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

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Summary

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

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Reproductive Health Surveys (13 datapoints, eight countries), and studies identified through systematic searches and unpublished data (162 datapoints, 40 countries) were included. 55 countries submitted additional data during WHO's country consultation process.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

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

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

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Introduction

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

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

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

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

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

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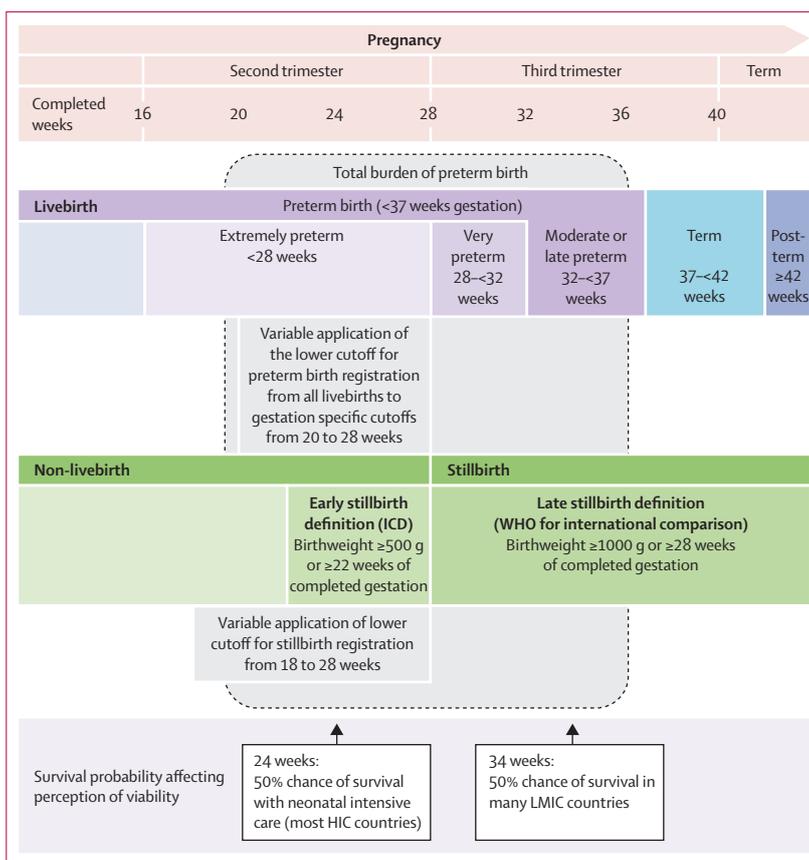

Figure 1: Overview of definitions and variable cutoffs applied for pregnancy outcomes related to preterm birth and stillbirths
Figure adapted from Lawn and colleagues.[17] HIC=high-income countries. LMIC=low-income and middle-income countries. *Very preterm group in this analysis includes babies 28–<32 weeks and extremely preterm births are defined as <28 weeks.

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

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

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

See **Online** for appendix

Methods

Data inputs

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

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

Data inclusion and exclusion criteria

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

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

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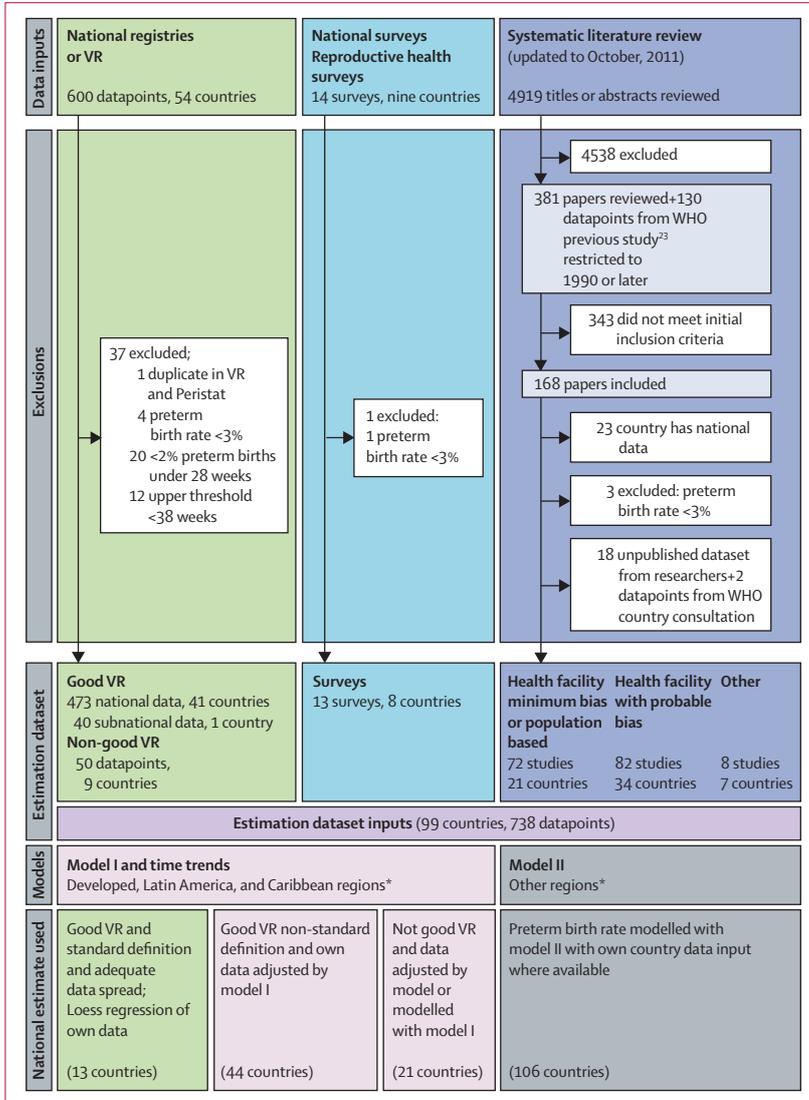

Figure 2: Preterm birth rate data search strategy, selection progress showing the methods, and models used for estimation
VR=vital registration. Good VR= national VR with high-quality reporting for maternal deaths.[25] *Millennium Development Goal regions.

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

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

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

Final dataset used as input for statistical models

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

Statistical models

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

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

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

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

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

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

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

suggest that the model fits the data well (overall R²=0·4; appendix p 62).

Variables retained in Model II included: linear log (low birthweight rate) (p<0·0001), malaria endemicity (p=0·06), female literacy rate (p=0·04), data source (p=0·02), method of gestational age assessment (p=0·01), and denominator (singleton or all births; p=0·40; table 2, see appendix p 60 for full model equation). Preterm birth rates increased with increasing low birthweight rate, malaria, and female literacy (table 2; appendix p 61). Regression diagnostic plots show the fit of the model to the data (overall R²=0·29; appendix p 63).

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

Statistical analysis

To estimate the distribution of preterm births by gestational age subgroup, we did a meta-analysis of all 345 datapoints in our input database which presented data by our agreed gestational age subgroups (N=131296765; table 1). The median year of these data was 2004 (range 1990–2010). A random effects model was used as some evidence of heterogeneity, assessed using I^2 and the χ^2 test, was present (p<0·10). The proportions were remarkably similar across these datasets suggesting a biological basis for the distribution. Given this consistency, we applied these proportions to our estimates of preterm births for all countries for 2010. However, only 13% (44 datapoints) were from outside the Developed region, with only seven datapoints from southern Asia, or sub-Saharan Africa. There was some evidence of a difference in the distributions of the subgroups for all other regions, compared with Developed region, reported on average slightly lower proportions of preterm births at less than 28 weeks (4·8% vs 5·3%; p=0·02); similar proportions of preterm births for 28 to less than 32 weeks (10·2% vs 10·6%; p=0·13); and higher proportions for births at 32 weeks to less than 37 weeks (85·1% vs 84·1%; p=0·03)). These differences are likely to represent differences in case ascertainment in the group of less than 28 weeks' gestation between regions. We did not estimate trends for the gestational age subgroups.

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

	Number of livebirths	Estimated mean preterm birth rate (%) (uncertainty range*)	Number of preterm births (uncertainty range*)
Developed regions	14300000	8·6% (8·3–9·4)	1233200 (1188500–1345100)
Eastern Asia	17400000	7·2% (5·4–9·0)	1262200 (943100–1564100)
Latin America	10200000	8·4% (6·8–11·4)	852800 (695500–1164000)
Northern Africa	3543100	7·3% (4·8–10·9)	259200 (168700–387900)
Oceania	263200	7·4% (4·5–15·6)	19500 (11800–41000)
Southeastern Asia	11000000	13·6% (9·3–18·6)	1497500 (1019400–2044700)
Southern Asia	38700000	13·3% (10·1–16·8)	5159300 (3900100–6504200)
Sub-Saharan Africa	32100000	12·3% (9·5–15·8)	3936800 (3039500–5068000)
Western Asia	4855300	10·1% (6·9–14·3)	488200 (334000–693700)
Caribbean	682800	11·2% (7·8–20·8)	76500 (53300–142000)
Caucasus and Central Asia	1643000	9·2% (6·0–13·0)	151300 (99100–212800)
Total worldwide	135000000	11·1% (9·1–13·4)	14936700 (12268200–18089700)

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

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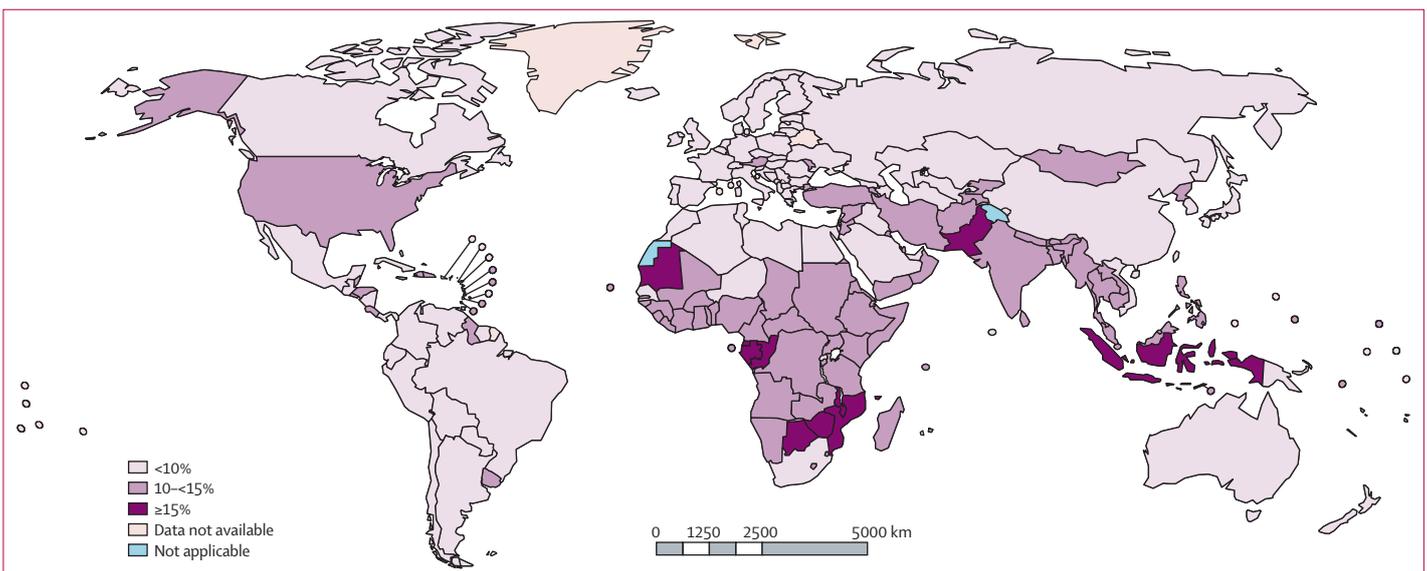

Figure 3: **Estimated preterm birth rates by country for the year 2010**

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

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

Funding

Results

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

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

No evidence of a systematic difference existed between the estimated preterm birth rates for 2010 and the nationally reported rate in the 26 countries with available data for 2009 or 2010 using the standard definition and of acceptable quality (paired *t* test p=0·84).[24] The median

difference between estimated and reported rates was −0·3% (IQR −1·3 to 2·3%; appendix pp 73–74).

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

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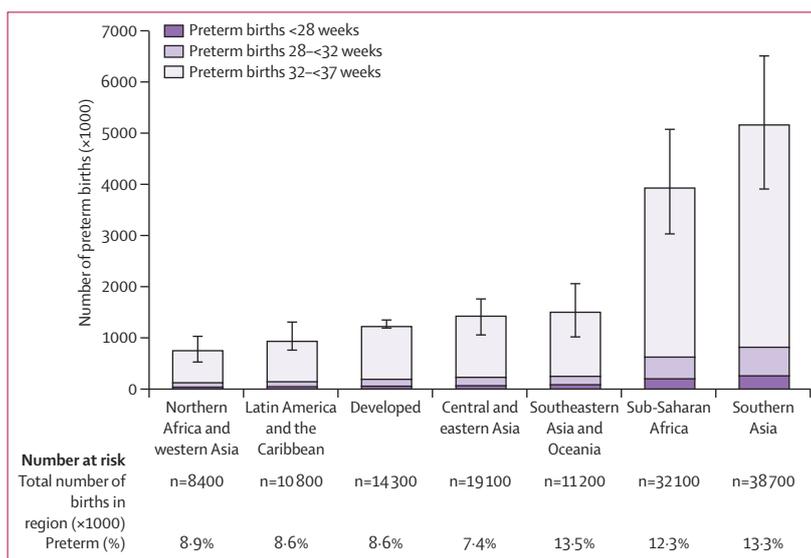

Figure 4: Estimated preterm births by region and by gestational age grouping for the year 2010

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

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

	1990			2010			1990–2010	
	Number of livebirths	Preterm birth rate (%)	Number of preterm births (uncertainty range*)	Number of livebirths	Preterm birth rate (%)	Number of preterm births (uncertainty range*)	Increase in preterm rate (%)	Average annual % increase in preterm birth rate
Developed regions	15 100 000	7·2%	1 090 000 (1 035 000 –1 179 000)	14 300 000	8·6%	1 233 000 (1 189 000–1 345 000)	19·4%	1·1%
Latin America	10 900 000	7·7%	845 000 (707 000–1 217 000)	10 200 000	8·4%	853 000 (696 000–1 164 000)	9·1%	0·5%
Caribbean	769 000	8·9%	68 000 (48 000–125 000)	683 000	11·2%	77 000 (53 000–142 000)	25·8%	1·5%
Total	26 769 000	7·5%	2 004 000 (1 839 000–2 468 000)	25 183 000	8·6%	2 163 000 (1 987 000–2 593 000)	14·7%	0·8%

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

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

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

Discussion

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

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

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

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

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

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

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

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

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

Data quality is particularly affected by under-registration of extremely preterm births, or their misclassification to stillbirths near the thresholds of perceived viability and stillbirth registration.[59] Countries using preterm birth definitions that include births from 20 weeks onwards report a higher proportion of preterm births under 28 weeks, possibly reflecting increased data capture of livebirths around the margins of viability (figure 5). Other countries with no specified lower cutoff have variable capture of

Panel: Research in context

Systematic review

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

Interpretation

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

extremely preterm babies. When reporting thresholds are changed it might take some time before recording of cases near the new threshold improves. For example, Denmark changed their lower threshold for registering preterm births from 28 to 22 weeks in 1997, but it was several years later that the proportion of all preterm births under 28 weeks increased from 4% to 7% (figure 6). We excluded 20 datapoints from our input dataset based on the implausibility criteria of less than 2% of preterm births being at less than 28 weeks' gestation (figure 2). We did a sensitivity analysis regarding these exclusions and found no evidence of a systematic difference between the estimated preterm birth rates at country level with and without these data included (paired *t* test p=0·44).

We applied statistical modelling to try to correct for definition variation, data limitations, and to estimate for countries for which no or poor data were available. The use of statistical models can never be a substitute for improved empirical data. Prediction of the prevalence of preterm birth, in essence a syndrome and with varying risk factors around the world, has presented modelling challenges. The predictor variables available as time series are poor when compared with the complex interplay of different factors leading to preterm birth. Particularly, it was not possible to distinguish between spontaneous and provider-initiated preterm births, since even in high-income countries, this distinction is not readily available
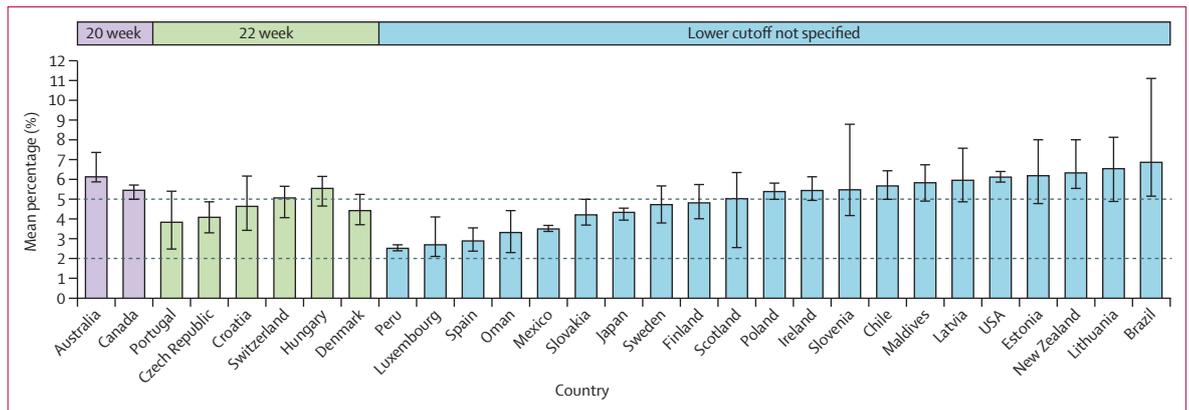
Figure 5: Percentage of reported preterm births that are less than 28 weeks by country showing variation with different lower gestational age thresholds
Data from 29 countries with more than one reported datapoint providing information on the proportion of preterm births that are <28 weeks from 1990 to 2010. Error bars show range of reported proportions. All these countries report using livebirths as numerator or denominator. The 5% standard is based on meta-analysis shown in table 1. For estimation input dataset <2% was considered implausible and the data were excluded.
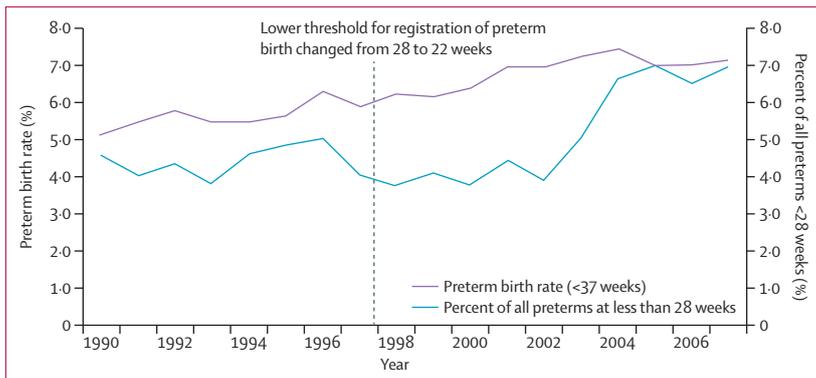
Figure 6: Variation in preterm birth rate and proportion of preterm births at less than 28 weeks with a reduction in the lower threshold for registration of preterm births from 28 to 22 weeks' gestation in Denmark
Analysis of 1 191 000 livebirths 1990 to 2007 Data source: National Board of Health.[60]

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

Improved quality and quantity of preterm birth data are needed in every country, but especially in low-income countries. Efforts in every country should be directed to the increase of coverage and systematic recording of all births, whether live or stillborn in a standard reporting format, which includes both birthweight and estimated gestational age. Application of a standard definition for preterm birth in terms of both the numerator and the denominator is essential. We have used the standard ICD 10 definition focusing on all livebirths at less than 37 weeks' gestation. A 28 week threshold was mentioned in ICD 10, but since the last edition, increased viability at lower gestational ages calls for this threshold to be reviewed, and consequently, very few countries are now applying this as a threshold for reporting (figure 5).[18] We recommend the use of an additional data quality marker regarding the percent of liveborn preterm babies under

1000 g or 28 weeks of gestation because of highly variable reporting of this group of babies and variable practices in resuscitation of the "micro preemie" group under 26 weeks' gestation.[61] The ICD 11 process provides an opportunity to give clear guidelines regarding this and other perinatal birth and death certificate issues, relevant to both high-income and low-income contexts.

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

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

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

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

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

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