



Making stillbirths visible: a systematic review of globally reported causes of stillbirth

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Background Stillbirth is a global health problem. The World Health Organization (WHO) application of the International Classification of Diseases for perinatal mortality (ICD-PM) aims to improve data on stillbirth to enable prevention.

Objectives To identify globally reported causes of stillbirth, classification systems, and alignment with the ICD-PM.

Search strategy We searched CINAHL, EMBASE, Medline, Global Health, and Pubmed from 2009 to 2016.

Selection criteria Reports of stillbirth causes in unselective cohorts.

Data collection and analysis Pooled estimates of causes were derived for country representative reports. Systems and causes were assessed for alignment with the ICD-PM. Data are presented

by income setting (low, middle, and high income countries; LIC, MIC, HIC).

Main results Eighty-five reports from 50 countries (489 089 stillbirths) were included. The most frequent categories were Unexplained, Antepartum haemorrhage, and Other (all settings); Infection and Hypoxic peripartum (LIC), and Placental (MIC, HIC). Overall report quality was low. Only one classification system fully aligned with ICD-PM. All stillbirth causes mapped to ICD-PM. In a subset from HIC, mapping obscured major causes.

Conclusions There is a paucity of quality information on causes of stillbirth globally. Improving investigation of stillbirths and standardisation of audit and classification is urgently needed and should be achievable in all well-resourced

settings. Implementation of the WHO Perinatal Mortality Audit and Review guide is needed, particularly across high burden settings.

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Keywords cause of death, classification, ICD, Stillbirth, systems.

Tweetable abstract Urgent need to improve data on causes of stillbirths across all settings to meet global targets.

Linked article This article is commented on by RL Goldenberg, p. 225 in this issue. To view this article visit <https://doi.org/10.1111/1471-0528.14984>.

Plain Language Summary

Background and methods

Nearly three million babies are stillborn every year. These deaths have deep and long-lasting effects on parents, healthcare providers, and the society. One of the major challenges to preventing stillbirths is the lack of information about why they happen. In this study, we collected reports on the causes of stillbirth from high-, middle-, and low-income countries to: (1) Understand the causes of stillbirth, and (2) Understand how to improve reporting of stillbirths.

Findings

We found 85 reports from 50 different countries. The information available from the reports was inconsistent and often of poor quality, so it was hard to get a clear picture about what are the causes of stillbirth across the world. Many different definitions of stillbirth were used. There was also wide variation in what investigations of the mother and baby were undertaken to identify the cause of stillbirth. Stillbirths in all income settings (low-, middle-, and high-income countries) were most frequently reported as *Unexplained*, *Other*, and *Haemorrhage (bleeding)*. *Unexplained* and *Other* are not helpful in understanding why a baby was stillborn. In low-income countries, stillbirths were often attributed to *Infection* and *Complications during labour and birth*. In middle- and high-income countries, stillbirths were often reported as *Placental complications*.

Limitations

We may have missed some reports as searches were carried out in English only. The available reports were of poor quality.

Implications

Many countries, particularly those where the majority of stillbirths occur, do not report any information about these deaths. Where there are reports, the quality is often poor. It is important to improve the investigation and reporting of stillbirth using a standardised system so that policy makers and healthcare workers can develop effective stillbirth prevention programs. All stillbirths should be investigated and reported in line with the World Health Organization standards.

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Introduction

The global stillbirth rate (≥ 28 completed weeks' gestation) is estimated to be 18.4 per 1000 births,¹ or around 2.6 million stillbirths each year.¹ The World Health Organization's (WHO's) *Every Newborn: An Action Plan To End Preventable Deaths* aims to reduce the stillbirth rate to 12 or fewer per 1000 births by 2030 in every country, and for countries already meeting this target to reduce equity gaps.² However, with an estimated annual reduction rate of 2.0% between 2000 and 2015,¹ half that for neonatal deaths, progress has been slow. Identifying interventions to achieve such a target would be facilitated by cross-country and inter-country comparisons of the causes of stillbirth. Moreover, while national neonatal causes of death are regularly

published through the United Nations,^{1,3} there is currently no systematic global reporting of causes of stillbirth. The WHO recommends use of the *International Statistical Classification of Diseases and Related Health Problems (ICD)*⁴ for classification of perinatal deaths for international reporting.⁵ However, limitations in ICD for classifying stillbirths⁶ has resulted in numerous disparate systems currently being in use,⁷ thus limiting global comparisons. In 2016, WHO released *ICD Perinatal Mortality (ICD-PM)* as part of the WHO *Perinatal Mortality Audit and Review* guide.⁸ The ICD-PM is an application of ICD and holds promise as an important step in improving global and local reporting of causes of stillbirths and neonatal deaths.⁹ At a minimum, the ICD-PM aims to collect timing of death and clinically defined causes and associated conditions.

Objectives

Following on the introduction of the ICD-PM, we aimed to identify globally reported causes of stillbirth in order to support progress toward the stillbirth rate target in the WHO's *Every Newborn* action plan. The specific objectives were to:

- 1 describe the current status of global reporting of stillbirth causes, including reported causes and classification systems used
- 2 pool results from country representative reports to identify commonly reported causes of stillbirth, stratified by income setting (high-, middle-, and low-income)
- 3 assess alignment of systems used and reported causes of stillbirths with the ICD-PM for country representative reports.

Methods

This systematic review was conducted and reported according to the PRISMA checklist.¹⁰ The protocol has not been published. Two authors independently undertook screening of reports, selection, data extraction, and quality assessment.

Eligibility criteria

All published and unpublished cohort and cross-sectional reports from 1 January 2009 to 31 December 2016 that presented causes of stillbirth were eligible. Reports were excluded if they: included non-consecutive or selected subgroups, e.g. preterm; aimed only to identify risk factors or did not provide data on causes in an extractable format (for complete study selection, see Figure S1).

Information sources

We searched PubMed, Global Health, Cinahl, Medline, and Embase with no language restrictions. We identified national reports through web-based systematic searches (Appendix S1) and cross-referenced included reports.

Study selection

Titles and abstracts of identified reports were screened for eligibility; full text papers were retrieved if potentially eligible or if eligibility could not readily be determined from the abstract. All reports presenting causes of stillbirth were included to address Objective 1. To address Objectives 2 and 3, the most recent national reports for each country were selected. If a national report was unavailable, a report was selected on the following criteria (in descending order): (1) population-based report with the largest number of stillbirths; (2) multi-centre health facility report covering the largest population.

Data extraction

A purpose-built data extraction form was used. For details on data items and definitions used, see Appendix S2.

Grouping reported stillbirth causes

The development of categories and mapping of reported causes of stillbirth to those categories were undertaken by a panel including maternal fetal medicine specialists (GG, BS, DE), a pathologist (RL), and an epidemiologist (VF), with guidance from The Amsterdam Classification Workshop¹¹ members. Categories were created by 'clustering' reported causes into 15 clinically meaningful groups for stillbirth prevention ('global categories') (Table S1). With the addition of 'Placental conditions', these categories generally coincided with previously suggested major causal groupings by Lawn et al.¹² We did not attempt to differentiate causes from associated conditions (Table S1).

Quality assessment

Quality assessment of country representative reports included in the pooled analysis of reported causes was performed using an adapted version of the *Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data*¹³ (Appendix S3). An overall quality rating was derived for each report (low, medium, or high quality). For subgroup analyses of 'good' quality reports, we combined data from reports assessed as high and medium quality.

Data presentation and analysis

Data were presented by income setting using World Bank groupings¹⁴ of low and lower-middle [LIC; Gross National Income (GNI) \leq \$3,955], upper-middle (MIC; GNI \$3,956–\$12,235), and high (HIC; GNI \geq \$12,236). Categories of stillbirth causes were presented as proportions of the total number of stillbirths classified. Results from country representative reports were statistically pooled to identify commonly reported causes stratified by country groupings. Analyses were done in R using the meta package¹⁵ with 95% prediction intervals (PI)^{16–18} (Appendix S4). Subgroup analyses by report quality and type of system (ICD versus clinical classification systems) were planned a priori. See Appendix S2 for definition of clinical classification systems⁷ and criteria for alignment of classification systems with ICD-PM.

Each reported cause was mapped to the relevant ICD-PM major category. The ICD-PM includes five major maternal condition categories (M1–5) and 13 fetal categories, six with antepartum timing (A1–6) and seven with intrapartum timing (I1–7).⁵ For the Unknown (U) timing category, we included the categories: U1, Congenital malformations, deformations, and chromosomal abnormalities; U2, Infection; U3, Other specified disorder; U4, Disorders related to fetal growth; U5, Death of unspecified cause. We added one category, 'Other', to all timings to accommodate the causes without ICD-PM coding.

Table 1. Characteristics of included papers. By income setting (85 reports; 489 089 stillbirths)

	All reports				Country representative reports			
	HIC <i>n</i> = 37 <i>n</i> (%)	MIC <i>n</i> = 20 <i>n</i> (%)	LIC <i>n</i> = 28 <i>n</i> (%)	Total <i>n</i> = 85 <i>n</i> (%)	HIC <i>n</i> = 15 <i>n</i> (%)	MIC <i>n</i> = 11 <i>n</i> (%)	LIC <i>n</i> = 7 <i>n</i> (%)	Total <i>n</i> = 33 <i>n</i> (%)
Countries included	20	14	15	49	15	11	7	33
Stillbirths classified	44 676	431 203	13 197	489 089	19 238	429 666	5629	454 533
Stillbirth definition								
20–24 weeks	29 (78)	10 (50)	5 (18)	44 (52)	13 (87)	4 (36)	0	17 (52)
28 weeks	2 (5)	6 (30)	19 (68)	27 (32)	2 (13)	3 (27)	4 (57)	9 (27)
Unknown	6 (16)	4 (20)	4 (14)	14 (16)	0	3 (27)	2 (29)	5 (15)
Terminations								
Excluded	9 (24)	2 (10)	0	11 (13)	2 (13)	0	0	2 (6)
Unknown	19 (51)	14 (70)	25 (89)	58 (68)	7 (47)	8 (73)	6 (86)	21 (64)
Multiple pregnancies								
Excluded	5 (14)	1 (5)	3 (11)	9 (11)	1 (7)	0	1 (14)	2 (6)
Unknown	11 (30)	12 (60)	8 (29)	31 (36)	4 (27)	8 (73)	1 (14)	13 (39)
Setting								
Population based	21 (57)	12 (60)	8 (29)	41 (48)	15 (100)	11 (100)	6 (86)	32 (97)
Hospital based	16 (43)	8 (40)	19 (68)	43 (51)	0	0	1 (14)	1 (3)
Unknown	0	0	1 (4)	1 (1)	0	0	0	0
Language								
English	33 (89)	7 (35)	26 (93)	66 (78)	11 (73)	2 (18)	6 (86)	19 (58)
Non-English	4 (11)	13 (65)	2 (7)	19 (22)	4 (27)	9 (82)	1 (14)	14 (42)
Classification systems								
ICD	14 (38)	7 (35)	3 (11)	24 (28)	9 (60)	7 (64)	1 (14)	17 (52)
Clinical classification system	20 (54)	6 (30)	15 (54)	41 (48)	6 (40)	2 (18)	3 (43)	11 (33)
No system	3 (8)	7 (35)	10 (36)	20 (24)	0	2 (18)	3 (43)	5 (15)

HIC, high-income countries; ICD, International Classification of Diseases; LIC, low-income countries; MIC, middle-income countries; Terminations, termination of pregnancy.

We calculated the proportions of stillbirths that could be mapped to a fetal cause and/or a maternal condition in ICD-PM. Mapping of data from good quality HIC reports to ICD-PM was compared descriptively with the 15 global categories.

Results

Of the 7415 abstracts screened for eligibility, 909 full-text papers were reviewed for inclusion and 824 records were excluded because: they did not discuss stillbirth (396); they contained no extractable data (217); they dealt only with sub-populations (145); or they included risk factors only (12) (for complete study selection, see Figure S1). Eighty-five reports (LIC 28, MIC 20, HIC 37) covering a total of 489 089 stillbirths were included in the review (LIC 13 197, MIC 431 216, HIC 44 676). Thirty-three country representative reports classifying 454 533 stillbirths were included in the pooled analysis of causes and mapping to ICD-PM.

Global stillbirth reporting

Description of included reports

The 85 included reports originated from 50 countries. Reports were published in English (66) and other languages (19; Table S2). Eleven reports excluded terminations of pregnancy. Half of the reports (including 2.4% of all stillbirths) were from hospital settings (LIC, 19 reports/7419 stillbirths; MIC, 8 reports/1134 stillbirths; HIC, 16 reports/3240 stillbirths) (Table 1; for full details, see Table S2).

Definitions of stillbirth

Stillbirth was defined in 71 reports (84%) using 34 discrete definitions (Figure S2). The majority of HIC reports (78%) used a lower gestational age limit of 20–24 weeks, while the majority of LIC reports (68%) used 28 weeks (Table 1).

Data available to classifiers

Systematic prospective perinatal mortality audits were used in 21 reports (LIC 2, MIC 4, HIC 15), of which 12 were

Figure 1. Proportion of stillbirths in each category for all studies. By income setting (85 reports; 489 089 stillbirths). (A) Reports from high-income countries (HIC): 37 reports with 44 676 stillbirths. (B) Reports from middle-income countries (MIC), 20 reports with 431 216 stillbirths. (C) Reports from low-income countries (LIC): 28 reports with 13 197 stillbirths. APH, antepartum haemorrhage; CA, congenital anomalies; FGR, fetal growth restriction; HT, hypertension; Hyp, hypoxic peripartum death; Inf, infection; Mat, maternal conditions; Other, other unspecified condition; Plac, placental conditions; SP, spontaneous preterm; SPF, specific fetal/placental condition; ToP, termination of pregnancy, unspecified; Umb, umbilical cord; UnC, unable to classify; Unex, unexplained.

hospital audits; seven used comprehensive investigation protocols (all from HIC) (Table S2). In 40 reports, retrospective audit data were used; 18 of these (LIC 2, MIC 6, HIC 10) sourced causes from *Civil Registration and Vital Statistics* (CRVS). Sixteen reports (LIC 13, MIC 3) were prospective studies; eight of these, all from LIC, used verbal autopsy. Reported autopsy rates in 20 reports [MIC 3 (14%), HIC 17 (47%)] ranged from 2.7 to 100%. In over half of the reports (55%) it was unclear whether autopsy had been performed. Placental pathology examination rates were included in 15 reports (18%) (none in LIC), with rates ranging from 22 to 100%. For full details on data available, see Table S2.

Classification systems

Twenty-one clinical classification systems^{19–39} were used in 41 of the 85 reports (LIC, 15 reports covering 30% of stillbirths; MIC, 6 reports covering 5% of stillbirths; HIC, 20 reports covering 27% of stillbirths). The ICD was used more frequently in HIC (14 reports covering 72% of stillbirths) and MIC (7 reports covering 94% of stillbirths) than LIC (3 reports covering 2% of stillbirths) (Table 1). The remaining 20 reports listed causes of death without reference to any classification system. Areas of origin for the 21 clinical systems are shown in Table S3. Three-quarters of the systems allow a single primary cause of death, and half the systems allow associated factors to be recorded (Table S4). Five systems provide comprehensive definitions of causes,^{21,28,31–33} and 13 systems provide rules for assigning cause of death (See Table S4 for full details on clinical classification systems).

Globally reported categories of stillbirth

The 85 included reports presented causes of stillbirth using 860 unique terms. These were grouped into 15 global categories and 46 minor categories, of which eight major categories were common to over half (53%) of the reports (Table S5).

Congenital anomalies was the most frequently reported category, included in 93% of all reports. The proportion of stillbirths assigned to this category ranged from 1.4% in Nigeria⁴⁰ to 64.4% in China⁴¹ (Figure 1, Table S5). The second category was *Unexplained*, included in 82% of all reports, ranging from 0.3% in Turkey²⁶ to 82.0% in Japan.⁴² *Maternal conditions* were included in 64% of all reports, with frequencies ranging from 0.6% in Ireland⁴³ to 36.5% in Italy²⁹ (Figure 1, Table S5).

The proportions of categories also differed across type of classification system. The most commonly categories for

reports using the ICD included *Other unspecified condition* (68% of reports) and *Hypoxic peripartum death* (64%), whereas for clinical systems these included *Antepartum haemorrhage* (72%) and *Infection* (67%).

Country representative reports

Description of included reports

Thirty-three reports classifying 454 533 stillbirths were included in the pooled analysis: seven LIC (5629 stillbirths), 11 MIC (429 666 stillbirths), and 15 HIC (19 238 stillbirths). Twenty-one reports included $\geq 95\%$ of total stillbirths in the country during the reporting period, one report included 72%, three included 6–49%, and eight included $\leq 5\%$ (Figure S3). In two reports (6%), terminations of pregnancy were excluded, and in 21 (64%), no reference was made to terminations. The ICD was used mainly in HIC and MIC reports (60 and 64%, respectively, versus 14% of LIC reports; Table 1, Table S2).

Quality assessment identified 13 good-quality reports (29% of all LIC reports, 36% of all MIC reports, 47% of all HIC reports); only one of these was high-quality.⁴⁴ The remaining reports were assessed as low-quality (Table S6, Figure S4).

Pooled estimates of commonly reported causes of stillbirths

The top five categories by frequency for each country grouping are shown in Figure 2. *Unexplained* was the top category across all settings, with pooled estimates ranging from 31.2 to 43.7% (Tables S7 and S8). Two additional categories were amongst the top five across all settings: *Other unspecified conditions* (9.3–11.6%) and *Antepartum haemorrhage* (8.4–9.3%; Tables S7, S9 and S10). In LIC, *Infection* (15.8%) and *Hypoxic peripartum death* (11.6%; Tables S7, S11 and S12) were also amongst the top five. In both HIC and MIC settings, *Placental conditions* (14.4 and 13.7%, respectively) ranked in the top five, with *Congenital anomalies* as the remaining category in HIC (14.0%) and *Specific fetal/pregnancy pathology* in MIC (11.0%) (Tables S7, S13–S15).

Details of pooled analyses of *Umbilical cord complications*, *Maternal conditions*, *Spontaneous preterm*, *Hypertension*, *Fetal growth restriction* and *Terminations* are presented in Tables S16–S21.

Subgroup analysis

Owing to insufficient data, subgroup analysis by report quality was only possible for HIC. The proportion of *Unexplained*

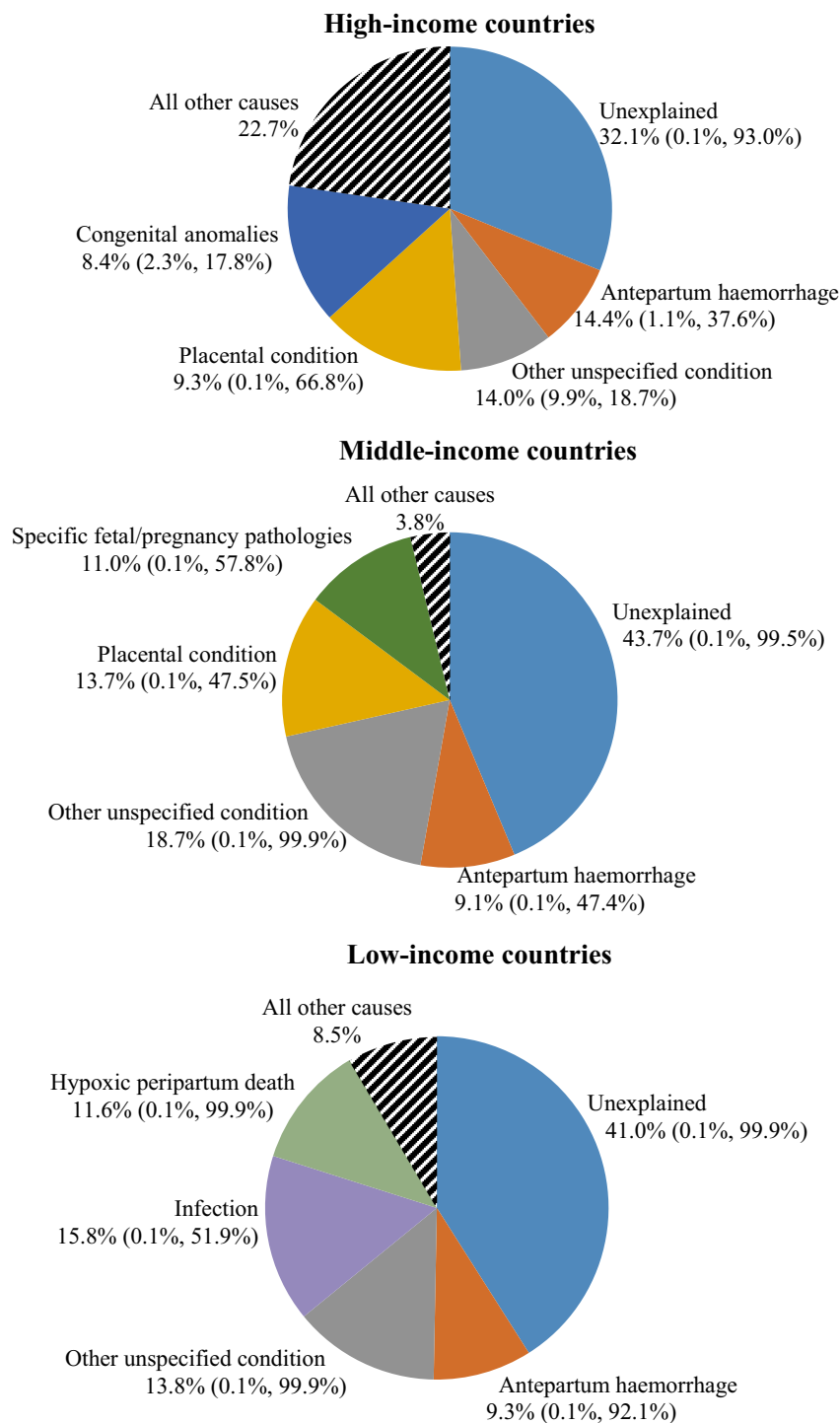


Figure 2. Top five pooled estimates of the global categories of stillbirth. Country-representative reports by income setting (33 reports, 454 533 stillbirths). Data presented as point estimate (95% prediction interval).

(15.4% versus 31.6%) and *Other unspecified conditions* (1.6% versus 9.3%) was lower in good quality reports versus all reports (Tables S8 and S9). Subgroup analyses by system type showed higher proportions of *Antepartum haemorrhage* using clinical

systems (14.1%) than using ICD (4.4%) in MIC (Table S10). Use of clinical systems resulted in lower proportions of *Other unspecified conditions* (1.6%) and *Unexplained* (17.7%) than use of ICD (13.2 and 43.4%, respectively) in HIC (Tables S9 and S8).

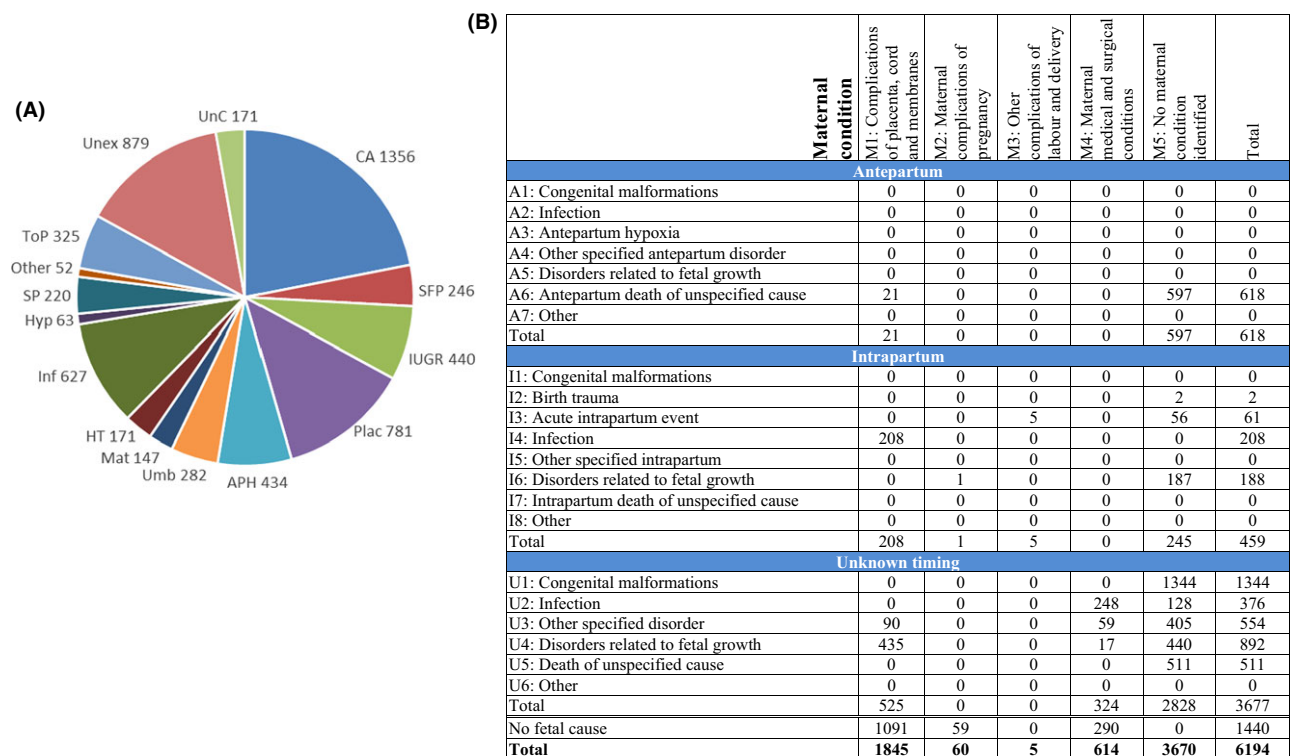


Figure 3. Mapping of causes from good quality reports using clinical classification systems from high income countries (5 reports; 6,194 stillbirths). (A) Grouping of causes of stillbirths into 15 global categories. (B) Stillbirths mapped to the ICD-PM matrix. APH, antepartum haemorrhage; CA, congenital anomalies; FGR, fetal growth restriction; HT, hypertension; Hyp, hypoxic peripartum death; Inf, infection; Mat, maternal conditions; Other, other unspecified condition; Plac, placental conditions; SFP, specific fetal/placental condition; SP, spontaneous preterm; ToP, termination of pregnancy, unspecified; Umb, umbilical cord; UnC, unable to classify; Unex, unexplained.

Alignment with the ICD-PM

Alignment of clinical classification systems with the ICD-PM

Of the 21 classification systems used, only Codac²⁰ was fully aligned with the ICD-PM. Four systems met two of the three criteria used to assess alignment, and 14 systems scored 0.5–1.5 out of a maximum of 3 (Table S3, Figure S5).

Mapping of reported causes to ICD-PM

Nearly all the 454 533 stillbirths reported in the 33 country representative reports were mapped to an ICD-PM fetal or maternal category, or both. Causes for 831 stillbirths (0.2%) mapped to ICD-PM neonatal rather than fetal codes (for example, ‘neonatal aspiration syndrome’). There were 264 480 stillbirths (58%) mapped to a fetal but not a maternal ICD-PM cause, and 140 319 (31%) to a maternal but not a fetal ICD-PM cause; 49 734 stillbirths (11%) were mapped to both (Tables S22 and S23).

Of the 204 545 stillbirths in the global category *Unexplained*, 113 558 (56%) were mapped to the ICD-PM category *Unknown timing unspecified* (no maternal condition), 90 335 (44%) to *Antepartum hypoxia* (no maternal condition), 602

(0.3%) to *Antepartum unspecified* (no maternal condition), and 50 (0.02%) to maternal condition *Other complications of labour and delivery* (no fetal cause) (Tables S22 and S23).

The global causes from the best available data (good quality reports using clinical classification systems in HIC: five reports, 6194 stillbirths) were mapped to ICD-PM. The global categories reflecting underlying placental causes of *Antepartum haemorrhage* and *Placental condition* (insufficiency) accounted for 20%, and *Intrauterine growth restriction* for 7% of stillbirths (Figure 3). When mapped to the ICD-PM, these global categories are included within the major maternal category *Complications of Placenta, cord, and membranes* and the fetal category *Disorders related to fetal growth*, accounting for 30 and 17% of stillbirths, respectively (Figure 3).

Discussion

Main findings

From 85 reports presenting causes of nearly half a million stillbirths from 50 countries and all income settings, we identified 15 major causal categories from nearly 900 causal terms; eight categories were common to the majority of

reports. Despite this overarching commonality, we found wide variation in frequency of stillbirth categories and in the systems used to classify them, with generally poor-quality data. Underlining one of the key challenges of achieving the *Every Newborn* action plan stillbirth target are the high proportions of stillbirths in all income settings recorded without information to guide prevention (*Unexplained* and *Other unspecified conditions*).

Strengths and limitations

We sought to include the most detailed causes of stillbirth available to allow identification of common groupings, and ultimately to enable consistent reporting across settings. In line with WHO recommendations^{4,5} and to maximize the utility of the data for prevention strategies, we excluded reports that assigned more than one cause of stillbirth and excluded all those reported as associated only. This may have resulted in a loss of information and limited our ability to assess the full value of the ICD-PM, which aims to record both a fetal and a maternal condition for every stillbirth. The need to assign multiple causes for some stillbirths has been highlighted. Further, the distinction between causes and associated conditions is often poorly defined,²⁷ and in this review, many reported 'causes' are not recognised as causal conditions. Further, although we imposed no language restrictions, we may have missed some reports by using English-language search terms.

Interpretation

Data quality

Data quality was generally poor, with only a small number of reports based on high-quality perinatal mortality audit. Further, many reports did not provide sufficient detail to adequately assess quality. As in other publications,^{1,6,45} we found global comparisons problematic because of differing definitions and systems. The inability to identify terminations of pregnancies in reporting of stillbirth causes is problematic: many are terminated as a consequence of congenital anomalies,⁴⁶ some of which may not have resulted in stillbirth.

Global causes of stillbirth

Results of the pooled analysis enabled comparisons of stillbirth causes across settings, providing additional evidence for key areas for prevention. The relatively high proportion of stillbirths attributed to intrapartum hypoxia (*Hypoxic peripartum*) in LIC versus HIC and MIC is in line with recent evidence from low- and middle-income countries (LMIC)^{47,48} and confirms the urgency of improving care during labour and birth, when half of all global stillbirths occur.^{1,3,47,49} Further, as in other reports,^{47,48} we identified infection as a top cause of stillbirths in LIC, confirming the

importance of infection prevention and management.^{3,49,50} Our findings clearly highlight the importance of placental conditions as a major contributor to stillbirths in all settings, consistent with other recent studies.^{47,51} However, many placental conditions were ill-defined and the causal links unclear (for instance delayed villous maturation).^{52,53} Many conditions that lead to stillbirth are also linked to neonatal deaths, and both must therefore be accommodated within a single system to ensure optimal pregnancy care and outcomes.⁵⁴

ICD-PM and progress towards global reporting

We confirmed findings of other studies, showing numerous disparate systems for classification of stillbirths are in use globally,^{6,45,55} further highlighting the need for a globally effective classification system. A recent consensus described user-identified characteristics for such a system,⁵⁶ but no existing systems meet these characteristics.⁵⁷ Further, robust evaluation of system performance is limited.⁷ The ICD-PM is the first system intended for global use in classification of perinatal deaths,^{5,58–60} aiming to facilitate comparisons by improving perinatal mortality data, particularly in high-burden settings. While evaluation of the performance of ICD-PM is currently limited, retrospective application to datasets in the UK and South Africa highlighted its values and provided insights to future improvements.⁵⁹ In our dataset, all causes of stillbirths reported globally could be accommodated within the ICD-PM. However, our mapping of causes from good quality reports in HIC using clinical classification systems highlights that classification system requirements differ across settings. Meeting the needs of diverse settings is essential for global comparisons to identify important variation and inform programmatic change to reduce deaths.

The WHO publication *Making Every Baby Count*,⁸ a perinatal mortality audit and review guide, provides a tool to initialize audits in low-income settings using the ICD-PM for classifying perinatal deaths. The ICD-PM maps ICD-10 codes to an underlying fetal cause of antepartum, intrapartum, or unknown timing, and a maternal condition; thus, data collection must include timing as well as a fetal and a maternal condition. While this approach aims to capture information on stillbirths from low resource settings (either cause and/or associated conditions), the ICD-PM faces challenges owing to its ICD-10 provenance, including insufficient differentiation of causes from associated conditions, and insufficient detail on maternal conditions.⁹ Conditions noted as maternal in the ICD-PM include not only fetal underlying causes (*Placenta, cord, and membranes*), but also maternal causes (*Maternal complications of pregnancy*) and maternal associated conditions (*Maternal medical and surgical conditions*). Further, one-fifth of stillbirths in the global category *Unexplained* mapped to ICD-PM *Antepartum asphyxia*. Classifying associated conditions is important, particularly in

data-poor settings where assigning causes may be difficult. However, confusing causes from associated conditions or mechanisms of death (ante-partum asphyxia), while reducing the number of *Unexplained* cases, may obscure key areas for prevention. The WHO is currently working towards ICD-11, which provides an opportunity to alleviate some of these issues.⁶¹

Differences in proportions of causal categories across countries were likely due to different classification approaches. Codac²⁰ was the only non-ICD system fully aligned with the ICD-PM. Although Codac has previously been shown to be the best-performing system,⁴⁵ the majority of stillbirths classified using Codac were mapped to unknown timing and cause within the ICD-PM (data not shown). Codac also resulted in a high proportion of *Unexplained* stillbirths, potentially influenced by the categories included. Moreover, this system was only aligned with nine of the 17 user-identified characteristics for an effective global system. Future enhancements to global classification of stillbirths need to incorporate user-identified characteristics for an effective global system. Further, optimisation of information from data-rich settings to incorporate recent advances in stillbirth aetiology such as the consensus on placental pathology⁵³ and other detailed laboratory investigations will serve to advance prevention of stillbirths globally. Implementation of any system must also be accompanied by appropriate training to ensure high-quality data.

Conclusion

To achieve the *Every Newborn* action plan global stillbirth rate target, priorities are improving the care of women in labour and giving birth, preventing and treating infections, and improving the quality of data on causes to drive change. Implementation of ICD-PM as part of the WHO *Perinatal Mortality Audit and Review* guide⁸ would be a major step forward. While the ICD-PM captures data from high-burden settings by allowing for a minimum of timing and clinically defined causes and associated conditions, a global system must also accommodate the needs of data-rich settings to enable global comparisons. Clearly ascertaining underlying causes, separating them from associated conditions, and enabling capture of more detailed information in data-rich settings will fully harness the ICD-PM's potential for global reporting and prevention of stillbirths. Further research is needed to improve the classification of placental causes of stillbirths. Enhancements to global classification of stillbirths and neonatal deaths must be based on comprehensive testing across diverse settings.

Disclosure of interests

Full disclosure of interests available to view online as supporting information.

Contribution to authorship

HR was responsible for the conduct of the study. VF conceptualized the study and developed methods and procedures with HR, MC, and SHL. HR, VF, SHL, AW, and ZT undertook searches, selection of studies, data extraction, and quality assessment. GG, DE, RL, and VF created the global stillbirth categories. MC oversaw all statistical aspects of the study and undertook the pooled analysis. VF and SHL undertook the assessment of ICD-PM alignment with advice from RP, JG, ÖT, and EA. HR and VF were responsible for interpretation of findings and preparation of the first draft of the manuscript. SH, AW, GG, RL, DE, ZT, EA, HB, ED, JJE, FF, JG, KG, SG, AG, AH, YK, FK, JL, EM, JO, RP, KP, DS, RS, GS, and ÖT have been actively involved throughout planning and consultation stages of the project and provided comments on the manuscript. HR, SHL, MC, SH, AW, GG, RL, DE, ZT, EA, HB, ED, JJE, FF, JG, KG, SG, AG, AH, YK, FK, JL, EM, JO, RP, KP, DS, RS, GS, and ÖT approved the final version. All authors are part of The International Stillbirth Alliance Collaborative for Improving Classification of Perinatal Deaths.

Details of ethics approvals

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Flow diagram of study selection.

Figure S2. Stillbirth definitions in included reports.

Figure S3. Proportion of national stillbirths included in country representative reports.

Figure S4. Quality assessment summary.

Figure S5. Alignment of 21 stillbirth classification systems with the ICD-PM.

Table S1. Mapping of reported causes of stillbirth into categories.

Table S2. Characteristics of included reports detailed (by country income-setting [$n = 85$]).

Table S3. Classification systems for causes of stillbirth: alignment with the ICD-PM.

Table S4. Classification systems for causes of stillbirth: selected characteristics.

Table S5. Major categories of causes of stillbirth (by income-setting [$n = 85$]).

Table S6. Detailed quality assessment detailed.

Table S7. Pooled estimates of global causes of stillbirth (by country income setting [$n = 33$]).

Table S8. Unexplained stillbirth, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S9. Other unspecified condition, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S10. Antepartum haemorrhage, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S11. Infection, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S12. Hypoxic peripartum death, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S13. Placental conditions, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S14. Congenital anomalies, detailed pooled estimates (country-representative studies [$n = 33$]).

Table S15. Specific fetal/pregnancy pathology, detailed pooled estimates.

Table S16. Hypertension, detailed pooled estimates.

Table S17. Fetal growth restriction, detailed pooled estimates.

Table S18. Umbilical cord conditions, detailed pooled estimates.

Table S19. Maternal conditions, detailed pooled estimates.

Table S20. Spontaneous preterm, detailed pooled estimates.

Table S21. Terminations (unspecified), detailed pooled estimates.

Table S22. Mapping of stillbirth causes to the ICD-PM.

Table S23. Stillbirth causes mapped to the ICD-PM matrix.

Appendix S1. Search string and systematic searches for national reports.

Appendix S2. Data collection and definitions.

Appendix S3. Checklist for quality assessment.

Appendix S4. Statistical methods for pooled estimates of reported causes. ■

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