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Original article

Development of criteria for identifying neonatal near-miss cases: analysis of two WHO multicountry cross-sectional studies

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Objective To develop and test markers of neonatal severe morbidity for the identification of neonatal near-miss cases.

Design This is a database analysis of two World Health Organization cross-sectional studies: the Global Survey on Maternal and Perinatal Health (WHOGS) and the Multicountry Survey on Maternal and Newborn Health (WHOMCS).

Setting The WHOGS was performed in 373 health facilities in 24 countries (2004–2008). The WHOMCS was conducted in 359 health facilities in 29 countries (2010–2011).

Population Data were collected from hospital records of all women admitted for delivery and their respective neonates.

Methods Pragmatic markers (birthweight <1750 g, Apgar score at 5 minutes <7, and gestational age <33 weeks) were developed with WHOGS data and validated with WHOMCS data. The diagnostic accuracy of neonatal characteristics and management markers of severity was determined in the WHOMCS.

Results This analysis included 290 610 liveborn neonates from WHOGS and 310 436 liveborn neonates from WHOMCS. The diagnostic accuracy of pragmatic and management markers of severity for identifying early neonatal deaths was very high: sensitivity, 92.8% (95% CI 91.8–93.7%); specificity, 92.7% (95% CI 92.6–92.8%); positive likelihood ratio, 12.7 (95% CI 12.5–12.9); negative likelihood ratio, 0.08 (95% CI 0.07–0.09); diagnostic odds ratio, 163.4 (95% CI 141.6–188.4). A positive association was found between the frequency of neonatal near-miss cases and Human Development Index.

Conclusion Newborn infants presenting selected markers of severity and surviving the first neonatal week could be considered as neonatal near-miss cases. This definition and criteria may be seen as a basis for future applications of the near-miss concept in neonatal health. These tools can be used to inform policy makers on how best to apply scarce resources for improving the quality of care and reducing neonatal mortality.

Keywords Early neonatal death, neonatal morbidity assessment, neonatal near-miss criteria, perinatal care assessment, quality of care.

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Introduction

The near-miss concept is being increasingly used as a tool to evaluate and improve the quality of care, especially for maternal health, where it has been used in clinical audits and epidemiological surveillance, similar to maternal deaths.[1] It has been hypothesised that this concept could also be useful in the neonatal context, to accelerate progress

towards achieving Millennium Development Goals four and five by facilitating the assessment of quality of perinatal care.[2] Nevertheless, until now, there is no standard definition or internationally agreed identification criteria for neonatal near-miss cases. The term neonatal near miss has been used inconsistently, and also to describe survivors of rare conditions.[3–6] Similarly to the maternal near-miss concept, a neonatal near-miss case would refer to 'an infant who nearly died but survived a severe complication that occurred during pregnancy, birth or within 7 days of extra-uterine life'.[7]

This is a new concept being proposed for addressing issues on quality of perinatal care, and should be differentiated from other already established entities such as apparent life-threatening events and survivors of sudden infant death syndrome.[6,8,9] The absence of standard identification criteria for near-miss cases makes it very difficult to establish the relationship between near-miss cases and neonatal deaths. This is a necessary step for quality of care assessments based on the near-miss concept.

The development of a standard benchmark for evaluating the quality of perinatal care would allow comparisons between different settings, regardless of the local development level and across time.[10] In this context, the development of tools able to contribute to the improvement of quality of perinatal care and the reduction of adverse neonatal outcomes is a priority for global health research.[11] The main purpose of this study is to explore traditional predictors of early neonatal mortality as criteria to identify neonatal near-miss cases among high-risk babies.

Therefore, we: (1) assessed the accuracy of the selected combination of criteria to predict early neonatal deaths; (2) developed and validated a set of pragmatic neonatal near-miss criteria; and (3) explored the relationship of these indicators with the Human Development Index (HDI).[2]

Methods

Study design and data collection

This article reports on the analysis of two large WHO data sets, the Global Survey on Maternal and Perinatal Health (WHOGS, a cross-sectional study carried out in 373 health facilities from 24 countries in Africa, Asia, and Latin America) and the Multicountry Survey on Maternal and Newborn Health (WHOMCS, a cross-sectional study carried out in 359 health facilities from 29 countries in Africa, Asia, Latin America, and the Middle East). The methodological details of both studies have been published elsewhere.[12–15] Briefly, in both surveys trained health professional staff retrieved data from the hospital records of women and newborns, including individual data on demographics and reproductive characteristics, medical conditions during pregnancy, birth outcomes, complications, and the health interventions deployed during the hospital stay, until 7 days after birth or hospital discharge. Using a different approach from WHOGS, the WHOMCS collected specific data on the management of severe neonatal morbidity. In addition, data on the capacity of the health facilities were obtained in both surveys, including laboratory tests, infrastructure, and the capacity of obstetrics and neonatal healthcare services. The data collection for WHOGS took place between 2004 and 2008, for 2–3 months per facility, and data were collected from May 2010 to December 2011 for WHOMCS, for 2–4 months in each facility. A multistage cluster sampling method was used to select countries, provinces, and health facilities to participate in the WHOGS; this network of health facilities was adjusted with a similar strategy, and for convenience, in the WHOMCS. Both studies were ethically approved by the WHO and by the relevant authorities and institutional review boards in all of the participating countries. Box S1 shows the operational definitions used in this analysis. Table S1 shows the tabulation of participating countries per HDI and number of liveborn neonates per participant country. Table S2 presents the number of neonatal near-miss cases, early neonatal deaths, severe neonatal outcomes, and case-fatality ratios, stratified by country.

Methodological considerations about the 'near-miss' concept

A fundamental aspect of the near-miss concept is the similarity between deaths and near-miss cases. Thus, near-miss cases should be as similar as possible to deaths. The ideal near-miss case would mirror a death, the only difference being that the infant is alive at the point of assessment of the vital status. The development of criteria to identify near-miss cases is challenged by the absence of a gold standard for near-miss cases. In addition, survival must be established first in order to attribute the near-miss status, which makes the identification of near-miss cases always retrospective. Taking a step back in the continuum of severity, and considering case identification criteria as a diagnostic test, a specific set of criteria able to identify only very severe cases would have true-positive cases as those resulting in death. Consequently, in a specific set of criteria (able to identify only very severe cases), false-positive cases could be considered as near-miss cases (i.e. those that narrowly survived). True-positive cases (deaths) would be similar to false-positive cases (near-miss cases), except for the vital status. This approach has been used in the development and validation of identification criteria for maternal near-miss cases.[10]

Study population and analysis

For this analysis, we used data of liveborn infants with known vital status at birth and at 7 days of life/hospital

discharge. This analysis was carried out in two steps: first, pragmatic markers of severe neonatal morbidity were developed using the WHOGS data set; second, a full set of criteria combining the previously developed pragmatic markers with management markers of severe neonatal morbidity was developed.

Pragmatic markers of severe neonatal morbidity

Prematurity and birth asphyxia are complications that are well known as major causes of neonatal deaths.[16] Using the WHOGS data set, we studied three conditions associated with prematurity and birth asphyxia: low Apgar score at 5 minutes of life (<7); low birthweight (<1750 g); and low gestational age (<33 weeks). The cut-offs for each condition were selected based on the diagnostic accuracy (DA) profile and on heterogeneity in the prediction of early neonatal death. These three variables were considered candidate predictors of intrahospital early neonatal mortality: neonatal death occurring within the first week of life. In each hospital, information from the best available method for estimating gestational age was used. Records with missing data on vital status at birth or on any of the exposure or outcome variables were excluded. Extreme outliers in terms of birthweight or gestational age were also excluded. These outliers are considered to most likely result from misreporting, and have been identified considering weight by gestational age curves. As the intention was to exclude only the extreme outliers, we used the intrauterine growth curve developed by Hadlock, Harrist, and Martinez-Poyer as the reference for determining the upper limit (percentile 99.99) and the WHOGS customised intrauterine growth curve for India for determining the lower limit (percentile 0.01).[17,18] The first curve was used to set the upper limit because it presents high weights by gestational age, even higher in comparison with those observed among the WHOGS country-customised curves. The WHOGS Indian customised curve was selected because it provides the lowest weights by gestational age among the WHOGS country-customised curves. We determined the relationship between early neonatal mortality and Apgar score. Similarly, the relationship between early neonatal mortality and birthweight and gestational age has been determined. Next, considering the mortality risk for each category of Apgar score, birthweight, and gestational age, we identified those categories with similar mortality risks (i.e. a certain Apgar score, gestational age, or birthweight). Then, these categories were grouped together and formed 'sets of conditions'. The stratum with the lowest mortality rate was used as the reference group. In order to promote some homogeneity in terms of death risk among the possible identification criteria, we searched for sets of cut-off points in each variable that could produce similar death risks. These sets of possible identification criteria were used to assess the predictive value as diagnostic tests in the identification of early neonatal deaths. In addition, a set of criteria used in a previous analysis of WHOGS was tested for comparison.[7] We evaluated the DA of each set of conditions in identifying neonatal near-miss cases by calculating sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and prevalence of near-miss cases identified by the proposed set of criteria. We used the I^2 test to assess the heterogeneity between the relative risks within the selected sets of criteria. In addition, we calculated the prevalence of the identified neonatal near-miss cases added to early neonatal deaths. We also determined the mortality rate among liveborn infants. Finally, an ideal set of criteria to identify neonatal near-miss cases should be simple and pragmatic, being as similar as possible to neonatal deaths, and homogeneous in terms of the severity of individual criteria. Considering all of this, we selected a set of criteria from the WHOGS that would be more appropriate to contribute to the development of a definition of neonatal near miss. The selected set of criteria was then tested in the WHOMCS data set.

Pragmatic and management markers of neonatal severity

Information about management markers of severity, based on life-saving interventions used in South African studies, were explored to assess the applicability of the near-miss concept in neonatal health in the WHOMCS.[4,19,20] The neonatal life-saving interventions surveyed were: use of therapeutic intravenous antibiotics; nasal continuous positive airway pressure (nasal CPAP); any intubation (anytime within the first week); use of phototherapy within the first 24 hours; need of cardiopulmonary resuscitation; use of any vasoactive drug; use of anticonvulsants; surfactant administration; use of any blood products; use of steroids to treat refractory hypoglycaemia; and any surgery during early neonatal life. We used the WHOMCS data set to test the previously developed pragmatic markers of neonatal severity, and to test the use of the set of management markers of severity adapted from South African studies.[4,19,20] We classed the frequency of pragmatic and management markers of neonatal morbidity in three groups: overall; among survivors (neonatal near-miss cases); and among infants that died in the first week after childbirth. We also determined the mortality associated with each severity marker. The accuracy of pragmatic markers of severity, management markers of severity, and of combined pragmatic and management markers of severity was estimated through sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, and diagnostic odds ratios.

Indicators

Based on the maternal near-miss indicators developed by WHO, we modified and adapted them to the neonatal

context.[21] We determined the number of early neonatal deaths per 1000 live births, the number of neonatal near-miss cases per 1000 live births, and the number of infants with severe neonatal outcomes (i.e. neonatal near misses plus early neonatal deaths). We also determined the case/fatality ratio (calculated as the ratio between neonatal near-miss cases and each neonatal death), together with the mortality index (calculated as the number of early neonatal deaths divided by the number of infants with severe neonatal outcomes). We stratified the countries according to the level of HDI estimated in 2012 by the United Nations Development Programme (very high, high, moderate, and low), and calculated the previously mentioned indicators by HDI country strata.

This analysis was conducted using STATA 11.2 (Statistics/Data Analysis; Statacorp LP, College Station, TX, USA, 1985–2009), EPI-INFO 3.5.3 statistical package (Centers for Disease Control and Prevention, Atlanta, GA, USA), Microsoft EXCEL 2007 and REVIEW MANAGER 5.0 Review Manager (RevMan) (Nordic Cochrane Centre, Copenhagan).

Results

From the WHOGS, a total of 277 706 liveborn infants were included in this analysis (2042 early neonatal deaths and 275 664 infants alive at hospital discharge or on the seventh day of life). From the WHOMCS, a total of 309 644 liveborn infants were included in this analysis (2850 early neonatal deaths and 306 794 infants alive at hospital discharge or on the seventh day of life). The summary analysis flow is illustrated in Figure 1. Several combinations of pragmatic markers of neonatal severity were developed and tested using the WHOGS data set. Table 1 presents the DA of three sets of pragmatic markers of neonatal severity selected to illustrate the relationship between these markers and the prediction of early neonatal deaths. Table S3 and Figure 2 present the relationship between early neonatal mortality and stratified categories of birthweight, gestational age, and Apgar score at 5 minutes. Considering the accuracy, prevalence, mortality, and heterogeneity, set 1 of the severity markers (i.e. Apgar score at 5 minutes less than <7, birthweight <1750 g, and gestational age <33 weeks) was selected to integrate the proposed neonatal near-miss definition.

Based on the WHOMCS data set, Table 2 presents the accuracy profile of pragmatic markers of severity, management markers of severity, and the combined set (pragmatic or management markers of severity). The pragmatic set showed a similar accuracy profile in the WHOMCS as compared with the accuracy profile observed in the WHOGS data set. Combining pragmatic and management markers of severity resulted in improved accuracy over the pragmatic markers alone for the prediction of early neonatal deaths, as shown in Table S4 (Diagnostic accuracy of selected markers of severity in the prediction of early neonatal deaths among all liveborn infants). The frequencies of individual pragmatic and management markers of severity (stratified by survival status, near-miss cases, and early neonatal deaths) are presented in Table 3, together with the mortality rates associated with each severity marker. The presence of any pragmatic or management marker identified 72.5/1000 among liveborn infants with a mortality rate within this group of 10.5%. Any intubation during the first week of life and need of cardiopulmonary resuscitation or use of vasoactive drug were associated with high mortality rates. Table 4 presents the number of liveborn infants, early neonatal deaths, neonatal near-miss cases, infants with severe neonatal outcomes, and the case/fatality ratio or mortality index (with relevant health indicators) according to HDI level. The case/fatality ratios decrease as the HDI decreases.

Discussion

This analysis studied various combinations of markers of neonatal morbidity for the identification of neonatal near-miss cases. The combined use of pragmatic and management markers of severity showed a very good performance as predictors of early neonatal deaths. Considering the methodological aspects of the development of near-miss definitions, the survivors of life-threatening conditions presented characteristics warranting the status of appropriate proxies of early neonatal deaths, and could be labelled as neonatal near-miss cases. Indicators derived from this analysis illustrated the strong connection between quality of care (evaluated by early neonatal mortality index and the case/fatality ratio) and the development of the country (measured by the 2012 HDI).[22]

A number of scoring systems have been developed to assess prognosis, quality of care, and to allow comparisons between health care services; however, most of these scoring systems may not be routinely applicable in developing or under-resourced settings.[7,23–27] The main constraint to the application of these systems is the need for more detailed and complex information, often requiring laboratory facilities. In this context, an accurate, pragmatic, and easily applicable indicator for assessing the quality of maternal, perinatal, and neonatal care, to be applied in health facilities and health systems, could be useful.[21] We believe that the use of the near-miss approach in neonatal health is a step forward in the direction of an innovative tool to improve the quality of antenatal, intrapartum, and postnatal care.

The WHOGS and WHOMCS produced large maternal and perinatal health databases, with information obtained from several countries around the world. One of the strengths of this analysis is the fact that the pragmatic

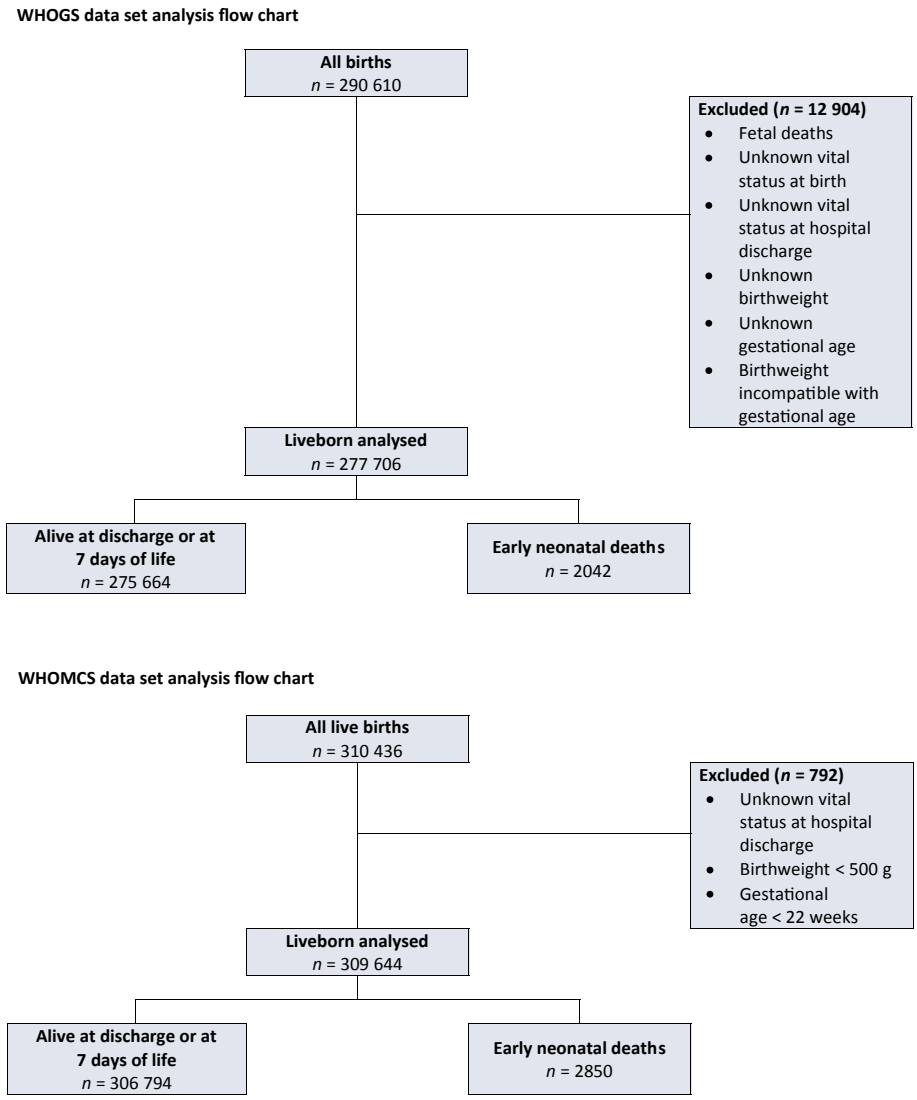

Figure 1. The analysis flow.

markers of severity were identified in the WHOGS database and then tested in an independent population using data from the WHOMCS. Some limitations should be acknowledged, however. These studies are facility-based, and may not be representative of a proportion of pregnant women and babies from areas where the coverage of institutional births is low; in addition, this data set might be biased towards larger and more equipped facilities, which may over-represent more complicated deliveries, and the collected sample may not represent the overall population at the country level. A second limitation is the source of data within health facilities, i.e. routine hospital records, which can lead to missing or misrecorded data. Another limitation is the relative paucity of data related to neonatal characteristics and care in the WHOGS database, mostly because the primary research questions of these studies were generally related to maternal health. The Apgar score at 5 minutes of life, gestational age, and birthweight were among the few neonatal characteristics available for analysis in the WHOGS study database; however, the WHOMCS study collected data on an expanded set of neonatal variables related to the management of complications that allowed the development of a more comprehensive and robust set of markers of severity. It is important to note that data on gestational age were obtained from medical records and reflected at each setting the best available method for gestational age estimation (i.e. in many settings this could be only the fundal height or weight at birth, if other methods such as ultrasound or reliable maternal information were not available).

Management markers of severity are essentially composed of life-saving interventions (e.g. surfactant, intuba-

Table 1. Diagnostic accuracy profiles for prediction of early neonatal death and other characteristics of selected sets of pragmatic markers of neonatal morbidity (n = 277 706)*

	Set 1 Apgar <7 or Birthweight <1750 g or Gestational age <33 weeks	Set 2 Apgar <5 or Birthweight <1500 g or Gestational age <31 weeks	Set 3 Apgar <7 or Birthweight <1500 g or Gestational age <30 weeks
Sensitivity	79.1% (77.3–80.8)	62.0% (59.9–64.1)	72.6% (70.6–74.5)
Specificity	96.5% (96.4–96.5)	98.7% (98.6–98.7)	97.4% (97.4–97.5)
Positive likelihood ratio	22.3 (21.7–23.0)	46.9 (44.7–49.1)	28.3 (27.7–29.4)
Negative likelihood ratio	0.22 (0.20–0.24)	0.39 (0.36–0.41)	0.28 (0.26–0.30)
Diagnostic odds ratio (95% CI)	103.1 (92.5–114.9)	121.7 (110.6–133.8)	100.7 (91.1–111.3)
Prevalence	3.5%	1.3%	2.5%
Mortality	14.2%	25.8%	17.3%
Heterogeneity**	0%	18%	98%

*Calculated using the data set of the WHO Global Survey on Maternal and Perinatal Health (2004–2008).
**Statistical heterogeneity between severity markers, assessed by the I^2 test.

tion, etc.). In some settings, these life-saving interventions may not be available, and the omissions of such life-saving interventions are likely to contribute to increased mortality. This should not compromise the applicability of the proposed definition in settings where some of the management markers are not available, because the performance of the health service can be assessed by the ratio between survivors and non-survivors (case/fatality ratio). In settings with poor quality of care, there are fewer survivors per neonatal death, and the case/fatality ratio can complement the information provided by early neonatal mortality. In settings where lower neonatal mortality rates are observed or in individual health facilities (where the number of neonatal deaths may provide insufficient information), reviewing near-miss cases as part of a clinical audit can function as a complementary source of information for understanding the performance of health services and identifying issues related to quality of care.

Only intrahospital early neonatal mortality was assessed in this analysis. Thus, the observed survival, particularly for infants at very early gestational ages, and among those born with very low birthweight, may not reflect the survival at the end of the full neonatal period. It is relevant to consider that the development of the near-miss concept is centred in neonates surviving severe perinatal and neonatal conditions, and this analysis assessed outcomes within the first postpartum week. The use of the near-miss concept in neonatal health might also be important to predict later developmental problems related to the life-threatening conditions to which these neonates were exposed. More research should be fostered to understand the impact of these neonatal life-threatening conditions in long-term survival and disabilities.

As learned from the maternal near-miss experience, audit processes of near-miss cases contribute to highlight specific issues and help to prioritise the implementation of effective interventions for improving maternal health care.[14] We believe that the assessment of medical records of neonatal near-miss cases in addition to neonatal death cases would function similarly to maternal near-miss audit processes, and would facilitate the selection and performance evaluation of interventions for improving perinatal health.

Lastly, the neonatal near-miss approach represents a simple and easily applicable tool for the quality assessment of perinatal health care, independently of the development level where the health institution is located. The calculation of proposed neonatal near-miss indicators enables an objective analysis of the performance of a health facility. Another advantage of this approach is to allow comparison of the performance of health facilities at different points in time and within the same country. Comparison of perinatal health services between countries with different development levels might be of use to assess the effectiveness of complex interventions, which might require the evaluation of softer outcomes instead of neonatal mortality.

Conclusion

Newborn infants presenting selected markers of severity and surviving the first neonatal week could be considered as neonatal near-miss cases. This definition and criteria may be seen as a basis for future applications of the near-miss concept in neonatal health. The neonatal near-miss concept represents an additional tool to complement the assessment of burden and quality of perinatal care. These tools can be used to inform policy makers on how best to

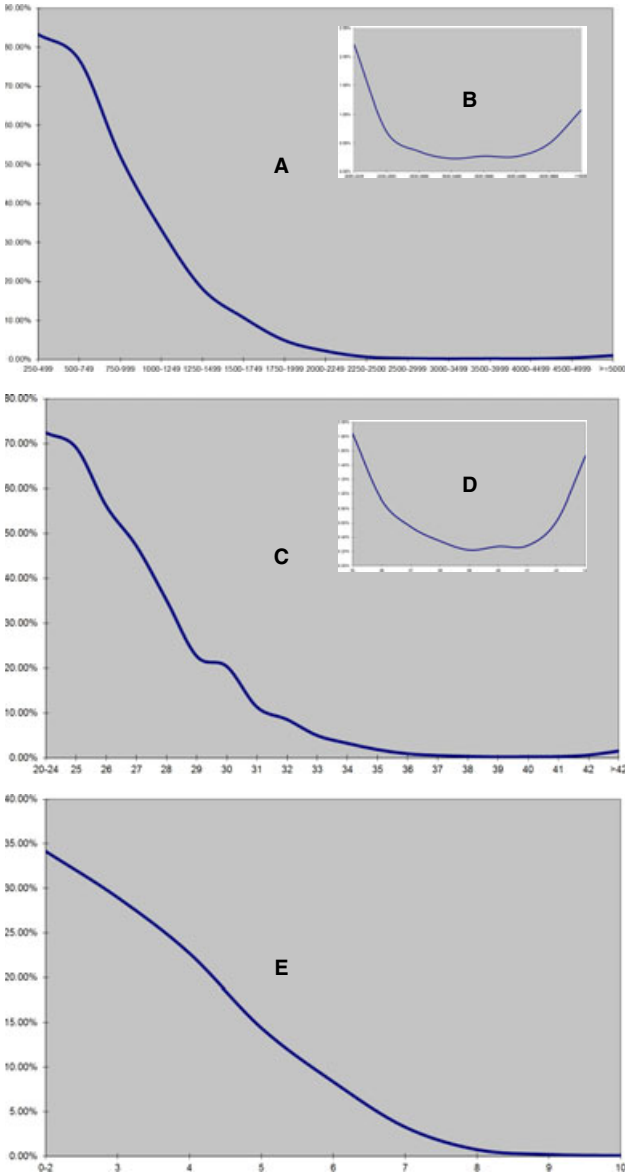

Figure 2. (A) Early neonatal mortality rates (ENM, %) by birth weight (in grams). (B) Detail on ENM from 2000 g to 5000 g. (C) ENM (%) by complete gestational week. (D) Detail on ENM from 35 to 42 complete weeks. (E) ENM (%) by Apgar score at 5 minutes of extra-uterine life.

apply scarce resources for improving the quality of care and reducing neonatal mortality.

Disclosure of interests

The authors declare no competing interests.

Contribution to authorship

CP and JPS designed the analysis. CP performed the analysis and drafted the article. All authors contributed to and approved the final version of the article.

Table 2. Diagnostic accuracy profiles of severity markers for early neonatal death among liveborn infants (n = 309 644)*

		Early neonatal death	
		+	–
Pragmatic set (any pragmatic marker of severity) (Set 1: Apgar< 7 or birthweight <1750 g or gestational age <33 weeks)	+	2208	11 587
	–	642	295 207
Sensitivity (95% CI)		77.5% (75.9–79.0%)	
Specificity (95% CI)		96.2% (96.2–96.3%)	
Positive likelihood ratio (95% CI)		20.5 (20.0–21.1)	
Negative likelihood ratio (95% CI)		0.23 (0.22–0.25)	
Diagnostic odds ratio (95% CI)		87.6 (80.1–95.9)	
Management set (any management marker of severity)	+	2252	16 421
	–	598	290 373
Sensitivity (95% CI)		79.0% (77.5–80.0%)	
Specificity (95% CI)		94.7% (94.6–94.7%)	
Positive likelihood ratio (95% CI)		14.8 (14.4–15.1)	
Negative likelihood ratio (95% CI)		0.22 (0.21–0.24)	
Diagnostic odds ratio (95% CI)		66.6 (60.8–73.0)	
Combined set (any pragmatic or management marker of severity)	+	2645	22 458
	–	205	284 336
Sensitivity (95% CI)		92.8% (91.8–93.7%)	
Specificity (95% CI)		92.7% (92.6–92.8%)	
Positive likelihood ratio (95% CI)		12.7 (12.5–12.9)	
Negative likelihood ratio (95% CI)		0.08 (0.07–0.09)	
Diagnostic odds ratio (95% CI)		163.4 (141.6–188.4)	

*Calculated using the data set of the WHO Multicountry Survey on Maternal and Newborn Health (2010–2011).

Details of ethics approval

The WHOGS (protocol ID, A25176; date of approval, 25 April 2003) and WHOMCS (protocol ID, A65661; date of approval, 27 October 2009) were conducted following ethical clearance from the Scientific and Ethical Review Group of the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Geneva, Switzerland. Both studies were independently reviewed by the relevant review board(s) of each country.

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Table 3. Frequency of severity markers among liveborn infants (n = 309 644)*

	Severe neonatal outcomes** *n* (‰)	Neonatal near-miss cases *n* (‰)	Early neonatal deaths *n* (‰)	Mortality rate %
Pragmatic set (any pragmatic marker of severity)				
Apgar score at 5 minutes <7	8033 (25.9)	6745 (21.8)	1288 (4.2)	16.0
Birthweight <1750 g	6099 (19.7)	4456 (14.4)	1643 (5.3)	26.9
Gestational age <33 weeks	4438 (14.3)	3424 (11.1)	1014 (3.3)	22.8
Any pragmatic marker of severity	13 795 (44.6)	11 587 (37.4)	2208 (7.1)	16.0
Management set (any management marker of severity)				
Use of therapeutic intravenous antibiotics	13 496 (43.6)	11 952 (38.6)	1544 (5.0)	11.4
Nasal CPAP	4772 (15.4)	3874 (12.5)	898 (2.9)	18.8
Any intubation (anytime within the first week)	3970 (12.8)	2811 (9.1)	1159 (3.7)	29.2
Use of phototherapy in the first 24 hours	3434 (11.1)	3222 (10.4)	212 (0.7)	6.2
Cardiopulmonary resuscitation	2961 (9.6)	1598 (5.2)	1363 (4.4)	46.0
Use of any vasoactive drug	1890 (6.1)	1176 (3.8)	714 (2.3)	37.8
Use of anticonvulsants	1441 (4.7)	1166 (3.8)	275 (0.9)	19.1
Surfactant administration	1366 (4.4)	1075 (3.5)	291 (0.9)	21.3
Use of any blood products	980 (3.2)	802 (2.6)	178 (0.6)	18.2
Use of steroids to treat refractory hypoglycaemia	895 (2.9)	736 (2.4)	159 (0.5)	17.8
Any surgery	247 (0.8)	216 (0.7)	31 (0.1)	12.6
Any management-based marker of severity	18 673 (60.3)	16 421 (53.0)	2252 (7.3)	12.1
Combined set (any pragmatic or management marker of severity)	25 103 (81.1)	22 458 (72.5)	2645 (8.5)	10.5

*Calculated using the data set of the WHO Multicountry Survey on Maternal and Newborn Health (2010–2011).
**Calculated by the sum of neonatal near-miss cases and early neonatal deaths.

Table 4. Number of liveborn infants, early neonatal deaths, neonatal near-miss cases, infants with severe neonatal outcomes, and case/fatality ratio (with relevant health indicators: ratios per 1000 live births in brackets) according to the HDI of the country, with data from WHOMCS (n = 309 644)

	Overall	Countries with very high HDI	Countries with high HDI	Countries with medium HDI	Countries with low HDI
Number of liveborn infants	309 644	30 397	67 247	88 979	119 388
Number of early neonatal deaths (per 1000 live births)	2850 (9.2)	79 (2.6)	390 (5.8)	882 (9.9)	1334 (11.2)
Number of neonatal near-miss cases* (per 1000 live births)	22 458 (72.5)	1187 (39.0)	5096 (75.8)	7345 (82.5)	7880 (66)
Number of infants with severe neonatal outcomes** ;(per 1000 live births)	25 308 (81.7)	1266 (41.6)	5486 (81.6)	8227 (92.5)	9214 (77.2)
Case/fatality ratio (mortality index***)	8:1 (11.3%)	15:1 (6.2%)	13:1 (7.1%)	8:1 (10.7%)	6:1 (14.5%)

Missing data with tabulation of HDI and early neonatal death: 3633.
*Calculated based on the presence of any pragmatic or management marker of morbidity or the occurrence of an early neonatal death.
**Severe neonatal outcome: early neonatal deaths plus neonatal near-miss cases.
***Mortality index: number of early neonatal deaths divided by the total number of severe neonatal outcomes.

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Supporting Information

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

Box S1. Operational definitions.

Table S1. Countries participating in the WHOGS and WHOMCS, stratified by HDI, with the total number of live births and respective percentages.

Table S2. Neonatal near-miss cases, early neonatal death, severe neonatal outcome, and case/fatality ratio, by country.

Table S3. Relationship between Apgar score at 5 minutes, birthweight, and gestational age with early neonatal mortality (n = 277 706).

Table S4. Diagnostic accuracy of selected markers of severity in the prediction of early neonatal deaths among all liveborn infants (n = 309 644). ■

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