- 1 Quantifying the burden of stillbirths before 28 weeks of completed gestational age in high income
- 2 countries: a population based study of 19 European countries.
- 3 Authors: Lucy Smith, PhD<sup>1</sup>, Ashna D Hindori-Mohangoo, PhD<sup>2,3,4</sup>, Marie Delnord, PhD<sup>5</sup>, Mélanie
- 4 Durox, MSc<sup>5</sup>, Prof Katarzyna Szamotulska, PhD<sup>6</sup>, Prof Alison Macfarlane, CStat<sup>7</sup>, Prof Sophie
- 5 Alexander, PhD<sup>8</sup>, Prof Henrique Barros, PhD<sup>9</sup>, Prof Mika Gissler, PhD<sup>10</sup>, Béatrice Blondel, PhD<sup>5</sup>, Prof
- 6 Jennifer Zeitlin, DSc<sup>5</sup> for the Euro-Peristat Scientific Committee<sup>11</sup>

#### 7 Affiliations

- 8 1. Department of Health Sciences, University of Leicester, Leicester, UK
- 9 2. Netherlands Organisation for Applied Scientific Research, TNO Healthy Living, Department
   Child Health, Leiden, the Netherlands
- 1 3. Perinatal Interventions Suriname, Perisur Foundation, Paramaribo, Suriname
- 12 4. Tulane University, School of Public Health and Tropical Medicine, New Orleans, USA
- Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé),
   Centre for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris
   Descartes University, Paris, France
- Department of Epidemiology and Biostatistics, National Research Institute of Mother and
   Child, Kasprzaka 17 a, 01-211 Warsaw, Poland
- 18 7. Centre for Maternal and Child Health Research, City, University of London, UK
- 19 8. Perinatal Epidemiology and Reproductive Health Unit, ULB, Brussels, Belgium
- 20 9. ISPUP-EPIUnit, Universidade do Porto, Porto, Portugal
- THL National Institute for Health and Welfare, Helsinki, Finland and Karolinska Institute,
   Stockholm, Sweden
- 23 10. The Euro-Peristat Scientific Committee

#### 24 Corresponding author:

- 25 Lucy K Smith; The Infant Mortality and Morbidity Studies (TIMMS), Department of Health Sciences,
- 26 College of Medicine, Biological Sciences and Psychology, University of Leicester, Centre for Medicine,
- 27 University Road, Leicester, LE1 7RH, UK
- 28 Email: <u>lks1@leicester.ac.uk</u>
- 29
- 30 Word count: 3183

#### 1 Abstract

- 2 Background: International comparisons of stillbirth allow assessment of variations in clinical practice
- 3 to reduce mortality. Currently such comparisons only include stillbirths from 28 or more completed
- 4 weeks of gestational age which underestimates the true burden of stillbirth. With increased
- 5 registration of early stillbirths in high income countries we assessed the reliability of including
- 6 stillbirths before 28 completed weeks.
- 7 **Methods:** We used national cohort data from 19 European countries participating in the Euro-
- 8 PERISTAT project on live births and stillbirths from 22 completed weeks of gestation in 2004, 2010
- 9 and 2015. Pooled stillbirth rates were calculated using a random-effects model and changes in rates
- 10 between 2004 and 2015 were calculated using risk ratios (RR) by gestational age and country.
- 11 **Results**: Stillbirths at 22<sup>+0</sup>-27<sup>+6</sup> weeks of gestation accounted for 32% of all stillbirths in 2015. The
- 12 pooled stillbirth rate at 24<sup>+0</sup>-27<sup>+6</sup> weeks declined from 0.97 to 0.71 per 1000 births from 2004 to
- 13 2015, a reduction of 24% (RR=0.77, 95% CI 0.68 to 0.88). The pooled stillbirth rate at 22<sup>+0</sup>-23<sup>+6</sup> weeks
- of gestation in 2015 was 0.53 per 1000 births and had not significantly changed over time (RR 0.97,
- 15 95% CI 0.80 to 1.16) although changes varied widely between countries (RRs 0.62 to 2.09). Wide
- 16 variation in the percentage of all births occurring at 22<sup>+0</sup>-23<sup>+6</sup> weeks of gestation suggest
- 17 international differences in the ascertainment.
- 18 **Conclusions**: Current definitions used for international comparisons exclude a third of stillbirths.
- 19 International consistency of reporting stillbirths at 24<sup>+0</sup>-27<sup>+6</sup> weeks suggests these deaths should be
- 20 included in routinely reported comparisons. This would have a major impact, acknowledging the
- 21 burden of perinatal death to families, and making international assessments more informative for
- 22 clinical practice and policy. Ascertainment of fetal deaths at 22<sup>+0</sup>-23<sup>+6</sup> weeks should be stabilised so
- that all stillbirths from 22 completed weeks of gestation onwards can be reliably compared.

24 **300 words** 

#### 1 Introduction

2 The 2016 Lancet stillbirth series highlighted the global impact of stillbirths on parents and families<sup>1</sup> with around 3.5 per 1000 births ending in stillbirths in high income countries<sup>2,3</sup> and a decline over the 3 4 last decade for stillbirths in the third trimester<sup>2,4</sup>. However, the full extent of the burden is generally 5 underestimated since a gestational age cut-off of 28 completed weeks for comparing the stillbirth 6 rate has been implemented widely as recommended by WHO for international purposes 7 (http://www.who.int/maternal\_child\_adolescent/epidemiology/stillbirth/en/ Accessed 07/03/2017). 8 Although WHO recommends a threshold of 22 completed weeks for ascertainment of stillbirths 9 within countries, there are major discrepancies between countries in their registration legislation and 10 within countries in the implementation of their legislation. These inhibit reliable international comparisons<sup>2,4,5</sup> using this limit. There are also differences in legislation about late termination of 11 12 pregnancy and the extent to which late terminations are reported as stillbirths and can be 13 distinguished from them. These have a major influence on reported stillbirth rates at early gestations, particularly at 22<sup>+0</sup> to 23<sup>+6</sup> weeks<sup>6,7</sup>. In addition international differences in the perception 14 15 of viability may lead to differences in legislation about the registration of stillbirths and their

16 ascertainment at early gestations<sup>1,8</sup>.

17 Because of the way these issues affect the comparability of stillbirth rates, there has been little international comparison of stillbirths below the gestational age threshold recommended by WHO of 18 19 28 completed weeks. Over the past few decades, however, there have been consistent increases 20 within countries in reported numbers of babies born before 28 completed weeks of gestation<sup>9</sup>, and 21 dramatic increases in their survival rates, with most babies born alive at 25 or more completed weeks 22 gestation surviving <sup>10</sup>. Flenady et al.<sup>2</sup> highlight that depending on the definition, between 35% and 23 50% of stillbirths occur before 28 completed weeks of gestation. The Lancet stillbirth series 24 suggested that stillbirth rates at earlier gestations are not showing the falls seen at 28 completed 25 weeks of gestation and over and may possibly even be increasing<sup>2</sup>, but international comparisons to 26 confirm this statement are lacking. By excluding these stillbirths, the burden of stillbirths in high 27 income countries could be seriously underestimated. This could therefore fail to acknowledge the 28 heartache suffered by many parents and their families experiencing fetal death or stillbirth<sup>11</sup>. 29 Furthermore, by excluding these deaths, international comparisons are limited in their ability to 30 assess the overall burden of stillbirth and the variations in clinical practice and therefore to identify 31 best strategies for improving care.

Only through international studies, such as the Euro-Peristat project, that collect data on births and
 deaths starting at 22 completed weeks of gestation using a standardised protocol, can cross-country

1 comparisons of stillbirth rates be made. This makes the case for consistent international reporting 2 practices for terminations of pregnancy and agreed definitions for reporting of stillbirths and live 3 births. Here we undertake analyses of data from the Euro-Peristat project on stillbirths from 22 4 completed weeks of gestation in 19 European countries to assess the additional burden of stillbirth at 5 early gestational ages and to quantify changes in stillbirth rates at these early gestations over time. 6 These analyses will also compare the consistency of the reporting of fetal deaths by gestational age 7 to assess the evidence for moving the gestational age cut-off for the international reporting of 8 stillbirths in the future.

9

#### 10 Methods

#### 11 Data sources

12 The data from this study are from the Euro-Peristat project, which developed a list of valid and reliable indicators for monitoring and evaluating perinatal health in the EU<sup>4,5,9,12</sup>. The Euro-Peristat 13 project collected national level data from routine population-based sources on its indicators in 2004, 14 15 2010 and 2015 using a common data collection instrument. Data come from medical birth registers, civil registration, child health systems and routine surveys, as described previously.<sup>4,5,9,12</sup> In 2004, 26 16 17 countries participated in Euro-Peristat, rising to 29 in 2010 and 31 in 2015. The project was based on 18 aggregated data collected routinely in each European country, following the ethics approval required 19 locally.

20 In this study, we use aggregated data on the numbers of live births and stillbirths by gestational age 21 for the years 2004, 2010 and 2015 for countries with data from all three periods, provided in a 22 comparable manner for the same geographic area. We excluded countries without national data on 23 stillbirths by gestational age in these periods (Cyprus, France and Spain), or where data available 24 were not comparable between 2004 and 2015 (due to changes in birth and death registration in Sweden and Slovakia; due to lack of national data in 2004 in Belgium). We also excluded those 25 countries with fewer than 10000 births per year as the proportion of stillbirths at 22<sup>+0</sup>-27<sup>+6</sup> weeks of 26 27 gestation is small and consequently the numbers of these deaths are extremely small (Malta and 28 Luxembourg). For the UK, data were provided separately for England and Wales combined, Northern Ireland and Scotland. Thus, 16 countries were included in the analyses of stillbirths at 22<sup>+0</sup> to 23<sup>+6</sup> 29 weeks of gestation and 19 in the analyses of stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation. For the first 30 31 period, data were for births in 2005 in England and Wales and for births in 2003 in Italy. In the latter 32 period, data from Poland were for 2014, not 2015. Data sources are provided in Table S1.

#### 1 Definitions and analysis

2 The stillbirth rate was defined as the number of deaths before or during birth per 1000 live and 3 stillbirths. Stillbirth rates were calculated separately for each country, year of the study (2004, 2010 4 and 2015) and for each gestational age subgroups (22<sup>+0</sup> to 23<sup>+6</sup> weeks; 24<sup>+0</sup> to 27<sup>+6</sup> weeks and 28<sup>+0</sup> weeks and over) <sup>12</sup>. The fetus at risk approach was used overall and by gestational age so, for 5 example the rate at 24<sup>+0</sup>–27<sup>+6</sup> weeks was defined as the number of stillbirths from 24<sup>+0</sup> to 27<sup>+6</sup> weeks 6 divided by the number of fetuses in utero at 24<sup>+0</sup> weeks <sup>13</sup>. Terminations of pregnancy were excluded 7 8 from stillbirth rates in countries where they were included in the data source and could be 9 differentiated from spontaneous stillbirths. In order to calculate the overall stillbirth rate in each of 10 the time periods, pooled estimates were calculated with 95% confidence intervals (CIs) for gestational age group in 2004, 2010 and 2015. Meta-analysis techniques were used to obtain the 11 12 pooled stillbirth rate. A random-effects model was fitted using the method of Der Simonian and Laird<sup>14</sup> to take account of variation between countries. The change in stillbirth rate over time was 13 14 calculated using risk ratios (RR) with 95% CIs for each gestational age group in 2015 vs 2004. Again 15 meta-analysis techniques were used to obtain a pooled RR using a random-effects model. We 16 explored changes in ascertainment of stillbirths by calculating the RR of total births rates in 2015 17 compared with total birth rates in 2004 by gestational age group.

18 Several sensitivity analyses were undertaken. For all analyses, the impact on stillbirth rates of including only those countries where terminations of pregnancy before 24<sup>+0</sup> weeks of gestation could 19 20 be excluded from the data was explored. We also assessed the impact of excluding stillbirths with 21 unknown gestations which were classified as being of 28 completed weeks gestation or above in the 22 main analyses. Finally, we compared the percentage of stillbirths occurring between 22<sup>+0</sup> and 27<sup>+6</sup> 23 week gestation in 2015 in the 8 countries excluded from our study because they did not have 24 comparable data across the 3 periods (Cyprus, Spain, Sweden, Slovakia, Malta, Luxembourg, Belgium 25 and France) to assess their comparability with the main results.

26 Analyses were performed with Stata, V.14.0 SE (Stata Corporation, College Station, Texas, USA).

#### 27 Role of the funding source

- 28 The funders of the study had no role in study design, data collection, data analysis, data
- 29 interpretation, or writing of the report. The corresponding author had full access to all the data in the
- 30 study and LS and JZ had final responsibility for the decision to submit for publication.

31

1

#### 2 Results

Table 1 shows the percentage of stillbirths at 22<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation in 2015. This shows that 3 4 32.0% of stillbirths overall would be excluded from stillbirth statistics when reporting only deaths at 5 28<sup>+0</sup> weeks of gestation and over. This proportion ranged from 20% in Estonia to 51% in the 6 Netherlands. Table 1 also shows that only a few countries could not exclude terminations of 7 pregnancy in 2004, 2010 and 2015 as, for example, the Netherlands where terminations could not be 8 separated from spontaneous stillbirths. In most countries, inclusion of terminations of pregnancy 9 after 24 weeks of gestation was rare. For countries reporting data on spontaneous stillbirths only, the highest rate of stillbirth at 22<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation in 2015 was 37% in Norway. This was 10 similar to the rate in 2004 (30%) and 2010 (35%) [see Supplementary table S2 & S3]. The percentage 11 12 of stillbirths at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation in 2015 varied widely between countries representing 13 between 6% in Ireland and 36% in the Netherlands or to 23% in Hungary if excluding countries where terminations were included. Less international variation was seen for stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks 14 in 2015 where they represented between 12% in Latvia and 29% in Slovenia or 23% in Northern 15 16 Ireland if excluding countries where terminations were included. In 2004 the variation was less for 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation births but similar for 24<sup>+0</sup> to 27<sup>+6</sup> weeks births (see supplementary 17

18 table S2 and S3).

19 The pooled estimate of the stillbirth rate at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation for the 16 countries in 2015 (Figure 1a) was 0.53 per 1000 births in 2015 (95% Cl 0.41 to 0.66). The relatively high I-squared 20 21 value of 94% suggested variation between countries. Ireland reported a rate of 0.26 per 1000 births 22 compared to 1.73 per 1000 births in the Netherlands, a six-fold difference. This range was reduced to 23 0.26 to 0.69 when excluding countries where terminations were included, a three-fold difference. For births at this gestation, the stillbirth rate barely changed over time from 0.56 per 1000 births in 2010 24 25 (95% CI 0.39 to 0.73) and 0.55 per 1000 births (95% CI 0.40 to 0.70) in 2004, see Figure 1a. In 2004 26 rates ranged from 0.15 per 1000 births in Portugal to 1.37 in the Netherlands, an approximately nine-27 fold difference in the most extreme rates. Comparing 2015 with 2004, there was no change over time 28 in the pooled estimate of the stillbirth rate (RR 0.97, 95% CI 0.80 to 1.16) (Figure 1a) but the changes 29 over time ranged widely between countries, from 0.62 to 2.09. A sensitivity analysis was undertaken which included only countries where terminations of pregnancy before 24<sup>+0</sup> weeks of gestation could 30 be excluded (see Table 1). This showed that the pooled rate did not change significantly over time 31 (RR 0.87; 95% CI 0.72 to 1.06) and variation in the changes over time between countries reduced but 32 33 was still wide ranging from 0.62 to 1.26.

This variation between countries at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation contrasted with the patterns for 1 stillbirths from 24 weeks of gestation onwards. The pooled estimate of the stillbirth rate at  $24^{+0}$  to 2 3 27<sup>+6</sup> weeks of gestation in 2015 (Figure 1b) in the 19 included countries was 0.71 per 1000 births 4 (95% CI 0.58 to 0.84) with rates ranging from 0.43 per 1000 births in Finland to 1.77 per 1000 births 5 in Slovenia, an approximately four-fold difference, with a relatively high I-squared value of 93%. 6 However this range was reduced to 0.43 to 0.78 when excluding countries where terminations were 7 included and could not be separated from spontaneous stillbirths, a two-fold difference. Over time, 8 the pooled rate had declined substantially from 0.97 stillbirths per 1000 births in 2004 (95% CI 0.79 9 to 1.14) and 0.81 stillbirths per 1000 births in 2010 (95% CI 0.69 to 0.93) (Figure 1b), with rates in 10 2004 ranging between 0.54 per 1000 births in Germany and 1.62 in Slovenia, an approximately 2.5 11 fold difference in rates. This represented a significant reduction over the decade from 2004 to 2015 12 in the stillbirth rate of 23% (RR=0.77, 95% CI 0.68 to 0.88) (Figure 1b) with moderate variation 13 between countries ranging from 0.42 to 1.18. A sensitivity analysis restricted to countries where terminations of pregnancy from 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation could be excluded (for countries 14 15 included see Table 1) showed a similar reduction of stillbirth over time (RR=0.78, 95% CI 0.67 to 16 0.92).

Over the three periods, there was wide variation in births occurring at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation as a proportion of all births (Figure 2a), ranging from a reduction of 30% in Lithuania to an increase of 187% in Portugal. Overall the proportion of births at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation increased by 14% from 2004 to 2015 (RR=1.14, 95% CI 0.99 to 1.31). In contrast, there was far less variation in the change over time at 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation (Figure 2b). Overall there was a slight reduction in births at 24<sup>+0</sup> to 27<sup>+6</sup> weeks of 10% (RR=0.90, 95%CI 0.84 to 0.96) and this varied from a reduction of 43% in Northern Ireland to an increase of 9% in Germany and Italy.

24 Sensitivity analyses excluding stillbirths of unknown gestational age had minimal impact on the

25 percentage of stillbirths occurring between 22<sup>+0</sup> to 27<sup>+6</sup> weeks gestation increasing the percentage of

stillbirths from 32.0% to 32.4%. Nor was there an impact on rates and relative risks over time.

27 Further sensitivity analyses exploring the percentage of stillbirths between 22<sup>+0</sup> to 27<sup>+6</sup> weeks

28 gestation in 2015 for the 8 countries excluded from our study found very similar results (33.5%).

29

#### 30 Discussion

31 We have used data from 19 European countries to explore stillbirths before 28 completed weeks of

32 gestation, a group that is often not included in international comparisons of deaths. This has shown

that around one in three stillbirths are not accounted for in standard stillbirth rates measured from

28 weeks of gestation<sup>1,2</sup>. Stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks represent around seven per 10 000 births 1 2 and are declining in a similar manner to stillbirths seen at later gestations in European and other high 3 income countries, although our data, similar to these other reports, reveal heterogeneity in trends across countries<sup>4</sup><sup>12</sup>. Stillbirths occurring at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation represent around six per 4 10 000 births. Stillbirth rates for these gestations have remained steady over time, but our 5 6 hypothesis is that this is likely to be related to improvements in the reporting of deaths at these gestations as there was an increase in all births at 22<sup>+0</sup> to 23<sup>+6</sup> weeks gestation compared to a fall in 7 births at  $24^{+0}$  to  $27^{+6}$  weeks gestation. 8

9 Interpretation and implications for policy

Stillbirth rates at 24<sup>+0</sup> to 27<sup>+6</sup> weeks appear to be falling by the same proportion as stillbirth rates at 28 weeks of gestation onwards<sup>12</sup>. The fall of 24% in stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks is extremely similar to that seen globally for stillbirths of 28 weeks of gestation and above for a similar time period of 2000 to 2015<sup>1</sup> suggesting consistent improvements over time in the reduction of stillbirths from 24 completed weeks of gestation.

15 In contrast, we found no change in the overall rate of stillbirth at  $22^{+0}$  to  $23^{+6}$  weeks between 2004, 16 2010 and 2015. It is possible that rates of stillbirth have remained stable at this gestation but this is 17 contrary to all other gestational age groups. In recent years the gestational age when a baby is 18 perceived as viable has decreased with changes in the approach to early management of these 19 babies. For example until recently, the American Academy of Pediatrics Neonatal Resuscitation Programme<sup>15</sup> recommended that resuscitation should be withheld when the gestational age is less 20 21 than 23 completed weeks or a birth-weight of less than 400 grams, but this has now been amended 22 to recommend that resuscitation should be withheld only below 22 completed weeks<sup>16</sup> and this is 23 supported by increases in reported survival in some countries. Consequently there has been an increased tendency for resuscitation of babies born at early gestations<sup>17,18</sup> and an increase in the 24 25 tendency to report babies as a neonatal death rather than stillborn<sup>18,19</sup> in some countries in Europe. 26 At the same time, the increase in viewing these early births as potential live births may also have 27 increased the reporting of early stillbirths.

Our study suggests that to ensure that the magnitude of the burden of stillbirth is better understood and to improve routine data for monitoring of the outcomes and management of extremely preterm births, WHO's threshold for international comparisons should be lowered, at least for high income countries. Mullan and Horton emphasised in the 2011 Lancet series on stillbirth that "to a mother and father, a stillbirth is no less a tragedy than the death of a newborn baby or child"<sup>20</sup> and that parents deserve "recognition of their loss and reassurance that an accurate record of it will add to the global knowledge required to prevent future ones"<sup>20</sup>. As part of the Lancet 2016 stillbirth series
Heazell et al. emphasised the major economic and psychosocial consequences of stillbirth. To a
mother or father a second trimester stillbirth is no less a tragedy than a stillbirth from 28 completed
weeks onwards and these parents too deserve recognition of their loss and accurate reporting of
deaths to improve care in the future.

#### 6 Strengths and limitations

7 A major strength of this work is the wide geographic coverage, the use of a standardised data 8 collection protocol and the ability to ensure that late terminations of pregnancies at or after 22 9 weeks wherever possible were disaggregated from the stillbirths so that they were not included in 10 the fetal death rate. Unfortunately terminations of pregnancy could not be excluded for a few countries; these occur principally at 22<sup>+0</sup> to 23<sup>+6</sup> weeks in many countries and while increases in late 11 12 terminations of pregnancy could contribute to the changes over time<sup>21</sup>, sensitivity analyses showed a similar increase over time for those countries where terminations could be excluded. While we had 13 14 to exclude some countries in the Euro-PERISTAT project that didn't have comparable data for all 15 periods, our sensitivity analyses support the generalizability of our results, as proportions of early 16 stillbirths in these countries were very similar.

#### 17 Conclusions

18 The consistency in reporting of births over time at 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation and the similarity 19 of reduction in the rate of stillbirth over time to births at 28 completed weeks of gestation and above suggests that stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation can be routinely included in rates of 20 21 stillbirth for international comparisons from now on. Improvements to ascertainment of stillbirths at 22 22 and 23 weeks of gestation within countries will allow the routine reporting of all stillbirths from 22 23 completed weeks of gestation onwards or even earlier internationally. This would lead to better 24 alignment of the gestational age at which stillbirths and neonatal deaths are reported as has already been done in some countries such as the US, Canada and Norway<sup>8</sup>. Such changes would enable a 25 26 fuller acknowledgment of the burden of perinatal death to health services and families and allow 27 assessment of variations in clinical practice in order to improve care.

28

#### 29 Funding statements

30 The Euro-Peristat project received funding from the European Union under the framework of the

Health Programme (grant numbers: 20101301, 2007114, 2003131) and the Bridge Health Project

32 (665691).

- 1 Lucy K Smith is funded by a National Institute for Health Research Career Development Fellowship.
- 2 This article presents independent research funded by the National Institute for Health Research
- 3 (NIHR). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR
- 4 or the Department of Health.
- 5 JZ, M Durox, M Delnord and LS had access to the full data and LS and JZ had final responsibility for
- 6 the decision to submit the manuscript for publication.
- 7 8

## 9 Contributors

- 10 All authors contributed to the overall conception and design of the study. JZ (2004, 2010, and 2015),
- 11 M Delnord (2010 and 2015) and M Durox (2015) and Ashna Hindori-Mohangoo (2004, 2010)
- 12 coordinated data collection. LS wrote the first draft of this manuscript, and analysed the data. All
- authors contributed to the interpretation of results and drafting of the manuscript. All authors read
- 14 and approved the final manuscript. LS is the guarantor.

## 1516 Data sharing

- 17 Aggregated data from the Euro-Peristat project can be downloaded from the project's website:
- 18 www.europeristat.com.
- 19

## 20 Acknowledgements

- 21 A full list of contributors to the European Perinatal Health Report: Health and Care of Pregnant
- 22 Women and Babies in Europe in 2010 can be found online <u>http://www.europeristat.com/our-</u>
- 23 <u>network/country-teams.html</u>
- 24
- 25 Competing interests: None declared. All authors have completed the ICMJE uniform disclosure form
- 26 at http://www.icmje.org/coi\_disclosure.pdf and declare: no support from any organisation for the
- 27 submitted work [or describe if any]; no financial relationships with any organisations that might have
- an interest in the submitted work in the previous three years [or describe if any], no other
- relationships or activities that could appear to have influenced the submitted work [or describe ifany].
- LS affirms that the manuscript is an honest, accurate, and transparent account of the study being
- reported; that no important aspects of the study have been omitted; and that any discrepancies from
- the study as planned (and, if relevant, registered) have been explained.
- 34 The Euro-Peristat Scientific Committee comprise: Gerald Haidinger (Austria), Sophie Alexander
- 35 (Belgium), Pavlos Pavlou (Cyprus), Petr Velebil (Czech Republic), Laust Mortensen (Denmark), Luule
- 36 Sakkeus (Estonia), Mika Gissler (Finland), Béatrice Blondel (France), Günther Heller, Nicholas Lack
- 37 (Germany), Aris Antsaklis (Greece), István Berbik (Hungary), Helga Sól Ólafsdóttir (Iceland), Sheelagh
- Bonham (Ireland), Marina Cuttini (Italy), Janis Misins (Latvia), Jelena Isakova (Lithuania), Yolande
- 39 Wagener (Luxembourg), Miriam Gatt (Malta), Jan Nijhuis (Netherlands), Kari Klungsøyr (Norway),
- 40 Katarzyna Szamotulska (Poland), Henrique Barros (Portugal), Mihai Horga (Romania), Jan Cap
- 41 (Slovakia), Natasa Tul (Slovenia), Francisco Bolúmar (Spain), Karin Gottvall (Sweden), Sylvan Berrut,
- 42 Mélanie Riggenbach (Switzerland), Alison Macfarlane (United Kingdom). Project coordination:
- 43 Jennifer Zeitlin, Marie Delnord, Ashna Hindori-Mohangoo.
- 44

#### 1 Research in context

- 2 Evidence before the study
- 3 Over the past decade there have been several systematic reviews and scoping studies that have
- 4 reviewed the literature in order to investigate the rates and risk factors for stillbirth internationally
- 5 and, specifically, in high income countries<sup>2,3,22</sup>. The most recent review was published in the Lancet
- 6 stillbirth series in 2016<sup>23</sup>. To update these reviews, we searched PubMed for international
- 7 comparisons of stillbirth published from Jan 1 2016 to the present using the search terms
- 8 "(international OR worldwide)" AND "(stillbirth\* OR fetal loss\* OR fetal death\*)" AND "(rate\*)" in
- 9 titles and abstracts. We only included studies in English. Research suggested that depending on the
- 10 definition, between 35% and 50% of stillbirths occur before 28 completed weeks of gestation and
- 11 that stillbirth rates at earlier gestations are not showing the falls seen at 28 completed weeks of
- 12 gestation and over and may possibly even be increasing but international comparisons to confirm
- this statement are lacking. Research also highlighted international variation in reporting of deaths at
- 14 22 and 23 weeks as a stillbirth or neonatal death which could impact on reported rates of stillbirth,
- 15 neonatal mortality and preterm birth.

## 16 Added value of this study

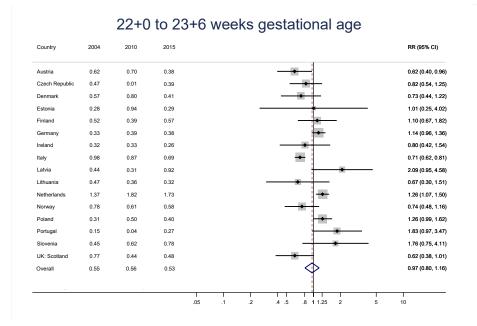
- 17 We used data from 19 countries participating in the international Euro-PERISTAT project, that
- 18 collected data on births and deaths starting at 22 completed weeks of gestation in 2004, 2010 and
- 19 2015. This project used a standardised protocol with consistent international reporting practices for
- 20 terminations of pregnancy and agreed definitions for reporting of stillbirths and live births. We
- estimated 32% of stillbirths were not identified using the gestational age cut-off of 28 weeks which is
- recommended for international studies. The pooled stillbirth rate at 24<sup>+0</sup>-27<sup>+6</sup> weeks declined from
- 23 0.97 to 0.70 per 1000 births from 2004 to 2015, a reduction of 24% (RR=0.76, 95% CI 0.67 to 0.87) in
- 24 line with that reported in international studies on stillbirths over 28 weeks gestation. The pooled
- stillbirth rate at 22<sup>+0</sup>-23<sup>+6</sup> weeks of gestation in 2015 was 0.54 and did not significantly change over
- time (RR 0.97, 95% Cl 0.81 to 1.16) but trends varied widely between countries (RRs 0.62 to 2.09)
- 27 with evidence of differing ascertainment between countries at these earlier gestations.
- 28 Implications of all the available evidence
- 29 Current definitions used for international comparisons exclude a third of stillbirths. International
- 30 consistency of reporting stillbirths at 24+0-27+6 weeks suggests that to ensure that the magnitude of
- 31 the burden of stillbirth is better understood and to improve routine data for monitoring of the
- 32 outcomes and management of extremely preterm births, WHO's threshold for international
- comparisons should be lowered, at least for high income countries. This would have a major impact,
- 34 acknowledging the burden of perinatal death to families, and making international assessments more
- 35 informative for clinical practice and policy. Ascertainment of fetal deaths at 22+0-23+6 weeks should
- 36 be stabilised so that all stillbirths from 22 completed weeks of gestation onwards can be reliably
- 37 compared. Contrary to speculation, stillbirths at 24<sup>+0</sup> to 27<sup>+6</sup> weeks are declining in a similar manner
- to stillbirths seen at later gestations in European and other high income countries. Stillbirths
- 39 occurring at 22<sup>+0</sup> to 23<sup>+6</sup> weeks of gestation have remained steady over time, but this is likely to be
- 40 related to improvements in the reporting of deaths at these gestations. Improvements to
- 41 ascertainment of stillbirths at 22 and 23 weeks of gestation within countries will allow the routine
- 42 reporting of all stillbirths from 22 completed weeks of gestation onwards or even earlier
- 43 internationally. This would lead to better alignment of the gestational age at which stillbirths and
- 44 neonatal deaths are reported.

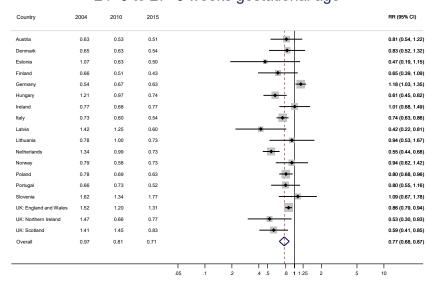
Number of stillbirths by gestational age Percentage of all stillbirths Total births 24<sup>+0</sup>-27<sup>+6</sup> 22<sup>+0</sup>-23<sup>+6</sup> >=28+0 22<sup>+0</sup>-23<sup>+6</sup> 24<sup>+0</sup>-27<sup>+6</sup> 22<sup>+0</sup>-27<sup>+6</sup> Inclusion of termination of Unknown >=22+0 Country weeks weeks weeks gestation weeks weeks weeks pregnancy weeks 15.5 Excluded Austria 83884 32 43 202 0 11.6 27.1 Czech Republic 43 296 23.9 Excluded 111162 52 7 10.8 13.1 32.4 Excluded Denmark 57847 24 31 115 0 14.1 18.2 20.4 Excluded 13961 4 7 43 7.4 Estonia 0 13.0 Finland 55759 32 24 114 1 18.7 14.0 32.7 Excluded 276 Germany 728505 461 1759 63 10.8 18.0 28.8 Excluded Hungary 92206 120 68 338 0 22.8 12.9 35.7 Excluded Ireland 65913 17 51 222 0 5.9 17.6 23.4 Excluded 486557 33.6 Excluded 338 261 1175 6 19.0 14.7 Italy 31.1 Included 22<sup>+0</sup>-23<sup>+6+</sup> Latvia 21826 20 13 73 0 18.9 12.3 Lithuania 31601 10 23 90 3 7.9 18.3 26.2 Excluded Included >= $22^{+0}$  but rare >= $24^{+0++}$ Netherlands 169234 292 124 358 35 36.1 15.3 51.4 59928 35 44 134 1 16.4 20.6 36.9 Excluded Norway Excluded Poland 376968 149 237 932 3 11.3 17.9 29.2 23.8 Included 22<sup>+0</sup>-23<sup>+6++</sup> Portugal 86048 23 45 218 0 15.7 8.0 41.9 Included >=22<sup>+0</sup> from 2010<sup>++</sup> Slovenia 20397 16 36 72 0 12.9 29.0 Included but rare >=24<sup>+0+</sup> N/A UK: England and Wales 699204 N/A 915 2232 0 N/A 27.1 UK: Northern Ireland 24544 N/A 19 63 0 N/A 23.2 N/A Excluded Included >=  $22^{+0}$  in 2004 & >=  $24^{+0}$  in 31.6 UK: Scotland 54513 26 45 153 1 11.6 20.0 2010 but rare >=24<sup>+0</sup>, excluded in 2015<sup>++</sup> Overall \* 2516309 1457 1565 6294 120 15.4 16.6 32.0

Table 1: Total births at all gestations, number of stillbirths by gestational age, percentage of all stillbirths occurring at  $22^{+0}$  to  $23^{+6}$  weeks, 24 to 27 weeks and 22 to 27 weeks of gestation in 2015 and information on inclusion of terminations of pregnancy by country (N/A=Not available)

<sup>+</sup> Excluded from sensitivity analysis for 22 to 23 weeks; <sup>++</sup> Excluded from sensitivity analysis of 22 to 23 and 24 to 27 weeks) \* Excluding England and Wales and Northern Ireland as data were not available on births and deaths at 22 to 23 weeks

Figure 1a and 1b: Rates of stillbirth per 1000 total births by country in 2004, 2010 and 2015 and risk ratio for 2015 vs. 2004 by country: 22<sup>+0</sup> to 23<sup>+6</sup> weeks and 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation.





### 24+0 to 27+6 weeks gestational age

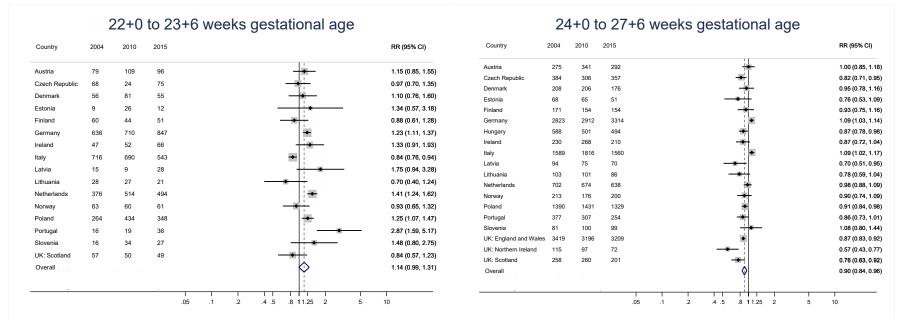


Figure 2a and 2b: Total births in 2004, 2010 and 2015 and rate ratio of gestation specific birth rate in 2015 compared to 2004 by country: 22<sup>+0</sup> to 23<sup>+6</sup> weeks and 24<sup>+0</sup> to 27<sup>+6</sup> weeks of gestation

# Supplemental Table S1. Routine Euro-Peristat data sources used to report on fetal mortality in 2004, 2010 and 2015

	Data	source, Institution					
Country	2004 2010 2015						
Austria	Birth statistics,	Same	Same				
	Statistics Austria						
Czech Republic	Institute for Health Statistics and	Institute for Health	CZSO				
	Information of the Czech Republic (UZIS	Statistics and Information	Czech Statistical Office				
	CR)	of the Czech Republic					
		(UZIS CR)					
Denmark	The Medical Birth Register	Same	Same				
Estonia	Estonian Medical Birth Register, National	Same	Same				
	Institute for Public Health						
Finland	Medical Birth Register, National Institute	Same	Same				
	for Health and Welfare						
Germany	Destatis (Federal Statistical Office) and BQS	AQUA and Destatis for	IQTIG Institut für				
	Institut für Qualität & Patientensicherheit	TOP data	Qualitätssicherung und				
	GmbH		Transparenz im				
			Gesundheitswesen (IQTIG)				
Hungary	Hungarian Central Statistical Office	Same	Same				
Ireland	National Perinatal Reporting System	Same	Same				
	(NPRS)						
Italy 1	Birth certificates CeDAP,	Same	Same				
	Ministry of Health – Office of statistics	Sume	Sume				
Italy 2	Survey on spontaneous abortions,	Same	Same				
	National Institute of Statistics Italy ISTAT	Same	Same				
	,						
Italy 3	Survey on induced abortions,	Same	Same				
	National Institute of Statistics Italy ISTAT						
Italy 4		Hospital discharge form,	Same as in 2010				
		Regional authorities and					
		Ministry of Health					
Latvia	Newborn register of Latvia & Cause-of-	Medical Birth Register,	Same as in 2010				
	Death register, Health Statistics and	Centre for Disease					
	Medical Technologies State Agency	Prevention and Control					
Lithuania	Medical Data of Births, Health Information	Same	Same				
	Centre (LHIC)						
Netherlands	Netherlands Perinatal Register PRN	Same	Same				
Norway	Medical Birth Register of Norway,	Same	Same				
	Norwegian Institute of Public Health						
Poland	Birth and death certificates,	Same	Same				
	Central Statistical Office						
Portugal	Demographic statistics on births and	Same	Same				
	deaths, National Institute of Statistics						
Classes		<b>C</b>	<b>C</b>				
Slovenia	National Perinatal Information System of	Same	Same				
	Slovenia	_	_				
United Kingdom:	Civil Registration of births and deaths,	Same	Same				
England & Wales	Office for National Statistics						
United Kingdom:	Confidential Enquiry into Maternal and	Child Health System, CHS	Northern Ireland Maternity				
Northern Ireland	Child health, CEMACH		System, NIMATS				
United Kingdom:	Scottish Stillbirth and Infant death Inquiry	Scottish Morbidity Record	Same as in 2010				
Scotland		(SMR02)					

Table S2: Total births at all gestations, number of stillbirths by gestational age, percentage of all stillbirths occurring at 22<sup>+0</sup> to 23<sup>+6</sup> weeks, 24<sup>+0</sup> to 27<sup>+6</sup> weeks and 22<sup>+0</sup> to 27<sup>+6</sup> weeks of gestational age in 2004 and information on inclusion of terminations of pregnancy by country (N/A=Not available)

	Tatal	Number of stillbirths by gestational age			% total stillbirths by gestational age			
Country	Total births	22 <sup>+0</sup> -23 <sup>+6</sup>	24 <sup>+0</sup> -27 <sup>+6</sup>	>=28+0	Unknown	22 <sup>+0</sup> -23 <sup>+6</sup>	24 <sup>+0</sup> -27 <sup>+6</sup>	22 <sup>+0</sup> -27 <sup>+6</sup>
		weeks	weeks	weeks	gestation	weeks	weeks	weeks
Austria	79243	49	50	196	0	16.6	16.9	33.6
Czech Republic	98058	46	100	241	0	11.9	25.8	37.7
Denmark	64853	37	42	239	14	11.1	12.7	23.8
Estonia	14053	4	15	44	0	6.3	23.8	30.2
Finland	57759	30	38	117	5	15.8	20.0	35.8
Germany	674436	224	362	1648	27	9.9	16.0	25.9
Hungary	95613	N/A	116	354	6	N/A	24.4	N/A
Ireland	62400	20	48	266	0	6.0	14.4	20.4
Italy	542003	531	395	2011	0	18.1	13.4	31.5
Latvia	20492	9	29	99	0	6.6	21.2	27.7
Lithuania	29633	14	23	116	0	9.2	15.0	24.2
Netherlands	182279	249	243	763	18	19.6	19.1	38.6
Norway	57370	45	45	167	0	17.5	17.5	35.0
Poland	358440	112	280	1345	6	6.4	16.1	22.5
Portugal	109778	16	72	294	40	3.8	17.1	20.9
Slovenia	17946	8	29	63	0	8.0	29.0	37.0
UK: England & Wales	649573	N/A	988	2630	68	N/A	26.8	N/A
UK: Northern Ireland	22504	25	33	84	0	17.6	23.2	40.8
UK: Scotland	53269	41	75	242	0	11.5	20.9	32.4
Overall*	2422012	1460	1879	7935	184	13.0	16.7	29.6

\*Excluding England and Wales and Hungary as data not available on births and deaths at 22<sup>+0</sup> to 23<sup>+6</sup>

weeks

Table S3: Total births at all gestations, number of stillbirths by gestational age, percentage of all stillbirths occurring at  $22^{+0}$  to  $23^{+6}$  weeks,  $24^{+0}$  to  $27^{+6}$  weeks and  $22^{+0}$  to  $27^{+6}$  weeks of gestational age in 2010 and information on inclusion of terminations of pregnancy by country (N/A=Not available)

	<b>T</b> . 1	Number of stillbirths by gestational age			% total stillbirths by gestational age			
Country	Total births	22 <sup>+0</sup> -23 <sup>+6</sup>	24 <sup>+0</sup> -27 <sup>+6</sup>	>=28+0	Unknown	22 <sup>+0</sup> -23 <sup>+6</sup>	24 <sup>+0</sup> -27 <sup>+6</sup>	22 <sup>+0</sup> -27 <sup>+6</sup>
		weeks	weeks	weeks	gestation	weeks	weeks	weeks
Austria	78989	55	42	194	0	18.9	14.4	33.3
Czech Republic	116569	N/A	N/A	169	0	N/A	N/A	N/A
Denmark	63510	51	40	146	0	21.5	16.9	38.4
Estonia	15884	15	10	43	0	22.1	14.7	36.8
Finland	61371	24	31	120	5	13.3	17.2	30.6
Germany	637664	246	428	1429	0	11.7	20.4	32.0
Hungary	90844	130	88	304	0	24.9	16.9	41.8
Ireland	75595	25	51	275	1	7.1	14.5	21.6
Italy	547087	474	330	1276	16	22.6	15.7	38.4
Latvia	19248	6	24	79	0	5.5	22.0	27.5
Lithuania	30977	11	31	104	0	7.5	21.2	28.8
Netherlands	178838	326	177	509	9	31.9	17.3	49.3
Norway	62058	38	36	164	2	15.8	15.0	30.8
Poland	415015	209	285	1226	0	12.2	16.6	28.7
Portugal	101790	4	74	242	0	1.2	22.6	23.9
Slovenia	22416	14	30	74	0	11.9	25.4	37.3
UK: England & Wales	721925	N/A	867	2684	108	N/A	23.7	N/A
UK: Northern Ireland	25690	N/A	17	87	0	N/A	16.3	N/A
UK: Scotland	57467	25	83	208	0	7.9	26.3	34.2
Overall *	2458753	1654	2644	9333	141	16.9	17.9	34.8

\* Excluding England and Wales, Northern Ireland and Czech Republic as data not available on births

and deaths at 22 to 23 weeks

References

1. Blencowe H, Cousens S, Jassir FB, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health 2016; 4(2): e98-e108.

2. Flenady V, Wojcieszek AM, Middleton P, et al. Stillbirths: recall to action in high-income countries. Lancet 2016; 387(10019): 691-702.

3. Flenady V, Koopmans L, Middleton P, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet 2011; 377(9774): 1331-40.

4. Zeitlin J, Mortensen L, Cuttini M, et al. Declines in stillbirth and neonatal mortality rates in Europe between 2004 and 2010: results from the Euro-Peristat project. J Epidemiol Community Health 2016; 70(6): 609-15.

5. Mohangoo AD, Blondel B, Gissler M, et al. International comparisons of fetal and neonatal mortality rates in high-income countries: should exclusion thresholds be based on birth weight or gestational age? PloS one 2013; 8(5): e64869.

6. Papiernik E, Zeitlin J, Delmas D, et al. Termination of pregnancy among very preterm births and its impact on very preterm mortality: results from ten European population-based cohorts in the MOSAIC study. BJOG 2008; 115(3): 361-8.

7. Blondel B, Cuttini M, Hindori-Mohangoo A, et al. How do late terminations of pregnancy affect comparisons of stillbirth rates in Europe? Analyses of aggregated routine data from the Euro-Peristat Project. BJOG 2018; 125(2): 226-34.

8. Joseph KS, Liu S, Rouleau J, et al. Influence of definition based versus pragmatic birth registration on international comparisons of perinatal and infant mortality: population based retrospective study. BMJ 2012; 344: e746.

9. Zeitlin J, Szamotulska K, Drewniak N, et al. Preterm birth time trends in Europe: a study of 19 countries. BJOG : an international journal of obstetrics and gynaecology 2013; 120(11): 1356-65.

10. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ 2012; 345: e7976.

11. Heazell AE, Siassakos D, Blencowe H, et al. Stillbirths: economic and psychosocial consequences. Lancet 2016; 387(10018): 604-16.

12. Mohangoo AD, Buitendijk SE, Szamotulska K, et al. Gestational age patterns of fetal and neonatal mortality in Europe: results from the Euro-Peristat project. PloS one 2011; 6(11): e24727.

13. Kramer MS, Liu S, Luo Z, et al. Analysis of perinatal mortality and its components: time for a change? Am J Epidemiol 2002; 156(6): 493-7.

14. Thorlund K, Imberger G, Johnston BC, et al. Evolution of heterogeneity (I2) estimates and their 95% confidence intervals in large meta-analyses. PloS one 2012; 7(7): e39471.

15. American Academy of Pediatrics Committee on F, Newborn, Bell EF. Noninitiation or withdrawal of intensive care for high-risk newborns. Pediatrics 2007; 119(2): 401-3.

16. Cummings J, Committee On F, Newborn. Antenatal Counseling Regarding Resuscitation and Intensive Care Before 25 Weeks of Gestation. Pediatrics 2015; 136(3): 588-95.

17. Bonet M, Cuttini M, Piedvache A, et al. Changes in management policies for extremely preterm births and neonatal outcomes from 2003 to 2012: two population-based studies in 10 European regions. BJOG 2017.

18. Smith LK, Blondel B, Van Reempts P, et al. Variability in the management and outcomes of extremely preterm births across five European countries: a population-based cohort study. Arch Dis Child Fetal Neonatal Ed 2017.

19. Smith L, Draper ES, Manktelow BN, Pritchard C, Field DJ. Comparing regional infant death rates: the influence of preterm births <24 weeks of gestation. Arch Dis Child Fetal Neonatal Ed 2012.

20. Mullan Z, Horton R. Bringing stillbirths out of the shadows. Lancet 2011; 377(9774): 1291-2.

21. Joseph KS, Kinniburgh B, Hutcheon JA, et al. Determinants of increases in stillbirth rates from 2000 to 2010. CMAJ 2013; 185(8): E345-51.

22. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. Lancet 2006; 367(9521): 1487-94.

23. Lawn JE, Blencowe H, Waiswa P, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet 2016; 387(10018): 587-603.

1. Blencowe H, Cousens S, Jassir FB, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. *Lancet Glob Health* 2016; **4**(2): e98-e108.

2. Flenady V, Wojcieszek AM, Middleton P, et al. Stillbirths: recall to action in high-income countries. *Lancet* 2016; **387**(10019): 691-702.

3. Flenady V, Koopmans L, Middleton P, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. *Lancet* 2011; **377**(9774): 1331-40.

4. Zeitlin J, Mortensen L, Cuttini M, et al. Declines in stillbirth and neonatal mortality rates in Europe between 2004 and 2010: results from the Euro-Peristat project. *J Epidemiol Community Health* 2016; **70**(6): 609-15.

5. Mohangoo AD, Blondel B, Gissler M, et al. International comparisons of fetal and neonatal mortality rates in high-income countries: should exclusion thresholds be based on birth weight or gestational age? *PloS one* 2013; **8**(5): e64869.

6. Papiernik E, Zeitlin J, Delmas D, et al. Termination of pregnancy among very preterm births and its impact on very preterm mortality: results from ten European population-based cohorts in the MOSAIC study. *BJOG* 2008; **115**(3): 361-8.

7. Blondel B, Cuttini M, Hindori-Mohangoo A, et al. How do late terminations of pregnancy affect comparisons of stillbirth rates in Europe? Analyses of aggregated routine data from the Euro-Peristat Project. *BJOG* 2018; **125**(2): 226-34.

8. Joseph KS, Liu S, Rouleau J, et al. Influence of definition based versus pragmatic birth registration on international comparisons of perinatal and infant mortality: population based retrospective study. *BMJ* 2012; **344**: e746.

9. Zeitlin J, Szamotulska K, Drewniak N, et al. Preterm birth time trends in Europe: a study of 19 countries. *BJOG : an international journal of obstetrics and gynaecology* 2013; **120**(11): 1356-65.

10. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). *BMJ* 2012; **345**: e7976.

11. Heazell AE, Siassakos D, Blencowe H, et al. Stillbirths: economic and psychosocial consequences. *Lancet* 2016; **387**(10018): 604-16.

 Mohangoo AD, Buitendijk SE, Szamotulska K, et al. Gestational age patterns of fetal and neonatal mortality in Europe: results from the Euro-Peristat project. *PloS one* 2011; 6(11): e24727.
 Kramer MS, Liu S, Luo Z, et al. Analysis of perinatal mortality and its components: time for a

change? *Am J Epidemiol* 2002; **156**(6): 493-7.

14. Thorlund K, Imberger G, Johnston BC, et al. Evolution of heterogeneity (I2) estimates and their 95% confidence intervals in large meta-analyses. *PloS one* 2012; **7**(7): e39471.

15. American Academy of Pediatrics Committee on F, Newborn, Bell EF. Noninitiation or withdrawal of intensive care for high-risk newborns. *Pediatrics* 2007; **119**(2): 401-3.

16. Cummings J, Committee On F, Newborn. Antenatal Counseling Regarding Resuscitation and Intensive Care Before 25 Weeks of Gestation. *Pediatrics* 2015; **136**(3): 588-95.

17. Bonet M, Cuttini M, Piedvache A, et al. Changes in management policies for extremely preterm births and neonatal outcomes from 2003 to 2012: two population-based studies in 10 European regions. *BJOG* 2017.

18. Smith LK, Blondel B, Van Reempts P, et al. Variability in the management and outcomes of extremely preterm births across five European countries: a population-based cohort study. *Arch Dis Child Fetal Neonatal Ed* 2017.

19. Smith L, Draper ES, Manktelow BN, Pritchard C, Field DJ. Comparing regional infant death rates: the influence of preterm births <24 weeks of gestation. *Arch Dis Child Fetal Neonatal Ed* 2012.

20. Mullan Z, Horton R. Bringing stillbirths out of the shadows. *Lancet* 2011; **377**(9774): 1291-2.

21. Joseph KS, Kinniburgh B, Hutcheon JA, et al. Determinants of increases in stillbirth rates from 2000 to 2010. *CMAJ* 2013; **185**(8): E345-51.

22. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. *Lancet* 2006; **367**(9521): 1487-94.

23. Lawn JE, Blencowe H, Waiswa P, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. *Lancet* 2016; **387**(10018): 587-603.