Stillbirths: rates, risk factors and potential for progress towards 2030

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Webappendix 35 pages more of details, plus 114 references to reduce manuscript

Abstract

There were an estimated 2.7 million third trimester stillbirths in 2015 (uncertainty range: 2.5 – 3.0 million). Stillbirths have reduced more slowly than maternal or child mortality, which were explicitly targeted in the Millennium Development Goals. The Every Newborn Action Plan targets ≤ 12 stillbirths per 1000 births in every country by 2030. Ninety-two mainly high-income countries have already met this target, although with marked disparities. At least 67 countries, particularly in Africa and conflict affected areas will have to double current progress. Most (98%) stillbirths are in low and middle-income countries. Improved care at birth is essential to prevent 1.3 million intrapartum stillbirths, end preventable maternal and neonatal deaths, and also improve child development. Estimates for stillbirth causation are impeded by multiple classification systems, but for 18 countries with reliable data, congenital abnormalities account for a median of only 7.4%. Many conditions associated with stillbirths are potentially modifiable, and often co-exist such as maternal infections (population attributable fraction (PAF): malaria 8.2%, syphilis 7.7%), non-communicable diseases, nutrition and lifestyle factors (PAF around 10%) and age >35 yrs (PAF: 6.7%). Common causal pathways are through impaired placental function, either leading to fetal growth restriction and/or preterm labour, or secondary to prolonged pregnancy (PAF: 14.2%). Two-thirds of newborns have their birth registered. However, less than 5% of neonatal deaths have death registration, and even fewer stillbirths. Recording and registering all facility births, stillbirths, neonatal, and maternal deaths would substantially increase data availability. Improved data alone will not save lives, but provide a tool for targeting interventions to reach >7500 women every day all over the world who experience the reality of stillbirth.

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Key messages

- **What is happening to stillbirth rates?** At the end of the Millennium Development Goal (MDG) era there are 2.7 million (uncertainty range: 2.5 – 3.0 million) third trimester stillbirths annually. Stillbirth rates have declined more slowly since 2000 (Average Annual Rate of Reduction (ARR), 1.8%), than either maternal (ARR=3.4%) or post-neonatal child mortality (ARR=4.5%) which had MDG targets and consequently received more global and country level attention. Better data are essential to accelerate progress towards the target of ≤ 12 stillbirths per 1000 births in every country by 2030 as outlined in the Every Newborn Action Plan (ENAP), linked to United Nations Secretary General's Every Woman Every Child.
- **Where to focus?** 10 countries account for two-thirds of stillbirths and most neonatal (60%) and maternal (58%) deaths estimated in 2015. Sixty-seven countries need to at least double current progress in reducing stillbirths, many of these in Africa. The highest stillbirth rates (SBR) are in conflict and emergency areas. Over 60% of stillbirths are in rural areas, affecting the poorest families. However, even in the 92 countries with a SBR less than 12 per 1000 marked disparities remain between and within countries.
- **When and where in the health system to focus?** Each year there are an estimated 1.3 million intrapartum stillbirths (deaths during labour), despite two-thirds of births worldwide now being in health facilities. High coverage of good quality care during labour and birth is key, and would also reduce maternal and neonatal deaths, prevent disability and improve child development, giving a high return on investment. Improved quality antenatal care is also important to maximise maternal and fetal well-being, to detect and manage underlying conditions, and to promote healthy behaviours and birth planning.
- **Which conditions to focus on?** There is a myth that most stillbirths are inevitable due to non-preventable congenital abnormalities, yet for countries with reliable data congenital abnormalities account for a median of only 7.4% of stillbirths. Conditions where population attributable fraction (PAF) could be estimated at global level include: maternal age >35yrs (PAF 6.7%), maternal infections (PAF malaria 8.2%, syphilis 7.7%), non-communicable diseases, nutrition and lifestyle factors, many of which co-exist (PAF each around 10%) and prolonged pregnancy (PAF 14.2%). Stillbirths commonly occur via fetal growth restriction and/or preterm labour.
- **Which data are required for action?** Two-thirds of the world's newborns have birth certificate, but death registration coverage is even lower at <5% of neonatal deaths and even fewer stillbirths. Recording and registering all facility births, stillbirths, neonatal deaths, and maternal deaths would substantially increase data availability. Reliable measurement of stillbirths outside facilities using household surveys remains problematic, yet no research is addressing this issue. Little has been invested in improving coverage data for maternal and newborn health interventions including those specific to stillbirths. The ENAP measurement improvement roadmap, includes coverage indicator validation, and development of tools such as a minimum perinatal dataset and perinatal audit, offering opportunities to improve data availability and use.

Introduction

The Millennium Development Goals (MDGs) demonstrated the value of health outcome targets to drive change. Maternal (MDG5) and under-five mortality (MDG4) have been halved, with progress still accelerating, most notably for child mortality, with the annual rate of reduction (ARR) improving from 1.2% (1990-1995) to 4% (2005-2013).¹ The world's 2.7 million neonatal deaths (first 28 days after birth) have increased prominence on national and global agendas, primarily since they account for 45% of under-five deaths globally.¹ Attention was not driven by numbers regarding millions of newborn deaths, but more by recognition that neonatal mortality reduction was essential for the MDG4 child mortality target, accounting for almost half of child deaths.^{2,3} In contrast, stillbirths (see panel 1 for definitions) were not included in the MDGs and are not tracked by either the United Nations or the Global Burden of Disease,⁴ both of which count burden only after a live birth.^{1,5} Despite previous estimates showing large numbers of stillbirths (2.6 million in 2009),⁶ global attention remains low. Analyses of development aid reveal how rarely stillbirths were mentioned by donors - only 4 times in more than 2 million disbursements totalling \$1,599 billion (constant 2013 USD) from 2002-13.^{7,8}

The mortality focus during the MDG-era has also catalysed investments in data improvement. For example, child mortality data have increased through nationally representative surveys, the largest source for child mortality data in low and lower-middle income countries (www.childinfo.org). Many middle income countries have strengthened child death reporting in routine systems including vital registration. The frequency and visibility of maternal, child and neonatal mortality estimates have increased, with inclusion of neonatal mortality to annual UNICEF reports since 2009.⁹ In contrast stillbirth rate (SBR) data, although available in over 100 countries through civil registration and vital statistics systems (CRVS) or registry data, have not been routinely collated. Nor has there been investment in improving stillbirth data through household surveys, which remain the main SBR data source for most high burden countries. To date, only one set of national SBR estimates has been undertaken with World Health Organization (WHO).⁶ Hence, stillbirths were without a high profile target or accountability loop, as highlighted in several MDG reports.¹⁰⁻¹²

The *Every Newborn Action Plan* (ENAP) launched in mid-2014 with a World Health Assembly resolution, endorsed by all countries and supported by over 80 partners,¹³ supports the UN Secretary General's global initiative *Every Woman Every Child*, linking with "Ending Preventable Maternal Mortality" and "A Promise Renewed" for children. During consultations for ENAP development country representatives repeatedly stated that a target for stillbirths was needed to ensure accountability.^{3,13} Analyses for targets to end preventable neonatal deaths and stillbirths in every country by 2030 are outlined in the Lancet Every Newborn series.^{3,13}

Objectives

This paper reviews the status of stillbirth around the world and progress since the 2011 *Lancet Stillbirth Series*. We summarise the following new analyses, with the aim of informing action to meet 2030 stillbirth targets:

1. **Progress and projections for stillbirth rates (SBRs)**, in 195 countries, with new estimates and trends from 2000-2015, plus analyses to examine national SBR reductions required to reach the ENAP target of 12 or fewer stillbirths per 1000 total births in all countries by 2030.
2. **Priorities to accelerate progress towards preventing stillbirths**, notably where and when to focus, including the first published global comparative risk factor analysis of potentially modifiable demographic, infectious, non-communicable disease (NCD) and lifestyle factors associated with stillbirth.
3. **Improvements in national stillbirth data** since the *Lancet Stillbirth 2011 series* **and gaps remaining**.

Methods

Definitions

There is now wider recognition and use of the International Classification of Disease (ICD) and WHO recommendations for international stillbirth rate reporting (panel 1),¹⁴ facilitating comparisons, whilst recognising that countries may apply other definitions for internal use. Definition variability occurs mainly amongst high income countries (HIC) with a range from 20 weeks gestational age (GA) upwards, with many countries lowering the gestational age for reporting due to increasing survival at earlier gestational ages with neonatal intensive care.^{4,15}

However, as more countries report stillbirth data, issues with respect to the ICD classification are now clearer. ICD was developed before GA reporting became standard and prioritises birthweight over GA, and incorrectly assumes equivalence between birth weight and GA (panel 1).¹⁶ GA-based cut off is more appropriate, as a better predictor of maturity and hence viability, than birthweight.¹⁷ We propose that for international comparison the definition focus on a GA threshold for stillbirths, rather than birthweight, and be included in ICD 11. In this Lancet series we use the ≥ 28 weeks definition for stillbirth epidemiological estimates.¹⁶

An intrapartum stillbirth (IPSB) is a stillbirth occurring after the onset of labour, but before birth. Fresh stillbirth is commonly used as surrogate marker (panel 1).¹⁸ Antepartum stillbirths (APSB) occur prior to the onset of labour.

Data inputs and analyses

Panel 2 and the webappendix summarise the data inputs and analyses. SBR data were available from 157 of 195 countries, with high quality CRVS data from 54 countries. SBR estimates were developed with WHO including country consultation and presented at UN Inter-agency Group for Mortality Estimation (UN-IGME).¹⁶

Data on timing of stillbirths (antepartum or intrapartum) are still lacking for the majority of countries, with 130 having no useable data (Panel 2, webappendix). Although Intrapartum Stillbirth rate (IPSBR) data should be available from most facility birth registers, these data are infrequently collated at a national level, even in HIC.

The analyses of causes, notably congenital abnormalities, and risk factors are summarised in Panel 2, and the webappendix.

Results and Discussion

Progress in reducing stillbirths and meeting 2030 targets

In 2015, an estimated 2.7 million babies (uncertainty range: 2.5 – 3.0 million) will die before birth during the last trimester of pregnancy, a worldwide rate of 18.9 stillbirths per 1000 total births (uncertainty range: 17.4 – 21.1).¹⁶ In 2000 the estimated SBR was 24.9, implying an ARR of 1.8% between 2000 and 2015. Thus, while some progress has been made, it has been slower than for maternal (ARR 3.4%), neonatal (ARR 3.1%) and post-neonatal under-5 child mortality (ARR 4.5%) over the same period. For every country to reach the [ENAP](#) stillbirth target of 12 or less by 2030¹³ (Figure 1A), a global average ARR of 4.3% will be required from 2015, more than double the current ARR. Yet this global average hides regional variation.

Despite slow progress overall, in every region some countries are reducing stillbirths faster than their neighbours (Figure 1B). In Bangladesh, where the SBR ARR is 2.8%, the total fertility rate (TFR) has halved since 2000, and coverage of key maternal-newborn interventions has increased including four antenatal care (ANC) visits (ANC4) (Average Annual Rate of Change (ARC)=6.5% (regional median=3.1%)) and birth with a skilled attendant (ARC=7.1% (regional median=2.9%)).¹⁹ Births by caesarean section increased from <5% to 10 – 20% of all births, however addressing the proportion of those non-medically indicated is crucial to maintain progress.¹⁹ Rwanda (SBR ARR=2.7%), although still with a high TFR, has increased coverage of care (ANC4: ARC=3.7%, (regional median 2.5%)) and skilled birth attendants (ARC=4.8%, (regional median 2.0%)). Similar improvements are seen in Cambodia, SBR ARR=2.9% (ANC4: ARC=8.5%, (regional median 1.6%)); skilled birth attendants ARC=2.9%, regional median 0.6%)). Nevertheless, two-thirds of women in Bangladesh and Rwanda still do not access four ANC visits, and over half in Bangladesh and a third in Rwanda and Cambodia give birth without a skilled attendant (webappendix). In 2000, Peru (SBR ARR=2.7%) had substantially lower coverage than its neighbours, but through strategic investment in maternal and newborn health, including national financial protection, now has almost universal coverage of ANC4 and skilled birth attendance.²⁰ Even in HIC, such as Netherlands, progress is possible, with improvements in ANC and care at birth, wide-scale perinatal audit, coupled with a focus on women's health before and during pregnancy.¹⁵

Priorities for action to accelerate progress to prevent stillbirths

Where geographically to focus to close the gap?

For many countries, achieving the SBR target by 2030 will require concerted efforts. At least 67 countries will need to more than double their current annual stillbirth ARR. The African region has the highest SBRs and the slowest rates of progress, especially countries with conflicts and emergencies (Figure 1B) (webappendix). Thus, at current rates of progress it will be over 160 years before the average pregnant woman in Africa has the same chance of her baby being born alive as does a woman in a HIC today (Figure 1C), and even longer for women in the countries making the slowest progress. While the Sustainable Development Goals (SDGs) aim for convergence within a generation, with women and babies in all countries having the same chance of survival, equity gaps between regions and countries will widen over time, unless current SBR trends change. This is true even for HICs which have an average SBR of 3.3 per 1000 total births, but with substantial variation between countries, from 1.4 (Finland) to 9.4 (Ukraine) (Figure 1B).

Almost all stillbirths occur in Low and Middle Income Countries (LMICs) (98%) with three-quarters in sub-Saharan Africa (SSA) and South Asia (Figure 2). The 10 countries with the most stillbirths account for 53% of all livebirths, 65% of all stillbirths and most maternal (58%) and neonatal (62%) deaths (Table 1). Population size is an important determining factor, but the rankings shift with changes in mortality risk and fertility. For example Brazil graduated from the ten countries with highest neonatal deaths and stillbirths through dramatic falls in both fertility and stillbirth risk. In contrast several African countries with continuing high fertility and SBRs are now among the ten countries with the most stillbirths, notably Tanzania and Uganda. Tanzania met MDG4 for child survival but reductions in maternal and neonatal mortality and especially stillbirths have been slower.²¹ Challenging the myth that SBR or MNR reduction results in population growth, in many countries the reductions in NMR and SBR coincided with transition to low fertility, including Peru and Bangladesh (webappendix).²²

When to focus?

Worldwide in 2015 around half of stillbirths, more than 1.3 million (range: 1.2 – 1.6 million), occurred during labour (Figure 2). The proportion of stillbirths that are intrapartum varies from 10.0% (range:5.5-18.4%) in Developed region to 59.3% (range: 32.0-84.0%) in South Asia (webappendix). The majority of intrapartum stillbirths occur in countries with low coverage of timely, high-quality care around the time of birth. More than

40 million women give birth unattended at home each year. Improving access to high quality intrapartum care is essential for reducing preventable stillbirths, with the added benefits of reducing the 46% of maternal deaths during labour, one million neonatal deaths occurring on their birthday, reducing long-term disability, and enhancing child development.³

Where in the health system?

Given two-thirds of births worldwide occur in health facilities, most stillbirths are delivered in facilities. Hence high quality facility care, along with investments including community demand and birth planning, should be the first focus for stillbirth prevention. Despite increasing urbanisation, with the majority of the world now residing in cities, in South Asia and especially in Africa, around two-thirds of stillbirths are still rural. Rural families are often the poorest, with limited access to midwifery care, family planning services, and emergency obstetric care, including Caesarean section, resulting in high birth rates, and high stillbirth risk.¹⁹ Even in high income countries, SBR may be higher for rural areas.²³ Even short delays in accessing appropriate care can result in death or disability for newborns and women.^{24,25} The three delays model developed for maternal deaths is relevant for stillbirths, including delays in: (1) danger sign recognition (2) care-seeking due to social or economic barriers, or distance/ lack of transport and (3) receiving quality facility care.²¹ Intrapartum stillbirth is a sensitive marker of delay and low quality of care. It reflects lack of intrapartum monitoring and delays in the rapid delivery of a compromised fetus. There has been debate as to whether this, whilst averting the intrapartum stillbirth, may result in a compromised neonate with neonatal encephalopathy, and potential long term associated disability. This is less likely where timely action is taken and delivery linked to high quality neonatal care, however tracking of longer term outcomes is required as intrapartum and neonatal intensive care are scaled-up.²⁶ In addition a woman experiencing stillbirth is at risk of obstetric fistula or death. An estimated 78% to 96% of women with obstetric fistula also experience stillbirth.^{27,28}

National SBRs show a strong ecological association with coverage of care (webappendix). Higher national coverage of ANC is strongly associated with lower antepartum SBRs. While WHO recommends a four-visit ANC model for low-risk populations, these policies are currently being reviewed.²⁹ Similarly, higher coverage of birth with a skilled attendant is strongly associated with lower intrapartum SBRs (IPSBR). The median IPSBR is higher for those countries with caesarean section rates below 10%. Across countries with caesarean section rates above 10% there does not appear to be a strong correlation with SBR. This finding is consistent with a recent systematic review in which failed to detect any improvement in maternal or newborn health with caesarean section rates above 10-15% after correcting for “development status”.^{30,31} In countries with higher caesarean section rate’s some may be inappropriate. Even if appropriate, they contribute to higher preterm birth rates³² and are associated with increased risk in subsequent pregnancies for mothers and their offspring.³³⁻³⁵ Policies should encourage appropriate caesarean sections, but more research is required to track and disincentivise “non-medically indicated” intervention.³⁶ In LMICs much of the caesarean section epidemic is in the private sector, with caesarean rates over 50% in private hospitals, many of which are not medically indicated.¹⁹ However the global challenge remains that the women who most need caesarean sections to save their or their babies lives, are least likely to get them.³⁷ In many poor communities women even if women are able to access emergency caesarean sections if required they may not get them on time, and frequently have to pay for them out of pocket.³⁷

Why do stillbirths occur?

Many countries, particularly HIC and MICs, collate data on conditions associated with stillbirths. However, given over 55 active classification systems, consistent estimation of stillbirth causation remains difficult even across HICs.^{7,38} In the 2011 Lancet stillbirth series we called for a simplified classification system which could be applied in Low Income Countries (LICs) onto which more detailed categories recorded in other settings could be

mapped.⁴ Since 2005, national estimates have been available for all United Nation (UN) member states for neonatal cause of death,³⁹ but the lack of similar information for stillbirths limits our ability to act. Even if a new classification system is agreed, there will be a time lag, maybe of a decade, before national estimates are possible for all the major conditions associated with stillbirth.

Congenital abnormalities are exceptional in being reported consistently across many stillbirth classification systems. Myths persist that stillbirths are inevitable, and mostly due to non-preventable congenital abnormalities. Yet in most national reports, congenital abnormalities account for <10% all stillbirths after 22 weeks of gestation, with a median of 7.4% and rates well under 1 per 1000 births (Table 2). In settings with limited diagnostics, under-ascertainment of congenital causes is likely, for example non-tertiary hospitals in South Africa (2.5%). Conversely with good diagnostics, where termination of pregnancy (TOP) is illegal a higher proportion is reported (e.g. 21% in Ireland). Furthermore, not all congenital abnormalities are inevitable, e.g. neural tube defect prevention through folic acid supplementation.

Babies at greatest risk

Males are at 10% higher risk of stillbirth than females.⁴⁰ The likely mechanisms include X-linked congenital conditions and increased risk of preterm labour and poor fetal growth for male babies. This may be related to a higher incidence of placental vascular conditions, including pre-eclampsia.⁴¹

The smallest babies face the highest risk of death. Worldwide around 20 million live births are estimated to be low birthweight (<2500g), but this simplistic, dichotomous cut-off fails to differentiate between fetal growth restriction (FGR) and preterm labour, or a combination of the two.⁴² There is a higher risk of both antepartum and intrapartum stillbirth among babies experiencing FGR. FGR is often part of a causal network, whereby an already compromised fetus is more susceptible to infection or hypoxic insults.⁴³ For example the risk of death is higher for those experiencing a hypoxic insult against a background of FGR and infection, and this applies both for stillbirths and liveborn babies who develop neonatal encephalopathy.⁴⁴

Where there is high quality obstetric and neonatal care, intrapartum stillbirth is now rare, and hence the majority of stillbirths are antepartum, many with FGR. In these settings, FGR or placental conditions are more likely to be detected and the balance of risks may favour early induction or Caesarean section, hence increasing the preterm birth rate.⁴⁵ However early detection of FGR remains a challenge even in HICs.¹⁵

Modifiable factors associated with stillbirth

We reviewed potential risk factors for stillbirths including over 35 maternal factors comprising demographic, environmental, nutrition and lifestyle factors, maternal infections and NCDs, and fetal factors (Table 3). We did not include distal determinants of stillbirth such as poverty and inequity, which affect underlying maternal health and access to quality care. Whilst highly important, data were not available to quantify the risk. FGR and preterm labour are frequently a final link in the causal pathway leading to stillbirth, however in this comparative risk factor analysis we focus on the biological risks.

Risk ratio data were available for twelve modifiable conditions associated with stillbirth, with prevalence data for all countries (Figure 3, webappendix). These risk factors are not mutually exclusive and many may coincide in the same woman, so the sum of the population attributable risks exceeds 100%. However, comparing categories with the greatest overall impact still provides a useful guide for programmatic priorities towards ending preventable stillbirths.

Worldwide, 6.7% (uncertainty: 6.3–7.3%) of stillbirths are attributable to older maternal age (>35 years). Adolescent pregnancy is also associated with increased risk, especially in those under 16.⁴⁶ We were unable to quantify this risk due to lack of robust age-specific risk data. However, due to a lower number of pregnancies in this group the population attributable contribution to stillbirth is relatively small compared to women over 35. Family planning programmes may lack clear messages regarding pregnancy risks at older ages, notably sub-fertility, severe maternal morbidity/death, stillbirth, preterm birth, low birthweight and neonatal death.⁴⁷ Such messages must be coupled with access to acceptable family planning methods and empowerment for informed choices.⁴⁸ Short inter-pregnancy interval is another important risk associated with other poor perinatal outcomes, modifiable with family planning, but the effect on stillbirth is yet to be quantified.⁴⁹

Infections during pregnancy remain important preventable factors, especially in SSA, although few studies report usable risk data. Improving prevention and treatment of malaria in pregnancy (estimated to be attributable for around 20% of stillbirths in SSA), and syphilis (7.7% (4.6–12.0%) of stillbirths globally, 11.0% (6.7–17.0%) in SSA), should be an important first step in preventing stillbirth in weaker health systems.^{50,51} It is notable that the campaigns for managing malaria and syphilis in pregnancy have tended to focus on neonatal deaths, despite the associated stillbirth burden being much higher. Data to assess the burden of stillbirths attributable to HIV/AIDS are limited. Based on data from the South African Programme for Identification of Perinatal Priorities we estimate that 0.7% (0.6–0.8%) of stillbirths in SSA may be attributable to HIV infection. The risk may be higher in settings without widespread availability of antiretroviral therapy (webappendix).

The global epidemics of obesity and NCDs, notably hypertension and diabetes, are affecting pregnancies in all regions,⁵² especially when combined with advanced maternal age. Our estimates suggest that around 10% of stillbirths are attributable to these conditions (Figure 3). Improving outcomes will require efforts aimed both at primary prevention and improved detection and management of affected women, where possible prior to pregnancy. Tobacco has a relatively small PAR (Figure 3), due to a low relative risk and also low prevalence of smoking even in South Asia where smoking has risen dramatically.

Over 200,000 stillbirths are attributable to pre-eclampsia and eclampsia (combined PAF 4.7%) with the highest burden in SSA and South Asia. Many of these deaths could be averted with detection and appropriate management in ANC, and improved intrapartum care.⁵³

Pregnancy lasting longer than 42 weeks is associated with an increased risk of stillbirth, accounting for an estimated 14.2% of stillbirths worldwide. Most HICs have introduced policies of induction of labour prior to 42 weeks, with some ecological analyses suggesting substantial impact.⁵⁴ This policy could be extended to MIC settings where accurate dating of pregnancies, through early ultrasound, and safe emergency obstetric care are widely available. Caution is needed in settings where these criteria cannot be met and there is real potential for harm to women and their babies.³⁷

For some other important conditions it was not possible to estimate the attributable stillbirths due to lack of prevalence or risk data (webappendix). For example regarding violence against pregnant women, although studies show an increased risk of stillbirth,^{55,56} and 30% of ever-partnered women experience physical or sexual abuse in their lifetime, there are no prevalence estimates specific to pregnant women.⁵⁷ Other factors associated with an increased risk of stillbirth include: bacterial infections (eg chorioamnionitis), viral infections (eg influenza and hepatitis),⁵⁸ other medical conditions such as thyroid disorders and liver disease;⁵⁹ and indoor air pollution (30% increased risk).^{60,61}

High quality ANC could identify and address many of these conditions. Currently over half of pregnant women are estimated to attend at least four ANC visits.⁶² However, there is a need to optimise timing and quality and reach the marginalised, including those with mental health conditions.^{63,64}

Whilst these biomedical conditions are important and must be addressed in order to improve fetal and maternal health, especially in LMIC, the common factor for many stillbirths is the absence or low quality of intrapartum care, including access to timely referral.^{65,66} This must be urgently addressed. It is clear that progress in preventing stillbirths will require working with groups who focus on issues beyond maternal and newborn care, notably family planning, NCDs, nutrition, and malaria and other infections, as well as wider health systems change, plus strategies for women's education, empowerment and community engagement including with men, mother-in-laws and other societal gatekeepers.

Counting stillbirths and making the data count

Some progress has been made in measurement since the 2011 Lancet Stillbirth Series (webappendix). Stillbirths are increasingly counted, which may be partly related to more visible SBR estimates and rankings.⁶ More data are available for SBRs, with the number of countries with no data reduced from 68 to 38. However, amongst those with data, 81 do not have nationally representative data and more do not have trend data. In many settings stillbirths are infrequently weighed at birth, especially for births occurring outside of health facilities. Shifting the stillbirth definition to one based on GA should further increase data quality and comparability, recognising further advances are needed in GA accuracy (panel 1).

Whilst SBR data have increased, data gaps remain for IPSBR and over 130 countries are without available data, despite being recorded in most routine labour ward registries. It should be a scandal that an estimated 1.3 million intrapartum stillbirths, the majority of which are preventable, are not collated in hospital or national information systems.

Improving data will require investments in national health information systems, as promoted by the "Measurement and Accountability for results" roadmap, which is crosscutting, and the [ENAP](#) measurement improvement roadmap which focuses on newborns and stillbirths.^{67,68} As part of ENAP, WHO is developing perinatal audit tools to assist in addressing modifiable factors,⁶⁹ and to link with a minimum perinatal dataset.⁷ These initiatives provide opportunities to develop better tools which can be applied to address important research questions. However, investment is needed in high burden countries to operationalise this.

All babies should be registered at birth. Birth registration now covers two-thirds of the world's livebirths, but <5% of stillbirths. Coverage of death registration is even lower, covering <5% of neonatal deaths and even fewer stillbirths. Recording all facility births, stillbirths (especially intrapartum) and newborn, child and maternal deaths using standard definitions is feasible, and linking these to birth registration would rapidly increase SBR data availability, even by 2020. The inclusion of gestational age, birth weight and associated maternal conditions on death certificates would greatly increase data utility allowing cross-tabulation of maternal and perinatal conditions. Including these data on birth certificates would provide important intergenerational information on health such as NCD outcomes.⁷

Accelerating progress to end preventable stillbirths requires improved data. Little investment has yet been made in improving coverage data for interventions that improve maternal and newborn health. This is an urgent priority and should include tracking content and quality of interventions specific to stillbirth prevention, particularly within ANC and intrapartum care.⁷⁰ For example coverage data for syphilis detection and treatment,

components of advanced ANC, and intrapartum monitoring remain absent in most countries, and in global tracking. In addition, data are needed regarding reduction of stigma and provision of bereavement care.¹⁵

The 2011 Lancet Stillbirth Series ranked research priorities for improving our understanding of stillbirth epidemiology (webappendix).⁴ The top five priorities centred on risk factors, and our review and analysis underline limited progress made on this knowledge base, even for conditions such as malaria and HIV (and new ones such as Ebola) with major investment but where SBR or IPSBR data are rarely collected. Household surveys, a potentially important source of data in countries lacking robust routine data collection systems, remain problematic for SBR capture, but no research to address this issue is ongoing. Methodological research is needed to address this issue, including improved understanding of which survey-based tools (e.g. birth history, pregnancy-history, truncated pregnancy-history) maximise the capture of stillbirths, and how these can be best implemented. Demographic surveillance sites such as the INDEPTH network provide a unique opportunity to test retrospective survey modules against prospective pregnancy capture data, and also assess the length of interviews which is a major constraint in DHS given the questionnaire already has long, complex questions.

Regarding classifying causes-of-stillbirth, the greatest challenge remains the development of a practical standardised classification system which is effective with varying complexity of data from verbal autopsy to clinical attribution possible in facilities to centres with more extensive laboratory testing.⁷¹ WHO is working on this issue. Resource-limited settings may rely on verbal autopsy especially for births outside health facilities.^{72,73} The commonly used WHO verbal autopsy tool, while retaining questions on the timing of stillbirth (fresh/macerated), no longer includes questions on the causes of stillbirth.

In each region of the world the fastest progressing country for SBR (Figure 1B, web appendix) also tended to make more progress than their neighbours in data improvement. For example Rwanda has increased birth registration and notably increased reporting of the baby's birth weight from under a third to over two-thirds (webappendix).

Conclusion

As we transition from the MDG to the SDG-era, the global architecture for accountability for health outcomes is more complex. Ending preventable deaths of newborns and under-five children by 2030 is a sub-target under SDG3 (the only health goal), with 16 other goals focused mainly on social and economic development and the environment. The discourse has shifted from health being essential for development, to development being necessary to improve health. Neonatal mortality is now an explicit SDG target. Many countries requested that WHO establish an explicit stillbirth target, which is why this was included in ENAP.³

Opportunities exist, with more investment planned for national health information systems, including CRVS, and ongoing calls for more use of data for accountability, but there is a pressing need for leadership to include stillbirths at a global level, especially in high burden countries.^{7,74} Leadership is needed at all levels, but it will be critical to have technical skills to improve and use programmatic data to close quality and equity gaps. This will require intentional investment in effective data systems and skills-building in communities most affected by stillbirth, including affected women.⁷⁴ Household surveys have been strengthened to improve the capture of neonatal and child deaths; this can also be done for stillbirth. At all health facilities, we call for systematic recording of stillbirths especially intrapartum stillbirth, with collation and review of these data at both a local and national level, such as through perinatal audit. The majority of stillbirths, particularly intrapartum stillbirths, are preventable and those due to syphilis and malaria should be considered unacceptable even in the weakest

health systems. Improving data will not alone lead to change, but provides accountability for targeting interventions, reaching the more than 7500 women every day all over the world who experience the reality of stillbirth. We call for a joint programmatic and measurement agenda that includes mothers, newborns *and stillbirths*, in order to end all these preventable deaths.

For The Lancet Ending Preventable Stillbirths Series study group

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Contributions

Joy E Lawn, Hannah Blencowe, (overall coordination, SBRs, IPSBRs, cause of death, RF analysis) and Simon Cousens overall statistical advice. Zeshan Qureshi (IPSBR and SBR data published studies searches and abstraction) Suhail Shiekh (registry data review). Claire Calderwood (IPSBR combined databases and risk factor reviews/abstraction) Fiorella Bianchi Jassir (Fastest progressor analysis). All the authors reviewed and input to the manuscript. The content of this Series paper does not necessarily indicate the view of the authors' organisations.

Conflicts of interest

We declare that we have no conflicts of interest.

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Panel 1 Defining stillbirth and intrapartum stillbirth

Fetal loss and stillbirth

International Classification of Disease 10th revision (ICD 10) definitions (note birth weight was given priority over gestational age (GA))

- late fetal death ≥ 1000 gms or ≥ 28 weeks or ≥ 35 cm
- early fetal death ≥ 500 gms or ≥ 22 weeks or ≥ 25 cm
- miscarriage as a pregnancy loss before 22 completed weeks of GA

World Health Organization (WHO) definitions

For international comparison WHO uses stillbirth to mean the ICD definitions of late fetal deaths (ie ≥ 1000 gms with an assumed equivalent of 28 weeks gestation).

However the birthweight and GA thresholds do not give equivalent results. For example in the US if stillbirths were defined by ≥ 500 gm birthweight definition, the stillbirth rate (SBR) is lower by 40% than using the at 22 week definition, and if ≥ 1000 gm then is lower by 21% than the 28 weeks definition.¹⁶ Hence the definition should be based on one parameter and we propose that a GA threshold is most appropriate as it is a better predictor of viability than birthweight and Information of gestational age is more widely available than birthweight for many stillbirths. In many Low-Middle income countries GA is primarily based on last menstrual period, and improving GA accuracy in these settings requires additional innovation but is more feasible than weighing all stillbirths at home.

For these **stillbirth rate estimates**, we use the ≥ 28 weeks definition, which represents third trimester stillbirths and hence undercounts the true burden if early stillbirths were included. We use the term stillbirth to refer to all early and late fetal deaths since ICD and many countries do count early stillbirths, mostly from 22 weeks.

Intrapartum stillbirth

An intrapartum stillbirth is a death which occurs after the onset of labour but before birth. Diagnosis of intrapartum stillbirth requires confirmation of the presence of a fetal heart rate at the onset of labour. In settings where fetal heart rate monitoring is lacking, examination of the skin appearance is frequently used to estimate the timing of the stillbirth. Signs of skin maceration begin at 6 – 12 hours after fetal death, and a “fresh” skin appearance with no signs of maceration is considered a surrogate measure for intrapartum stillbirth.⁷⁵ However this may be unreliable and can underestimate intrapartum stillbirth, especially where fetal death during labour occurs at home, and delays in access to care are more than 6 – 12 hours.⁷⁶ The intrapartum or fresh SBR is a useful marker of stillbirths that may be preventable due to improved care during labour, however it might be an over estimate as it will include babies with underlying conditions, such as FGR, infections or congenital abnormalities. For programmatic action, where possible the intrapartum stillbirth rate should be calculated, excluding those with severe congenital abnormalities, as antenatal diagnosis of these will affect the level of intervention during labour.

See web appendix A1 for details of relevant time periods and definitions of related birth outcomes

Panel 2 Overview of data inputs and methods

Stillbirth rates

Inputs

Stillbirth rate (SBR) data were identified through web-based searches of National Statistical Office and Ministry of Health websites of all countries. In addition, for countries outside the Millennium Development Goal Developed region, systematic searches were undertaken, covering the published literature and all Demographic and Reproductive Health Surveys. A Stillbirth Epidemiology Investigator group was created, with calls for data distributed via relevant groups and list serves and individual PIs approached. Data were assessed using specified inclusion criteria, and were adjusted to the ≥ 28 week definition where required. 157 countries in total contributed data. High quality Civil Registration and Vital Statistics (CRVS) data were available from 54 countries, lower quality CRVS or Health Management Information Systems (HMIS) data from 60 countries. In addition, 127 retrospective household surveys were included (57 countries) and 329 studies from 57 countries.

Stillbirth estimation

For 31 countries, with “complete” time series high quality national data the country’s own reported rates, adjusted where necessary (see above), were smoothed with loess regression to produce estimated trends for 2000-2015. For 164 countries without high quality time-series CRVS data, a regression model was developed to predict national stillbirth rates using stillbirth rate data identified from all countries meeting the inclusion criteria. For 164 countries without recent, national high quality SBR data, their subnational or other data were included as inputs, and national predictor covariates were used to model 2015 estimates and time trends. The final model included $\ln(\text{nmr})$, $\ln(\text{gni})$, $\ln(\text{lbw})$, mean years of adult female education, the context of the study and the region as the main variables for prediction purposes. Details are given elsewhere.¹⁶

Projections to 2030 at national level were based on trends for SBR 2000– 2015, assuming the same national ARR, and combining with UN PopDivision medium birth cohort projections by country by year, to estimate rates and numbers for each country, region and globally to 2030.

Uncertainty

Uncertainty estimates were derived using a bootstrap approach by drawing 1000 bootstrap samples with replacement from the input data and re-running the model to produce estimates and taking the 2.5 and 97.5 percentile values for each cause as the uncertainty bounds. For countries with high quality time-series data where reported rates were used we assumed a Poisson distribution.¹⁶

Intrapartum stillbirth rates

Inputs

Data on intrapartum stillbirths were identified through web-based searches of National Statistical Office and Ministry of Health websites and systematic literature searches for all countries. Further data were requested from the Stillbirth Epidemiology Investigator group. Data were assessed using specified inclusion/ exclusion criteria. Where CRVS and routine data were available for more than one year, the latest full year of data availability was used. Data were included from 65 countries (41 outside the developed region). This included 173 data points covering over 37 million births with 1.1 million stillbirths.

Estimation

Various strategies to fit a regression model to estimate the national intrapartum stillbirth rate were attempted, including approaches to predict intrapartum stillbirth rate, the proportion of all stillbirths that are intrapartum and the logodds of stillbirth (see webappendix). In view of data limitations it was not possible to identify a satisfactory model. Therefore to estimate the intrapartum stillbirth rate for each country we first calculated the median proportion of stillbirths that are intrapartum from all data inputs from a given region. For all countries in a given MDG region the intrapartum stillbirth rate was estimated by applying the regional median to the country estimated stillbirth rate for 2015.

Uncertainty

Uncertainty estimates for the proportion of stillbirths that are intrapartum were derived by the use of regional IQR for regions with more than 10 data inputs. For regions with 10 or fewer data points, the upper and lower datapoints were used. We simulated uncertainty estimates for intrapartum stillbirth rates by using 1000 independent random draws of the uncertainty around the total stillbirth estimated for the proportion of total stillbirths that were intrapartum.

Congenital conditions associated with stillbirth

Inputs

A web-based search of National Statistical Office and Ministry of Health websites of all countries was undertaken to identify databases and reports providing data on cause of death for stillbirths was undertaken. National data were available from 22 countries. Data were excluded when countries reported with an early stillbirth definition (≥ 20 weeks or ≥ 22 weeks) and

included terminations of pregnancy or did not provide consistent data on all stillbirths (Italy had data on <50% of stillbirths and >25% garbage codes (deaths assigned to ill-defined causes that are not useful for public health analyses)); Philippines only reported on the top 10 causes of stillbirth (which included 74% of all stillbirths)). Data on were abstracted regarding the definition of stillbirth used, the proportion of stillbirths where a congenital abnormality was associated with the stillbirth, and the proportion of stillbirths with no cause recorded. Data regarding the current status of screening and the legal status of Termination of Pregnancy for congenital abnormalities was abstracted from these reports, and supplemented by web-based searches where necessary.

Risk factor analyses for stillbirth

Inputs

We undertook a review of the literature to identify potentially modifiable risk factors associated with stillbirth reported in the published literature. We grouped these risk factors into the following categories: 1) Maternal - demographic/ fertility related, infection, nutrition, lifestyle, non-communicable disease, environmental; and 2) Fetal. (Table 2)

We prioritized inclusion of risk factors with strong evidence of an association with stillbirth, and available prevalence data on the exposure for countries from all worldwide regions. Recent systematic reviews (published 2010 – 2015) were searched for data to inform the risk associations. We included studies with median data collection from 1995, restricting to more recent data were possible. Data on the population prevalence of the risk factor by country were searched from publically available databases. (see webappendix) For important potentially modifiable exposures with available prevalence data, but with no risk association data from recent systematic reviews, further systematic reviews were undertaken.

Estimation process

For included conditions, we calculated the proportion of cases in the whole population that may be attributed to the exposure (population attributable fraction (PAF)). PAF is the proportional reduction in stillbirth that would occur if exposure to a risk factor were reduced to an alternative ideal comparative scenario (the counterfactual e.g. no active syphilis in pregnancy). However, as stillbirths may be caused by multiple risk factors, and individual risk factors may interact in their impact on overall risk of stillbirth, PAFs for individual risk factors overlap. This calculation assumes causality and complete control of possible confounding factors, and hence will over-estimate the effect.

Uncertainty

We quantified uncertainty around these estimates by taking 1000 random draws of the national number of stillbirths and the risk associated with the condition, and the prevalence of the risk factor (where available), assuming a normal distribution with mean equal to the point estimate of the parameter and the standard deviation equal to the estimated standard error. We summed these data at the regional level for each draw and present the 2.5th and 97.5th percentiles of the resulting distributions as the uncertainty range.

See Webappendix for more details of inputs and methods

Figure 1: Projections of progress for stillbirth rates at global and regional level

A. Projections to 2030 for the national stillbirth rate targets of 12 or less per 1000 total births as set in the Every Newborn Action Plan

B: Variation in national average annual rates of reduction of stillbirth rates (2000 – 2015), showing the fastest progressing country in each Millennium Development Goal region

See web appendix for details and Blencowe et al for details of stillbirth rate estimates

C. Time for each region to reach the same stillbirth rate as high-income countries in 2015, based on ARR from 2000–2015

Figure 2: Regional variation in estimated stillbirth rates, showing uncertainty ranges, and the proportion of intrapartum stillbirths for 2015

	TOTAL	Developed region	Eastern Asia	Latin America and Caribbean	Caucasus and Central Asia	South-eastern Asia	N.Africa and W.Asia	Southern Asia	Sub-Saharan Africa
Estimated stillbirth rate per 1000 total births (uncertainty range)	18.9 (17.4 - 21.1)	3.3 (3.2 - 3.4)	7.3 (5.6 - 10.3)	8.6 (8.0 - 9.6)	11.7 (9.9 - 14.4)	13.5 (11.8 - 15.7)	14.7 (13.3 - 16.5)	26.3 (23.5 - 29.6)	29.4 (26.0 - 35.0)
Number of stillbirths	2,682,000	47,000	139,400	94,500	20,600	157,100	131,300	988,100	1,103,900
Estimated intrapartum stillbirths (%)	49.6%	10.0%	19.9%	16.8%	19.9%	45.7%	42.0%	59.3%	51.1%
Percentage of stillbirths in rural areas*	58.9%	23.0%	43.8%	24.9%	58.9%	54.5%	41.8%	65.5%	61.8%
Percentage of stillbirths born in health facilities*	61.2%	99.4%	99.5%	89.3%	97.1%	79.6%	81.5%	58.8%	49.0%

See web appendix for details and Blencowe et al for details of stillbirth rate estimates.

*Based on urban/rural birth cohorts with national SBR so may underestimate rural SBR which is expected to be higher than urban. For facility/home SBR differential, the direction of increased SBR is unpredictable as may be lower at home if high risk cases are in facilities, or higher at home if very low access to care

Figure 3: Regional variation in stillbirth population-attributable risk for factors with adequate risk and appropriate prevalence data

Note that these factors are not mutually exclusive and some, particularly older age and non-communicable and lifestyle factors may coincide
See table 3 for conditions considered and Webappendix for more details

Table 1: Top ten countries for absolute numbers of stillbirths, maternal and neonatal deaths in 2015

Country	Rank for stillbirth numbers in 2015 (2000)	Number of stillbirths in 2015 (ARR:2000-15)	Rank for numbers of neonatal deaths in 2015	Number of neonatal deaths in 2015 (ARR:2000-15)	Rank for numbers of maternal deaths in 2015	Number of maternal deaths in 2015 (ARR:2000-15)	GFR in 2015 (ARR:2000-15)
India	1 (1)	617,800 (-2.2)	1	703,600 (-3.2)	1	47,200 (-4.4)	0.08 (-1.9)
Nigeria	2 (2)	341,800 (-1.3)	2	255,200 (-2.3)	2	39,100 (-3.9)	0.18 (-0.3)
Pakistan	3 (3)	222,500 (-1.2)	3	209,200 (-1.9)	7	7,400 (-3.7)	0.09 (-2.5)
China	4 (4)	131,300 (-4.6)	4	99,500 (-8.6)	9	5,800 (-4.4)	0.05 (0.5)
Ethiopia	5 (6)	99,200 (-2.1)	6	87,800 (-3.7)	4	12,200 (-6.1)	0.13 (-2.7)
Democratic Republic of the Congo	6 (8)	95,200 (-1.0)	5	89,900 (-1.7)	3	20,300 (-3.1)	0.18 (-1.2)
Bangladesh	7 (5)	89,900 (-2.8)	7	72,300 (-3.9)	14	4,800 (-5.2)	0.07 (-3.1)
Indonesia	8 (7)	65,200 (-1.8)	8	62,200 (-3.2)	5	8,500 (-3.4)	0.07 (-1.0)
United Republic of Tanzania	9 (11)	41,400 (-2.2)	11	36,600 (-3.5)	6	7,600 (-4.6)	0.17 (-0.6)
Uganda	10 (13)	38,500 (-2.0)	14	35,100 (-2.7)	10	5,700 (-4.3)	0.19 (-1.2)
Total		1.7 million stillbirths (65% world total)		1.7 million neonatal deaths (62% world total)		158,600 maternal deaths (58% world total)	

See web appendix for details and Blencowe et al for details of stillbirth rate estimates

Table 2: Proportion of all stillbirths reported to be associated with congenital abnormalities in 18 national reports (2009-2013) and subnational in South Africa (2012-13) showing status of screening and legality of termination of pregnancy

Country	(Year)	Stillbirth definition	Stillbirth rate	Congenital cause-specific stillbirth rate	Percentage of all stillbirths attributed to congenital	Status of screening for congenital abnormalities	Legal status of Termination of Pregnancy (TOP) for congenital abnormalities
Australia	2011	>=28 weeks	2.9	0.3	10	Widely available	Legal in most regions
Colombia	2013	>=28 weeks	8	0.7	8.3	Availability <50%	Legal (severe only)
Kuwait	2012	>=28 weeks	5.9	0.4	7.3	Widely available	Legal
Suriname	2010-11	>=28 weeks	22.4	1.5	6.7	Limited availability	Not permitted
Argentina	2012	>=1000g	5.2	0.3	6	Widely available	Not permitted
Panama	2013	>=7 months	5	0.4	7	Limited availability	Not permitted
Wales	2013	>=24 weeks	4.2	0.3	7.1	Widely available	Legal
UK	2009	>=24 weeks	5.2	0.4	7.4	Widely available	Legal
Portugal	2012	>=22 weeks	3.6	0.3	8	Widely available	Legal
Lithuania	2013	>=22 weeks	4.8	0.5	9.7	Widely available	Legal
Costa Rica	2013	>=22 weeks	6.8	0.4	6.4	Widely available	Legal
Canada	2010	>=500g	3.8	0.4	11.4	Widely available	Legal
Ireland	2012	>=500g	3.9	0.8	21	Widely available	Not permitted
Scotland	2012	>=500g	4.7	0.5	11	Widely available	Legal
Guatemala*	2013	>=20 weeks	8.6	0.5	5.4	Limited availability	Not permitted
Mexico*	2012	All fetal deaths	8.7	0.6	7.3	Variable	Not permitted
Ecuador*	2013	All fetal deaths	7.4	0.5	6.4	Not known	Not permitted
Qatar*	2009	Not stated	6.7	0.8	11.4	Widely available	Legal (<5th Month)
Subnational							
South Africa - non-tertiary hospitals**	2012-13	>=1000g	14	0.4	2.5	Very limited availability	Legal
South Africa - tertiary referral**	2012-13	>=1000g	27.2	2.1	7.7	Limited availability	Legal

* stillbirth ascertainment at <22 weeks likely low in these settings

**Programme for identification of Perinatal Priorities (PIPP) covered 73% of all births nationally in these years

See WebAppendix for full details of the sources

Table 3: Conditions associated with stillbirth reviewed for risk factor analysis

Potentially modifiable risk factors	Prevalence data	Risk data	Comment
MATERNAL FACTORS			
Demographic / fertility			
Maternal age >35	✓	✓	Data only available for girls aged 15 – 19 years old suggesting no increased risk but likely to be higher risk for younger age group
Maternal age <18	X	X	
Primiparity	X	X	
Short inter-pregnancy interval	X	X	
Assisted reproductive therapy	X	X	
Infections			
Syphilis	✓	✓	
HIV	✓	✓	
Malaria	✓	✓	
Rubella	X	X	
Varicella	X	X	
Parvovirus	X	X	
Toxoplasmosis	X	X	
CMV	X	X	
Tuberculosis	✓	X	
Influenza	X	X	
Hepatitis	X	X	
Chorioamnionitis	X	X	
Nutritional			
Overweight	✓	✓	No studies showing convincing risk when confounding considered 1 study - no adjustment for potential confounders
Obesity	✓	✓	
Short maternal stature	X	X	
Undernutrition	✓	X	
Maternal anaemia	Limited	X	
Non-communicable diseases			
Maternal diabetes (pre-existing)	✓	✓	Adult females prevalence data
Gestational Diabetes	X	✓	
Maternal hypertensive disorders:			Prevalence data based on adult female hypertension
Pre-existing	✓	✓	
Pregnancy-induced	X	✓	
Pre-eclampsia	✓	✓	
Eclampsia	✓	✓	
Untreated thyroid disease	X	X	
Obstetric Cholestasis	X	X	

Maternal mental health disorders	X	X	Studies report non-standard exposures, and close association with substance abuse
Maternal HbSS	✓	✓	
<i>Lifestyle influences</i>			
Tobacco	✓	✓	Adult females prevalence data
Alcohol	✓	X	Adult females prevalence data
Illicit drug use	X	✓	
Violence against women	✓	✓	
<i>Environmental factors</i>			
Indoor air pollution	✓	✓	
FETAL FACTORS			
Male sex	✓	✓	Not modifiable
Post-term pregnancy	✓	✓	
Small for Gestational age	<i>Only for LMICs</i>	NA	<i>On the causal pathway for many of the risk factors</i>
Congenital abnormalities	X	NA	Considered as direct cause
Rhesus Disease	✓	✓	
✓ = data available X = no data available. LMIC=Low-Middle income country <i>See WebAppendix for detail</i>			