Stillbirth in Low- and Middle-Income Countries

A conceptual framework

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CONTENTS

- **Background** 4
  - Why a conceptual framework on stillbirth? 4
- **Aim and overview of work** 6
- **Methods** 7
  - Developing and drafting the high-level framework 7
  - Refining and detailing framework domains 7
    - Individual factors 7
    - Health system factors 8
- **Findings** 9
  - High-level framework on factors impacting stillbirth in LMICs 9
  - High-level review of individual factors associated with stillbirth 11
  - Refining and detailing different domains of the framework 12
    - Social determinants and behavioural factor domains 12
    - Medical, obstetric and index pregnancy domains 15
    - Scoping review of delays in receiving adequate care and stillbirth ... 15
- **Summary** 16
- **References** 17
- **Annex** 20
  - Annex 1: Identifying published frameworks of pathways to stillbirth .. 20
    or related outcome of maternal or child mortality
  - Annex 2: Identifying published umbrella and systematic reviews of ... 21
    specific risk factors associated with stillbirth in LMIC settings

BACKGROUND

Over the past two decades, the global stillbirth rate declined from 21.4 per 1,000 total births in 2000 to 13.9 in 2019. While this is a sign of modest progress, there were still an estimated 2.0 million stillbirths in 2019 (1, 2). There are large disparities, both in absolute overall stillbirth rates and in progress towards reducing these deaths, between global regions, between countries in regions, and within countries (2).

Only a few countries – for instance, Australia and the United States – provide subnational and other disaggregated stillbirth data. This means that disparities at subnational level or between different population groups are often obscured by a lack of data. Work is underway to close these data gaps and thus further our understanding of the true burden of stillbirth across settings.

Improved data on the number of stillbirths are vitally needed to track progress towards achieving the vision of the 2030 Agenda for Sustainable Development and ensure that no child is left behind. These data are also critical to monitoring progress toward the Every Newborn Action Plan (ENAP) target of 12 or fewer stillbirths per 1,000 total births in every country by 2030 (3). To ensure we achieve the Sustainable Development Goals and the ENAP target, we must not only improve data on stillbirths, but also deepen our understanding of why these babies are dying and what we can do to prevent these tragic losses.

Why a conceptual framework on stillbirth?

A conceptual framework offers an important tool to map specific factors that can influence stillbirth outcomes. It arms policymakers and health care practitioners with valuable guidance on predictors of stillbirth, thus providing vital information on where interventions are most needed and where they can be most effective.

A more comprehensive understanding of the pathways to stillbirth is important. With progress in reducing these deaths not keeping pace with reductions in child mortality, stillbirth has become an increasingly important public health issue. Today, stillbirths account for a larger share of deaths that took place between 28 weeks gestation and 5 years of age than they did 20 years ago: As of 2019, stillbirths comprised 36 per cent of these losses, an increase from 23 per cent in 2000 (1, 2). But limited knowledge

and misperceptions of the causes of stillbirth stand in the way of solutions, both in closing the stillbirth disparity gap and in ending preventable stillbirth deaths.

Most stillbirths are preventable with improved women's health and access to high quality care along the continuum, from pre-pregnancy and family planning, through antenatal to intrapartum (childbirth) care (4–6). The most significant biomedical causes of stillbirth include antepartum haemorrhage, maternal conditions affecting placental sufficiency and fetal growth (e.g., hypertension and diabetes), infections (e.g., syphilis and group B streptococcus), complications during childbirth, and genetic conditions. But in most settings, data that reflect the health conditions and circumstances that led to a stillbirth are limited (7) – meaning that in many scenarios, policymakers and health practitioners do not have the information at hand to plan and implement interventions.

A stillbirth conceptual framework illustrates expected relationships between variables of interest, how those variables relate to each other, and stillbirth (8), thus fostering understanding of the pathways to stillbirth. A conceptual framework can also guide and inform research that investigates the contribution of a given variable on stillbirth outcomes (accounting for potential confounders) and help pinpoint the predictors (covariates) that could be useful for modelling stillbirth rates.

In addition to the direct importance of this framework for stillbirth, the work described here informs the wider maternal, newborn and child health agenda, and beyond. Fetal health is critical to health throughout the life-course. When compromised fetuses are detected in utero and timely delivery is initiated, stillbirths can be averted. But many of these babies will have increased inpatient care needs during the neonatal period and be at risk of stunting and reduced fat free mass as they mature. While stillbirth prevention is the immediate focus of this work, there are also important outcomes beyond saving babies' lives: When we strengthen our understanding of the pathways to suboptimal fetal health, we are not only helping to avert needless loss of young lives, but we are also improving the health of the next generation.

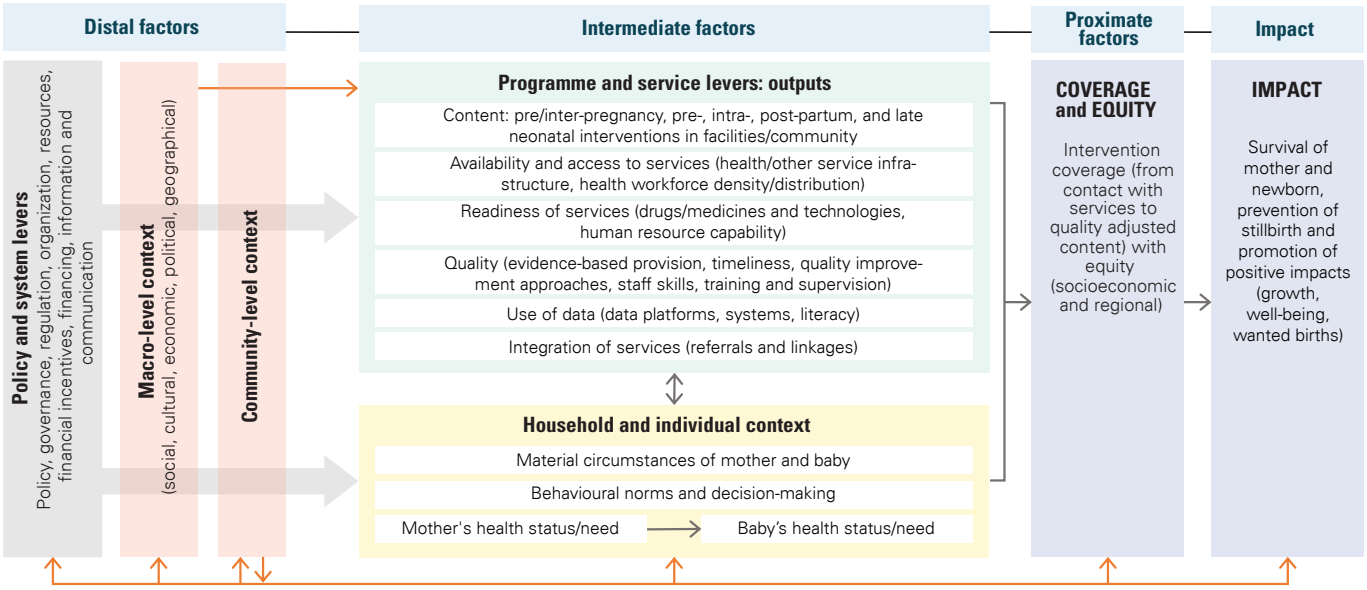
AIM AND OVERVIEW OF WORK

The overall aim of this work is to develop an initial conceptual framework on the specific factors that impact stillbirth in low- and middle-income countries (LMICs). It is designed to go beyond the biomedical causes of stillbirth by exploring the interactions between underlying medical conditions and other proximal and distal factors.

The specific focus here is on LMIC contexts, which accounted for 98 per cent of all stillbirths in 2019. While the underlying biomedical causes of stillbirth may be similar across contexts, access to high quality peri-conceptual, antenatal and obstetric health care varies widely between contexts. Where relevant, some of the background work that contributed to this framework included stillbirths in high-income contexts.

Development of this framework took place in parallel to a broader piece of work undertaken as part of the GATES Exemplars in Global Health programme to develop a holistic framework for research on maternal, late fetal and newborn survival and health (see Figure 1) (9). While the stillbirth-specific framework drew from the Exemplars project, the GATES work was designed to be a more holistic, interdisciplinary overview of the range of factors that explains reductions in mortality.

Figure 1. Holistic framework for research on maternal, late fetal and newborn survival and health, reproduced from Singh et al. (9)



METHODS

Developing and drafting the high-level framework

A draft framework was developed based on the findings of a literature review, which identified previously published frameworks of pathways to stillbirth or related outcome of maternal or child mortality (see Annex 1).

Each selected framework was reviewed in detail and factors potentially relevant to stillbirth were extracted and combined to form a draft high-level framework that highlighted five domains – medical history, obstetric history, index pregnancy factors, social determinants and behavioural determinants (see Figure 2). The resulting high-level framework is meant to be a working document to inform ongoing work on understanding pathways to stillbirth.

Next, a brief review was undertaken to identify previously published umbrella and systematic reviews of specific risk factors associated with stillbirth in LMIC settings to provide further granularity to broad domains included in the high-level framework (see Annex 2). The aim of this review was to select reviews that sought to provide an overview of factors associated with stillbirth in a given context.

Refining and detailing framework domains

This work was undertaken by students from King's College and London School of Hygiene & Tropical Medicine (LSHTM) as part of the PRECISE-DYAD network work on conceptual models, which also includes frameworks for pre-eclampsia, preterm birth and fetal growth restriction.

Individual factors

Domains from the high-level initial framework described above were used to develop a more detailed framework and quantify the evidence and strength of association, adapted from the Hiatt et al. approach for assessing determinants of breast cancer (10). Individual women-baby DYAD potential determinants of stillbirth were divided into the high-level framework's five domains. A sixth domain, biochemical predictors (biomarkers) of stillbirth, was added to be consistent with the other PRECISE-DYAD conceptual models work. To date, work has been completed on the first five domains. Details on cross-cutting health system-related factors from the high-level framework will be considered in future updates to the framework.

Literature searches for all possible direct associations between the direct determinants of stillbirth across each domain were undertaken in June 2021 using a single database (Ovid MEDLINE), covering a 10-year period from March 2011 to May 2021. Searches were repeated separately for each determinant. A hierarchical approach was used to prioritize the evidence: Umbrella review > systematic reviews > observational studies with more than 1,000 participants. The strength of association was assessed using the Harvard Cancer Risk Index (HCRI) (11):

Table 1. Harvard Cancer Risk Index

Strength of association	Relative risk or odds ratio	
	Negative relationship	Positive relationship
Definite	<0.40	≥3.00
Probable	0.40–0.69	1.50–2.99
Possible	0.70–0.89	1.10–1.49
Not significant	0.90–1.09	

The quality of evidence was assessed using GRADE (12–17).

Health system factors

As noted, this more detailed work did not consider cross-cutting health system-related factors, which are known to be important both in terms of the supply-side provision of high quality care and in women's demand for care.

To further understand the impact of delays and quality and content of care gaps experienced by women during pregnancy and delivery, existing literature on the ways in which delays in providing appropriate and timely care at the facility level (during pregnancy and intrapartum) contribute to stillbirths in sub-Saharan Africa was synthesized. Searches of five databases were conducted in June 2021 – Ovid MEDLINE, Embase, CINAHL Plus, Africa-Wide Information and Web of Science – using search terms 'delays and quality of care', 'pregnancy and intrapartum', 'stillbirth' and 'sub-Saharan Africa', and studies published between 2000 and 2021 were included. Data quality of included studies was appraised using the Joanna Brigg's Institute Critical Appraisal tools (18).

FINDINGS

Five relevant frameworks were located based on previous expert knowledge (19–23). In many cases, although these included a framework diagram, they were not labelled as 'conceptual frameworks'. An additional 355 titles and abstracts were screened from the literature review; this led to the identification of a further seven frameworks (24–30), for a total of 12 relevant published frameworks. All included frameworks contributed to the initial high-level framework on factors impacting stillbirth in LMICs.

High-level framework on factors impacting stillbirth in LMICs

The high-level framework developed based on the 12 relevant frameworks included two pathways to stillbirth. The first pathway focuses on suboptimal care. Here, stillbirths occur due to lack of availability of access to optimal care along the continuum, either in a healthy fetus or in a fetus comprised in utero. These stillbirths are potentially preventable through improved access to timely high quality care along the continuum, including adequate monitoring of pregnancy and labour and timely detection and action in case of complications. Most intrapartum and a substantial number of antepartum stillbirths in LMIC contexts occur through this suboptimal care pathway.

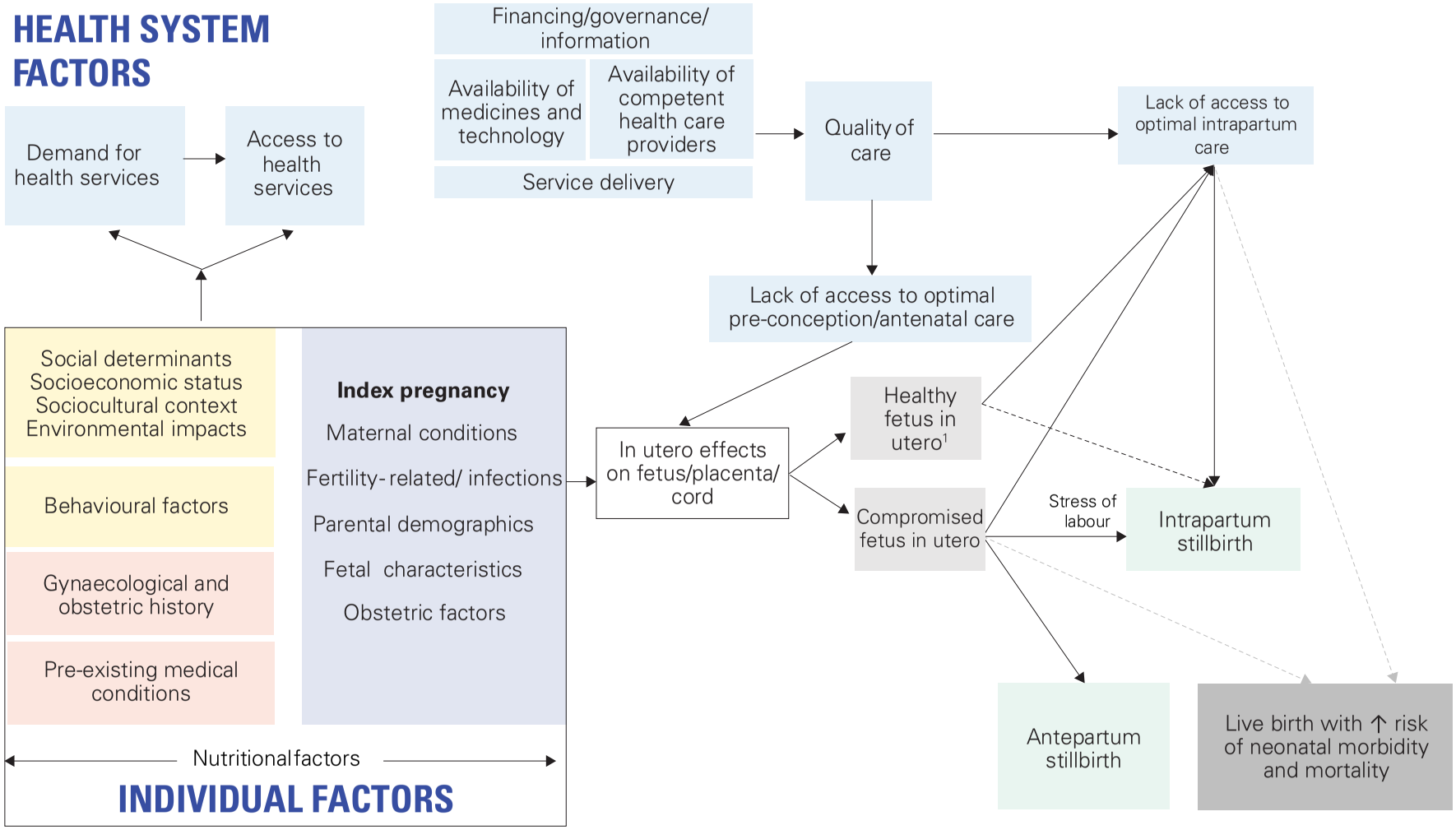
The second pathway focuses on situations where a fetus is compromised and at-risk in utero, yet current routine high quality antenatal care is not able to detect this. In data-rich settings where full investigation of cause of death is possible, these stillbirths are frequently classified as 'unexplained antenatal stillbirths'. These stillbirths are not currently preventable; however, as technologies improve, it is likely that the number of stillbirths in this category will decrease.

In rare instances, a stillbirth occurs in an otherwise healthy fetus due to a catastrophic cord accident and insufficient time to reach emergency care and delivery. This is shown in a footnote to the framework.

These pathways demonstrate the important dynamic interaction between individual women-baby DYAD factors and health system factors. All five of the identified individual-level factor domains – medical history, obstetric history, index pregnancy factors, social determinants and behavioural determinants – may influence either demand or access to health care, as well as have a direct impact on the health of the fetus.

The framework also highlights the close link between in utero fetal health, access to optimal high quality care and neonatal morbidity and mortality. In addition to early impacts on neonatal outcomes, this link can also result in long-term health and developmental impacts through pathways of preterm birth, fetal growth restriction or neurological insults, e.g., due to infections or hypoxia.

Figure 2. High-level framework on factors impacting stillbirth in LMICs



[1]In rare instances, a fetal death resulting in stillbirth may occur in an otherwise healthy fetus due to a catastrophic cord accident with insufficient time to receive care.

High-level review of individual factors associated with stillbirth

The literature review examining risk factors and determinants of stillbirth screened 234 titles and abstracts. A single recent umbrella review was identified that included determinants/risk factors associated with stillbirth worldwide but presented findings relevant to LMIC settings separately from those from high-income countries (31). A further 21 relevant reviews were located (6, 32–49), alongside an unpublished work undertaken by an LSHTM MSc student (50).

Additional searches were carried out to identify evidence for the following factors -- thyroid disorders, SLE, epilepsy, maternal underweight, ambient air pollution, rhesus disease, fetal hydrops, and inter-pregnancy interval – but no evidence was identified from this scope of the review.

A summary table of all associations between categories in different domains of the individual women-baby DYAD part of the draft conceptual framework was created.

Domain	Description	Factors
Gynaecological/ Obstetric history	Previous gynaecological or obstetric history	Female genital mutilation (44), previous adverse pregnancy outcome (stillbirth, preterm birth, or fetal growth restriction) (31), previous caesarean section birth (31)
Medical history	Maternal co-morbidities presenting prior to the index pregnancy	Diabetes mellitus (31), chronic kidney disease (31), sickle cell (31), Sjögren's (31), thyroid disorders (51), hypertensive disorders (31), SLE (52), epilepsy (53), anaemia (34), increased BMI (31), maternal underweight (54), mental health conditions (31)
Index pregnancy	New co-morbidities presenting for the first time during the index pregnancy	Gestational diabetes (31), hypertensive disorders of pregnancy (31, 36), anaemia (34), mental health conditions (31)
	Fertility-related	Primiparity (31), assisted-fertility (e.g., IVF) (31), short inter-pregnancy interval (56, 57), consanguinity (46)
	Infections	McClure et al. review identified 40 pathogens associated with stillbirth, with varying mechanisms such as chorioamnionitis, placental infection, systemic maternal sepsis or direct fetal infections (47) Important infections identified in McClure at al.'s review include: syphilis, malaria, dengue, GBS, rubella, HIV, influenza A (H1N1), zika, hepatitis C and E, HSV, parvovirus, toxoplasmosis, varicella, TB, Ebola. Epidemics/pandemics can impact stillbirth by disrupting health services, e.g., Ebola (58) and COVID-19 (59, 60)
	Parental demographic factors[2]	Maternal age (31), paternal age (31)
	Fetal characteristics	***Fetal characteristics:*** male sex (31), multiple gestation (50), congenital anomalies (46), rhesus incompatibility (55) ***Fetal in utero impacts:*** fetal hydrops (61), fetal growth restriction (31), macrosomia (50), reduced fetal movements (31)
	Obstetric factors	Bleeding in pregnancy (APH) (31), abruption (31), prolonged/obstructed labour (34, 46), cord accidents (34), prolonged pregnancy (6)
	Access to and utilization of high quality health care	Antenatal care attendance (31), contraceptive services (56, 57), use of traditional herbal medications/ uterotonics in the community (62), delayed care seeking (19)

Domain	Description	Factors
Social determinants	The conditions in the places where women and their babies are born, grow, live, work and age that affect the risk of stillbirth	***Socioeconomic status:*** marginalized groups/ethnic minorities (31), social deprivation/inequity (31), urban/rural (31), maternal education (31), geography/ political context and conflict (19) ***Sociocultural context:*** poor water/sanitation, physical workload (19), psychological stress (49), interpersonal violence (19), other sociocultural (19) ***Environmental impacts:*** exposure to external teratogens (19), indoor air pollution (33), ambient air pollution (63), climate impacts (high temperatures) (32, 43)
Behavioural factors	Factors related to lifestyle choices, activities and attitudes that affect the risk of stillbirth	Smoking (31), alcohol (31), smokeless tobacco (31), caffeine consumption (31), alcohol/substance abuse (48), sleep position (48)

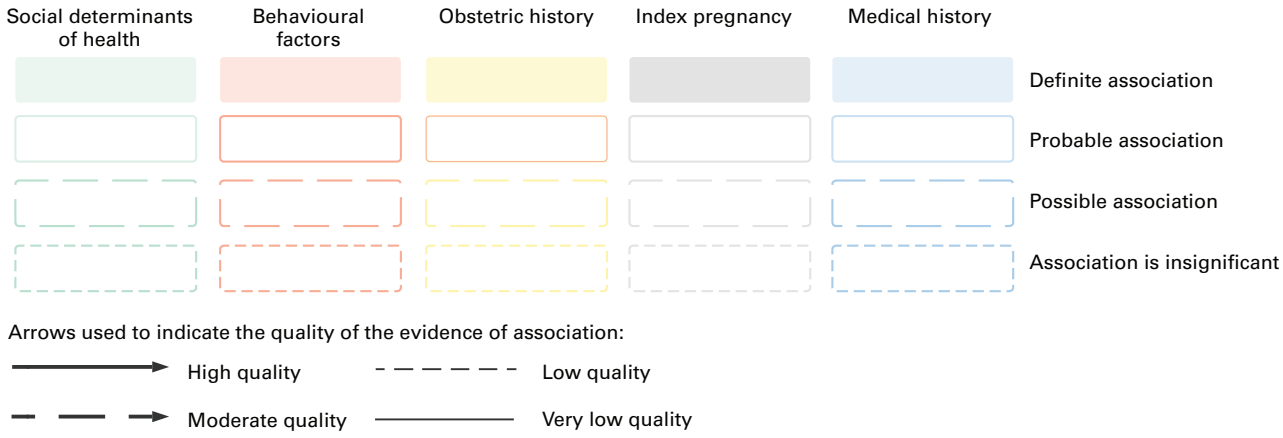
[2] Only demographic factors related to the index pregnancy are listed here. Other demographic factors – such as income and maternal education – are listed under social determinants.
Factors in italics were mentioned in some reviews, but no strong evidence was found during the high-level review.

Refining and detailing different domains of the framework

The section below provides preliminary findings from the ongoing work to detail the different domains of the stillbirth conceptual framework.

Design elements were used to clearly and intuitively display findings in the final conceptual framework. Solid colour shading indicates a definite association found between the factor and stillbirth in the detailed literature review, a solid border with empty cell indicates a probable association, and possible and insignificant associations are indicated by dashed borders (see Figure 3). Different arrows are used to indicate the quality of the evidence of association.

Figure 3. Understanding the visuals used to illustrate the refined conceptual framework for stillbirth

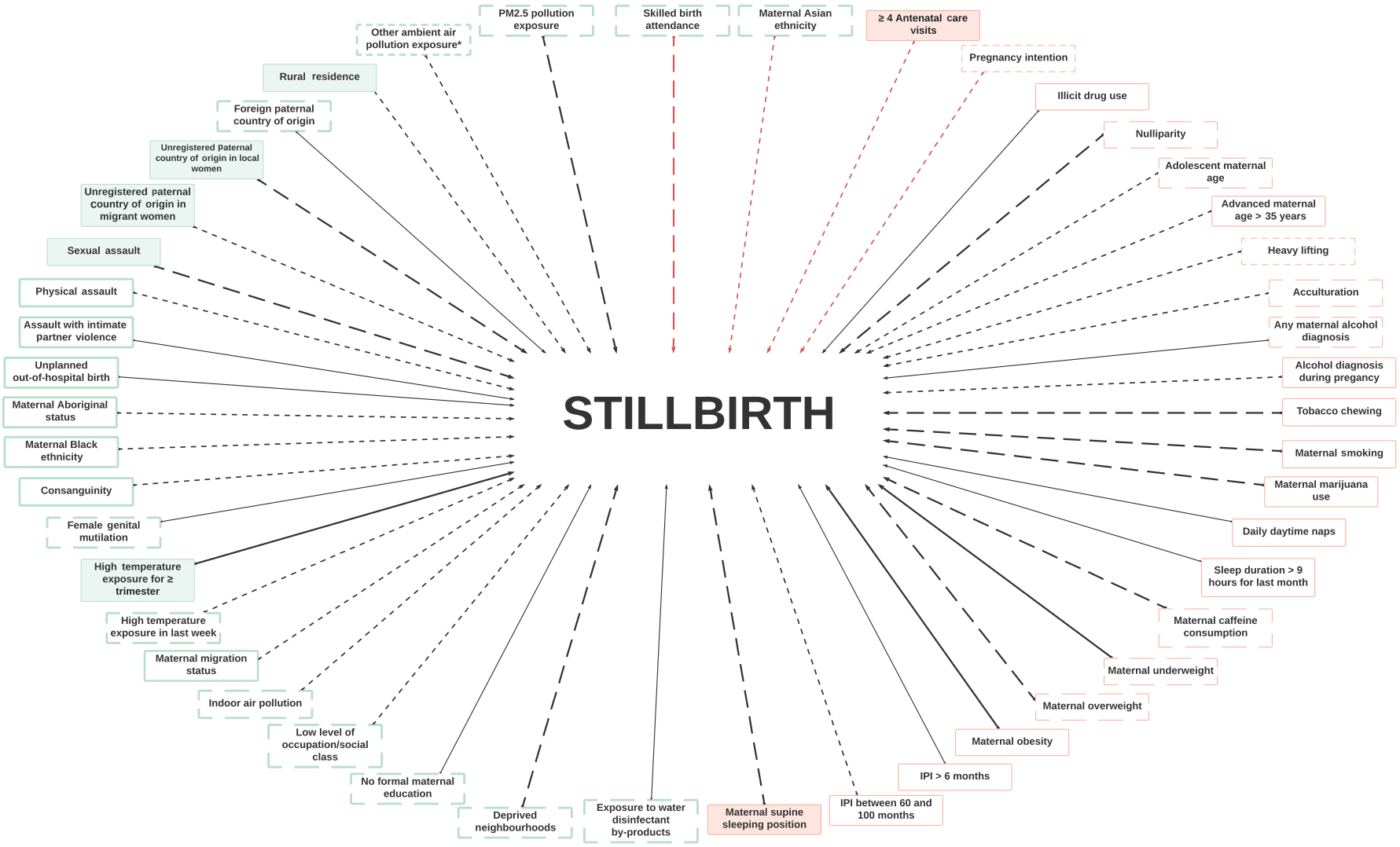


Social determinants and behavioural factor domains

In total, evidence for 20 potential social determinants and 22 behavioural factors was sought. Screening of 2,522 potential umbrella reviews, systematic reviews and observational studies took place. Further determinants were added as relevant.

For 14 determinants, no evidence was found. In total, 34 papers covering 46 determinants were included. The strength of association and quality of the evidence of association for these included determinants is shown in Figure 4.

Figure 4. Overview of social determinants and behavioural factors associated with stillbirth



Source: Dalle Piagge et al. full manuscript write-up in preparation

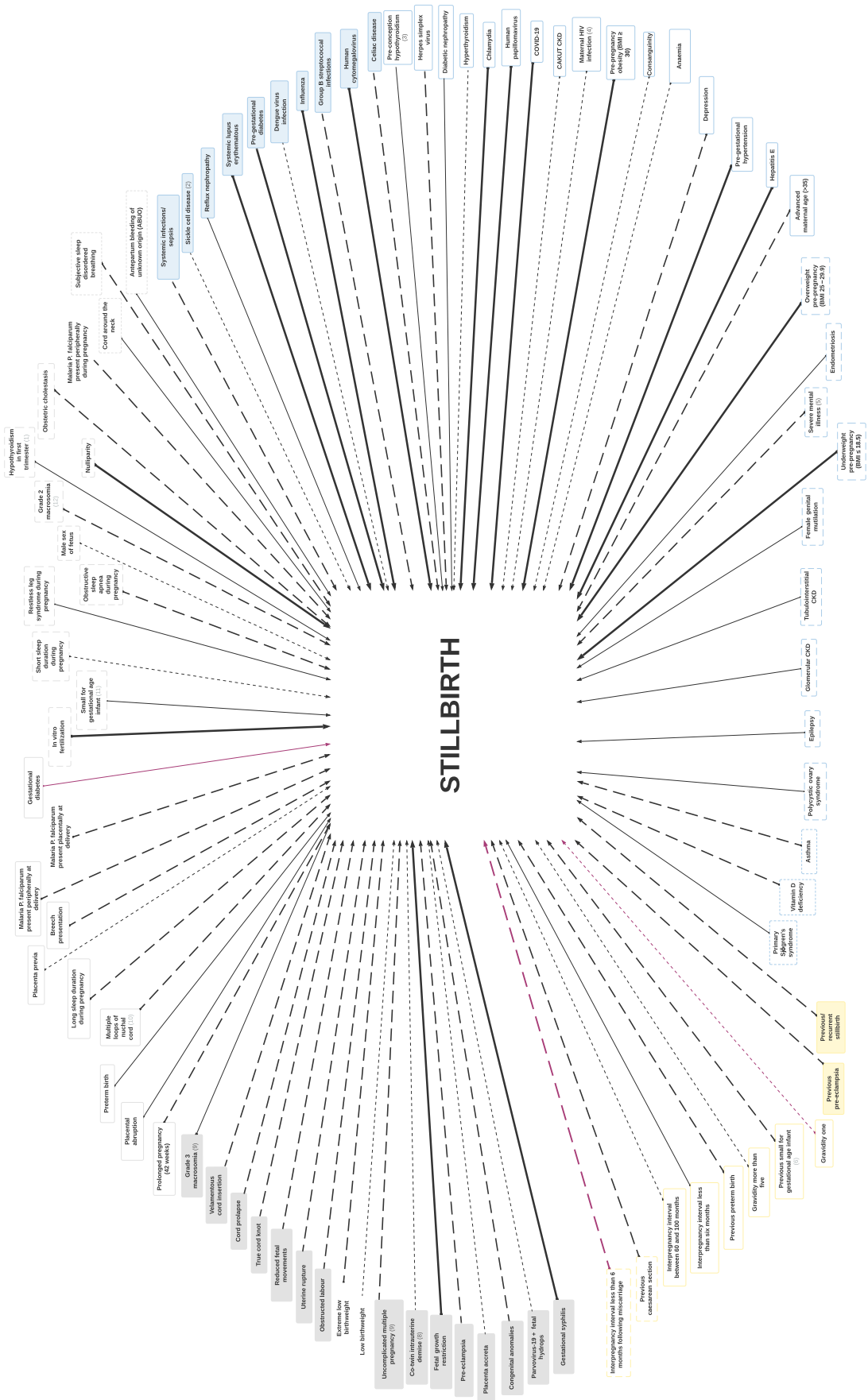


Figure 5. Overview of gynaecological, obstetric, medical and index pregnancy factors associated with stillbirth

Source: Stokes et al. full manuscript write-up in preparation

Medical, obstetric and index pregnancy domains

The initial framework was expanded to 73 potential determinants. Some 4,902 umbrella reviews, systematic reviews and observational studies were screened for evidence.

Based on the literature review, a further six determinants were added (four related to medical history, two to index pregnancy) and 16 determinants were further subdivided, creating 28 determinants.

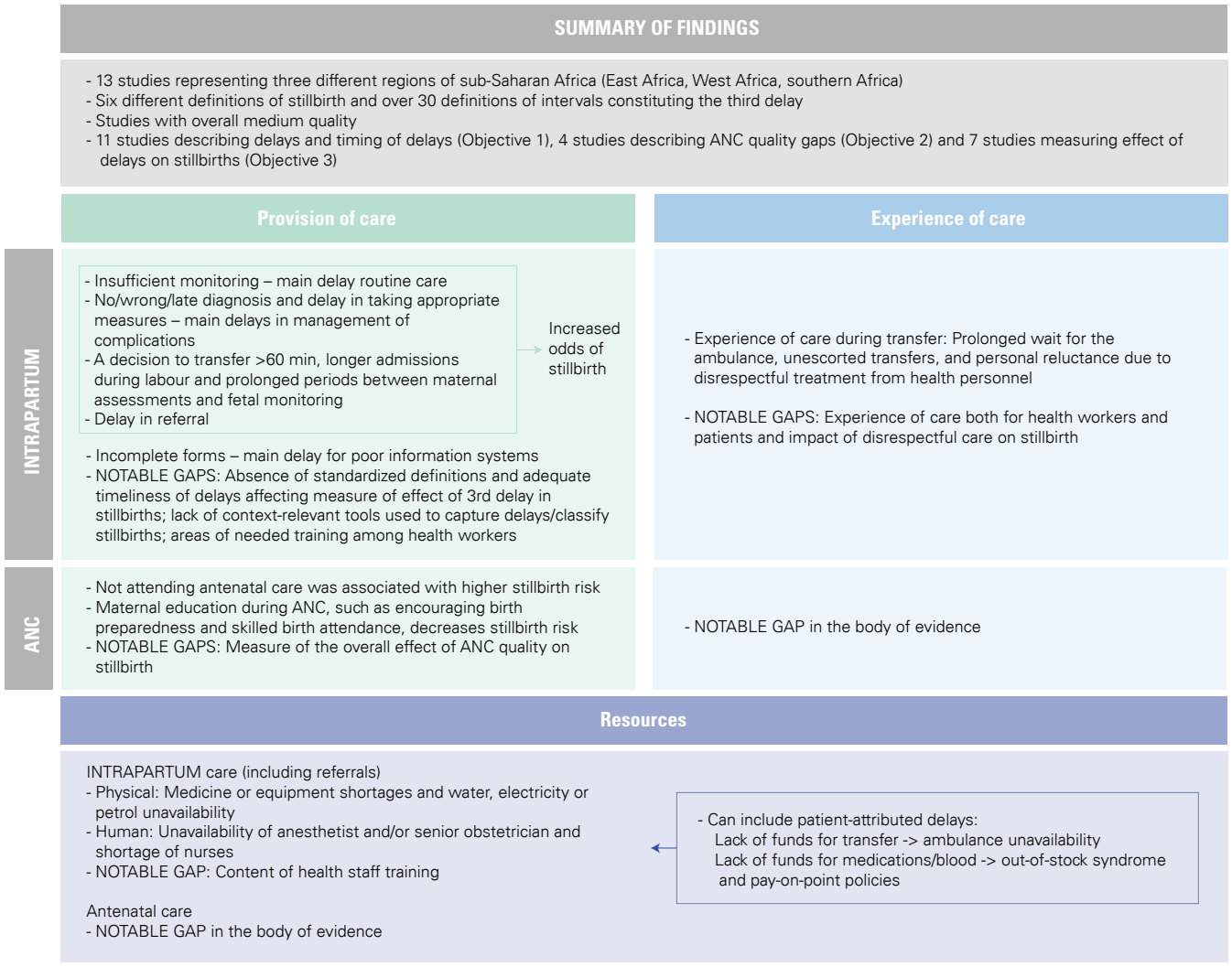
In total, 63 papers covering 81 determinants were included. The strength of association and quality of the evidence of association for these included determinants is shown in Figure 5.

For 10 determinants, no evidence was found. These include eight infections, rhesus disease and eclampsia, which may reflect the limitation of including only papers published since 2011 in the initial search.

Scoping review of delays in receiving adequate care and stillbirth

Overall, 3,882 titles were screened, and 13 studies conducted in sub-Saharan Africa were included. The most common reported causes of delays during intrapartum (childbirth care)

Figure 6: Summary of findings of scoping review of delays in receiving adequate care during pregnancy and childbirth in sub-Saharan Africa and their association with stillbirth



Source: Barreto et al. - in preparation
ANC=antenatal care

associated with stillbirth were inadequate monitoring, inter-facility transfer delay, and inappropriate management of obstetric emergencies. Not attending antenatal care was associated with higher stillbirth risk. Evidence regarding the overall effect of antenatal care quality on stillbirths was ambiguous; however, maternal education during antenatal care, such as encouraging birth preparedness and skilled birth attendance, was shown to decrease stillbirth risk. Evidence gaps were identified on care experiences, absence of standardized definitions and timeliness of delays (see Figure 6).

The review found that delays in providing timely antenatal and intrapartum care are critical modifiable factors that can reduce the high stillbirth rates found in sub-Saharan Africa.

SUMMARY

This work reviewed factors associated with stillbirth relevant to LMIC contexts. The initial framework produced from this review is high level and generic; it seeks to simply and succinctly illustrate the high-level pathways to and complexity of factors associated with stillbirth in a 2-D figure.

While the focus of this work was to produce a framework relevant to LMIC contexts, it should be noted that LMIC contexts vary substantially. The pathways to and factors associated with stillbirth categories shown in the framework are generic to all contexts, including those that are high income, but the contribution of each will vary by setting. For example, health system factors are more likely to be an important contributor to stillbirth in a rural area in a country with a weak health system, while some infections, such as malaria, are limited to some geographical settings only.

It should be noted that the interactions between different factors in each domain are frequently more complex than the depictions in the framework; it can be challenging to categorize potential determinants into specific domains. For example, in fetal characteristics, fetal hydrops may be a complication of an infection in the index pregnancy, such as parvovirus B-19 or rhesus disease. In addition, many proposed determinants in the 'Behavioural factors' category have complex multifaceted causes, e.g., engagement with formal health services; further work is required to refine these.

The work underway to refine and provide more supporting detail for the high-level framework has focused to date on using the epidemiological methods of Hiatt et al. to expand and detail the individual women-baby DYAD-level factors contributing to stillbirth. The initial searches for these reviews were only undertaken from March 2011, thereby limiting the evidence for some important known contributors to stillbirth that are no longer subject to current scientific exploration, such as rhesus disease. Future steps should extend the search for those factors without evidence further back in time.

With regards to health system factors, one scoping review has been undertaken to date to review published reports of delays in receiving adequate care during pregnancy and childbirth in sub-Saharan Africa and their association with stillbirth. This work is currently in progress; however, future work is required to fully capture and refine all health system impacts from the initial high-level framework.

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ANNEX

Annex 1: Identifying published frameworks of pathways to stillbirth or related outcome of maternal or child mortality

A broad search was undertaken using a single database (PubMed) in November 2020. Search terms for 'stillbirth' and 'child death' were combined with terms related to 'conceptual frameworks'.

	Concept	Search terms
1 OR 2	Stillbirth	("stillbirth"[MeSH Terms] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields]) OR ("foetal death"[All Fields] OR "fetal death"[MeSH Terms] OR ("fetal"[All Fields] AND "death"[All Fields]) OR "fetal death"[All Fields])
	Child death	("child mortality"[MeSH Terms] OR ("child"[All Fields] AND "mortality"[All Fields]) OR "child mortality"[All Fields]) OR (("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields]) AND ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields]))
AND		
3 OR 4	3. Conceptual framework	(("concept formation"[MeSH Terms] OR ("concept"[All Fields] AND "formation"[All Fields]) OR "concept formation"[All Fields] OR "conceptualisation"[All Fields] OR "conceptualization"[All Fields] OR "conceptual"[All Fields] OR "conceptualisations"[All Fields] OR "conceptualise"[All Fields] OR "conceptualised"[All Fields] OR "conceptualises"[All Fields] OR "conceptualising"[All Fields] OR "conceptualism"[All Fields] OR "conceptualizations"[All Fields] OR "conceptualize"[All Fields] OR "conceptualized"[All Fields] OR "conceptualizes"[All Fields] OR "conceptualizing"[All Fields] OR "conceptually"[All Fields]) AND ("framework"[All Fields] OR "framework s"[All Fields] OR "frameworks"[All Fields]))
	4. Conceptual model	(("concept formation"[MeSH Terms] OR ("concept"[All Fields] AND "formation"[All Fields]) OR "concept formation"[All Fields] OR "conceptualisation"[All Fields] OR "conceptualization"[All Fields] OR "conceptual"[All Fields] OR "conceptualisations"[All Fields] OR "conceptualise"[All Fields] OR "conceptualised"[All Fields] OR "conceptualises"[All Fields] OR "conceptualising"[All Fields] OR "conceptualism"[All Fields] OR "conceptualizations"[All Fields] OR "conceptualize"[All Fields] OR "conceptualized"[All Fields] OR "conceptualizes"[All Fields] OR "conceptualizing"[All Fields] OR "conceptually"[All Fields]) AND ("model"[All Fields] OR "models"[All Fields] OR "modeled"[All Fields] OR "modeler"[All Fields] OR "modeler s"[All Fields] OR "modelers"[All Fields] OR "modeling"[All Fields] OR "modelings"[All Fields] OR "modelization"[All Fields] OR "modelizations"[All Fields] OR "modelize"[All Fields] OR "modelized"[All Fields] OR "modelled"[All Fields] OR "modeller"[All Fields] OR "modellers"[All Fields] OR "modelling"[All Fields] OR "modellings"[All Fields] OR "models"[All Fields]))

Annex 2: Identifying published umbrella and systematic reviews of specific risk factors associated with stillbirth in LMIC settings

A broad search was undertaken using a single database (PubMed) in May 2021. Search terms for 'stillbirth' were combined with terms related to 'risk factors/determinants' and LMICs. Only reviews or systematic reviews were included.

	Concept	Search terms
1	Stillbirth	("stillbirth"[MeSH Terms] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields]) OR ("foetal death"[All Fields] OR "fetal death"[MeSH Terms] OR ("fetal"[All Fields] AND "death"[All Fields]) OR "fetal death"[All Fields])
AND		
2 OR 3	2. Risk factor	(("concept formation"[MeSH Terms] OR ("concept"[All Fields] AND "formation"[All Fields]) OR "concept formation"[All Fields] OR "conceptualisation"[All Fields] OR "conceptualization"[All Fields] OR "conceptual"[All Fields] OR "conceptualisations"[All Fields] OR "conceptualise"[All Fields] OR "conceptualised"[All Fields] OR "conceptualises"[All Fields] OR "conceptualising"[All Fields] OR "conceptualism"[All Fields] OR "conceptualizations"[All Fields] OR "conceptualize"[All Fields] OR "conceptualized"[All Fields] OR "conceptualizes"[All Fields] OR "conceptualizing"[All Fields] OR "conceptually"[All Fields]) AND ("framework"[All Fields] OR "framework s"[All Fields] OR "frameworks"[All Fields]))
	3. Determinant	(("concept formation"[MeSH Terms] OR ("concept"[All Fields] AND "formation"[All Fields]) OR "concept formation"[All Fields] OR "conceptualisation"[All Fields] OR "conceptualization"[All Fields] OR "conceptual"[All Fields] OR "conceptualisations"[All Fields] OR "conceptualise"[All Fields] OR "conceptualised"[All Fields] OR "conceptualises"[All Fields] OR "conceptualising"[All Fields] OR "conceptualism"[All Fields] OR "conceptualizations"[All Fields] OR "conceptualize"[All Fields] OR "conceptualized"[All Fields] OR "conceptualizes"[All Fields] OR "conceptualizing"[All Fields] OR "conceptually"[All Fields]) AND ("model"[All Fields] OR "models"[All Fields] OR "modeled"[All Fields] OR "modeler"[All Fields] OR "modeler s"[All Fields] OR "modelers"[All Fields] OR "modeling"[All Fields] OR "modelings"[All Fields] OR "modelization"[All Fields] OR "modelizations"[All Fields] OR "modelize"[All Fields] OR "modelized"[All Fields] OR "modelled"[All Fields] OR "modeller"[All Fields] OR "modellers"[All Fields] OR "modelling"[All Fields] OR "modellings"[All Fields] OR "models"[All Fields]))
AND		
4 OR 5 OR 6	4. Low-income countries	("poverty"[MeSH Terms] OR "poverty"[All Fields] OR ("low"[All Fields] AND "income"[All Fields]) OR "low income"[All Fields]) AND ("countries"[All Fields] OR "country"[All Fields] OR "country s"[All Fields] OR "countrys"[All Fields])
	5. Africa	"africa"[MeSH Terms] OR "africa"[All Fields] OR "africa s"[All Fields] OR "africas"[All Fields]
	6. South Asia	"south asia"[Journal] OR ("south"[All Fields] AND "asia"[All Fields]) OR "south asia"[All Fields]
AND review or systematic review		

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