcomes

	Main data platforms		
	CRVS	**HMIS**	**Nationally representative household surveys**
Stillbirth	✓✓	✓✓	✓
Preterm Birth	?	✓✓	X
Low Birthweight	?	✓✓	✓

✓✓= important platform for capture of the outcome medium to long term in all settings. Preferred platform currently in HICs. Investment required in most LMICs to enable high quality data to be collated.
✓= currently an important data platform for the outcome in LMICs in the short to medium term, until alternative data collection systems generating highly quality data with high population-level coverage. Further research required to inform measures to improve capture and data quality.
?= may be important in the short term, but longer term, as births within the health system approach 100% improved data inter-operability can enable linking of key data elements captured in HMIS such as birthweight and gestational age to be linked to CRVS.
X=not currently used. Potential source in the short to medium term, if gestational age assessment can be improved.

Looking forward, data interoperability will be key to allow collection of the key data elements to be focussed on the most relevant data platforms, and then linked to other platforms to maximise efficiency and reduce duplication and burden on data collection systems, including frontline health workers. In all settings, sustained investment in healthcare workers and HMIS systems, linked to CRVS is required to enable high quality data on these outcomes. In addition, in settings with weak or non-existent HMIS or CRVS systems, in the short to mid-term household surveys will remain an important source of population-level data on stillbirth and low birthweight, as discussed in this thesis, further effort will be required to improve the quality of these data.

All three of these main data platforms have faced challenges in collecting data for stillbirth, preterm birth and low birthweight. Concerns over data quality have led to an ongoing assumption that these data are not robust or valid.[404] Going forward, greater attention to improving data quality could lead to improved and increasing 'socially robust' data which can be used to drive action. This thesis has discussed some of the data challenges and limitations summarised in the five gaps in Chapter 7. It has also outlined steps that can be taken to close these gaps. Improving the measurement, quality and completeness of these data is possible in all settings, and important lessons, potential solutions, and pitfalls to avoid can be gleaned from looking both at lessons learnt historically in HICs, as well as the data drama currently unfolding in many LMICs settings.

Reviewing the current status of data to inform stillbirth, preterm birth and low birthweight rates has necessitated at times going back to the history of the collection of data around these outcomes. It seems that the old adage "Those who cannot remember the past are condemned to repeat it" by George Santayana is true here. In particular, with respect to stillbirths we are failing to learn lessons from history. When the Registration (Scotland) Act of 1854 mandated registration of births, deaths, and marriages, the exclusion of both the birth and the death of a stillborn child was immediately seen as a contentious issue. As the leading Scottish newspaper put it in 1855 "Most assuredly they are born, and why should they not be registered?"[408]; and again in 1875 "Stillbirths, however which are notoriously far more dangerous to the lives of mothers than ordinary live births are not recorded".[409] This sentiment has been echoed by many bereaved families, health practitioners and general public alike worldwide. Scotland finally mandated stillbirth registration in 1939, and only following this was it possible for stillbirth to gain widespread attention there as a public health issue.[410] Despite the 'data revolution' of the Sustainable Development Goal era, stillbirth registration is still not legally mandated in many countries, and these deaths too often remain invisible.

Whilst this PhD thesis has highlighted substantial gaps in the data, it has also proposed some potential actions to close these gaps through improving the coverage (REACH), assessment, recording, collation and use of stillbirth, preterm birth and low birthweight data. The next section will briefly consider some examples of how steps can be taken to close these gaps through policy and programmatic action and future research.

8.2. Principles for policy and research to improve data

8.2.1. For policy and practice

Chapter 7 discussed the five steps required to close data gaps for stillbirth, preterm birth and low birthweight. Addressing these steps will require financial investment, but also increased attention to these issues and local leadership.

Table 8-2 below provides illustrative examples of some potential policy and practice actions to close the data gaps for the three key data systems CRVS, HMIS and household surveys following the five steps outlined in Figure 7-2 (see Annex A.6. for further details).

Several cross-cutting issues emerge when considering potential solutions to close these gaps. The first is the need for clear, consistent normative standards for measurement and definitions. The UN has an important role in this, and urgent attention is required to update and standardise guidance across different UN bodies including WHO, UNICEF and UN statistics division. The next is the need to build capacity in the data system to accurately capture these outcomes. All stakeholders, including frontline healthcare workers and bereaved parents, should be involved in all steps to design data system changes and training packages to overcome current barriers to accurately capturing stillbirth, preterm birth and low birthweight. In this age of increasing electronic data, interoperability between different data platforms offers an important method to streamline these data systems and increase efficiency.

However, to be equitable further innovation is required to design systems that can also function in settings with intermittent or limited electricity and internet. Action to improve attention to data quality is required. One important step would be to develop a short set of data coverage and quality indicators for adaptation to different contexts, to be used to drive improvements in the data and present a summary of these data quality indicators in all reports in a format interpretable to their intended audience.

Closing data gaps will require political will and adequate investments both in the data systems as highlighted above, but also in the legislative framework in which they operate. Currently in most settings there is no legal obligation for hospitals or health care providers, especially private ones, to report vital events to civil authorities. Public hospitals usually report these to the ministry of health, but private facilities are rarely required to. A legal framework is required for this, and to ensure adequate (ideally seamless) linking of data collected in both the health and the administrative data systems in a given country. Much investment is currently being undertaken in data systems for health in many settings, however, unless specific attention is paid to addressing the particular needs of data for stillbirth, preterm birth and low birthweight, these risk being left behind.

Table 8-2 Examples of policy and practice action to improve birth outcome data

	Policy and practice action: illustrative examples
STEP 1: REACH EVERY BIRTH	***Knowledge and awareness:*** Increase public awareness on importance of including all births in data systems in all settings through media campaigns and targeted education ***Data systems design:*** *CRVS:* Follow UN recommendation to provide for the collection of fetal death data with all CRVS,[246] ensure registration is free of charge,[253] services and forms are available in local languages and are flexible to meet cultural requirements. *Survey:* Use a pregnancy history approach coupled with improved training. *Humanitarian settings:* Include perinatal events in efforts to sustain civil registration and in rapid assessment tools in conflict and emergency situations[411] ***Data linkage and innovation:*** *CRVS and HMIS:* Collect information and notify events occurring outside of the health system to community health extension workers or volunteers.[317-320] Link to other pregnancy and child mortality surveillance e.g. MPDSR, birth defect surveillance. *CRVS*: Use innovations such as conditional cash transfers, mobile technology, birth notification through handheld records, one-stop shops and outreach services.[330 331 332] *HMIS:* Develop formal data sharing structures and consider innovations to incentivise data sharing with the private sector[337]
STEP 2: ASSESS KEY DATA ELEMENTS	***Knowledge and awareness:*** *Health workers:* Improve knowledge and skills in resuscitation and assessment of vital status at birth, gestational age and birthweight for facility and community healthcare workers e.g. through pre and in-service training. *Surveys:* Improve training of interviewers on birth outcomes ***Data systems design:*** *Surveys:* Add questions to standard questionnaires to assess gestational age and birthweight for all births, and vital status at birth for all stillbirths and neonatal deaths. Improve coverage and completeness of handheld records ***Standards and guidance:*** Set UN standards for ultrasound and weighing machines, guidance on calibration, use and care for devices
STEP 3: RECORD KEY DATA ELEMENTS	***Knowledge and awareness:*** *All:* Increase awareness on accurately recording/ registering every birth and death: for health workers, civil registrars, families and communities. Assess barriers such as stigma, fear and blame. Include in pre- and in-service training for all cadres of health workers and data collectors. *HMIS:* Promote a culture of no-blame perinatal audit with adequate supervision and support ***Data systems design:*** *All:* Ensure same reporting requirements for all births, whether live or stillbirths. Include gestational age and birthweight in all relevant registers and data forms or enable linkage to these data by building interoperability into data systems. *CRVS:* Place the responsibility on the facility to register stillbirths and early neonatal deaths. *HMIS:* Review, revise, harmonise and streamline registers and data capture to minimise duplication. Develop systems designed to capture missing birth outcomes e.g. DHIS-2 Tracker 'pregnancy registry approach' in HMIS

STEP 4: COLLATE DATA IN COMPARABLE WAY	***Standards and guidance:*** Revise UN ICD-11 definitions and normative guidance to be consistent with current practice and reporting needs of countries and standardise throughout all UN bodies. Provide guidance and support on standard definitions and their applications in formats accessible to designers and implementers of data systems. Improve awareness, guidance, training and supervision for all those involved in the data aggregation to improve adherence to the definitions and correct classification of every birth.
STEP 5: USE DATA TO INFORM PROGRAMMES AND POLICY	***Reporting and dissemination:*** Include stillbirth, preterm birth and low birthweight data in all relevant standard maternal and child health reporting. Disaggregate data by subnational, equity and other relevant groupings. Make data publicly accessible, allowing parent groups and communities to use these data to advocate for these issues

8.2.2. For research

Whilst there is much that can be done to improve these data now based on current knowledge, this PhD has highlighted some areas where research could further improve understanding and tailoring of data collection systems to improve the capture of stillbirth, preterm birth and low birthweight data. It is beyond the scope of this PhD to undertake a full research scoping exercise however,

Table 8-3 below provides illustrative examples of some remaining research questions to close the five data gaps for stillbirth, preterm birth and low birthweight. These examples are presented by the five steps outlined in Figure 7-2 (see Annex A.6. for further details).

Table 8-3 Examples of research questions to improve birth outcome data

	Research questions: illustrative examples
STEP 1: REACH EVERY BIRTH	***Barriers:*** What are the perceived barriers to data systems reaching stillbirths and births around the threshold of viability, including women's, families', communities' and data systems (CRVS, HMIS, surveys) perspectives? How do they differ by setting? How could these be addressed? ***Financial:*** What are the costs (direct and indirect) to families of birth and death registration – how can these be mitigated through a "one-stop shop"? ***Data system design:*** What models can be used to promote data sharing with private sector? How can these be incentivised? ***Humanitarian settings:*** How can information on birth outcomes be best collected in humanitarian settings?
STEP 2: ASSESS KEY DATA ELEMENTS	***Barriers***: *Families and communities:* How do women/ communities perceive signs of life at birth? How important are these in terms of personhood, religious ceremonies or other factors? Can assessment of vital status at birth be improved for home births through community interventions? *Health:* What are health worker and families' attitudes to weighing stillborn babies?

	What behaviour change interventions could improve coverage of the practice of weighing stillborn babies? ***Technology and innovation:*** How can existing and new technology be incorporated into low-cost, robust innovative methods for gestational age and birthweight assessment capable of being implemented at scale in LMICs?[a] What is the role of handheld medical records in improving the accuracy of gestational age and birthweight information availability in household surveys?
STEP 3: RECORD KEY DATA ELEMENTS	***Barriers:*** *All:* How do health workers, civil registrars, families and communities perceive the value of recording these data? How common is misreporting of these birth outcomes? What are the most effective ways to reduce this in different settings? *CRVS and HMIS:* What are the barriers to recording/ registering birth outcomes for births reached by the data system? How do they differ by settings? How can these be addressed? What role could incentives have in addressing these? ***Data system design:*** *Families and communities*: What are the needs of health providers and bereaved parents. How can these be balanced with the needs of the data system? *CRVS and HMIS:* How can interoperable data systems be developed where different government ministries are responsible for CRVS and HMIS? *HMIS:* How can time-motion studies be used to understand data flow, time and cost implications to support streamlining of data collection within the health system? ***Technology and innovation:*** *All:* What role can training and job aides (electronic and paper based) play in improving recording of key data elements? *HMIS:* Can longitudinal electronic records e.g. DHIS-2 tracker be used to reduce the burden of recording for frontline healthcare workers?
STEPS 4 and 5: COLLATE and USE DATA TO INFORM PROGRAMMES AND POLICY	***Barriers:*** What factors affect data use? How can these be addressed? ***Knowledge and awareness:*** *All:* Which formats of guidance are most effective in improving the consistency of data collation? Which data outputs are most applicable to varying audiences e.g. women, families and communities, health workers, managers, programmes, policy makers, politicians? ***Data system design:*** *All:* What are the most effective ways to integrate quality indicators into current standard processes for collating and reporting data to improve accuracy and social robustness of these data? What are the best indicators of data quality in a given context? How can they be integrated into the data system? ***Technology and innovation:*** *All:* How can new technologies and innovations be used to increase data use?

[a] Including home-based methods such as moon-beads and diaries to improve LMP awareness and recall?

8.3. Setting priorities for improving the data

The proceeding section has considered some examples of how steps can be taken to close the data gaps identified in the reaching every birth with data systems, assessment, recording, collation and use of stillbirth, preterm birth and low birthweight data. An overview of the steps with illustrative examples has been presented. In some settings, these data gaps may be minimal. For example, in a setting where facility birth is near 100%, all facility births are weighed on functional calibrated weighing scales, data are entered into electronic registers at the time of birth, and collated in a comparable way data on stillbirth and low birthweight rates would be readily available. However, if information on gestational age from early pregnancy ultrasound dating in this setting was entered in the woman's handheld health records but no field for gestational age is available in the electronic birth record, changing the electronic register with accompanying training for users may be sufficient to close the data gap and improve data for preterm birth outcomes. However, in most settings the solutions may be more challenging and go across several of the data improvement steps. In addition, whilst technically it may be possible to close many of these data gaps across all data platforms simultaneously, in reality budgets for health data improvement are constrained and programmes and policy makers are required to prioritise data improvement interventions within limited budget.

In order to set priorities for improving the data in a given setting an initial mapping of the current status of stillbirth, preterm birth and low birthweight data in the data system, and the requirement for these data should be undertaken. For example, using the framework in Figure 7-1 what proportion of estimated births in the population are reached currently by which data system? Are data currently collated for stillbirth, preterm birth and low birthweight rates? If yes, are they using standard comparable definitions? Decisions on where to prioritise efforts can be made based on this information in consultation with other key stakeholders such as frontline health workers, health information system team members, hospital managers, district health officers and community and parent representatives.

In many LMIC settings with increasing facility birth rates and current investment in HMIS data systems focusing on improving data in facility-based HMIS systems may be the preferred initial step. If data across all outcomes are currently weak, initial priority should be given to recording every facility birth, including stillbirths, with vital status at birth. As described above, this is required for accurate data for all of the 3 outcomes. First setting-specific barriers to recording every facility birth with information on vital status at birth and potential solutions should be identified. Illustrative examples of potential barriers include poor assessment of vital status at birth by health workers compounded by lack of resuscitation equipment, and

stillbirths being recorded in a separate register rather than the main birth register which is the register used for collating data for hospital reporting. Once the specific target area for data improvement has been agreed a logic model could be used to guide the planning of the programme to define the inputs (e.g. staff, resuscitation equipment, finances), activities (e.g. local adaptation of training materials, adaptation of main birth register to include stillbirths), outputs (e.g. number of staff trained, number of facilities with new registers) and impact expected (e.g. increased proportion of all births, including stillbirths, entered in the birth register and collated into routine hospital reporting).[412] Once this is achieved, the next step in improving data in HMIS across these outcomes could be to review and address barriers to assessing and recording birthweight on all facility births. This would enable the calculation of facility-based stillbirth rates and low birthweight rates, and inform monitoring of progress in facility births towards the Every Newborn stillbirth rate and Global Nutrition low birthweight targets. Where it is not yet possible to routinely record accurate gestational age to calculate preterm birth rates, low birthweight rates can continue to be used as a proxy for increased healthcare needs and increased mortality, especially when further disaggregated into birthweight groupings (<1000g, 1000-1499g, 1500-2000g, and 2000-2499g). Finally, attention and resources could be directed towards improving the capture of gestational age in the system. As detailed above, the measurement may be more complex than the others as relies on accurate dating of a pregnancy, ideally in the first trimester, communication of this information at the time of birth, using this information to estimate gestational age at delivery, but lessons learned from improving the recording and collating of information on vital status and birthweight could also be applied to gestational age. Once these data are strengthened within the HMIS, linking these data to CRVS systems through direct (ideally electronic) birth notification to the civil registrar of all births in facilities, including stillbirths, could strengthen the inclusion of these events in national vital statistics, with minimum additional costs or human resource burden.

8.4. Conclusion

Stillbirth, preterm birth and low birthweight are important public health challenges, that are still relatively new in terms of global health attention. Action to address these has been hampered by absent or low quality data in many settings. This PhD has reviewed in detail the current available data, developed and implemented methods to produce national estimates, summarised data gaps and proposed solutions for improving stillbirth, preterm birth and low birthweight data. Whilst many LMICs have previously relied on household surveys for data regarding these outcomes, increasing rates of facility births and investments in strengthening HMIS and CRVS systems are leading to a rapid expansion in routine data. Many LMICs are now becoming data-rich, but unless attention is paid to closing the measurement gaps and improving data quality, many countries will remain information poor with regards to these birth outcomes.

Improving the counting of these deaths and other adverse birth outcomes is only the first step towards action to improve the health and survival of babies worldwide. This information is necessary but not sufficient to improve outcomes. From an intervention design perspective, more detailed information is needed for some of these outcomes, such as information on antepartum versus intrapartum timing for stillbirths, cause of death and associated conditions for all mortality outcomes, and long term morbidity for preterm birth and low birthweight survivors.

As well as improved data, these data need to be accessible to and valued by frontline health workers, public health professionals, programme managers and policy makers, to drive action, investment and political commitment to result in real change for these babies and their mothers and families. Such transformation will require increased investment in the overall data systems, and also specific attention, leadership and data capacity regarding perinatal data. Only then will the smallest be counted and visible, and allocation of resources to prevent and track progress towards global targets for these outcomes commensurate with their burden be possible. Enabling every child to survive, thrive and transform.

9. References

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10. Annexes

A.1. Summary of role of the candidate in the work presented in this thesis

This thesis contains some content which was undertaken as part of a wider body of work. In addition to the cover sheets included in the main body of the thesis on the candidate's role in the component published papers, the following table summarises the role of the candidate in the work presented in each chapter of this thesis.

Table 1 - Summary of role of the candidate in the work presented in this thesis

Chapter	Component (or paper if relevant)	Activity	Responsibility	Additional input
Chapter 1	Background	Conceptualisation and writing	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn
Chapter 2	Review of definitions, Indicators and data platform	Conceptualisation, research and initial drafting of fetal and neonatal components of Blencowe et al.[1]	**Hannah Blencowe**, Simon Cousens	Clara Calvert, Oona Campbell
	Review of definitions, Indicators and data platform	Conceptualisation and writing of further expansion of work published in Blencowe et al.[1]	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn
	Introduction to measurement of stillbirth, preterm birth and low birthweight	Conceptualisation and writing	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn
Chapter 3	Stillbirth estimates	Conceptualisation of paper	Joy Lawn, **Hannah Blencowe**	
		Undertaking systematic data searches	**Hannah Blencowe**	Suhail Sheikh, Zeshan Qureshi
		Model fitting and estimation process	**Hannah Blencowe,** Simon Cousens	
		Drafting of manuscript	**Hannah Blencowe,** Simon Cousens, Joy Lawn	

		Review of drafts and approval of final manuscript	All authors	
Chapter 4	Preterm birth estimates	Conceptualisation of paper	Joy Lawn, Lale Say, **Hannah Blencowe**	
		Undertaking systematic data searches	**Hannah Blencowe**	Doris Chou, Ann-Beth Moller, Lale Say, Rajesh Narwal, Claudia Vera Garcia, Lale Say, Alma Adler, Sarah Rhodes
		Model fitting and estimation process	**Hannah Blencowe,** Joy Lawn, Simon Cousens, Mikkel Oestergaard	
		Drafting of manuscript	**Hannah Blencowe,** Joy Lawn, Simon Cousens, Mikkel Oestergaard	
		Review of drafts and approval of final manuscript	All authors	
Chapter 5	Low birthweight estimates	Conceptualisation of paper	Joy Lawn, **Hannah Blencowe,**	
		Undertaking systematic data searches	**Hannah Blencowe**	Suhail Sheikh, Luca Cegolon
		Household survey data collation and adjustment	Xiaoyi An, Julia Krasevec, Simon Cousens, **Hannah Blencowe**	Suhail Sheikh, Yadigar Coskun
		Model fitting and estimation process	**Hannah Blencowe**, Suhail Sheikh	Simon Cousens, Gretchen Stevens, Luca Cegolon
		Drafting of manuscript[a]	**Hannah Blencowe,** Simon Cousens, Joy Lawn, Julia Krasevec	
		Review of drafts and approval of final manuscript	All authors	

Chapter 6		Conceptualisation and writing	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn
Chapter 7		Conceptualisation and writing	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn
Chapter 8		Conceptualisation and writing	**Hannah Blencowe**	Review by Oona Campbell, Simon Cousens, Joy Lawn

[a] Figures 2 – 4 were produced by UNIECF graphic designers

A.2. Measuring maternal, fetal and neonatal mortality: Challenges and solutions.

Citation: Blencowe H, Calvert C, Lawn JE, Cousens S, Campbell OM. **Measuring maternal, foetal and neonatal mortality: Challenges and solutions.** Best Pract Res Clin Obstet Gynaecol 2016 Oct;36:14-29. doi: 10.1016/j.bpobgyn.2016.05.006.

A.2.1. Ethics approval

This work does not contain any new primary or secondary data collection or analysis and no ethics approval was required.

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Best Practice & Research Clinical Obstetrics and Gynaecology 36 (2016) 14–29

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

2

Measuring maternal, foetal and neonatal mortality: Challenges and solutions

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Keywords:
stillbirth
neonatal
maternal
mortality measurement
indicators
data sources

Levels and causes of mortality in mothers and babies are intrinsically linked, occurring at the same time and often to the same mother–baby dyad, although mortality rates are substantially higher in babies. Measuring levels, trends and causes of maternal, neonatal and foetal mortality are important for understanding priority areas for interventions and tracking the success of interventions at the global, national, regional and local level. However, there are many measurement challenges.

This paper provides an overview of the definitions and indicators for measuring mortality in pregnant and post-partum women (maternal and pregnancy-related mortality) and their babies (foetal and neonatal mortality). We then discuss current issues in the measurement of the levels and causes of maternal, foetal and neonatal mortality, and present options for improving measurement of these outcomes. Finally, we illustrate some important uses of mortality data, including for the development of models to estimate mortality rates at the global and national level and for audits.

Introduction

Monitoring levels of maternal mortality has been a priority on the global health agenda. Millennium development goal (MDG) 5 aimed to reduce the maternal mortality ratio (MMR) by 75% between 1990 and 2015. However, measuring progress over this time period was challenging, primarily because of

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http://dx.doi.org/10.1016/j.bpobgyn.2016.05.006
1521-6934/

the scarcity of empirical data. Global tracking relied instead on modelled estimates to monitor the success [1]. These estimates suggested that maternal mortality decreased by 44% worldwide in the MDG era [2]. Similar challenges were faced in tracking foetal and neonatal mortality. Neonatal deaths were not explicitly mentioned in MDG 4, which sought to reduce under-5 child mortality by two-thirds, but they were increasingly recognised as comprising almost half of child mortality globally and progressing more slowly. Neonatal mortality was estimated to have decreased by 47% worldwide during this period [3]. Stillbirths (late foetal deaths) were excluded from the MDG targets, and consequently received less attention, although the major associated burden has been quantified more recently [4]. At the end of the MDG era, the number of deaths, albeit based on modelled estimates, remains unacceptably high: 303,000 maternal deaths [2], 2.6 million stillbirths (late foetal deaths) [5] and 2.7 million neonatal deaths [3].

Measuring the levels and trends of maternal, neonatal and foetal mortality is important for quantifying disease burden, understanding risk factors and determinants, identifying priority areas for interventions, programmes and policies, and evaluating the success of interventions at the global, national, regional and local level [6,7]. Knowing the biomedical causes of mortality in pregnant or recently delivered women, or in their babies, is essential to direct interventions to prevent such deaths. Unfortunately, there are many challenges to measurement, but there are also numerous potential options and solutions.

This paper provides an overview of current issues and options in measuring the levels and causes of maternal, foetal and neonatal mortality. We define these deaths and associated indicators, and then focus on the measurement methods, challenges and solutions, and where possible, present potential opportunities to improve measurement of maternal, neonatal and foetal deaths.

Definitions

To compare maternal, foetal and neonatal mortality across populations or over time requires standardised definitions for each outcome. These definitions were included in the 10th revision of the International Classification of Diseases (ICD-10) [8], as summarised in Table 1 and described below. Various dimensions of these definitions require an ability to assess pregnancy status of women, the timing of death in relation to delivery, gestational age (or alternatively birth weight or birth length) at delivery, vital status at the start of labour and at birth and, cause of death. The dimensions and critical time periods are shown schematically in Fig. 1.

Maternal and pregnancy-related mortality

'Maternal death', is defined in the ICD-10 [8] as 'the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes' (Table 1). This definition encompasses direct obstetric deaths, when death occurs because of an obstetric complication such as haemorrhage or eclampsia, and indirect obstetric deaths, when an underlying, previously existing medical condition or non-obstetric medical condition developed during pregnancy, is aggravated by pregnancy. Since deaths that are accidental or incidental to the pregnancy need to be excluded, information on cause-of-death is required to apply this definition.

However, the definition of maternal death is conceptually problematic from a measurement perspective [9]. Distinguishing indirect maternal death from incidental or accidental deaths during pregnancy or post partum is epidemiologically challenging, and consequently coding can be difficult. The decision whether a condition is aggravated by pregnancy or its management can either be made on a case-by-case basis, be ascribed to conditions based on epidemiologic data showing elevated incidence or case fatality in pregnant women with the condition compared with non-pregnant women, or be decided for entire classes of conditions (e.g., deaths from external causes). Guidance is provided but is not particularly helpful; for example, ICD maternal mortality (ICD-MM) instructs that HIV-related deaths should be classified as maternal when 'there is an aggravating effect of pregnancy on HIV and the interaction between pregnancy and HIV is the underlying cause-of-death' [10]. It further states that if 'the woman's pregnancy status is incidental to the course of her HIV infection' then the death should not be classified as maternal. Unfortunately, ICD-MM provides no guidance on how to identify

Table 1
ICD-10 definitions of maternal, foetal and neonatal deaths [8].

Indicator	Primary threshold	Alternative threshold/definition
Maternal death	A death while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes	90 days [13] or 40 days [13,74]
Late maternal death	A maternal death from direct or indirect obstetric causes >42 days, but <1 year, after termination of pregnancy	
Pregnancy-related death	A death while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death	
Early foetal death*	A baby born with no signs of life with birth weight ≥500 to <1000 g	Gestational age ≥22 weeks or length ≥25 cm (if birth weight is not available)
Late foetal death	A baby born with no signs of life with birth weight ≥1000 g	Gestational age ≥28 weeks or length ≥35 cm (if birth weight is not available)
Intrapartum foetal death	A foetal death occurring after the onset of labour, but before birth	A baby born with no signs of life and no evidence of skin maceration (fresh stillbirth) is commonly used as a surrogate marker [22]
Antepartum foetal death	A foetal death occurring before the onset of labour	A baby born with no signs of life, with evidence of skin maceration (macerated stillbirth) is commonly used as a surrogate marker [22]
Perinatal death	Composite indicator including all late foetal deaths and early neonatal deaths	Other composite indicators for perinatal deaths are described in the text
Early neonatal death	A death of a live-born baby at 0–6 days of age regardless of gestational age or birth weight	
Late neonatal death	A death of a live-born baby at 7–27 days of age regardless of gestational age or birth weight	
Neonatal death	A death of a live-born baby at 0–27 days of age regardless of gestational age or birth weight	Deaths in the first month of life

*Non-induced pregnancy losses with a birth weight <500 g (or gestational age <22 weeks or length <25 cm) are defined as miscarriages in ICD-10, although many countries (e.g., the USA and Australia) report foetal deaths using a lower gestational age (≥20 weeks definition).

when HIV disease progression has been accelerated by pregnancy, making the coding of these deaths very difficult, particularly in the absence of detailed data. Furthermore, epidemiological studies suggest that certain causes of death that are often excluded from maternal mortality estimates, such as suicide or homicide, are more likely to occur in certain subsets of pregnant women compared with non-pregnant women (notably amongst younger age groups) [11].

Although maternal death is the most widely used mortality definition in pregnant and post-partum women, the ICD-10 gives two further definitions that expand the deaths captured in two different ways. First, 'late maternal death' lengthens the time period to capture maternal deaths occurring from 42 days up to 1 year post partum. The 42-day post-partum cut-off has a weak evidence base, and a few studies show women remain at elevated risk for several months after delivery [12]. Historically, a 90-day cut-off has been used [13,14], and some even argue that the increased mortality risk may extend beyond 1 year post partum [15]. Second, 'pregnancy-related death' includes any 'death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause-of-death', without excluding accidental or incidental deaths in this specified time period. This latter definition only requires information on the timing of death in relation to pregnancy (or the end of pregnancy), and not on the cause of death (Fig. 1). As such, pregnancy-related death is comparable to neonatal and foetal deaths that are also defined primarily by time periods, as described below.

Foetal and neonatal mortality

Live birth is defined in ICD-10 [8] as 'the expulsion or extraction from its mother of a product of human conception, irrespective of the duration of the pregnancy, which, after such expulsion or

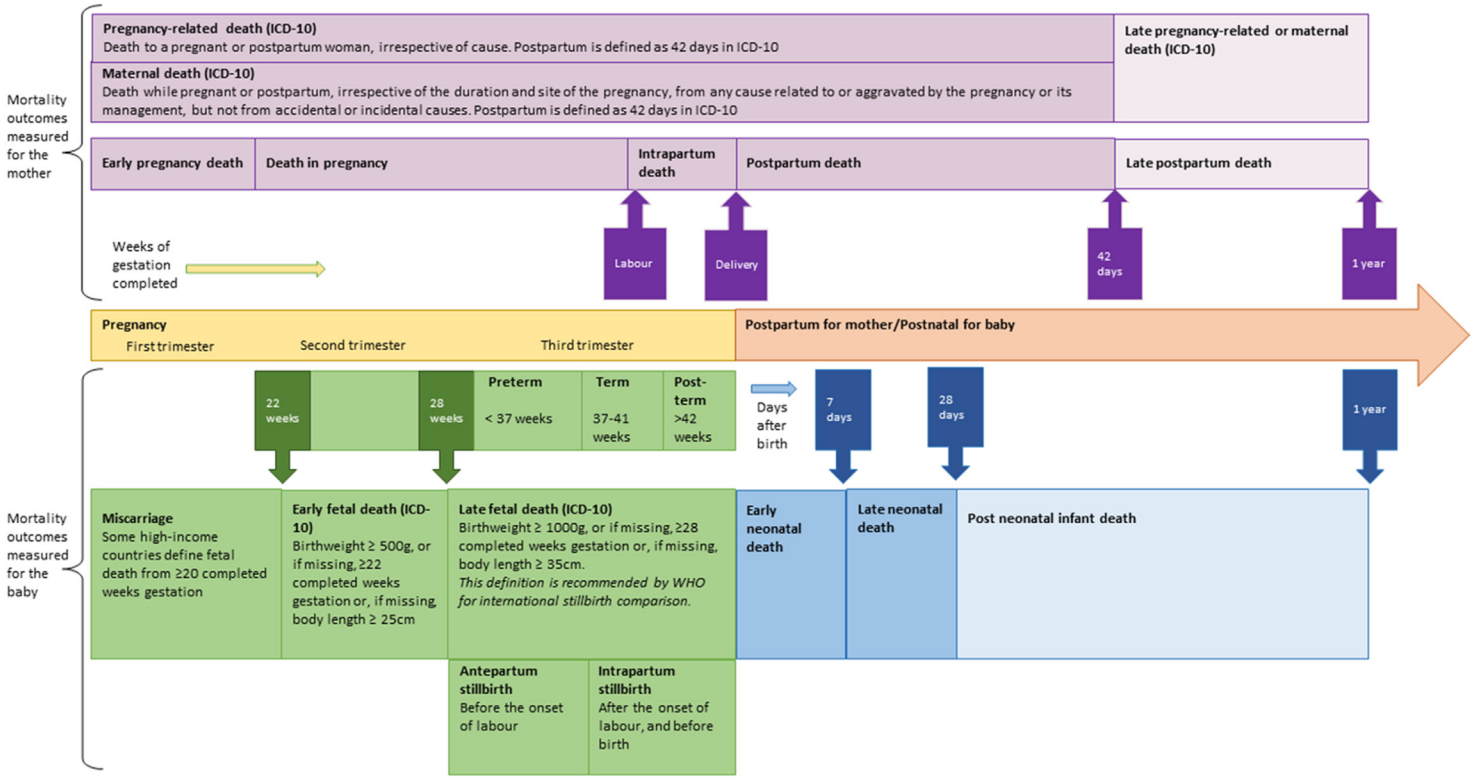

Figure 1. Schematic representation of times when maternal, foetal and neonatal deaths occur in relation to pregnancy. Adapted from Lawn et al., 2011 [17].

extraction, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached. Heartbeats are to be distinguished from transient cardiac contractions; respirations are to be distinguished from fleeting respiratory efforts or gasps'. The ICD-10 [8] definition for neonatal death is the death of a live-born infant in the first 28 days of life; this definition is applied nearly universally (Table 1 and Fig. 1).

Foetal death is 'death prior to the complete expulsion or extraction from its mother of a product of human conception, irrespective of the duration of pregnancy and which is not an induced termination of pregnancy'. Death is indicated by the foetus not showing signs of being a live birth, as described above. ICD-10 defines foetal deaths as occurring from ≥500 g, or ≥22 weeks, or ≥25 cm only. Deaths before this period are spontaneous abortions or miscarriages in lay terminology. Definitions and terminology for foetal deaths are applied more inconsistently – especially amongst high-income countries with thresholds ranging from 20-week gestational age upwards (Fig. 1) [16,17]. ICD-10 distinguishes early from late foetal deaths using birth weight, gestational age or length criteria. ICD-10 recommends reporting both early and late foetal mortality rates, while WHO recommends using the stillbirth rate or late foetal death rate for international comparisons. The term 'stillbirth' is often used in clinical practice and common parlance to refer to any foetal death; however, it is used epidemiologically and in global estimates to refer to late foetal deaths only.

Since ICD-10 was developed several decades ago, the foetal death threshold was set to be based first on birthweight criterion then gestational age and then length. However, birthweight and gestational age thresholds do not give equivalent results. For example, in the USA the Stillbirth rate (SBR) would be 40% lower than with a 500-g threshold compared with a 22-week gestational threshold. Hence, the threshold should be based on one parameter as it is not accurate to assume equivalence. In practice, most health facilities could measure birth weight at the time of delivery, yet in reality less than half of the world's births are weighed and fewer stillbirths are weighed. Gestational age can be difficult to assess without records from early ultrasound as the gold standard or dating based on last menstrual period [18–20]. Nevertheless, we would argue that assessment of gestational age is essential to enable correct classification of a foetal death to the early or late category to allow for international comparisons. This is used in practice in middle- and high-income countries, and increasingly in low-income settings. It is proposed that the 11th ICD revision change to a gestational-age-based foetal death threshold, in line with most high-income country reporting.

Assessing the intrapartum versus antepartum timing of foetal death is another area where definitions may be applied differently in different settings with lower-level care. If evidence of a foetal heartbeat at the start of labour is not available, classification as intrapartum or antepartum often relies on an assessment of the skin of the baby (fresh vs. macerated), which is not a very reliable indicator of antepartum or intrapartum timing of foetal death [21,22].

Indicators

Counting numbers of maternal, foetal and neonatal deaths can identify countries, regions or subgroups with the largest numeric burden, but often we are also interested in knowing where the risk of such deaths is highest. For example, due to its large population, India has a much greater number of maternal deaths than Sierra Leone, yet the risk of a woman in India dying of maternal causes is much lower than in Sierra Leone [2]. Identifying the risk faced by individual women or babies requires the numbers of deaths be considered in relation to a denominator at risk of these deaths. Below we have described commonly used indicators of risk, as well as others used in mortality measurement.

Maternal indicators

Assessing the risk of maternal or pregnancy-related mortality requires relating the number of such deaths in a given time period and a given country or area, to the number of women at risk. The ideal denominator for this – the number of pregnant woman entering into the pregnancy/post-partum period, or time spent pregnant or post-partum – is difficult to obtain without conducting prospective studies of large groups of women. Instead, routine data sources are commonly used to calculate

MMR: the number of maternal deaths per 100,000 live births in a given time period: (number of deaths/live births) × 100,000. This live-birth denominator approximates the number of pregnancies, but excludes women who have miscarriages, induced abortions or stillbirths, while women having multiple live births (e.g., twins or triplets) are counted multiple times in the denominator. In some settings, all maternity cases, including those resulting in foetal deaths, and even induced abortions, are included in the denominator [23].

Three additional, less commonly reported, indicators are defined below:

1. MMR (or pregnancy-related): deaths per 100,000 women aged 15–49 per year (midpoint population)
2. Lifetime risk of maternal (or pregnancy-related) death: the probability that a 15-year-old girl will die eventually from maternal (or pregnancy-related) causes, assuming that current levels of fertility and mortality (including maternal (or pregnancy-related) mortality) do not change in the future, considering competing causes of death [24].
3. Proportion of deaths: proportion of maternal (or pregnancy-related) deaths among all deaths of women of reproductive age.

The MMR (or pregnancy-related) and the level of fertility influence all three indicators. For any given MMR, the higher the level of fertility, the higher the level of the three indicators. The lifetime risk indicator and the proportion of deaths are also influenced by death rates among non-pregnant/non-post-partum women: all else being equal, the higher the death rates in non-pregnant/non-post-partum women, the lower these two indicators will be.

Foetal and neonatal indicators

Mortality indicators for outcomes in babies are usually measured per 1000 births. Neonatal mortality rates use live births as the denominator: (number of neonatal deaths)/(live births) × 1000. Foetal mortality rates can be calculated as (number of foetal deaths)/(live births + foetal deaths) × 1000. A combined indicator for all 'perinatal deaths' [8] is used, which includes all late foetal deaths (≥1000 g or ≥28 weeks) and all early neonatal deaths (days 0–6): (number of perinatal deaths)/(live births + foetal deaths) × 1000.

It is recommended that all deaths in babies <28 days of age, whether in utero above a specified threshold or in the neonatal period, are recorded by gestational age, birth weight and timing (antepartum or intrapartum and day of neonatal death). Such reporting of outcomes is of programmatic relevance. For example, the 'intrapartum stillbirth and early neonatal death indicator', may be used to monitor improvements of the quality of obstetric and newborn care provided at birth. It can be calculated at a facility level as (intrapartum stillbirths + neonatal deaths within the first 24 h of life (≥2500 g))/(live births + foetal deaths (≥2500 g)) [25,26].

Another, less frequently used, measure is the 'prospective foetal mortality rate': (number of foetal deaths at a gestational age per 1000 foetal deaths at that gestational age or greater, plus live births). This is a more accurate denominator for those at risk, and provides an estimate of the risk of foetal death at a given gestational age [27,28]. In high-income settings, this indicator has been used to compare the risk of foetal death with the neonatal mortality rate to determine the optimal gestational age for delivery [29].

Current issues in measuring mortality

Despite the existence of definitions and indicators, measuring mortality can be problematic. First, deaths need to be identified, and then categorised and counted. Deaths may be misclassified because aspects of their definitions (including pregnancy/post-partum status, incidental/accidental cause of death, gestational age, survival status at the start of labour and at delivery and day of death post partum) are difficult to recognise, determine, capture or remember. They can also be misclassified because information is deliberately misreported for reasons related to blame or stigma or to protect women or avoid bureaucracy. Comparisons may be difficult because inconsistent definitions or classification systems are used, or data are not collected at all.

Table 2
Mechanisms for identifying maternal, foetal and neonatal deaths.

Mechanism	Active vs. passive data collection	Frequency	Notes
Civil registration	Passive	Continuous	Works well with high coverage, completeness of births and deaths registration and with good ascertainment of cause of death. Can be easier to implement in urban areas. Low coverage in highest-burden areas (see Fig. 2 for maternal mortality estimates). Sample vital registration approaches are taken in China and India.
Health Information Management Systems	Passive	Continuous	Widespread in public-sector facilities in many countries. Quality variable, and data may not filter-up to aggregated levels. Frequently, low inclusion of private sector. Platforms include District Health Information Systems 2 (www.dhis2.org/).
Surveillance	Predominantly active	Continuous or periodic	Surveillance can be of whole populations, of pregnancies and their outcomes, or of deaths (either all deaths of reproductive-aged females or all pregnancy-related deaths). Can occur for short or prolonged periods (e.g., demographic surveillance sites). Surveillance can range from continuous case detection, to surveillance visits up to 1 year apart.
Population-based surveys (e.g., RHS, DHS and MICS) or Census	Active	Intermittent	Surveys are the main source of mortality outcomes on the 45 million births occurring outside facilities. Foetal deaths are frequently omitted, and capture of foetal and early neonatal deaths may be of poor quality. Measuring maternal mortality based on reported household deaths via surveys requires very large sample sizes or a census. Sisterhood method approaches reduce this requirement but limits the capture of information on cause of death or on co-variates (see main text for reasons).

RHS = Reproductive Health Surveys (http://ghdx.healthdata.org/series/reproductive-health-survey-rhs).
DHS = Demographic and Health Surveys (http://www.dhsprogram.com/).
MICS = Multiple Indicator Cluster Surveys (http://mics.unicef.org/).

Sources for identifying deaths

Table 2 provides a brief overview of four main data collection systems that can be used to identify and count maternal (or pregnancy-related), foetal and neonatal deaths. In practice, all four have strengths, and as with most measurement systems, there are generally trade-offs between the reliability of the estimates and practical considerations such as cost or time.

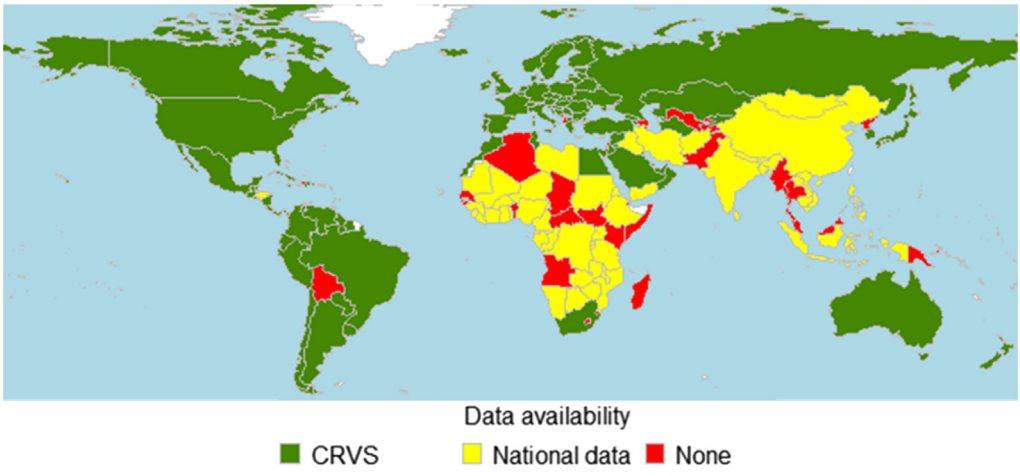

Figure 2. Empirically measured data available for producing maternal mortality estimates (since 2010). Source: produced using information from Alkema et al., 2015 [2] and WHO, trends in maternal mortality: 1990–2015 (available at http://apps.who.int/iris/bitstream/10665/194254/1/9789241565141_eng.pdf?ua=1).

Civil registration and vital statistics (CRVS) should capture all births and deaths (including cause-of-death information assigned by a medically qualified person) in a country, on an ongoing basis, issuing certificates for these vital events. In ICD-10, WHO recommended a checkbox on the death certificate to record a woman's pregnancy status at the time of death, enabling such systems to identify whether death was pregnancy-related [30]. Alternative systems have been used in China and India, where a 'sample registration system' (sample CRVS system), is in place for a number of population clusters, which have been randomly selected from a national sampling frame [31]. In theory, the national scope and the ongoing effort makes CRVS the 'gold standard' for measuring all deaths. Unfortunately, CRVS systems remain weak in most areas of highest mortality burden [32–34], missing deaths and failing to cover certain areas. Moreover, cause-of-death ascertainment, needed to define maternal deaths, is frequently poor, and substantial proportions of maternal deaths are misclassified even in high-income settings with complete CRVS. The lack of CRVS is illustrated, for maternal mortality, in Fig. 2. Foetal and early neonatal deaths, especially around viability are frequently under captured, with <5% globally having either a birth of death certificate [35].

Health management information systems (HMIS) are a source of data on births and deaths that occur in health facilities. They usually fail to capture births and deaths that occur at home even after discharge from a facility. In addition deaths when a women is readmitted post-partum may not be recognised as pregnancy-related, and hence missed. Further, many settings also exclude events in private sector facilities. However, HMIS can be useful for monitoring trends within facilities, particularly for foetal and early neonatal outcomes, noting the limitation that facility use, and the case mix of woman/babies using facilities, may change over time.

Other alternatives include surveillance, through systems such as demographic surveillance sites or special studies such as confidential enquiries. These may focus on deaths to women of reproductive age, and then retrospectively seek to ascertain whether the woman was pregnant or recently delivered at the time of death or may focus on deaths of pregnant or post-partum women. Alternatively, they may adopt a cohort approach and seek to identify all pregnancies and the resulting outcome for both the mother and her baby. These studies tend to operate at a subnational level as they are resource-intensive. They may also be too small to provide precise estimates of maternal mortality unless aggregated over many years.

Cross-sectional, population-based household surveys are an important source of data, particularly for neonatal mortality. A full live birth or pregnancy history is typically used to identify births and neonatal deaths. Surveys using full pregnancy history are also potentially able to capture foetal deaths or stillbirths. Some surveys using a live-birth history have added a question regarding stillbirth; for example, the core Demographic and Health Survey (DHS) module, but for many surveys the capture of stillbirths is implausibly low [35,36]. Measuring maternal mortality directly via surveys by asking household members about deaths of pregnant or recently delivered women within a given time period (often in the last 1 or 2 years) requires very large sample sizes [37] or a census [38]. Sisterhood method approaches ask siblings to report on the pregnancy-related deaths of their sisters, and reduces the required sample size. However, they cannot capture information on cause of death or on predictors associated with increased risk because it is unreasonable to expect a sibling to know and report such details [39].

Sources for ascertaining cause of death

Information on the causes of maternal, foetal and neonatal deaths is important for identifying priority interventions to reduce mortality, and is a pre-requisite for defining maternal deaths, as the definition excludes causes that are incidental to pregnancy.

Comparison of cause-of-death distributions between countries has been hampered by different classification systems, particularly for causes of stillbirths or foetal deaths. To improve comparability, countries using ICD-10 should include all deaths coded to the maternal chapter (O codes) and maternal tetanus (A34) as maternal deaths, while all foetal and neonatal deaths should be coded to the perinatal chapter (P codes), congenital chapter (Q codes) or to a limited number of exceptions, including specific infections such as neonatal tetanus (A33) or congenital syphilis (A50) [8]. In 2012, the World Health Organization (WHO) published the ICD-MM to be used in conjunction with the three ICD-10 volumes to reduce errors in coding maternal deaths, and to improve attribution [10]. A similar manual (ICD-PM)

to improve the coding of both stillbirths and neonatal deaths in ICD-10 is planned for release by the WHO in 2016.

Ideally, detailed information on cause of death, distinguishing between immediate and underlying causes, should be possible to obtain from CRVS, with medical certification. Clinical diagnoses of causes can be supported with laboratory tests and even autopsies. WHO introduced a separate perinatal death certificate to obtain information on maternal and foetal conditions, but this has had limited uptake. However, population-based data on the causes of maternal, foetal and neonatal deaths are scarce in many high-burden countries due to the lack of CRVS and medical certification [33].

Facility records can provide information on causes of death, but the extent to which these data represent causes of these deaths at the population level is questionable given low levels of institutional delivery across many parts of Asia and sub-Saharan Africa. For example, women delivering at home and experiencing post-partum haemorrhage may die very rapidly before reaching a facility for emergency care, potentially underestimating the proportion of deaths attributable to haemorrhage if only facility-level data are used.

Surveillance and surveys aiming to ascertain causes of maternal foetal and neonatal deaths in most high-burden settings frequently rely on verbal autopsy (VA) [41,42]. In VA, family members or caregivers (lay reporters) of the deceased are asked about the signs and symptoms occurring before the death. Symptom data from VA interviews are then interpreted by physicians or by automated methods [41,43]. VA has some validity for causes of neonatal death in low-resource settings; however, its performance is generally worse for foetal deaths [44–47]. VA performs better at identifying overall maternal deaths when compared with identifying direct causes of maternal death [48]. Overall, however, the imprecise nature of VA, and the potential for misclassification of cause-of-death at the individual level, means results from VA are usually presented at the population level rather than being used for individual level diagnoses.

Issues with establishing timing of death and survival status

All of these sources rely on informants, be they health professionals with access to medical records or family members, and they are therefore subject to some important limitations. Omission or misclassification of deaths can occur for several reasons. First, where the information is not known by the informant (e.g., pregnancy status in a maternal death occurring in early pregnancy or in the post-partum period or gestational age at the time of foetal death). Other examples include misclassification between intrapartum foetal death and early neonatal death, which is thought to be common in low-resource settings, particularly when relying on VA.

Second, omission or misclassification can occur where an informant deliberately withholds or alters information. This can be motivated by desire to avoid stigma; for example, families may not report pregnancy status in a young unmarried woman, termination of pregnancy, suicide or homicide. In facilities, healthcare workers may fear blame, and not report or misclassify deaths (e.g., record intra-partum stillbirths (potentially due to substandard care) as antepartum stillbirths (less incriminating for the birth attendant)) [11,45]. Furthermore, responses to VAs can be influenced by other factors including the sex of the interviewer [49]. It has been reported that women may be unwilling to report a foetal death to a male interviewer from her village [36].

Third, accuracy and comparability can be hampered by inconsistent application of definitions; for example, when foetal deaths are reported using variable definitions or for neonatal deaths where understanding the distribution of the day of death has been hampered by inconsistent use of day 0 versus day 1 for the day of birth, and heaping of deaths on day 7 (1 week) affects the classification of early versus late neonatal deaths [50].

Potential solutions to identifying deaths and defining them accurately and consistently

We would argue that to ensure that all deaths are identified at a national level requires complete vital registration, ideally with proper medical certification of deaths and a good classification system. ICD-11 is currently under development, along with a new single death certificate to include deaths at all ages, including stillbirths or foetal deaths. This will record women's pregnancy status and allow for

the inclusion of both maternal and foetal/neonatal contributing causes. Widespread use of this method of medical certification could improve our understanding of maternal, foetal and neonatal causes of death, and the links between them, and provide comparable estimates across different settings. Some settings link deaths of women to records of live births or foetal deaths as a further way to identify possible maternal deaths [51]. Improving the classification of stillbirths and neonatal deaths and to increase comparability across settings will require a classification system with a limited number of programmatically relevant, causal categories that can be assigned using VA, but can be further expanded in settings where detailed clinical data and diagnostics are available [52]. The new ICD perinatal mortality (ICD-PM) seeks to provide such a resource to improve coding of these deaths. It has been proposed for the 11th ICD revision to change to a gestational-age-based stillbirth or foetal death threshold, in line with most high-income country reporting.

For the many countries where complete vital registration is unlikely to become a reality for some years, if not decades, there are interim solutions. One solution to the challenge of capturing all maternal deaths, as is used in maternal death surveillance and response, is to first capture all deaths in women of reproductive age and then investigate the pregnancy status of the woman within 42 days of death, including the linkage to birth and foetal death records [53]. A potential solution for foetal and neonatal deaths is to investigate which survey-based methods (e.g., birth history, pregnancy history and truncated pregnancy history) best capture these deaths. Undoubtedly, e-health can form part of the solution in a number of ways, including more timely data collection through mobile devices (m-health) and through improved HMIS.

Improving the ascertainment of the timing of deaths is clearly a major challenge, particularly between foetal and very early neonatal deaths, and better efforts are needed to redress drivers of misclassification. Improving gestational age assessment could include improving recall of last menstrual period, use of biomarkers, ultrasound assessment of gestational age after the first trimester and improved algorithms to enable a 'best gestational age estimate' [18,54]. In addition, collecting information on foetal heartbeat on admission for all facility births could improve the categorisations of a death as either in the antepartum or intrapartum period. A positive, but unintended consequence of improved training in neonatal resuscitation may be improved by recording the distinction between intrapartum foetal and early neonatal death [55].

Solutions are also needed to address sensitivities associated with reporting foetal, neonatal or maternal deaths. In facilities, fostering a no-blame culture of maternal and perinatal audit could have a role. Further investigation of methods to improve reporting in household surveys may focus on the interviewer, the informant, the role of stigma associated with these deaths as well as the content of the questions.

To accurately ascertain causes of death in pregnant and post-partum women, and their babies, clearly requires more precise methods. New simplified methods for collecting cause-of-death data in resource-poor settings are needed, and investigations are currently underway to assess whether minimally invasive autopsies are feasible and acceptable [56]. Until other methods are available, we should strive to improve the quality of VAs and to understand the pitfalls of current methods of interpreting the data and the effects these may have on the estimated cause-specific mortality fractions. Estimates produced from VAs are likely to remain imprecise, and great caution should be applied when comparing cause-specific mortality fractions over time or in different places, given that the extent to which imprecise tools provide correct estimates will vary depending on the sensitivity, specificity and the true percentage of deaths attributable to the cause in the population.

Even with improved methods to diagnose causes of deaths, problems will still remain in how to distinguish deaths that should be classified as 'maternal' (i.e., directly or indirectly related to pregnancy) from those assumed to be unrelated to the pregnancy. Recent evidence suggests it is not possible to distinguish indirect and coincidental HIV/AIDS-related deaths which calls into question the entire concept of maternal death as is currently defined [57]. Difficulties in identifying deaths aggravated by pregnancy have also been identified for other causes (e.g., malaria). We therefore agree with authors who argue that we should focus on measuring direct obstetric causes of deaths [9]. However, given that treatment provided to women within Antenatal care (ANC)/ delivery services may prevent deaths that are not strictly related to the pregnancy – for example, given that HIV-related deaths during pregnancy or the postpartum may be preventable with timely access to Anti-retroviral

treatment (ART) in the prenatal period – we believe it is also important, and relatively simple, to monitor all deaths to pregnant and post-partum women as well (i.e., pregnancy-related deaths). As such, we call on researchers to focus on measuring pregnancy-related mortality and, where possible, disaggregate these estimates by cause of death, ideally reporting cause-specific mortality ratios.

Using and interpreting mortality data

Maternal, foetal and neonatal mortality data are used for numerous purposes including examining the burden of mortality and trends in this over time, for identification of risk factors for mortality and for exploring effects of mortality on other outcomes (e.g., effect of a foetal death on maternal mental health or effect of maternal death on infant survival). It can be useful to adopt a life course perspective on health problems; for example, the effect of maternal health on long-term outcomes for the newborn or acute infections such as Zika virus. Mortality data can be used by a variety of end users, from individual women and their families, to communities, front-line health providers, managers at a local or district level, national and global policymakers and researchers.

Where possible, mortality data should be available by geographical area, rural or urban, place of death, timing, underlying cause (which can include both proximal biomedical causes and wider social determinants and factors) and other disaggregations such as socio-economic status. This can help in identifying priorities, planning and monitoring progress and for advocacy purposes. For example, understanding the timing of deaths in relation to pregnancy is programmatically useful. It has been repeatedly shown that the highest risk of pregnancy-related death occurs during delivery and in the immediate post-partum period [58]; but as direct obstetric causes of deaths decline and other causes of death including non-communicable disease become more important, this pattern may shift. This has programmatic implications, increasing the importance of providing care in the antenatal and postnatal period, and requiring linkages and integration of general health services beyond just those addressing obstetric causes. However, while such disaggregations are usually possible for neonatal and foetal mortality, for maternal mortality this is more challenging as it is a relatively rare outcome. At the facility level, for example, there are only likely to be one or two maternal deaths over a year.

Cause-of-death data need to be interpreted with some caution. Changes in the percentage of deaths due to each cause can be driven by changes in one specific cause (see Fig. 3). For example, as the percentage of deaths attributable to direct obstetric causes decrease with safe motherhood

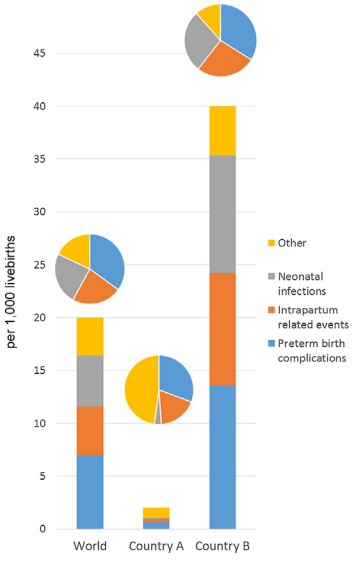

Figure 3.

programmes, we may see an increase in the proportion of deaths assigned to HIV/AIDS. This may either be due to an increase in HIV/AIDS-related deaths, or simply because the number of deaths attributable to HIV/AIDS is coming down at a slower pace than direct obstetric causes. In addition to proportions, therefore, the absolute numbers of each type of death should be related to the number at risk of dying (e.g., number of pregnant and post-partum women, number of births or the appropriate person years) to obtain absolute risks. This is particularly helpful for understanding how the risk of each cause of death is changing over time or between groups.

In the next sections, we present two very different uses of empirical data on maternal, neonatal and foetal mortality for [1] producing global mathematical models and [2] audit.

Estimating the mortality burden

Attempts to quantify the global burden of maternal, foetal and neonatal mortality have been hampered by a lack of data. For maternal mortality, for example, only 52% of countries have any CRVS data since 2010 (with only 40% having high-quality CRVS data), while other countries must rely on modelled estimates (Fig. 2). Three main groups have developed models to estimate the levels and trends of maternal and/or neonatal mortality, the Institute for Health Metrics and Evaluation (IHME), the Maternal Mortality Estimation Inter-agency Group (MMEIG) and the UN Inter-agency Group for Child Mortality Estimation (UN-IGME). To date, there have not been regular attempts to quantify the global burden of foetal deaths, although WHO has led two exercises to estimate stillbirths (late foetal deaths) [3,59].

Although estimates can play an important role, especially to guide resource allocation and action in settings where high-quality empirical data are not available, it is important to distinguish estimates from data and to recognise that not all estimates are equally robust [60]. Some national estimates are derived from nationally representative data for those countries over multiple years; for example, the UN-IGME estimates of overall neonatal mortality rates [61], and therefore can track mortality in each country. For other estimates, for example, maternal mortality, stillbirth rate estimates and neonatal cause of death, the estimates for many high-burden countries are not based on data from that country but from a model bringing together data from many countries, predicting the rates and changes in rates based on country-specific covariate values. Some countries contribute little or no input data to the modelling process. The resulting estimates do not track actual changes occurring, but provide predictions of what may be occurring in countries. One example of this is seen with respect to the drop in the percentage of maternal deaths attributable to HIV/AIDS from 9.0% in 2008 to 3.8% in 2013 in the MMEIG models and from 32% in 2008 to 1.5% in 2013 in the IHME models [62,63]. This is likely to principally reflect changes in the model assumptions. These changes to the models have been driven by not being able to accurately estimate which HIV-related deaths should be classified as indirect or coincidental to pregnancy, and will undoubtedly change as more evidence becomes available. The utility of results that is so sensitive to model assumptions is questionable, strengthening the case for focusing on improving measurement systems [64].

Audit

Our inability to accurately measure levels and trends in mortality, as is the case in many high-burden settings, contributes to the lack of an accountability mechanism in such countries, which in turn is likely to contribute to the lack of progress in reducing levels of maternal, foetal and neonatal mortality. To overcome this, audit is increasingly being used, particularly at the facility level, as a mechanism for surveillance and to identify avoidable factors leading to death to improve quality of care. It requires a number of steps as follows:[53]

1. Establish the objectives of the audit systems
2. Identify maternal, neonatal or foetal deaths based on an appropriate case definition
3. Collect data (facilities and/or communities)
4. Investigate causes and circumstances of deaths

5. Analyse and interpret the data
6. Develop dissemination mechanism
7. Respond
8. Evaluate the audit system

Such systems have been implemented across a range of settings for investigating maternal deaths including Malawi [65], South Africa [66] and Nigeria [67], though not without challenges. There is evidence that audits and feedback can lead to quality improvement [68], and positive effects have been observed in the settings of maternal health services where the audit system is underpinned by a national framework with properly implemented feedback mechanisms, leadership both from committed health professionals and the ministry of health, an enabling legal framework and a workplace culture promoting learning [69,70].

Despite the link among maternal, foetal and neonatal mortality, perinatal reviews have not been as widely adopted as maternal death reviews [70,71]. A policy review found that of the 51 'Countdown to 2015 for Maternal, Newborn and Child Health' priority countries, which had a policy for maternal death notification, only 17 had a similar policy for perinatal death reviews in 2014 [70]. Even in countries with a national policy on perinatal review, they are not necessarily implemented. For example, a qualitative study of maternal and perinatal death reviews in one region of Tanzania found that perinatal deaths are rarely reviewed [72]. There is, however, some limited evidence to suggest that reviewing foetal and neonatal deaths can lead to mortality reductions of about 30%, suggesting that audit could be an important tool for reducing the death of babies in high-burden settings if it is effectively implemented [73].

Conclusion

Accurate and timely measurement is important to achieve change and inhibit preventable maternal, neonatal and foetal mortality. However, as we have illustrated in this paper, there are numerous obstacles to achieving this goal, particularly in high-burden settings. These challenges range from conceptual difficulties in the definitions of maternal and foetal mortality, to challenges faced in data collection systems making it impossible to count each birth and death, to problems of intentional or unintentional misclassification and inconsistent use of definitions or use of inconsistent classification systems or indicators.

Equally there are many potential solutions, some of which we have presented in this paper. These might include expanded use of e-health platforms for data collection and increased efforts to reduce the stigma around reporting a maternal, neonatal or foetal death. Certainly, we should consider how we can improve our definitions to enable comparable estimates, and limit the potential for misclassification. The close link among maternal, neonatal and foetal mortality – in, for example, timing and risks factors – means that many of the potential solutions will lead to improvement in measurements of all outcomes, and suggests the maternal and neonatal research communities for the need to collaborate to most efficiently improve measurement.

Ultimately, however, solutions to measurement issues are only likely to be properly implemented if we have the political will to do so. This has become an even more challenging task in the era of the sustainable development goals, where only one of 17 goals is dedicated to health, and sub-goals are nested within this for reducing maternal and newborn mortality. In particular, it is critical to improve visibility for tracking foetal deaths, in addition to maternal and neonatal ones.

Research Agenda

The close link among maternal, neonatal and foetal mortality – in, for example, timing and risks factors – means that many of the potential solutions will lead to improvement in measurements of all outcomes, and suggests the maternal and neonatal research communities for the need to collaborate to most efficiently improve measurement.

Practice Points

Maternal, foetal and neonatal mortality data should be reported using standard definitions and, where possible, disaggregated by cause of death, ideally reporting cause-specific mortality ratios.
These mortality data can be used for numerous purposes including examining the burden of mortality and trends in this over time, for identification of risk factors for mortality and for exploring effects of mortality on other outcomes.

Conflict of interest

The authors declare that they have no conflict of interest.

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A.3. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Global Health 2016.

A.3.1 Ethics approval

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Dr Hannah Blencowe
LSHTM

21 September 2015

Dear Dr Blencowe,

Study Title: The epidemiology of stillbirths worldwide

LSHTM ethics ref: 10188

Thank you for your application for the above research, which has now been considered by the Observational Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

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

Document Type	File Name	Date	Version
Investigator CV	CV Hannah Blencowe 25th November ARL	23/06/2015	v1
Local Approval	ethics	23/06/2015	1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

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

Yours sincerely,

[redacted]

Professor John DH Porter
Chair

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

Improving health worldwide

Page 1 of 1

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A.3.3. Webappendix of published paper

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A.4. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 2012

A.4.1 Ethics approval

This work contained only secondary data analysis of publicly available data and hence at the time of publication no ethics approval was required.

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Expected completion date	Oct 2017
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INTRODUCTION

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A.5. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis

A.5.1. Ethics approval

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Observational / Interventions Research Ethics Committee

Dr Hannah Blencowe
Assistant Professor
Department of Infectious Disease Epidemiology (IDE)
Epidemiology and Population Health (EPH)
LSHTM

11 January 2017

Dear Hannah

Study Title: Low birthweight: national, regional and global estimates

LSHTM Ethics Ref: 11991

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

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

Document Type	File Name	Date	Version
Protocol / Proposal	Low birthweight study overview	10/11/2016	v1
Investigator CV	cv_blencowe	10/11/2016	1
Investigator CV	CV Joy Lawn_sept 2016	10/11/2016	1
Investigator CV	Simon_Cousens_CV_2016	10/11/2016	1
Covering Letter	response_6thjan	06/01/2017	1

After ethical review

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At the end of the study, the CI or delegate must notify the committee using an End of Study form.

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

Yours sincerely

[redacted]

Professor John DH Porter
Chair

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A.5.3. Webappendix of published paper

Available at https://www.thelancet.com/cms/10.1016/S2214-109X(18)30565-5/attachment/7950f057-2932-4eaf-9270-d47ecc7462e1/mmc1.pdf

A.6. Additional tables

A.6.1. Closing data gaps 1. REACH

Challenge	Policy and practice action: examples	Research questions: examples
CRVS specific		
No current legal framework for inclusion of stillbirths	• Follow WHO recommendation to provide for the collection of fetal death data with all CRVS, even if collecting this information is not yet viable.[1]	
Low coverage of the CRVS system, including failure of system to cover births and deaths in the most marginalised	• Follow UN recommendation that birth and death registration should be free of charge.[2] • Consider use of health registers, community health extension workers or community volunteers to collect information and notify events occurring outside of the health system.[3] • Consider innovations such as conditional cash transfers, mobile technology, birth notification through handheld records and outreach services.[4] • Include perinatal events in efforts to sustain civil registration in conflict and emergency situations • Include those with refugee status in system as per UN recommendation.[5] • Ensure services and forms are available in all local languages and are flexible to meet cultural requirements (e.g. infant naming traditions) • Involve stakeholders, including women and families in the CRVS system design	• What are the costs and opportunity costs (direct and indirect) to families of birth and death registration – how can these be mitigated through a one-stop shop? • Which innovations are most cost effective in which settings?
HMIS specific		
Low coverage, including failure of system to cover births in the most	• Consider use of community health extension workers or community volunteers to collect information on births	• What models can be used to promote data sharing with private sector? How can these be incentivised?

marginalised and those born in the private sector	occurring outside of the health system, using mhealth innovations where available[a] • Link to other pregnancy and child mortality surveillance e.g. MPDSR • Develop formal data sharing structures and consider innovations to incentivise data sharing between the private sector and the HMIS system[6]	
Household survey specific		
Lack of surveys in most vulnerable settings e.g. fragile states or less stable areas of countries	• Add perinatal outcome component to rapid assessment tools used in humanitarian settings	• How is information on birth outcomes best collected in humanitarian settings?
Stillbirths and early neonatal deaths most commonly omitted from surveys	• Use a pregnancy history approach to capture all birth outcomes (rather than live births only) • Increase training of interviewers in administering pregnancy history and sensitivities/ stigma around stillbirths and early neonatal deaths that could prevent disclosure • Involve bereaved parents from various settings in the design of the training modules.	• How can wording of questions improve the capture of birth events in household surveys? • How can interviewer training be refined to improve the disclosure of birth events in household surveys?

[a] For example in a rural district in Indonesia local health registers to include a register of pregnancies coupled with training of community health workers led to stillbirth rates four times (13.5 vs 3.5 per 1,000 total births) those previously reported using the standard 'Maternal and Child Health program information system'.[266]

[1] World Health Organization. Strengthening civil registration and vital statistics for births, deaths and causes of death resource kit. 2013.

[2] United Nations Department of Economic and Social Affairs Statistical Division. Principles and Recommendations for a Vital Statistics System. Statistical Papers Series M 2014; 19(Rev3).

[3] Helleringer et al. Using community-based reporting of vital events to monitor child mortality: Lessons from rural Ghana. PloS one 2018; 13(1): e0192034. Amouzou et al. Monitoring child mortality through community health worker reporting of births and deaths in Malawi: validation against a household mortality survey. PloS one 2014; 9(2): e88939. Amouzou et al. Using Health Extension Workers for Monitoring Child Mortality in Real-Time: Validation against Household Survey Data in Rural Ethiopia. PloS one 2015; 10(11): e0126909. Joos et al. Strengthening Community-Based Vital Events Reporting for Real-Time Monitoring of Under-Five Mortality: Lessons Learned from the Balaka and Salima Districts in Malawi. PloS one 2016; 11(1): e0138406

[4] Pega et al. Unconditional cash transfers for reducing poverty and vulnerabilities: effect on use of health services and health outcomes in low- and middle-income countries. The Cochrane database of systematic reviews 2017; 11: Cd011135. University of Oslo, HISP India, HMN. Systematic Review of eCRVS and mCRVS Interventions in Low and Middle Income

Countries.http://wwwwhoint/healthinfo/civil_registration/crvs_report_ecrvs_mcrvs_2013pdf 2013. Kaneko et al. Effectiveness of the Maternal and Child Health handbook in Burundi for increasing notification of birth at health facilities and postnatal care uptake. Global health action 2017; 10(1): 1297604.

[5] APAI-CRVS. Civil Registration in Conflict and Emergency Situations. accessed 13th July 2018 from https://auint/sites/default/files/newsevents/workingdocuments/33070-wd-civil_registration_in_conflict_and_emergency_situations_enpdf 2016.

[6] Bhattacharyya et al. District decision-making for health in low-income settings: a case study of the potential of public and private sector data in India and Ethiopia. Health policy and planning 2016; 31 Suppl 2: ii25-ii34

A.6.2. Closing data gaps 2. ASSESS

Challenge	Policy and practice action: examples	Research questions: examples
Cross-cutting across data systems		
Assessment of vital status at birth	• Work with Ministries of Health and pre and in-service training institutions to improve knowledge and skills in resuscitation and assessment of vital status at birth for facility and community healthcare workers and traditional birth attendants	• Equipment: Development of low-cost, robust and accurate weighing devices and ultrasound machines • Training and supervision: What training packages are most effective to improve knowledge and skills of health workers in assessment of key data elements at different levels of the health sector? What role can job aides (electronic and paper based) play in improving measurement of these outcomes? What is the role of supervision and mentoring in improving accuracy of assessment? • Development of algorithms to improve accuracy of gestational age assessment in 3rd trimester of pregnancy
Assessment of gestational age	• Work with Ministries of Health and global suppliers such as UNICEF supplies division to set standards for ultrasound machines, including guidance on calibration and care for devices	
Assessment of birthweight	• Work with Ministries of Health and global suppliers such as UNICEF supplies division to set standards for weighing devices, including guidance on calibration and care for devices	
Household survey specific		
Poor understanding of the assessment of these data elements by informants and interviewers Poor recall of key data elements	• Work with developers and implementers of large-scale household surveys to improve the training of interviewers • Work with Ministries of Health to improve coverage and completeness of handheld records, and ensure that these data are used by interviewers to supplement women's responses.	• What factors affect women's reporting of these data items in household surveys? How could these be improved?
Gestational age collected for stillbirths only (and in months not weeks)	• Add questions to standard survey questionnaires to assess gestational age for all births, in weeks where possible	• How reliable is gestational in months/ weeks reported in surveys? How can this be improved e.g. use of handheld cards or linkage to facility records?
Birthweight collected for recent live births only	• Add questions to standard survey questionnaires to assess birthweight for all recent births (live and stillbirths)	• How reliable is birthweight reported in surveys for stillbirths? How accuracy be improved?

A.6.3. Closing data gaps 3. RECORD

Challenge	Policy and practice action: examples	Research questions: examples
Cross-cutting across data systems		
Lack of awareness of public health importance of recording or registering every birth reached by the data system including those born very preterm and stillbirths	• Increase awareness on requirement and importance of recording/ registering every birth and death, even in the case of stillbirth or early neonatal death or very preterm babies around the threshold of viability in all settings amongst healthcare workers, civil registrars, families and communities; for example through pre- and in-service training for professional staff and media and targeted educational campaigns for communities.	• Which methods are most effective in increasing the awareness on importance of reporting, recording and registration of all births and perinatal deaths amongst healthcare workers, civil registrars, families and communities? • What are the perceived barriers to recording/ registering birth outcomes in births reached by the data system? How do they differ by settings?
CRVS specific		
Logistically complex systems for grieving parents following a stillbirth or a neonatal death to navigate	• Place the responsibility on the facility to register stillbirths and early neonatal deaths prior to discharge to increase capture of events occurring within the health system. • Where not possible, streamline the process of registration to avoid multiple visits. Bedside registration where possible • Consider reviewing incentives for reporting (context specific) • Involve stakeholders, including bereaved parents in any improvement processes.	• What kind of incentives work and in which settings? • What are the needs of bereaved families and health providers and how can these be balanced with the needs of the CRVS system?
Failure to include data on birthweight and/or gestational age within the birth and death certification process	• Add recommendation to include birthweight and gestational age on the birth, stillbirth and neonatal death notification form or design CRVS systems with data interoperability capabilities to enable linking of data to HMIS and birth registry systems to UN normative guidance.[1]	• How can interoperable data systems be developed especially when different government ministries are responsible for CRVS and health data including HMIS?

HMIS specific		
Standard Facility-based and Community Registers not capturing all data elements required	• Review standard registers ensuring that key data elements of minimum perinatal dataset, including gestational age and birthweight are captured for all births, including stillbirths • Involve frontline healthcare workers in this process	• How can longitudinal electronic records e.g. DHIS-2 tracker be used to reduce the burden of recording for frontline healthcare workers
Low understanding of importance of recording such data by healthcare workers	• Include in pre- and in-service training for all cadres of healthcare and health data workforce	• How do health workers perceive the value of recording these data?
Incentives for healthcare workers to misreport e.g. fear of blame, to protect the mother, to meet targets, to reduce paperwork, or other reasons	• Ensure that the same reporting requirements are made for all births, whether live or stillbirths • Provide adequate supervision and support • Promote a culture of no-blame audit	• How common is misreporting? How can data systems work together with healthcare workers to reduce this?
Poor understanding of flow of data within HMIS system, with large burden of reporting on healthcare workers	• Review flow of birth outcome data within HMIS system • Review, revise, harmonise and streamline registers and data capture to minimise duplication – involving all stakeholders[a] • Build interoperability into data systems[b] • Where data linkage is required, provide clear guidance at each step of data linkage to enhance accuracy, validity and reproducibility of the data.[2]	• Time-motion studies to understand data flow and time and cost implications • What role can training and job aides (electronic and paper based) play in improving recording of key data elements?
Missing information on birth outcomes, especially for births outside public sector facilities	• Develop systems designed to capture missing birth outcomes e.g. in settings with high antenatal care coverage use individual-level data e.g. DHIS-2 to create a 'pregnancy registry approach' to identify and follow-up all women accessing antenatal care without a birth outcome recorded in the system	•

	• Report all live births in a system and all fetal deaths at 28 or more completed weeks in all settings. Where possible capture all fetal deaths from 22 weeks gestation.	
Household survey specific		
Willingness of mothers to report events to interviewers	• Improve women's understanding of the importance for maternal and child public health of accurate reporting of these events • Improve empathy and understanding amongst interviewers through training.[3] • Involve bereaved parents in the design of the training modules.	• How can interviewer training, guidelines and supervision be improved to increase accurate maternal reporting of birth outcomes especially stillbirths?
Women may misunderstand question	• Carefully review wording of the questions in each context to check understanding of potential respondents, with special attention and pilot testing of translations. • Review and improve training for DHS interviewers in capture of pregnancy outcomes including stillbirth	
Incentives for mothers or interviewers to misreport (see Section 6.4)	• Ensure that the same reporting requirements are made for all births, whether live or stillbirths • Address potential factors influencing maternal misreporting such as stigma, fear and blame in introductions to questions. Highlight confidentiality.	• What are the underlying reasons for misreporting in a given setting? How can training and probes be adapted to reduce this?

[a]Stakeholders may include community - women, families; healthcare providers: facility and community-based, Traditional Birth Attendants, private sector; other systems collecting data on vital events – village administration units, community volunteers etc…

[b]For example between registers using DHIS-2 tracker where data are entered once and 'tracks' through system at each visit from antenatal care-delivery care – postnatal care – child health services/ immunisations; or between health data systems e.g. HMIS and Logistics Management Information Systems, MPDSR, data from the private sector or externally with CRVS

[1] United Nations Department of Economic and Social Affairs Statistical Division. Principles and Recommendations for a Vital Statistics System. Statistical Papers Series M 2014; 19(Rev3)

[2] Gilbert et al. GUILD: GUidance for Information about Linking Data sets. Journal of public health (Oxford, England) 2018; 40(1): 191-8.

[3] Munos et al. Strengthening Community Networks for Vital Event Reporting: Community-Based Reporting of Vital Events in Rural Mali. PloS one 2015; 10(11): e0132164. Rasch et al. Self-reports of induced abortion: an empathetic setting can improve the quality of data. Am J Public Health 2000; 90(7): 1141-4.

WHO minimum perinatal dataset

Section	Variables
Identification	ID of mother and baby, facility name, district name
Pregnancy progress and care	# previous pregnancies (gravidity) and total live births (parity), mother's age, singleton/ multiple pregnancy, number of antenatal care contacts, HIV status
Labour and birth	Last menstrual period, Date and time of Birth, Gestational Age (Method of assessment), Place of delivery, Delivery attendant, Mode of Delivery (Cephalic vaginal, breech vaginal, assisted vaginal, caesarean section)[a], sex of the baby, Birthweight
Details of death (if applicable)	Date of death, time of death, type of death (neonatal death, intrapartum stillbirth, antepartum stillbirth, stillbirth unknown timing)

[a] Though not included in initial minimum perinatal dataset, it is recommended that Termination of Pregnancy (TOP) be included as an additional category.

A.6.4. Closing data gaps 4. COLLATE

Challenge	Policy and practice action: examples	Research questions: examples
Cross-cutting across data systems		
UN normative guidance (ICD) not in line with current practice or reporting needs of countries	• Revise UN ICD-11 definitions and normative guidance to be consistent with current practice and reporting needs of countries	
Non-standard definitions used in data system legal framework or guidance	• United Nations organisations to provide normative guidance and support on definitions and their applications in formats accessible to designers and implementers of data systems (health sector and CRVS) • Standard guidance to be given regarding handling of fetal deaths secondary to elective termination of pregnancy (TOP)[a]	
Lack of adherence to standard definitions	• Improve awareness, guidance, training and supervision for all those involved in the collection and aggregation of data to improve practical adherence to the definitions and correct classification of every birth and use of correct denominators for the calculation of rates.[b]	
CRVS specific		
Inconsistencies in current global CRVS normative guidance	• United Nation organisations with a mandate for setting normative standards to review and standardise advice given across relevant CRVS guidance.[1]	
Delay in notification and registration of births	• Where delayed birth registration permitted for logistical reasons, require compulsory notification of all births (both live and stillbirths) by maternity units and community health workers to the civil registrar to enable their timely inclusion in vital statistics.	
HMIS specific		

Low birthweight data collated despite missing birthweight data on a large proportion of births	• In data collation and reporting, ensure that the total number of babies with a birthweight is used as the denominator and the proportion with missing birthweights is reported alongside the low birthweight rate, with details of how this may impact the result	
Household survey specific		
Use of non-standard definitions e.g. stillbirths defined as fetal death at 7 or more months of gestation	• Seek to capture gestational in weeks (see ASSESS section above) and apply standard definitions for stillbirth and preterm birth	
Data on preterm birth not collated due to lack of gestational age data captured for live births or where captured concerns with data quality	• Capture information on gestational age for all births, monitor data quality and collate data where data quality permits.	
Low birthweight data collated despite missing birthweight data on a large proportion of births	• In data collation and reporting, ensure that the proportion with missing birthweights is reported alongside the low birthweight rate, with details of how this may impact the result	

[a] Especially in high-income settings with low stillbirth rates and when early fetal deaths are included as a relatively higher proportion of stillbirths may be elective termination of pregnancies

[b] Particular focus to be placed on training on the processes and practices around recording of very preterm babies around the threshold of viability in all settings

[1] United Nations Department of Economic and Social Affairs Statistical Division. Principles and Recommendations for a Vital Statistics System. Statistical Papers Series M 2014; 19(Rev3).

A.6.5. Closing data gaps 5. USE

Challenge	Policy and practice action: examples	Research questions: examples
Cross-cutting across data systems		
Failure to include stillbirth, preterm birth and low birthweight data in standard health indicator reports	• Include stillbirth, preterm birth and low birthweight data in all relevant standard maternal and child health reporting formats. Present disaggregated data by subnational, equity and other relevant groupings to track progress towards targets. Where available include information on stillbirth timing (antepartum or intrapartum) and cause of death. • Potential role for parent groups and communities to use these data to place further pressure on policy makers to assess these issues.	
Low perceived social robustness/ plausibility of data	• Develop a short set of data coverage and quality indicators for adaptation to different contexts • Present a summary of the data quality assessment in a format interpretable to the policy or lay audience	• What are the best indicators of data quality in a given context? • How best can these indicators be integrated into current standard reporting?
CRVS specific		
Low perceived value of data collected in the 'fetal death register'	• Include stillbirth rates, alongside live birth data	
HMIS specific		
Low perceived value of data at local level by those collecting these data	• Involve all stakeholders (community, healthcare providers) in designing systems that facilitate generation of real-time actionable data e.g. DHIS-2 dashboards	• How do frontline health workers perceive the data that they collect? • How could the design of data systems be tailored to the needs of health workers and local managers
Household survey specific		
See cross-cutting above		

A.7. Data Management plan

This data management plan was prepared at the time of my PhD upgrading, when the focus of the PhD was on stillbirth alone. The data management plan followed for the low birthweight was similar to this plan. For preterm birth, whilst data were managed in a similar way, the final input data and code were not made available by data compass – which was in keeping with standard practice for global estimates at that time, prior to the publication of the GATHER guidelines.

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Data Management Plan for Research Students

Name	**Hannah Blencowe**
Email	Hannah.Blencowe@lshtm.ac.uk
Title	Dr
Date	15th December 2015
Supervisor	Prof Joy E Lawn

Support

Information on writing a Data Management Plan can be found at
http://www.lshtm.ac.uk/research/researchdataman/plan/

One-to-one advice is available through the RDM Support Service
researchdatamanagement@lshtm.ac.uk

DATA DESCRIPTION

What data will you collect or create?

Describe the data that you are collecting or creating in your project. Relevant information to provide includes:

The type of information that will be contained. E.g. MRI scans, interview transcripts, spatial data, etc.

Methods of capture. E.g. face-to-face interview, web survey, etc.

Amount of data. E.g. 100 patients will undergo an MRI scan, 500 people will be interviewed.

Data on stillbirth rate were collected via systematic searches (national statistical office, ministry of health, nationally representative household survey websites, and published literature). All these data are available in the public domain. Data on number of stillbirths, number of live births and other associated predictors of stillbirths was being abstracted from these publicly available data sources and collated into an excel database.
In addition to this, unpublished data were sought through consultation with a group of stillbirth investigators, and once the provisional estimates are completed, these were circulated by the World Health Organization to their country offices for further feedback, alongside an invitation to provide any further national stillbirth data not identified in the initial searches.

Briefly describe the key activities that will be performed on your data, from its creation/capture to its eventual archiving or deletion.

Consider the lifecycle of your research data and the actions that will be performed during that time. For example, data may be captured using a web form, anonymised to remove personal information using software X, cleaned using Tool Y to enable it to be analysed, analysed using software Z, and so on. The lifecycle may be written as text or pictorial form (e.g. a gantt chart).

In addition, it's useful to consider the approximate time period when you will perform each action (e.g. data capture in month 2, data cleansing in month 4, etc.).

All data used in this project are at a population level, and no personal information or identifiers are available.
Data will be collected as above over a 9-month period, abstracted into excel, then exported into STATA v13 for cleaning and data analysis.

What data formats or standards will you use to store data produced by your project?

Outline the data formats, encoding standards, or software tools that you will use to create, analyse, or use data. E.g. data will be captured using a MySQL database and analysed using STATA and MS Access.

Data will be captured in excel and analysed using STATA.

What quality controls and thresholds will you establish to ensure that your data is fit for purpose?

Quality controls may be applied prior, during and following data capture and processing. Possible QC practices include: testing instrumentation to ensure it is correctly calibrated, recording multiple measures, double-entry of information, checking validity of entered values

Excel data abstraction forms were piloted and refined prior to roll out. Data from systematic review and household survey data were double entered. All data were checked in STATA to identify potential outliers, and data abstraction for all outliers was subject to a further data check.

What documentation or metadata is needed to understand your data?

Describe the documentation or metadata that you will create to enable the data to be understood and used by your future self and others. It is helpful to consider the following questions:

What information is needed to understand the content and context of its creation?

What documentation and metadata standards will be used?

How will potential users find out about your data?

The methods and results will be written up and submitted for publication in an open access peer-reviewed journal. The STATA code and final input dataset will be made available via the LSHTM data repository.

DATA STORAGE AND MANAGEMENT

Where will you store data during the project lifetime? (tick one or more)

School PC local drive (drive C: or D:)	X	Personal area on School network (drive H:)		LSHTM Shared Network drive (e.g. I: drive)		Dedicated server maintained at partner institution	
LSHTM-based project server		School laptop or tablet		LSHTM Secure Data Server (for confidential data)		LSHTM Novell Filr	
For-cost cloud service (e.g. Amazon S3)		Free cloud service (e.g. Dropbox, Google Docs)		Portable storage (e.g.USB disk or memory stick)	X	Other. Please indicate	

Other

How will you organise and label your data?

Describe the approach you will take to structure and label your data. E.g. files and folders on a storage device, database tables and labels.

All data will be organised by data source, and all primary data sources stored alongside the database. These will be arranged in folders according to source of data eg; National statistical office, household survey, literature review etc… The main input database and all associated STATA files and output files will be labelled and stored in a folder alongside the input data.

What security measures, if any, will you apply to protect data? (tick one or more)

Controlled access limited to authorized users only		Physical security		Remove identifiable information (e.g. anonymisation)	
Data storage encryption		Data transfer encryption		Password protection	
Process on isolated machine in secure room		Secure deletion following analysis			
Avoid use of third party storage, such as Dropbox		Other			

Other

As all data are publicly available, no additional security measures were applied

DATA ARCHIVING AND SHARING

What data do you need to keep after your project ends and for how long?

The main input database and details of the estimates produced will be kept in an open access depository (LSHTM Datacompass). The output data results will also be made publicly available via the World Health Organization Global Observatory website.
All other primary data sources will remain in the current personal storage to be made available for the next update of the stillbirth rate estimates.

Where will data be kept after your project has finished (tick one or more)

Research data may be submitted to a data repository or data archive, which will handle the process of curation, preservation and sharing on your behalf.

I will keep the data myself	X	My supervisor will look after the data		It will be looked after by the project team	
Held in the LSHTM Research Data Repository	X	Held in a LSHTM-maintained project system		Held in a 3rd party data repository. Please specify in Other field	

Other

Can data be made available to anyone? If not state the reason it needs to be restricted and criteria for gaining access.

Can data be made freely available to anyone or do restrictions need to be applied? This question will help you to consider whether access controls need to be applied to limit data access. Potential reasons for restriction include the need to comply with consent agreements, which state:

Data can only be used by specific users, e.g. researchers working in an academic environment, a specific skill set, etc.

Data can be analysed only for specific purposes compatible with the consent agreement.

If data does need to be restricted, state the reason and the criteria that users would need to meet to gain access

The individual data are publicly available, and the combined database that has been created can be made available to any researchers. The output data (results) will be widely disseminated in excel format, for media, academics, policy makers and other interested groups.

What actions will be performed to prepare your data for access? (tick one or more)

Removal of personal information		Add synthetic data (e.g. pseudonyms)		Copyright clearance	
Establish participant consent		Develop an access agreement			

Other

No actions required

RESOURCING

What do you consider to be the primary data management challenges in your project?

What problems or issues do you need to address in your project.

Underlying quality of stillbirth data and definitions used which varied across countries and data types and can limit comparability of input data.
This project will seek to standardise stillbirth rate data to a common definition for international comparison (≥28 weeks) and to review and apply data quality criteria.

What resources would it be helpful for the School to provide to help deliver your plan?

How can the School help you to manage your data? E.g. training, specific IT Services, etc.

I will undertake some training in the use of LSHTM Data Compass