Declines in stillbirth and neonatal mortality rates in Europe between 2004 and 2010: results from the Euro-Peristat project

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ABSTRACT
Background Stillbirth and neonatal mortality rates declined in Europe between 2004 and 2010. We hypothesised that declines might be greater for countries with higher mortality in 2004 and disproportionately affect very preterm infants at highest risk.

Methods Data about live births, stillbirths and neonatal deaths by gestational age (GA) were collected using a common protocol by the Euro-Peristat project in 2004 and 2010. We analysed stillbirths at ≥28 weeks GA in 22 countries and live births ≥24 weeks GA for neonatal mortality in 18 countries. Per cent changes over time were assessed by calculating risk ratios (RR) for stillbirth, neonatal mortality and preterm birth rates in 2010 vs 2004. We used meta-analysis techniques to derive pooled RR using random-effects models overall, by GA subgroups and by mortality level in 2004.

Results Between 2004 and 2010, stillbirths declined by 17% (95% CI 10% to 23%), with a range from 1% to 39% by country. Neonatal mortality declined by 29% (95% CI 23% to 35%) with a range from 9% to 67%. Preterm birth rates did not change: 0% (95% CI −3% to 3%). Mortality declines were of a similar magnitude at all GA; mortality levels in 2004 were not associated with RRs.

Conclusions Stillbirths and neonatal deaths declined at all gestational ages in countries with both high and low levels of mortality in 2004. These results raise questions about how low-mortality countries achieve continued declines and highlight the importance of improving care across the GA spectrum.

INTRODUCTION
Perinatal birth outcomes have improved markedly in high-income countries over past decades: rates of neonatal mortality (deaths of live born infants in the first 28 days of life) were between 10 and 20/1000 live births in the 1970s and are now under 3/1000 in most countries.¹ ² Rates of stillbirth (infants born without signs of life) have also declined since the 1970s, although recent research suggests that declines have slowed or stopped in many countries.³ Despite these generally positive trends, the burden of mortality remains high, with an estimated 40 000–45 000 stillbirths and neonatal deaths per year in the countries of the European Union (EU).¹ ³

There are striking inequalities in mortality between European countries. The first Euro-Peristat report documented wide variations in stillbirth and neonatal mortality rates in Europe in 2004.⁴ Owing to the differences in registration practices for births and deaths at very early gestations, cross-country comparisons are often interpreted with caution or disbelief.⁵ ⁶ However, differences persist even when births most likely to be affected by registration practices are excluded.⁷ Further, while some of the variation was explained by higher mortality in the new member countries from the Baltic and Eastern and Central Europe, substantial differences were also observed in Western Europe.

The second Euro-Peristat report found that stillbirth and neonatal mortality rates declined between 2004 and 2010,¹ ⁸ but the patterns of this decline and its impact on disparities between countries have not been explored. Over time, higher mortality countries may experience steeper declines in mortality, thus leading to a narrowing of the gap between countries. While audits of perinatal deaths find that between 20% and 50% of deaths are associated with suboptimal care,⁹ ¹⁰ many fetal and neonatal deaths are not preventable—in particular, those related to lethal congenital anomalies or extremely preterm birth. Further, audits have shown that countries with lower mortality have fewer potentially preventable deaths.¹¹ These studies raise the question of whether there is an irreducible minimum in countries with low mortality. In addition, economic development and the spread of specialised medical technology may have fuelled more rapid declines in the new member states where mortality was higher in 2004.

Declines may also be greater for higher risk preterm infants in these countries because of the specialist technology and resources needed for their care.¹² More generally, changes may disproportionately affect very preterm infants who face the highest risks of mortality. Recent studies have reported mortality reductions for this population, attributed to continued medical advances and more active perinatal management.¹² ¹³ A final question relates to how much these declines reflect changes in gestation-specific mortality or whether they could result from changes in the gestational age distribution and, in particular, reductions in the preterm birth rate.

To better understand recent trends in stillbirth and neonatal mortality in Europe, we used data from the Euro-Peristat project collected in 2004 and 2010 to investigate the changes in stillbirths and neonatal mortality by gestational age and...
across countries according to their level of mortality in 2004. We hypothesised that declines would be greater for countries with higher mortality in 2004 and disproportionately affect very preterm infants.

METHODS
Data sources
This study was embedded within the Euro-Peristat project, which developed a list of valid and reliable indicators for monitoring and evaluating perinatal health in the EU and has produced perinatal health reports on 2004 and 2010 data.\textsuperscript{1, 4, 8} Twenty-five EU member states and Norway participated in data collection in 2004 and 2010. The Euro-Peristat project collects data from routine national-level population-based sources. Data come from medical birth registers, civil registration, child health systems and routine surveys, as described previously.\textsuperscript{1, 4, 7, 14}

In this study, we used aggregate data on the numbers of live births, stillbirths and neonatal deaths by gestational age for the years 2004 and 2010. Owing to missing data on mortality by gestational age, Cyprus, Greece and Spain were excluded for all comparisons and France, Germany, Hungary, Ireland and Italy were excluded for comparisons of neonatal mortality. Slovakia was excluded because birth and death registration procedures changed substantially over the study period. Thus, 22 and 18 countries were included for the analyses of stillbirths and neonatal mortality, respectively. Data for Belgium came from the Flanders region only and for the UK, data were provided separately for England and Wales, Northern Ireland and Scotland. Data from France came from national representative surveys in 2003 and 2010. For the first period, data for England and Wales were for births in 2005, and for Italy for births in 2003.

Variables and definitions
Our principal outcomes were stillbirth and neonatal mortality rates overall and by gestational age subgroup. We also calculated preterm birth rates in order to relate changes in the gestational age distribution to those observed for mortality. Euro-Peristat requests gestational age data using the best obstetrical estimate in completed weeks (ie, 28 weeks is equal to 28\textsuperscript{0} to 28\textsuperscript{6} weeks).

The stillbirth rate was defined as the number of deaths before or during birth at or after 28 weeks of gestation in a given year per 1000 live and stillbirths in the same year. The threshold of \geq 28 weeks was used because of differences in limits for registration of stillbirths and in policies towards screening for congenital anomalies and terminations of pregnancies. The neonatal mortality rate was defined as the number of deaths after live birth during the neonatal period (days 0–27) at or after 24 completed weeks of gestation in a given year per 1000 live births in the same year. For the Netherlands and Slovenia, we used cohort neonatal mortality rates (deaths occurring to infants born in the year), as annual rates are not reported. Births and deaths at 22–23 weeks were excluded because recording practices vary for these very early births. The preterm birth rate was defined as the per cent of live births before 37 completed weeks of gestation. To be consistent with the indicator of neonatal mortality, we excluded births at 22 and 23 weeks.

We derived gestation-specific mortality rates for the following subgroups: 24–27 weeks (for neonatal deaths only), 28–31, 32–36 and 37+ weeks. For stillbirths, a fetus at risk approach was used overall and by gestational age (ie, the rate at 28–31 weeks was defined as the number of stillbirths from 28 to 31 weeks divided by the number of fetuses in utero at 28 weeks).\textsuperscript{13}

Analysis strategy
To estimate the per cent change in mortality between the 2 years, we calculated risk ratios (RR) with 95% CIs for each outcome in 2010 vs 2004. We used meta-analysis techniques to derive pooled RR using random-effects models with the method of DerSimonian and Laird. Random-effects measures are interpretable as the association in an average country and relevant for inferences for the population of countries. We used Cochran’s homogeneity test statistic (Q) as a measure of heterogeneity and the I\textsuperscript{2} statistic and CIs, computed using the test-based method,\textsuperscript{16} to assess the percentage of total variation between countries that is due to true heterogeneity rather than chance.

To test the hypothesis that mortality declines were greater in countries with higher mortality in 2004, pooled RR were calculated for subgroups of countries defined by their mortality in 2004. Countries with low, intermediate and high mortality in 2004 were respectively defined as a rate under the 25th centile, between the 25th and 75th centiles, and above the 75th centile. We also tested the correlation between RRs and absolute rates of mortality in 2004 using non-parametric Spearman’s rank correlation tests. Spearman’s rank correlation tests were also used to assess the association between changes in mortality indicators and the change in the preterm birth rate.

To further explore the impact of the change of mortality by gestational age, we estimated absolute declines in the number of deaths for each gestational age subgroup. We computed expected deaths in 2010 given the 2010 distribution of births under the assumption that gestation-specific mortality was the same as in 2004. Absolute declines were estimated as the difference between the expected and the observed number of deaths in 2010.

Analyses were performed with Stata, V13.0 SE (Stata Corporation, College Station, Texas, USA).

RESULTS
Changes in stillbirth rates
Stillbirth rates at \geq 28 weeks in 2010 ranged from 2/1000 total births in the Czech Republic (1.5%) to over 4/1000 in Latvia (4.1%) and France (4.3%) (table 1). In 2004, rates ranged from 2.0/1000 in Finland to almost 5/1000 in Latvia (4.9%) and France (4.9%). Stillbirth rates declined in almost all countries and were significant in seven countries (figure 1A). The pooled RR across all countries was 0.83 (95% CI 0.77 to 0.90), representing a 17% decline. The heterogeneity in RRs was highly significant and the differences between the countries, as opposed to chance, accounted for an estimated 82% of the variation in the pooled rate (p<0.001, I\textsuperscript{2}=82.1% (95% CI 63.8% to 100%).

Changes in neonatal mortality rates
Neonatal mortality rates at \geq 24 weeks ranged from 1.1/1000 live births in Slovenia to 4.0/1000 in Malta in 2010 and from \geq 2/1000 live births in the Czech Republic, Luxembourg, Norway and Sweden (1.9%) to 5.5/1000 in Latvia in 2004 (table 1). Neonatal mortality declined in all countries except Northern Ireland and the decline was significant in 13 of 19 countries (figure 1B). The overall pooled RR was 0.71 (95% CI 0.65 to 0.77), representing a 29% decline. The test for heterogeneity was significant and between country differences accounted for an estimated 67% of the variation in the pooled RR (p<0.001; I\textsuperscript{2}=67.4% (95% CI 43.1% to 91.6%).

Changes in preterm birth rates
Preterm birth rates ranged from 3.3% to 8.8% in 2004 and from 5.4% to 8.9% in 2010 (table 1). Changes over this period
were compared as minimal with those observed for mortality (figure 1C), with a pooled RR of 1.00 (95% CI 0.97 to 1.03). There was significant heterogeneity between countries and very little variation due to chance in the pooled RR (p<0.001; \( I^2=96.0\% \) (95% CI 84.2% to 100%)). Changes in preterm live birth rates between 2004 and 2010, as measured by RR, were minimal compared with those observed for mortality and intermediate countries. The Spearman rank correlations coefficient test for the association of mortality levels in 2004 with changes between 2004 and 2010 was not significant (\( \rho=-0.18, p=0.47 \)).

**Declines in the number of deaths**

Figure 2 presents the additional deaths that would have occurred in participating countries in 2010 if gestational age-specific mortality had stayed the same as in 2004. For stillbirths, these were highest at 32–36 weeks (475 stillbirths) and 37+ weeks (426 stillbirths), accounting for 80% of the total. Decreases for neonatal mortality were highest at 37+ weeks (513 neonatal deaths) followed by 24–27 weeks (488 neonatal deaths), accounting for 68% of the total.

**DISCUSSION**

Stillbirth rates at 28 weeks of gestational age and over and neonatal mortality rates at 24 weeks of gestation age and over declined between 2004 and 2010 in most European countries. Overall, neonatal deaths declined more than stillbirths, but there was significant heterogeneity across countries. In contrast to our

| Table 1 | Stillbirth rates, neonatal mortality rates and preterm live birth rates in 2004 and 2010 in participating countries |
|---------|--------------------------------------------------------------------------------------------------------------------------|
| Country/coverage | Total births | Rate/1000 | Total births | Rate/1000 | Total births | Rate/1000 | Total births | Rate/1000 |
| Belgium: Flanders | 60 679 | 2.9 | 69 613 | 2.8 | 60 657 | 2.2 | 69 614 | 2.0 |
| Czech Republic | 97 480 | 2.4 | 116 239 | 1.5 | 97 649 | 1.9 | 116 376 | 1.6 |
| Denmark | 64 521 | 3.7 | 63 223 | 2.3 | 64 448 | 3.0 | 63 243 | 1.5 |
| Germany | 645 401 | 2.6 | 634 042 | 2.3 | 646 214 | – | 635 097 | – |
| Estonia | 13 939 | 3.2 | 15 790 | 2.7 | 13 948 | 3.9 | 15 802 | 1.3 |
| Ireland | 62 097 | 4.3 | 75 266 | 3.7 | 62 013 | – | 75 635 | – |
| France | 14 540 | 4.9 | 14 753 | 4.3 | 14 507 | – | 14 712 | – |
| Italy | 539 698 | 3.7 | 539 749 | 2.4 | 538 881 | – | 539 959 | – |
| Latvia | 20 382 | 4.9 | 19 164 | 4.1 | 20 348 | 5.5 | 19 136 | 3.3 |
| Lithuania | 29 502 | 3.9 | 30 849 | 3.4 | 29 466 | 4.2 | 30 815 | 2.3 |
| Luxembourg | 559 658 | 2.8 | 651 729 | 2.9 | 560 185 | 1.9 | 651 729 | 1.2 |
| Hungary | 94 900 | 3.7 | 90 155 | 3.4 | 95 018 | – | 90 259 | – |
| Malta | 3894 | 3.9 | 4020 | 3.5 | 3887 | 4.4 | 4016 | 4.0 |
| The Netherlands | 178 710 | 4.3 | 176 261 | 2.9 | 178 406 | 2.8 | 176 249 | 2.2 |
| Austria | 78 874 | 2.5 | 78 539 | 2.5 | 78 903 | 2.5 | 78 644 | 1.7 |
| Poland | 356 734 | 3.8 | 413 150 | 3.0 | 356 499 | 4.4 | 413 070 | 3.1 |
| Portugal | 202 382 | 3.5 | 228 282 | 3.3 | 202 488 | 2.2 | 228 278 | 1.9 |
| Slovenia | 57 407 | 2.0 | 61 123 | 2.0 | 57 423 | 2.0 | 61 123 | 1.6 |
| Finland | 100 111 | 3.2 | 114 649 | 2.8 | 100 053 | 1.9 | 114 472 | 1.3 |
| Sweden | 639 966 | 4.0 | 711 217 | 3.8 | 639 952 | 2.5 | 710 862 | 2.0 |
| UK: England and Wales | 114 125 | 3.8 | 125 259 | 3.4 | 114 051 | 2.4 | 125 252 | 3.0 |
| UK: Scotland | 52 860 | 4.6 | 57 133 | 3.6 | 52 801 | 2.5 | 57 102 | 2.1 |
| Norway | 57 092 | 2.9 | 62 106 | 2.7 | 57 093 | 1.9 | 62 086 | 1.3 |

*Data from Belgium cover Flanders only and data from the UK are provided separately for England and Wales, Northern Ireland and Scotland. Scotland; ‡Data are from the French National Perinatal Surveys. †Data from Belgium cover Flanders only and data from the UK are provided separately for England and Wales, Northern Ireland and Scotland. Data from 2005. ‡Data are from 2003. Data are from 2004. ©Coversions in 2004 was not complete.
Figure 1 (A) Risk ratios (95% CI) of stillbirths in 2010 vs 2004 for 22 European countries. (B) Risk ratios (95% CI) of neonatal mortality in 2010 vs 2004 for 18 European countries. (C) Risk ratios (95% CI) of preterm births in 2010 vs 2004 for 22 European countries. Data from Belgium cover Flanders only and data from the UK are provided separately for England and Wales, Northern Ireland and Scotland.

Table 2 Pooled risk ratios (RRs) of stillbirths in 2010 vs 2004 overall, by mortality level in 2004 and by gestational age

| Country          | RR (95% CI) | RR (95% CI) | RR (95% CI) | RR (95% CI) |
|------------------|-------------|-------------|-------------|-------------|
| Overall          | 0.83 (0.77~0.90) | 0.83 (0.77~0.90) | 0.83 (0.77~0.90) | 0.83 (0.77~0.90) |
| Mortality in 2004|             |             |             |             |
| Low mortality*   | 0.86 (0.75~0.99) | 0.90 (0.70~1.14) | 0.77 (0.65~0.92) | 0.92 (0.75~1.14) |
| Intermediate mortality† | 0.83 (0.74~0.92) | 0.90 (0.76~1.08) | 0.80 (0.75~0.86) | 0.77 (0.64~0.93) |
| High mortality‡  | 0.83 (0.71~0.96) | 0.86 (0.68~1.10) | 0.80 (0.67~0.95) | 0.82 (0.69~0.98) |

*Finland 2.0%, Czech Republic 2.4%, Austria 2.5%, Germany 2.6%, Portugal 2.7% and Luxembourg 2.8%.
†Belgium: Flanders 2.9%, Norway 2.9%, Estonia 3.2%, Sweden 3.2%, Slovenia 3.5%, Denmark 3.7%, Italy 3.7%, Hungary 3.7%, Poland 3.8%, UK: Northern Ireland 3.8%, Lithuania 3.9% and Malta 3.9%.
‡France 4.9%, Latvia 4.9%, UK: Scotland 4.6%, Ireland 4.3%, the Netherlands 4.3% and England and Wales 4.0%.

GA, gestational age.
initial hypotheses, these declines were not more pronounced among countries with higher mortality in 2004, indicating that continued gains occurred both in low-mortality and high-mortality countries. Marked disparities remained, and in 2010, high-mortality countries still had rates double those of lower mortality countries. These declines were not driven by a change in the gestational age distribution, but by gestation-specific reductions in mortality that were not restricted to the highest risk babies but affected all gestational age subgroups. In fact, absolute declines in the number of deaths were highest for term births, followed by births between 24 and 27 weeks. For stillbirths, reductions were greatest among moderately preterm and term births. These results underscore the importance of a focus on improving outcomes across the gestational age spectrum.

This study has strengths and limitations. Euro-Peristat collects population-based data on births and deaths using a common protocol. Information is requested by week of gestation making it possible to compute gestation-specific mortality rates which are unavailable in other international databases. Owing to differences in recording practices for births and deaths in Europe, we excluded stillbirths at 22–27 weeks and neonatal deaths at 22–23 weeks, allowing like-with-like comparisons across countries and across time.17 However, owing to these exclusions, we were unable to assess changes in stillbirth before 28 weeks. Another limitation is that we had only two time points, as Euro-Peristat collects data periodically for its reports. This increases variation due to annual fluctuations, especially in small countries, and the influence of specific situations linked to the years selected for our studies. In Italy, for instance, data covering the first period were produced after institutional changes in the processing of birth certificates; weights were used to compute total numbers, a procedure that was no longer used in 2010.18 Finally, as Euro-Peristat collects national-level aggregate data, we are limited by the lack of information on other factors to explain the observed changes in outcomes.

Our results corroborate studies showing steady declines in neonatal mortality in high-income countries,19 but contrast with some studies that have shown stagnating or increasing stillbirth rates.20–22 Part of these differences may be related to how stillbirth rates are measured. For instance, a Canadian study found that the reported increases in stillbirth rates were due to increasing terminations of pregnancies, not spontaneous stillbirths.21 The fact that some countries count terminations of pregnancy as stillbirths, while others do not,14 is one of the justifications for Euro-Peristat 28 week inclusion threshold since terminations are rare after this gestational age in most countries.22 It is also possible that stillbirth rates have begun to decline in some countries after a period of stagnation.24

We did not find marked changes in preterm birth rates, in contrast with recent reports of declining rates from the USA, although baseline rates were higher.23 While there was substantial heterogeneity in changes in the preterm birth rate over the study period, confirming previous Euro-Peristat analyses,24 these changes were not correlated with changes in mortality. Efforts to prevent preterm births have generally been unsuccessful,25 although the fact that some countries have experienced declines over the past decade has spurred interest in understanding the drivers of these changes.26 Further, the relationship between higher preterm birth rates and mortality may not be straightforward as some preterm births are the result of intervention undertaken to prevent stillbirths and improve neonatal outcomes.27

Gestation-specific mortality declined at all gestational ages, suggesting that explanations are multifactorial. Several non-exclusive hypotheses can be put forth. Changes in screening policies for congenital anomalies could have lowered reported stillbirths and neonatal mortality rates if screening led to early terminations for lethal anomalies or better postnatal management of certain anomalies such as congenital heart defects.31 Studies from the Netherlands and Denmark, where declines

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Table 3  Pooled risk ratios (RRs) of neonatal mortality in 2010 vs 2004 overall, by mortality level in 2004 and by gestational age

| Overall | Gestational age subgroup |
|---------|---------------------------|
|         | All countries | 24–27 Weeks | 28–31 Weeks | 32–36 Weeks | 37+ Weeks |
| RR (95% CI) | RR (95% CI) | RR (95% CI) | RR (95% CI) | RR (95% CI) |
| Mortality in 2004 | | | | | |
| Low mortality | 0.71 (0.65 to 0.77) | 0.75 (0.66 to 0.83) | 0.74 (0.65 to 0.83) | 0.78 (0.68 to 0.90) | 0.70 (0.60 to 0.81) |
| Intermediate mortality | 0.71 (0.63 to 0.81) | 0.74 (0.63 to 0.86) | 0.79 (0.66 to 0.94) | 0.77 (0.63 to 0.93) | 0.71 (0.57 to 0.89) |
| High mortality | 0.65 (0.57 to 0.75) | 0.78 (0.71 to 0.86) | 0.66 (0.57 to 0.77) | 0.70 (0.60 to 0.82) | 0.68 (0.48 to 0.96) |

*Czech Republic 1.9%, Finland 2.0%, Luxembourg 1.9% and Norway 1.9%.
†Finland 2%, Belgium: Flanders 2.2%, Slovenia 2.2%, Portugal 2.3%, UK: Northern Ireland 2.4%, Austria 2.5%, UK: England and Wales 2.5%, UK: Scotland 2.5%, the Netherlands 2.8%, Denmark 3% and Estonia 3.9%.
‡Latvia 3.5%, Poland 4.4%, Malta 4.4% and Lithuania 4.2%.

Figure 2  Estimated reduction in the number of stillbirths and neonatal deaths by gestational age subgroup in 2010 compared to 2004. Reduction computed as the difference in the number of observed and expected deaths with the number of expected deaths in 2010 calculated if gestational age-specific mortality had been the same as in 2004.
were particularly steep, suggest that newly introduced screening policies may have contributed to declines. Changes may also result from other policies, including preconception counseling, or programmes to improve the detection of fetal growth restriction. The decline in the prevalence of congenital heart defects in Europe has been associated with more periconceptional use of folic acid, for instance. Studies also find that more very preterm infants are receiving appropriate treatments, such as antenatal steroids and surfactants. Finally, the increasing emphasis on quality of care in obstetrics and neonatology, through the development of clinical guidelines and audits, may have improved the outcome.

Changes in the prevalence of risk factors in the population of childbearing women may also contribute to declines. In particular, smoking during pregnancy, considered to be the major risk factor for stillbirth, has decreased in many countries over this period. However, other risk factors for stillbirth and neonatal death—such as older maternal age and overweight—have increased and would have a negative effect on population indicators.

These results raise multiple questions for future research, including on the specific impact of policy initiatives as well as the relative contribution of changes in population characteristics to mortality declines. Further, we focused on stillbirth and neonatal mortality as separate indicators because of their distinct aetiological determinants in high-income countries with a high proportion of antepartum deaths and the need for different analytical approaches (fetus at risk approach for stillbirths). However, future studies should consider whether changes in policies related to stillbirths affect neonatal mortality and vice versa. Finally, while these results relate to countries in Europe, Euro-Peristat methodology could be applied in other countries, including middle-income and some low-income countries with population-based data of births and early prenatal care enabling accurate measurement of gestational age.

In conclusion, substantial declines in neonatal and stillbirth rates in Europe between 2004 and 2010 affected all gestational ages and were observed in high-mortality and low-mortality countries. Many low-mortality countries achieved continued decreases in rates, raising the global benchmarks for high performance for these key indicators of population health. These results also highlighted the importance of term and moderate preterm births to overall survival gains in high-mortality and low-mortality countries.

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