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**International versus national growth charts for
identifying small and large-for-gestational age newborns:
A population-based study in 15 European countries**

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1 **International versus national growth charts for identifying small and**
2 **large-for-gestational age newborns: a population-based study in 15**
3 **European countries**

4 Short title

5 International or national charts to evaluate intrauterine growth in Europe

6 Authors

7 Alice Hocquette, MSc¹; Mélanie Durox, MSc¹; Rachael Wood, PhD²; Kari Klungsoyr, MD³;
8 Katarzyna Szamotulska, PhD⁴; Sylvan Berrut, MSc⁵; Tonia Rihs, PhD⁵; Theopisti Kyprianou⁶; Luule
9 Sakkeus, PhD⁷; Aline Lecomte, MSc⁸; Irisa Zile, PhD⁹; Sophie Alexander, PhD¹⁰; Jeannette
10 Klimont, Mag¹¹; Henrique Barros, PhD¹²; Miriam Gatt¹³; Jelena Isakova¹⁴; Béatrice Blondel, PhD
11 ¹; Mika Gissler, PhD¹⁵; Jennifer Zeitlin, DSc¹

12 Affiliations

- 13 1. Université de Paris, CRESS, Obstetrical Perinatal and Pediatric Epidemiology Research
14 Team, EPOPé, INSERM, INRA, F-75004 Paris, France
- 15 2. Public Health Scotland, Edinburgh and University of Edinburgh, Edinburgh
- 16 3. Division of Mental and Physical Health, Norwegian Institute of Public Health, Bergen,
17 Norway and Department of Global Public Health and Primary Care, University of Bergen,
18 Norway
- 19 4. Institute of Mother and Child, Department of Epidemiology and Biostatistics, Warsaw
- 20 5. Federal Statistical Office FSO, Neuchâtel, Switzerland

- 21 6. Health Monitoring Unit, Ministry of Health, Nicosia
- 22 7. Estonian Institute for Population Studies, Tallinn University, Tallinn
- 23 8. Department of Population Health, Luxembourg Institute of Health, Luxembourg
- 24 9. The Centre for Disease Prevention and Control of Latvia, Riga
- 25 10. Université Libre de Bruxelles, School of Public Health, Perinatal Epidemiology and
- 26 Reproductive health Unit, Brussels
- 27 11. Statistics Austria, Vienna
- 28 12. University of Porto Medical School, Department of Public Health, Forensic Sciences and
- 29 Medical Education, Porto
- 30 13. Directorate for Health Information and Research, National Obstetric Information
- 31 Systems (NOIS) Register, Tal-Pietà
- 32 14. Institute of Hygiene, Health Information Centre, Health Statistics Department, Vilnius
- 33 15. THL Finnish Institute for Health and Welfare, Information Services Department, Helsinki
- 34 and Karolinska Institute, Department of Neurobiology, Care Sciences and Society,
- 35 Stockholm, Sweden

36

37 Corresponding author:

38 Alice HOCQUETTE

39 INSERM Equipe EPOPé, Maternité Port Royal

40 53 avenue de l'Observatoire, 75014 Paris, France

41 alice.hocquette@inserm.fr

42 Telephone : 06 32 98 83 22

43 Abstract

44 **Background:** To inform the on-going debate about the use of universal prescriptive versus
45 national intrauterine growth charts, we compared perinatal mortality for small and large-for-
46 gestational-age (SGA/LGA) infants according to international and national charts in Europe.

47 **Methods:** We classified singleton births from 33 to 42 weeks of gestation in 2010 and 2014
48 from 15 countries (N=1,475,457) as SGA (birthweight <10th percentile) and LGA (>90th
49 percentile) using the international Intergrowth-21st newborn standards and national charts
50 based on the customised charts methodology. We computed sex-adjusted odds ratios (aOR) for
51 stillbirth, neonatal and extended perinatal mortality by this classification using multilevel
52 models.

53 **Findings:** SGA and LGA prevalence using national charts were near 10% in all countries, but
54 varied according to international charts with a north to south gradient (3·0% to 10·1% and
55 24·9% to 8·0%, respectively). Compared with appropriate for gestational age (AGA) infants by
56 both charts, risk of perinatal mortality was increased for SGA by both charts (aOR[95%
57 confidence interval (CI)]=6·1 [5·6-6·7]) and infants reclassified by international charts from SGA
58 to AGA (2·7 [2·3-3·1]), but decreased for those reclassified from AGA to LGA (0·6 [0·4-0·7]).
59 Results were similar for stillbirth and neonatal death.

60 **Interpretation:** Using international instead of national charts in Europe could lead to growth
61 restricted infants being reclassified as having normal growth, while infants with low risks of
62 mortality could be reclassified as having excessive growth.

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65

66 Introduction

67 Restricted and excessive growth are severe pregnancy complications associated with short and
68 long-term adverse health outcomes. Fetal growth restriction, defined by insufficient growth in
69 relation to the fetus' genetic potential,^{1,2} is associated with risks of stillbirth and neonatal death,
70 major neonatal morbidity, neuro-developmental and metabolic disorders.³⁻⁵ Excessive growth ,
71 a complication of gestational diabetes, is also associated with fetal and neonatal death as well
72 as hypoxic ischaemic encephalopathy, shoulder dystocia and childhood obesity.⁶⁻¹⁰ While
73 restricted and excessive growth are defined in relation to the fetus' genetic potential, proxies
74 based on weight are used in clinical practice and research. Small-for-gestational-age (SGA) is
75 commonly defined as a birthweight under the 10th percentile and large-for-gestational-age
76 (LGA) as a birthweight over the 90th percentile. While there is a broad consensus on these
77 thresholds,^{1,10,11} there is an on-going debate about which growth charts should be used and, in
78 particular, whether charts should be universal or specific to national populations.

79 In line with the World Health Organization charts for children project,¹² the Intergrowth-21st
80 project developed intrauterine growth charts based on the assumption that fetal growth is
81 similar across diverse geographical settings as long as nutrition and access to health care are
82 guaranteed and environmental constraints on growth are low.¹³⁻¹⁵ Others claim that the
83 physiological characteristics of each population are essential for defining risk and that national
84 charts are more appropriate.¹⁶⁻¹⁹ Proponents of national charts point to studies showing the
85 impact of geographic and ethnic origin on birthweight,¹⁷⁻¹⁹ while proponents of using a
86 universal chart argue that population differences are minimal and that international norms are
87 needed to assess deviation from normal growth.²⁰ This debate is of particular relevance in an

88 international context for studies investigating differences between countries in the prevalence
89 of SGA or LGA births or developing protocols and synthesising evidence across multiple settings.
90 The objective of this study is to compare the capacity of international neonatal charts, as
91 proposed by the Intergrowth-21st project,¹³ and national charts customised to each country^{21,22}
92 to identify newborns at risk of perinatal mortality in 15 European countries. The European
93 context is of interest given geographically proximate countries with similar standards of living,
94 universal health insurance for pregnant women , but population differences in adult height and
95 weight which may affect fetal size and corresponding thresholds for defining sub-optimal
96 growth.^{23,24}

97 Methods

98 This study was undertaken by the Euro-Peristat network to underpin recommendations for
99 selecting growth charts in the ConcePTION project, a European consortium on medications
100 during pregnancy and breastfeeding. The Euro-Peristat network, constituted in 1999, aims to
101 monitor and evaluate the health and care of pregnant women and babies in Europe based on
102 national population data on perinatal health indicators.^{25,26}

103 Data source

104 The data source is a network study on intrauterine growth conducted in 2016-2017 which
105 included 15 countries (Austria, Belgium, Cyprus, Estonia, Finland, France, Latvia, Lithuania,
106 Luxemburg, Malta, Norway, Poland, Portugal, Scotland and Switzerland). Individual-level
107 information was collected on five variables (birthweight, gestational age at birth, infant sex, vital
108 status at birth (termination of pregnancy, stillbirth, livebirth), and neonatal death before 28

109 days of life) for all singleton births in the years 2010 and 2014. Data came from birth registers,
110 civil registration systems and routine surveys (see Appendix A). Inclusion criteria, based on Euro-
111 Peristat definitions, were a gestational age of at least 22 weeks of gestation or, if gestational age
112 was missing, birthweight of at least 500g. Gestational age was requested in complete weeks of
113 gestation (e.g. a birth at 37 weeks and 6 days of gestation was recorded with a gestational age
114 of 37 weeks). The definition of gestational age was the final estimate in the obstetrical records
115 at birth.

116 Most countries provided data for their whole population for the given years, except for France
117 where data come from a national survey including all births during a one-week period in all
118 maternity hospitals in France. France and Poland provided information on stillbirths, but not on
119 neonatal deaths since they weren't collected in the French Perinatal Survey and they couldn't
120 be linked for the Polish data. France and Poland provided data for the year 2010 only, Portugal
121 and Switzerland provided data for the years 2010 and 2013, and Cyprus provided data from
122 2007 to 2013 to allow for larger sample sizes in this small country.

123 Ethical approvals

124 This study uses a sub-set of Euro-Peristat's core variables, which include no indirect or direct
125 personal identifiers. Data are provided to Euro-Peristat in accordance with each data provider's
126 regulations for data use. The procedures for obtaining and maintaining the Euro-Peristat core
127 indicator database were authorised by the French Advisory Committee on Use of Health Data in
128 Medical Research (N°17-048, 30/03/17) and the French National Commission for Data
129 Protection and Liberties (CNIL, DR-2019-089, 26/03/19).

130 Study Population

131 Among the 1,496,321 singleton births in the 15 countries during the study period, we included
132 live births and stillbirths from 33 to 42 weeks of gestation because the Intergrowth-21st
133 newborn charts use these gestational age limits (N=1,477,840). We excluded terminations of
134 pregnancy when it was possible to distinguish them from stillbirths in the dataset (N=5); this
135 was not possible in Belgium, Cyprus and Luxemburg (in 2010 only). Newborns with
136 undetermined or unknown sex and with missing data on birthweight or gestational age were
137 excluded (N=2,378). Missing data constituted less than 1% of all data, except for Luxembourg
138 (1.8%). The final sample included 1,475,457 births from 15 countries with data on stillbirths and
139 1,062,154 births from 13 countries with data on neonatal deaths and stillbirths.

140 Outcomes

141 The study's principal outcomes were stillbirth, neonatal mortality and extended perinatal
142 mortality (stillbirth or neonatal death). Countries have different lower gestational age limits for
143 recording stillbirth,²⁷ but this does not affect births at 33 weeks of GA and over which are
144 registered in all countries. Neonatal death was defined as death before 28 days after a live birth.
145 Rates were calculated per 1000 total births for stillbirth and extended perinatal mortality, and
146 per 1000 live births for neonatal mortality.

147 Defining SGA and LGA births

148 International prescriptive charts

149 To define SGA and LGA by international charts, we used the Intergrowth-21st standards for
150 newborn weight.¹³ These charts are part of a suite of charts developed by the Intergrowth 21st

151 project for monitoring intrauterine growth from a sample of rigorously selected low-risk
152 pregnancies from 8 countries (Brazil, Italy, Oman, UK, USA, China, India, and Kenya).^{13,14}
153 Selection criteria included medical and obstetrical history, socio-demographic and behavioural
154 (nutrition, smoking) characteristics, health service accessibility and current pregnancy
155 complications. The newborn weight chart distinguishes boys and girls and covers births from 33
156 weeks of gestation up to 42 weeks. Centiles were fitted using fractional polynomials assuming a
157 skew t distribution with four parameters (mean, standard deviation, skewness and kurtosis). Its
158 published values are expressed in exact weeks (specifying the number of weeks and days; for
159 example, 28 exact weeks corresponds to 28+0 days as opposed to 28 completed weeks which
160 covers 28+0 to 28+6 days).²⁸ To adapt to our data in completed weeks, we used the midpoint
161 weight for each week.

162 National descriptive charts based on the customised chart methodology

163 The national charts were modelled based on the customised chart methodology developed by
164 Gardosi et al.¹⁶ Customised charts are widely used in the international literature on growth
165 restriction and were adapted by Mikolajczyk et al.²¹ and others^{22,29} for use at the country-level.
166 The customised chart's principle is based on the calculation of an individual ideal birthweight at
167 40 weeks of gestation taking into consideration factors which physiologically affect growth (fetal
168 sex, maternal height, pre-pregnancy weight, parity and ethnicity). To transpose this ideal
169 birthweight to each week of gestation, Hadlock's growth trajectory (expressing estimated fetal
170 weight by gestational age) is used to model individual intrauterine growth trajectories.³⁰
171 Assuming a normal distribution, the 10th and 90th percentiles are calculated as a proportion of
172 this individual trajectory using a constant coefficient of variation (calculated as standard

173 deviation over mean of birthweight at 40 weeks of gestation).For our study, in line with
174 previous applications of this model on the country level,^{21,22} we used each country's mean
175 birthweight and coefficient of variation at 40 weeks of gestation to create national charts for
176 girls and boys separately.

177 Equations for the national charts 50th percentile (1), 10th percentile (2) and 90th percentile (3)
178 are:

$$179 \quad (1) P_{50} = \frac{\exp(0.578+0.332w-0.00354w^2) \times m_C}{m_H}$$

$$180 \quad (2) P_{10} = P_{50} \times \left(1 - 1.28 \times \frac{s_C}{m_C}\right)$$

$$181 \quad (3) P_{90} = P_{50} \times \left(1 + 1.28 \times \frac{s_C}{m_C}\right)$$

182 Where: m_C is the mean birthweight at 40 weeks of gestation of the country (for boys and girls
183 separately), m_H is the mean birthweight at 40 completed weeks of gestation as derived from
184 Hadlock's study sample by Mikolajczyk et al²¹ (3705g), s_C is the standard deviation of
185 birthweight at 40 weeks of gestation of the country (for boys and girls separately) and w is
186 gestational age expressed in exact weeks. The country-specific coefficients for the models are
187 provided in Supplementary Table 1.

188 Analysis strategy

189 First, we compared the prevalence of SGA and LGA infants in each country according to the
190 international and national charts^{13,21} and assessed geographic patterns with maps as there are
191 known gradients of birthweight in Europe from north to south.³¹ Second, we classified our
192 sample by both charts as: (1) SGA according to both charts; (2) SGA according to the

193 international chart only; (3) SGA according to the national chart only; (4) AGA according to both
194 charts; (5) LGA according to the international chart only; (6) LGA according to the national chart
195 only; and (7) LGA according to both charts. We compared stillbirth, neonatal mortality and
196 extended perinatal mortality rates by this classification and then derived adjusted odds ratios
197 (aOR) using a multi-level logistic regression to take into consideration the clustering of births
198 within countries. We adjusted our model on sex, but not on gestational age since it is an
199 intermediate factor on the pathway between growth restriction and perinatal death (see
200 directed acyclic graph in supplemental Figure 1). However, we carried out sub-group analysis for
201 term births (37 weeks of gestation and over). As our outcomes are rare, odds ratios
202 approximate relative risks.

203 All analyses were performed using Stata 14.0.³²

204 Role of the funding source

205 The funders of the study had no role in study design, data collection, data analysis, data
206 interpretation, or writing of the report. The corresponding author had full access to all the data
207 in the study and AH and JZ had final responsibility for the decision to submit for publication.

208 Results

209 There was a wide range in the number of total births from 7,984 in Malta to 398,764 in Poland
210 (Table 1). The overall stillbirth rate was 1.8 per 1000 total births (95% confidence interval (CI):
211 1.8 to 1.9, 15 countries) with variation from 1.3 stillbirths per 1000 (CI: 1.1 to 1.4) in Portugal to
212 2.9 per 1000 (CI: 2.4 to 3.4) in Latvia. There were 0.8 neonatal deaths per 1000 live births (CI:
213 0.7 to 0.8, 13 countries) ranging from 0.2 per 1000 (CI: 0.1 to 0.7) in Luxembourg to 1.5 per 1000

214 (CI: 1.1 to 1.9) in Latvia. Extended perinatal deaths were 2.5 per 1000 total births (CI: 2.4 to 2.6,
215 13 countries), with a range from 1.6 (CI: 1.1 to 2.5) in Luxembourg to 4.8 (CI: 3.5 to 6.5) in Malta.
216 The proportions of SGA and LGA based on national charts were close to the 10% expected
217 values, with a minimum of 8.5% in Cyprus to a maximum of 10.6% in France for SGA, and from
218 10.3% in Latvia to 14.8% in Malta for LGA (Table 2). However, these proportions varied
219 markedly when using the international charts: from 3.0% in Estonia to 10.1% in Portugal for SGA
220 and from 8.0% in Portugal to 24.9% in Estonia for LGA. Differences in prevalence between the
221 international and national charts were up to -6.7% for SGA prevalence and to 14.3% for LGA
222 prevalence in Estonia. These discrepancies were geographically patterned, with a lower
223 prevalence of SGA in the north and a higher prevalence of SGA in the south, and higher
224 prevalence of LGA in the north and lower prevalence of LGA in the south when using the
225 international chart (Figure 1).

226 As shown in Table 3, 6.3% of infants in the overall sample were SGA according to both charts,
227 3.4% were SGA by national charts but AGA by the international charts, 73.2% were AGA by both
228 charts, 5.4% were considered LGA by international charts but AGA by national charts and 10.7%
229 were LGA according to both charts. Very few births were SGA according to international charts
230 but AGA by national charts (0.2%) and AGA by international charts but LGA by national charts
231 (0.9%); most of these births occurred in Portugal (99.4% and 56.2% respectively).
232 Supplementary Table 2 provides these distributions by country. Infants considered AGA by both
233 charts had mortality rates of 1.3, 0.6 and 1.9 per 1000 for stillbirth, neonatal death and
234 perinatal death, respectively. These rates were highest for infants who were SGA according to
235 both charts (8.5, 3.0 and 10.9 per 1000), followed by those SGA by national charts only (4.3, 1.4

236 and 5.6 per 1000). They were lowest for infants considered LGA by international charts only
237 (0.7, 0.4 and 1.2 per 1000). These patterns were similar among term births.

238 In mixed effects models adjusted for sex, infants classified as SGA by both charts faced highest
239 mortality risks (aOR for perinatal death: 6.1 [5.6; 6.7]) compared to infants who were AGA
240 according to both charts. Infants considered SGA by the national chart but AGA by the
241 international chart also had increased risks of mortality (aOR for perinatal death: 2.7 [2.3; 3.1]).
242 Being classified as LGA by the international chart only was associated with lower risks (aOR for
243 perinatal death: 0.6 [0.4; 0.7]). Finally, being LGA according to both charts was not associated
244 with an increased risk of mortality. Models for stillbirths and neonatal mortality yielded similar
245 results, as did analyses restricted to term births.

246 Discussion

247 Main findings

248 Our results showed marked discordance between international and national charts for
249 identifying SGA and LGA infants in European countries. Using national charts led to about 10%
250 of infants being classified as SGA and LGA in all the countries, as expected. In contrast, applying
251 international charts led to wide between-country variation from 3.0% to 10.1% for SGA and
252 from 8.0% to 24.9% for LGA, following a geographic pattern of higher SGA prevalence in the
253 south and higher LGA prevalence in the north. Compared to infants considered AGA by both
254 charts, those reclassified from SGA to AGA using the international charts were at 2.7 (2.3 to 3.1)
255 increased risk of perinatal death, whereas those reclassified from AGA to LGA using the
256 international chart were at reduced risk 0.6 (0.4 to 0.7). Very few infants were reclassified from

257 AGA to SGA using the international charts. Taken together, these results do not provide support
258 for the use of international birthweight charts in Europe.

259 Interpretation

260 Intergrowth-21st international charts for intrauterine growth monitoring were published in
261 2014, but their application in daily practice is an on-going debate. Multiple single-country
262 studies have compared Intergrowth-21st's newborn charts with national charts. Similar to our
263 results, local birthweight charts^{33–35} as well as Gardosi's customised model^{36,37} have found that
264 using Intergrowth-21st yielded a lower prevalence of SGA and a higher prevalence of LGA than
265 national or customised charts. We add to this literature by showing that the differences in the
266 prevalence of SGA and LGA when using international charts varied greatly between European
267 countries and followed a geographic gradient from north to south. Our results support the
268 position that population anthropometric characteristics should be considered in growth
269 monitoring.^{8,37–39}

270 Our results also corroborate studies comparing mortality risks using international versus local or
271 customised charts. Francis et al. found that being SGA by customised charts alone led to higher
272 risks of stillbirth and adverse neonatal outcomes,³⁶ and a Canadian study showed that detection
273 rates for their composite mortality and morbidity outcome were higher among newborns
274 considered SGA according to their local chart than among SGA according to Intergrowth-21st.³³ A
275 Swedish study revealed that the risk of perinatal mortality was significantly increased up to the
276 35th percentile of the Intergrowth-21st chart but only up to the 15th percentile of their local
277 chart.³⁷ We found that infants classified as SGA according to national charts, but considered

278 AGA by the international chart, had an over two-fold increased risk of perinatal death when
279 compared to those AGA by both charts. Since the national charts' tenth percentile was higher
280 than the international chart for all countries except Portugal, and mortality decreases linearly
281 with weight percentile to an optimum which has been shown to be higher than the mean,⁸ an
282 elevated risk in this group could be expected. However, the magnitude of the increased risk is of
283 concern given the proportion and unequal geographic distribution of reclassified infants: 3.4%
284 of the overall sample and over 6% in Estonia and Norway. Ideally, we would compare the
285 performance of the charts in terms of sensitivity and specificity, however there is no consensual
286 gold-standard as all current definitions of fetal growth restriction include at least one criterion
287 based on a weight percentile defined in relation to a growth chart.^{2,40-42}

288 Infants reclassified as LGA according to the international chart had significantly lower risks of
289 mortality than those AGA by both charts and represented about 10% or more of the births in
290 the Nordic and Baltic countries. Infants considered LGA by both charts were not at higher risk
291 for any of the outcomes compared to AGA infants according to both charts. This result differed
292 from what was expected but may be explained by the fact that the association between
293 excessive growth and mortality or morbidity has previously been investigated using absolute
294 weights, over 4000 or 4500 grams, rather than percentiles^{7,43}. Using a higher percentile cutoff,
295 such as the 97th, may be more appropriate for capturing the mortality risks associated with LGA
296 and should be explored in further studies. Our models also confirmed the well-documented
297 increased risk of neonatal mortality among boys; risk of stillbirth did not differ which is in line
298 with some recent studies showing no sex differences in overall stillbirth rates.⁴⁴

299 We derived national charts based on the customised model, which uses Hadlock's fetal growth
300 model. This approach has been previously used to derive country-specific charts^{16,21,22} and
301 allowed for consistency across countries and provided proportions of SGA and LGA births in line
302 with expectations. However, it differed from the methodology used in the Intergrowth project
303 and from other birthweight charts. Differences in these charts occur primarily at preterm
304 gestations because birthweight charts include preterm infants with abnormal growth and
305 therefore preterm percentiles are generally lower.^{45,46} Differences in the classification of
306 preterm births do not explain our findings, however, as our results were similar when the
307 sample was restricted to term births only. Results from other studies comparing Intergrowth
308 with national curves have been similar for both types of national charts.^{33,47}

309 In our observational study of birthweight, we can only measure the differences between
310 international and national newborn charts for identifying births facing higher risks of perinatal
311 mortality. However, our study is in line with research on charts of ultrasound measures (in
312 particular, abdominal circumference) or estimated fetal weight, showing a lower proportion of
313 fetuses with growth parameters under the tenth percentile as well as lower sensitivity of the
314 Intergrowth 21st charts for identifying growth restricted fetuses during pregnancy compared to
315 local or customised charts.⁴⁷⁻⁴⁹ The population used to build the Intergrowth 21st charts are the
316 same for the fetal and the newborn charts, and therefore concerns about this reference
317 population apply more broadly. Antenatal screening using charts that are not adapted to the
318 population could lead to failure to identify SGA fetuses and insufficient monitoring of high risk
319 pregnancies, while over-identification of LGA fetuses could increase iatrogenic interventions,
320 parental stress and healthcare costs.⁵⁰ Accurate identification of fetuses and newborns at risk is

321 vital to enable appropriate antenatal monitoring and interventions that prevent stillbirth and
322 neonatal morbidity⁵¹⁻⁵³ and to guide management after birth.

323 Strengths and Limitations

324 This study's strengths are its use of population data from a diverse sample of countries, enabling
325 assessment of the consequences of using international charts on comparisons of sub-optimal
326 growth in Europe. By cumulating data from many countries and over several years, we were
327 able to attain a sample sufficient for investigating fetal and neonatal mortality which are rare
328 events. Limitations are the absence of data on other environmental and maternal characteristics
329 which influence growth. More research is warranted on the factors that influence birthweight in
330 Europe, including the cultural and environmental context (diet or pollutants, for example),
331 physiological characteristics (maternal and paternal height, genetic factors) and risk factors for
332 sub-optimal growth (maternal smoking, maternal obesity and underweight, older maternal age,
333 social disadvantage) to assess their relevance for antenatal and neonatal growth monitoring.
334 Data were from 2010 and 2014, but birthweight as an indicator is stable over time,^{26,54} the
335 current rate of change in perinatal mortality in Europe is low²⁶ and the question of whether
336 universal charts should be applied is not time-bound. Because data come from diverse routine
337 sources, we were not able to clearly assess methods for determining gestational age, although
338 countries in Europe all provide early prenatal care, with widespread use of dating ultrasounds.⁵⁵
339 Finally, although we had large samples from a geographically diverse sample, we were not able
340 to study mortality risks stratified at the country-level because the number of deaths was too
341 small in some countries.

342 Conclusion

343 Our results do not provide support for the use of the Intergrowth 21st international charts for
344 defining SGA and LGA at birth in Europe as this could lead to the underestimation of infants with
345 SGA and overestimation of LGA in some countries. Their use for comparative surveillance and
346 research is also problematic as differences in SGA and LGA prevalence between countries were
347 influenced strongly by population anthropometric characteristics and cannot be interpreted as
348 reflecting variations in perinatal health risks.

349

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360 conducted as part of the ConcePTION consortium, this paper only reflects the personal views of
361 the stated authors.

362 **Authors' contribution**

363 AH and JZ had full access to all of the data in the study and take responsibility for the integrity of
364 the data and the accuracy of the data analyses.

365 Study concept and design: JZ, AH

366 Data acquisition and interpretation AH, MD, KS, RW, KK, SB, TR, TK, LS, AL, IZ, SA, JK, HB, MG, JI,
367 BB, MG, JZ

368 Drafting of the manuscript: AH, JZ, KS, RW, KK, SB, TR

369 Critical revision of the manuscript for important intellectual content and approval of final
370 version of the manuscript: AH, MD, KS, RW, KK, SB, TR, TK, LS, AL, IZ, SA, JK, HB, MG, JI, BB, MG,
371 JZ

372 Data management and statistical analysis AH, JZ, MD

373 **Declaration of interest**

374 No conflict of interest to disclose.

375 Data sharing statement

376 Individual participant data will not be available to others. Data on birthweight percentiles
377 modeled for each participating country are available upon request from the authors.

378 Research in context

379 **Evidence before this study**

380 The Intergrowth-21st project published prescriptive international intrauterine and newborn
381 growth charts in 2014, launching a vigorous debate about whether these charts should be used
382 in clinical practice and research for the identification of small and large for gestational age
383 infants (SGA and LGA) or whether local charts should be preferred. To review the papers
384 evaluating these charts we searched PubMed for comparisons of the Intergrowth-21st charts
385 with other local charts published from September 2014 to February 2020, combining the search
386 terms “intergrowth” AND “fetal/intrauterine growth OR fetal/intrauterine growth restriction OR
387 fetal/intrauterine growth retardation OR small for gestational age OR birthweight OR low
388 birthweight OR large for gestational age OR macrosomia OR references OR standards OR growth
389 charts OR growth curves OR biometric measures OR anthropometry”. Results from this
390 literature review show that local or customised charts more accurately described the
391 birthweight distribution and the mortality risks associated with low and high birthweight than
392 the Intergrowth-21st charts in many settings. These studies have been single-country studies
393 and international comparisons of the Intergrowth-21st charts are lacking.

394 **Added value of this study**

395 This study adds to the scientific literature by comparing the Intergrowth-21st newborn charts
396 with national charts customised to each country’s population in 15 European countries, making
397 it possible to assess the consequences of using one universal chart versus country specific charts
398 in an international context. The study uses routine population data on birthweight from 1.5
399 million births in European countries participating in the Euro-Peristat network. We find large
400 differences in the prevalence of both SGA and LGA infants between international and national
401 charts, with a strong north to south gradient when using international charts, demonstrating the

402 major impact of the choice of chart on the comparative assessment of the burden of fetal
403 growth anomalies by country and their relative rankings. Further, we show that births
404 reclassified by the international chart from SGA to appropriate for gestational age (AGA) had
405 over two-fold higher risks of perinatal mortality, whereas births reclassified from AGA to LGA
406 had lower risk.

407 **Implications of all the available evidence**

408 Our results corroborate previous comparative single-country studies evaluating the
409 Intergrowth-21st intrauterine growth charts. They provide further evidence in favour of using
410 national or local growth charts for monitoring growth during pregnancy and at birth and suggest
411 that physiological differences in population anthropometric characteristics should be taken into
412 consideration when constructing growth charts. Moreover, our study sheds new light on the
413 capacity of the Intergrowth-21st charts to identify SGA and LGA infants at risk of fetal and
414 neonatal mortality in a European context; it illustrates limitations at both extremes of the
415 birthweight spectrum in some settings which may create risks of underestimating SGA births
416 and overestimating LGA births. All these elements do not provide support for the use of the
417 Intergrowth-21st international chart for defining SGA and LGA at birth in Europe.

418 References

- 419 1. Vayssière C, Sentilhes L, Ego A, Bernard C, Cambourieu D, Flamant C, et al. Fetal growth restriction
420 and intra-uterine growth restriction: guidelines for clinical practice from the French College of
421 Gynaecologists and Obstetricians. *Eur J Obstet Gynecol Reprod Biol.* 2015 Oct;193:10–8.
- 422 2. ACOG Practice Bulletin No. 204: Fetal Growth Restriction. *Obstet Gynecol.* 2019;133(2):e97–109.
- 423 3. Flenady V, Koopmans L, Middleton P, Frøen JF, Smith GC, Gibbons K, et al. Major risk factors for
424 stillbirth in high-income countries: a systematic review and meta-analysis. *Lancet.* 2011 Apr
425 16;377(9774):1331–40.

- 426 4. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for
427 stillbirth: population based study. *BMJ*. 2013 Jan 24;346:f108.
- 428 5. Baschat AA, Viscardi RM, Hussey-Gardner B, Hashmi N, Harman C. Infant neurodevelopment
429 following fetal growth restriction: relationship with antepartum surveillance parameters.
430 *Ultrasound Obstet Gynecol*. 2009 Jan;33(1):44–50.
- 431 6. Beta J, Khan N, Khalil A, Fiolna M, Ramadan G, Akolekar R. Maternal and neonatal complications of
432 fetal macrosomia: systematic review and meta-analysis. *Ultrasound Obstet Gynecol Off J Int Soc*
433 *Ultrasound Obstet Gynecol*. 2019 Sep;54(3):308–18.
- 434 7. Wang D, Zhu L, Zhang S, Wu X, Wang X, Lv Q, et al. Predictive macrosomia birthweight thresholds
435 for adverse maternal and neonatal outcomes. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat*
436 *Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet*. 2016 Dec;29(23):3745–50.
- 437 8. Graafmans WC, Richardus JH, Borsboom GJJM, Bakketeig L, Langhoff-Roos J, Bergsjø P, et al. Birth
438 weight and perinatal mortality: a comparison of “optimal” birth weight in seven Western European
439 countries. *Epidemiol Camb Mass*. 2002 Sep;13(5):569–74.
- 440 9. Sparano S, Ahrens W, De Henauw S, Marild S, Molnar D, Moreno LA, et al. Being macrosomic at
441 birth is an independent predictor of overweight in children: results from the IDEFICS study. *Matern*
442 *Child Health J*. 2013 Oct;17(8):1373–81.
- 443 10. Committee on Practice Bulletins—Obstetrics. Macrosomia: ACOG Practice Bulletin, Number 216.
444 *Obstet Gynecol*. 2020;135(1):e18–35.
- 445 11. McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of
446 suspected fetal growth restriction: comparison, consensus, and controversy. *Am J Obstet Gynecol*.
447 2018 Feb;218(2S):S855–68.
- 448 12. de Onis M, Garza C, Onyango AW, Rolland-Cachera M-F, le Comité de nutrition de la Société
449 française de pédiatrie. [WHO growth standards for infants and young children]. *Arch Pediatr*
450 *Organe Off Soc Francaise Pediatr*. 2009 Jan;16(1):47–53.
- 451 13. Villar J, Ismail LC, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards for
452 newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-
453 Sectional Study of the INTERGROWTH-21st Project. *The Lancet*. 2014 Sep 6;384(9946):857–68.
- 454 14. Stirnemann J, Villar J, Salomon LJ, Ohuma E, Ruyan P, Altman DG, et al. International estimated
455 fetal weight standards of the INTERGROWTH-21st Project. *Ultrasound Obstet Gynecol*. 2017
456 Apr;49(4):478–86.
- 457 15. Papageorgiou AT, Ohuma EO, Altman DG, Todros T, Cheikh Ismail L, Lambert A, et al. International
458 standards for fetal growth based on serial ultrasound measurements: the Fetal Growth
459 Longitudinal Study of the INTERGROWTH-21st Project. *Lancet Lond Engl*. 2014 Sep
460 6;384(9946):869–79.
- 461 16. Gardosi J, Mongelli M, Wilcox M, Chang A. An adjustable fetal weight standard. *Ultrasound Obstet*
462 *Gynecol*. 1995 Sep;6(3):168–74.

- 463 17. Gardosi J. Fetal growth and ethnic variation. *Lancet Diabetes Endocrinol.* 2014 Oct;2(10):773–4.
- 464 18. Albert PS, Grantz KL. Fetal growth and ethnic variation. *Lancet Diabetes Endocrinol.* 2014
465 Oct;2(10):773.
- 466 19. Alexander GR, Kogan MD, Himes JH, Mor JM, Goldenberg R. Racial differences in birthweight for
467 gestational age and infant mortality in extremely-low-risk US populations. *Paediatr Perinat
468 Epidemiol.* 1999 Apr;13(2):205–17.
- 469 20. Villar J, Papageorghiou AT, Pang R, Ohuma EO, Cheikh Ismail L, Barros FC, et al. The likeness of fetal
470 growth and newborn size across non-isolated populations in the INTERGROWTH-21st Project: the
471 Fetal Growth Longitudinal Study and Newborn Cross-Sectional Study. *Lancet Diabetes Endocrinol.*
472 2014 Oct;2(10):781–92.
- 473 21. Mikolajczyk RT, Zhang J, Betran AP, Souza JP, Mori R, Gülmezoglu AM, et al. A global reference for
474 fetal-weight and birthweight percentiles. *Lancet Lond Engl.* 2011 May 28;377(9780):1855–61.
- 475 22. Zeitlin J, Bonamy A-KE, Piedvache A, Cuttini M, Barros H, Van Reempts P, et al. Variation in term
476 birthweight across European countries affects the prevalence of small for gestational age among
477 very preterm infants. *Acta Paediatr Oslo Nor* 1992. 2017 Sep;106(9):1447–55.
- 478 23. Robinson MR, Hemani G, Medina-Gomez C, Mezzavilla M, Esko T, Shakhbazov K, et al. Population
479 genetic differentiation of height and body mass index across Europe. *Nat Genet.* 2015
480 Nov;47(11):1357–62.
- 481 24. NCD Risk Factor Collaboration (NCD-RisC). A century of trends in adult human height. *eLife.* 2016
482 26;5.
- 483 25. Zeitlin J, Mortensen L, Cuttini M, Lack N, Nijhuis J, Haidinger G, et al. Declines in stillbirth and
484 neonatal mortality rates in Europe between 2004 and 2010: results from the Euro-Peristat project.
485 *J Epidemiol Community Health.* 2016 Jun;70(6):609–15.
- 486 26. Zeitlin J, Alexander S, Barros H, Blondel B, Delnord M, Durox M, et al. Perinatal health monitoring
487 through a European lens: eight lessons from the Euro-Peristat report on 2015 births. *BJOG Int J
488 Obstet Gynaecol.* 2019;126(13):1518–22.
- 489 27. Smith LK, Hindori-Mohangoo AD, Delnord M, Durox M, Szamotulska K, Macfarlane A, et al.
490 Quantifying the burden of stillbirths before 28 weeks of completed gestational age in high-income
491 countries: a population-based study of 19 European countries. *Lancet Lond Engl.* 2018
492 03;392(10158):1639–46.
- 493 28. Zeitlin J, Monier I. Clarification of INTERGROWTH-21st newborn birthweight standards. *Lancet Lond
494 Engl.* 2018 19;391(10134):1995–6.
- 495 29. A. Ego, C. Prunet, E. Lebreton, B. Blondel, M. Kaminski, F. Goffinet, et al. Courbes de croissance in
496 utero ajustées et non ajustées adaptées à la population française. I — Méthodes de construction. *J
497 Gynecol Obstet Biol Reprod.* 2015 Aug 25;45(2):165–76.

- 498 30. Hadlock FP, Harrist RB, Martinez-Poyer J. In utero analysis of fetal growth a sonographic weight
499 standard. *Radiology*. 1991 Oct;181(1):129–33.
- 500 31. Lack N, Blondel B, Mohangoo AD, Sakkeus L, Cans C, Bouvier-Colle MH, et al. Reporting of perinatal
501 health indicators for international comparisons--enhancing the appearance of geographical plots.
502 *Eur J Public Health*. 2013 Dec;23(6):957–63.
- 503 32. StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP.
- 504 33. Liu S, Metcalfe A, León JA, Sauve R, Kramer MS, Joseph KS, et al. Evaluation of the INTERGROWTH-
505 21st project newborn standard for use in Canada. *PLoS One*. 2017;12(3):e0172910.
- 506 34. Poon LCY, Tan MY, Yerlikaya G, Syngelaki A, Nicolaides KH. Birth weight in live births and stillbirths.
507 *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol*. 2016 Nov;48(5):602–6.
- 508 35. Choi SKY, Gordon A, Hilder L, Henry A, Hyett JA, Brew BK, et al. Performance of six birthweight and
509 estimated fetal weight standards for predicting adverse perinatal outcomes: a 10-year nationwide
510 population-based study. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol*. 2020
511 Jul 16;
- 512 36. Francis A, Hugh O, Gardosi J. Customized vs INTERGROWTH-21st standards for the assessment of
513 birthweight and stillbirth risk at term. *Am J Obstet Gynecol*. 2018;218(2S):S692–9.
- 514 37. Vieira MC, Relph S, Persson M, Seed PT, Pasupathy D. Determination of birth-weight centile
515 thresholds associated with adverse perinatal outcomes using population, customised, and
516 Intergrowth charts: A Swedish population-based cohort study. *PLoS Med*. 2019;16(9):e1002902.
- 517 38. BUCK LOUIS GM, GREWAL J, ALBERT PS, SCISCIONE A, WING DA, GROBMAN WA, et al. Racial/Ethnic
518 Standards for Fetal Growth, the NICHD Fetal Growth Studies. *Am J Obstet Gynecol*. 2015
519 Oct;213(4):449.e1-449.e41.
- 520 39. Kiserud T, Piaggio G, Carroli G, Widmer M, Carvalho J, Neerup Jensen L, et al. The World Health
521 Organization Fetal Growth Charts: A Multinational Longitudinal Study of Ultrasound Biometric
522 Measurements and Estimated Fetal Weight. *PLoS Med* [Internet]. 2017 Jan 24 [cited 2019 Dec
523 18];14(1). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5261648/>
- 524 40. Gordijn SJ, Beune IM, Thilaganathan B, Papageorgiou A, Baschat AA, Baker PN, et al. Consensus
525 definition of fetal growth restriction: a Delphi procedure. *Ultrasound Obstet Gynecol Off J Int Soc
526 Ultrasound Obstet Gynecol*. 2016 Sep;48(3):333–9.
- 527 41. Beune IM, Bloomfield FH, Ganzevoort W, Embleton ND, Rozance PJ, van Wassenaer-Leemhuis AG,
528 et al. Consensus Based Definition of Growth Restriction in the Newborn. *J Pediatr*. 2018
529 May;196:71-76.e1.
- 530 42. Collège National des Gynécologues et Obstétriciens Français. Recommandations pour la pratique
531 clinique - Le retard de croissance intra-utérin. *J Gynecol Obstet Biol Reprod*. 2013;42:1018–25.

- 532 43. Beta J, Khan N, Fiolna M, Khalil A, Ramadan G, Akolekar R. Maternal and neonatal complications of
533 fetal macrosomia: cohort study. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet*
534 *Gynecol*. 2019 Sep;54(3):319–25.
- 535 44. Voskamp BJ, Peelen MJCS, Ravelli ACJ, van der Lee R, Mol BWJ, Pajkrt E, et al. Association between
536 fetal sex, birthweight percentile and adverse pregnancy outcome. *Acta Obstet Gynecol Scand*.
537 2020;99(1):48–58.
- 538 45. Ego A, Prunet C, Blondel B, Kaminski M, Goffinet F, Zeitlin J. [Customized and non-customized
539 French intrauterine growth curves. II - Comparison with existing curves and benefits of
540 customization]. *J Gynecol Obstet Biol Reprod (Paris)*. 2016 Feb;45(2):165–76.
- 541 46. Zaw W, Gagnon R, da Silva O. The risks of adverse neonatal outcome among preterm small for
542 gestational age infants according to neonatal versus fetal growth standards. *Pediatrics*. 2003
543 Jun;111(6 Pt 1):1273–7.
- 544 47. Nwabuobi C, Odibo L, Camisasca-Lopina H, Leavitt K, Tuuli M, Odibo AO. Comparing
545 INTERGROWTH-21st Century and Hadlock growth standards to predict small for gestational age
546 and short-term neonatal outcomes. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed*
547 *Asia Ocean Perinat Soc Int Soc Perinat Obstet*. 2020 Jun;33(11):1906–12.
- 548 48. Sovio U, Smith GCS. Comparison of estimated fetal weight percentiles near term for predicting
549 extremes of birthweight percentile. *Am J Obstet Gynecol*. 2020 Aug 21;
- 550 49. Hua X, Shen M, Reddy UM, Louis GB, Souza JP, Gülmezoglu AM, et al. Comparison of the
551 INTERGROWTH-21st, National Institute of Child Health and Human Development, and WHO fetal
552 growth standards. *Int J Gynecol Obstet*. 2018;143(2):156–63.
- 553 50. Melamed N, Yogev Y, Meizner I, Mashiach R, Ben-Haroush A. Sonographic prediction of fetal
554 macrosomia: the consequences of false diagnosis. *J Ultrasound Med Off J Am Inst Ultrasound Med*.
555 2010 Feb;29(2):225–30.
- 556 51. Boers KE, Vijgen SMC, Bijlenga D, van der Post J a. M, Bekedam DJ, Kwee A, et al. Induction versus
557 expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial
558 (DIGITAT). *BMJ*. 2010 Dec 21;341:c7087.
- 559 52. Ganzevoort W, Mensing Van Charante N, Thilaganathan B, Prefumo F, Arabin B, Bilardo CM, et al.
560 How to monitor pregnancies complicated by fetal growth restriction and delivery before 32 weeks:
561 post-hoc analysis of TRUFFLE study. *Ultrasound Obstet Gynecol*. 2017 Jun;49(6):769–77.
- 562 53. Ego A, Monier I, Skaare K, Zeitlin J. Antenatal detection of fetal growth restriction and stillbirth risk:
563 a population-based case-control study. *Ultrasound Obstet Gynecol*. 2019 Jul 31;
- 564 54. Schneider EB. Fetal health stagnation: Have health conditions in utero improved in the United
565 States and Western and Northern Europe over the past 150 years? *Soc Sci Med* 1982. 2017
566 Apr;179:18–26.

567 55. Zeitlin J, Mohangoo AD, Delnord M, Cuttini M, EURO-PERISTAT Scientific Committee. The second
568 European Perinatal Health Report: documenting changes over 6 years in the health of mothers and
569 babies in Europe. *J Epidemiol Community Health*. 2013 Dec 1;67(12):983–5.

570

571 Tables and Figures

572 *Table 1: Total births in the study sample and stillbirth and neonatal mortality rates between 33*
 573 *and 42 weeks of gestation by country*

Country	Total births	Stillbirth rate		Neonatal mortality rate		Extended perinatal mortality rate	
		n	% total birth [CI 95%]	n	% live births[CI 95%]	n	% total births [CI 95%]
Austria	153410	258	1.7 [1.5 ; 1.9]	92	0.6 [0.5 ; 0.7]	350	2.3 [2.1 ; 2.5]
Belgium	71988	156	2.2 [1.9 ; 2.5]	70	1.0 [0.8 ; 1.2]	226	3.1 [2.8 ; 3.6]
Cyprus	20290	39	1.9 [1.4 ; 2.6]	18	0.9 [0.6 ; 1.4]	57	2.8 [2.2 ; 3.6]
Estonia	28284	57	2.0 [1.6 ; 2.6]	24	0.9 [0.6 ; 1.3]	81	2.9 [2.3 ; 3.6]
Finland	114610	161	1.4 [1.2 ; 1.6]	82	0.7 [0.6 ; 0.9]	243	2.1 [1.9 ; 2.4]
France	14539	25	1.7 [1.2 ; 2.5]	-	-	-	-
Latvia	39166	112	2.9 [2.4 ; 3.4]	57	1.5 [1.1 ; 1.9]	169	4.3 [3.7 ; 5.0]
Lithuania	57 024	138	2.4 [2.0 ; 2.9]	84	1.5 [1.2 ; 1.8]	222	3.9 [3.4 ; 4.4]
Luxembourg	12854	18	1.4 [0.9 ; 2.2]	3	0.2 [0.1 ; 0.7]	21	1.6 [1.1 ; 2.5]
Malta	7984	19	2.4 [1.5 ; 3.7]	19	2.4 [1.5 ; 3.7]	38	4.8 [3.5 ; 6.5]
Norway	116603	239	2.1 [1.8 ; 2.3]	81	0.7 [0.6 ; 0.9]	320	2.7 [2.5 ; 3.1]
Poland	398764	826	2.1 [1.9 ; 2.2]	-	-	-	-
Portugal	177013	225	1.3 [1.1 ; 1.4]	84	0.5 [0.4 ; 0.6]	309	1.7 [1.6 ; 2.0]
Scotland	107791	230	2.2 [1.9 ; 2.4]	75	0.7 [0.6 ; 0.9]	305	2.8 [2.5 ; 3.2]
Switzerland	155137	217	1.4 [1.2 ; 1.6]	122	0.8 [0.7 ; 0.9]	339	2.2 [2.0 ; 2.4]
Total	1475457	2720	1.8 [1.8 ; 1.9]	811	0.8 [0.7 ; 0.8]	2680	2.5 [2.4 ; 2.6]

574 *NOTE: Combined data from the years 2010 and 2014, except Cyprus (2007-2013), Poland and France*
 575 *(2010 only) and Portugal and Switzerland (2010, 2013).*

576

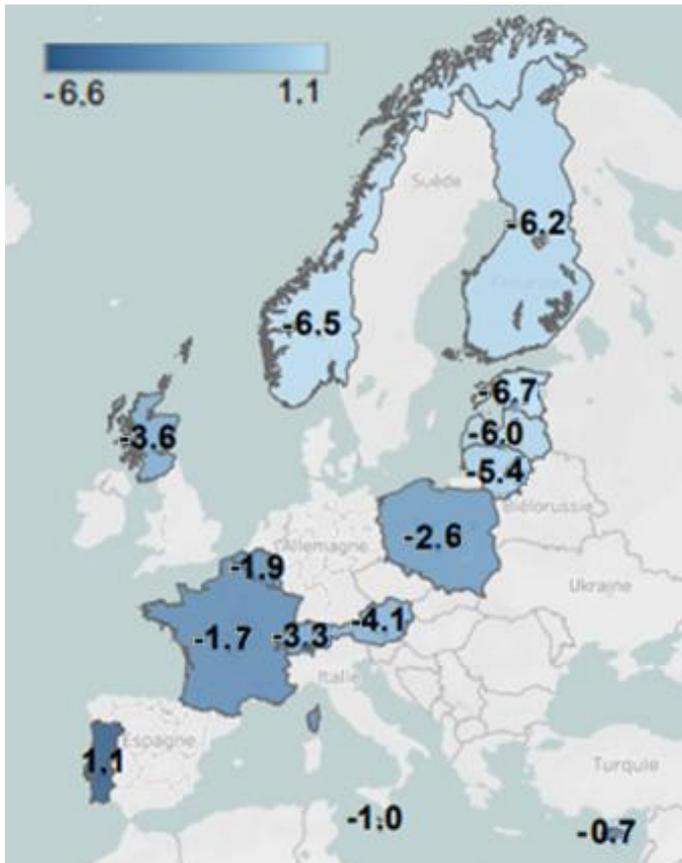
577 *Table 2: Prevalence of small and large for gestational age births in European countries according*
 578 *to international and national charts*

Country	Total births (N)	International			National		
		SGA (%)	AGA (%)	LGA (%)	SGA (%)	AGA (%)	LGA (%)
Austria	153410	5.9	80.0	14.1	10.0	78.4	11.6
Belgium	71988	8.2	80.1	11.7	10.1	77.8	12.1
Cyprus	20290	7.7	81.5	10.8	8.5	77.4	14.1
Estonia	28284	3.0	72.1	24.9	9.7	79.7	10.6
Finland	114610	3.9	73.0	23.0	10.1	78	11.9
France	14539	8.8	80.5	10.7	10.6	78.3	11.2
Latvia	39166	4.0	72.8	23.2	10.1	79.6	10.3
Lithuania	57 024	4.4	75.2	20.5	9.7	79.3	11.1
Luxembourg	12854	6.5	81.0	12.5	9.4	77.8	12.8
Malta	7984	8.6	80.8	10.6	9.6	75.6	14.8
Norway	116603	3.9	72.8	23.3	10.4	78.5	11.1
Poland	398764	6.7	77.0	16.3	9.3	79.3	11.4
Portugal	177013	10.1	81.9	8.0	9.0	78.5	12.4
Scotland	107791	6.5	75.1	18.4	10.1	78.6	11.3
Switzerland	155137	6.4	80.4	13.2	9.6	78.5	11.9
Total	1475 457	6.4	77.5	16.1	9.7	78.7	10.7

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580

581 *Figure 1 a: Difference in prevalence of SGA between international and national charts*



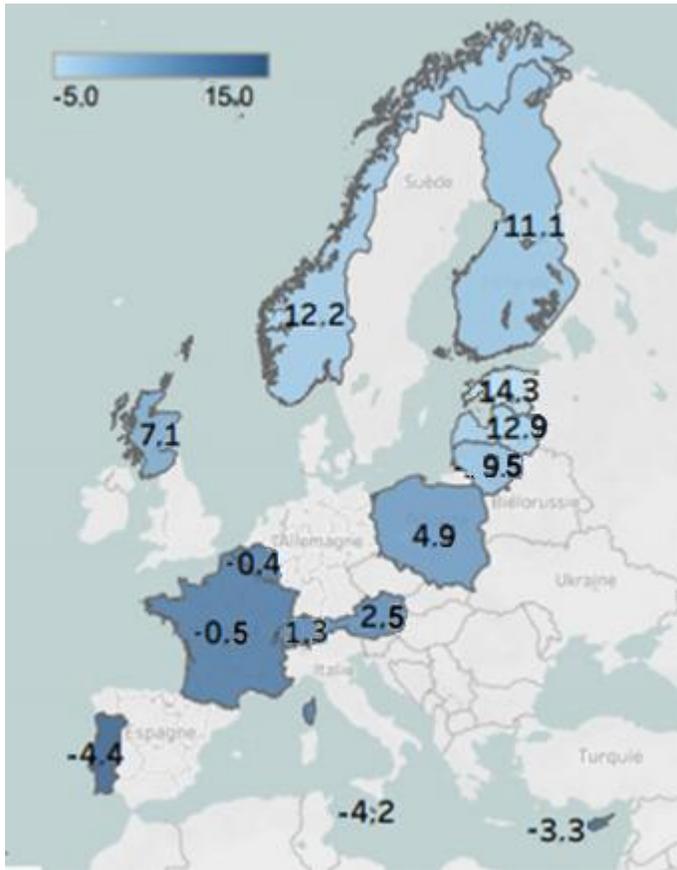
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	% difference [CI 95%]
Austria	-4.1 [-4.3 ; -3.9]
Belgium	-1.9 [-2.2 ; -1.6]
Cyprus	-0.7 [-1.3 ; -0.2]
Estonia	-6.7 [-7.1 ; -6.3]
Finland	-6.2 [-6.4 ; -6.0]
France	-1.7 [-2.4 ; -1.1]
Latvia	-6.0 [-5.7 ; -6.4]
Lithuania	-5.4 [-5.7 ; -5.1]
Luxembourg	-3.0 [-3.6 ; -2.3]
Malta	-1.0 [-1.9 ; -0.1]
Norway	-6.5 [-6.7 ; -6.3]
Poland	-2.6 [-2.8 ; -2.5]
Portugal	1.1 [0.9 ; 1.3]
Scotland	-3.6 [-3.9 ; -3.4]
Switzerland	-3.3 [-3.4 ; -3.1]

585 *Figure 1 b: Difference in prevalence of LGA between international and national charts*



	% difference [CI 95%]
Austria	2.5 [2.3 ; 2.7]
Belgium	-0.4 [-0.7 ; -0.0]
Cyprus	-3.3 [-3.9 ; -2.6]
Estonia	14.3 [13.7 ; 15.0]
Finland	11.1 [10.8 ; 11.4]
France	-0.5 [-1.2 ; 0.2]
Latvia	12.9 [12.4 ; 13.4]
Lithuania	9.5 [9.1 ; 9.9]
Luxembourg	-0.3 [-1.1 ; 0.6]
Malta	-4.2 [-5.2 ; -3.2]
Norway	12.2 [11.9 ; 12.5]
Poland	4.9 [4.7 ; 5.0]
Portugal	-4.4 [-4.6 ; -4.2]
Scotland	7.1 [6.8 ; 7.4]
Switzerland	1.3 [1.0 ; 1.5]

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587

Stillbirth		All births ¹ N (%)	Stillbirths n (rate per 1000)	Adjusted model ² aOR [95% CI]	All term births ¹ N (%)	Term stillbirths n (rate per 1000)	Adjusted model ² aOR [95% CI]
BW group	SGA both	92 559 (6.3)	791 (8.5)	6.7 [6.1 ; 7.3]	85 035 (6.0)	434 (5.1)	5.9 [5.3 ; 6.6]
	SGA international only	2 188 (0.2)	2 (0.9)	1.1 [0.3 ; 4.3]	2 163 (0.2)	2 (0.9)	1.8 [0.4 ; 7.3]
	SGA national only	50 245 (3.4)	218 (4.3)	3.1 [2.7 ; 3.6]	45 744 (3.3)	101 (2.2)	2.2 [1.8 ; 2.8]
	AGA both	1 079 324 (73.2)	1424 (1.3)	Reference	1 033 397 (73.4)	927 (0.9)	Reference
	LGA national only	13 885 (0.9)	31 (2.2)	2.2 [1.5 ; 3.1]	10 745 (0.8)	5 (0.5)	0.8 [0.3 ; 1.8]
	LGA international only	79 251 (5.4)	58 (0.7)	0.5 [0.4 ; 0.6]	79 216 (5.6)	58 (0.7)	0.7 [0.5 ; 0.9]
	LGA both	158 005 (10.7)	196 (1.2)	0.9 [0.8 ; 1.1]	151 267 (10.8)	148 (1.0)	1.1 [0.9 ; 1.3]
Sex	Female	716 647 (48.6)	1 321 (1.8)	Reference	685 846 (48.7)	819 (1.2)	Reference
	Male	758 810 (51.4)	1 399 (1.8)	1.0 [0.9 ; 1.1]	721 721 (51.3)	856 (1.1)	1.0 [0.9 ; 1.1]
Variance at country level				0.06 [0.03 ; 0.14]			0.08 [0.03 ; 0.20]
Neonatal death		Live births ^{1,3} N (%)	Neonatal deaths n (rate per 1000)	Adjusted model ² aOR [95% CI]	Term live births ¹ N (%)	Term neonatal deaths n (rate per 1000)	Adjusted model ² aOR [95% CI]
BW group	SGA both	64 082 (6.0)	194 (3.0)	5.4 [4.6 ; 6.4]	58 881 (5.8)	131 (2.2)	5.0 [4.1 ; 6.1]
	SGA international only	2 186 (0.2)	1 (0.5)	1.3 [0.2 ; 9.6]	2 161 (0.2)	1 (0.5)	1.5 [0.2 ; 11.2]
	SGA national only	39 271 (3.7)	56 (1.4)	2.2 [1.7 ; 2.9]	35 850 (3.6)	32 (0.9)	1.7 [1.2 ; 2.5]
	AGA both	771 619 (72.8)	452 (0.6)	Reference	738 348 (73.0)	343 (0.5)	Reference
	LGA national only	12 596 (1.2)	9 (0.7)	1.6 [0.8 ; 3.0]	10 211 (1.0)	1 (0.1)	0.3 [0.0 ; 1.9]
	LGA international only	58 485 (5.5)	22 (0.4)	0.5 [0.4 ; 0.8]	58 450 (5.8)	22 (0.4)	0.7 [0.5 ; 1.1]
	LGA both	112 046 (10.6)	77 (0.7)	1.1 [0.9 ; 1.5]	107 365 (10.6)	52 (0.5)	1.0 [0.8 ; 1.4]
Sex	Female	516 953 (48.8)	372 (0.7)	Reference	494 524 (48.9)	272 (0.6)	Reference
	Male	543 332 (51.2)	439 (0.8)	1.1 [1.0 ; 1.3]	516 742 (51.1)	310 (0.6)	1.1 [0.9 ; 1.3]
Variance at country level				0.19 [0.07 ; 0.49]			0.16 [0.06 ; 0.42]
Perinatal death		All births ^{1,3} N (%)	Perinatal deaths n (rate per 1000)	Adjusted model ² aOR [95% CI]	All term births ¹ N (%)	Term perinatal deaths n (rate per 1000)	Adjusted model ² aOR [95% CI]
BW group	SGA both	64 590 (6.1)	702 (10.9)	6.1 [5.6 ; 6.7]	59 161 (5.8)	411 (6.9)	5.5 [4.9 ; 6.2]
	SGA international only	2 188 (0.2)	3 (1.4)	1.1 [0.4 ; 3.6]	2 163 (0.2)	3 (1.4)	1.7 [0.6 ; 5.4]
	SGA national only	39 436 (3.7)	221 (5.6)	2.7 [2.3 ; 3.1]	35 932 (3.6)	114 (3.2)	2.1 [1.7 ; 2.6]
	AGA both	772 613 (72.7)	1446 (1.9)	Reference	738 987 (73.0)	982 (1.3)	Reference
	LGA national only	12 618 (1.2)	31 (2.5)	1.7 [1.2 ; 2.4]	10 215 (1.0)	5 (0.5)	0.5 [0.2 ; 1.2]
	LGA international only	12 618 (5.5)	72 (1.2)	0.6 [0.4 ; 0.7]	58 500 (5.8)	72 (1.2)	0.8 [0.6 ; 1.0]
	LGA both	112 174 (10.6)	205 (1.8)	1.0 [0.8 ; 1.1]	107 461 (10.6)	148 (1.4)	1.0 [0.8 ; 1.2]
Sex	Female	517 853 (48.8)	1 272 (2.5)	Reference	495 080 (48.9)	828 (1.7)	Reference
	Male	544 301 (51.2)	1 408 (2.6)	1.1 [1.0 ; 1.2]	517 339 (51.1)	907 (1.8)	1.1 [1.0 ; 1.2]
Variance at country level				0.09 [0.04 ; 0.22]			0.09 [0.04 ; 0.21]

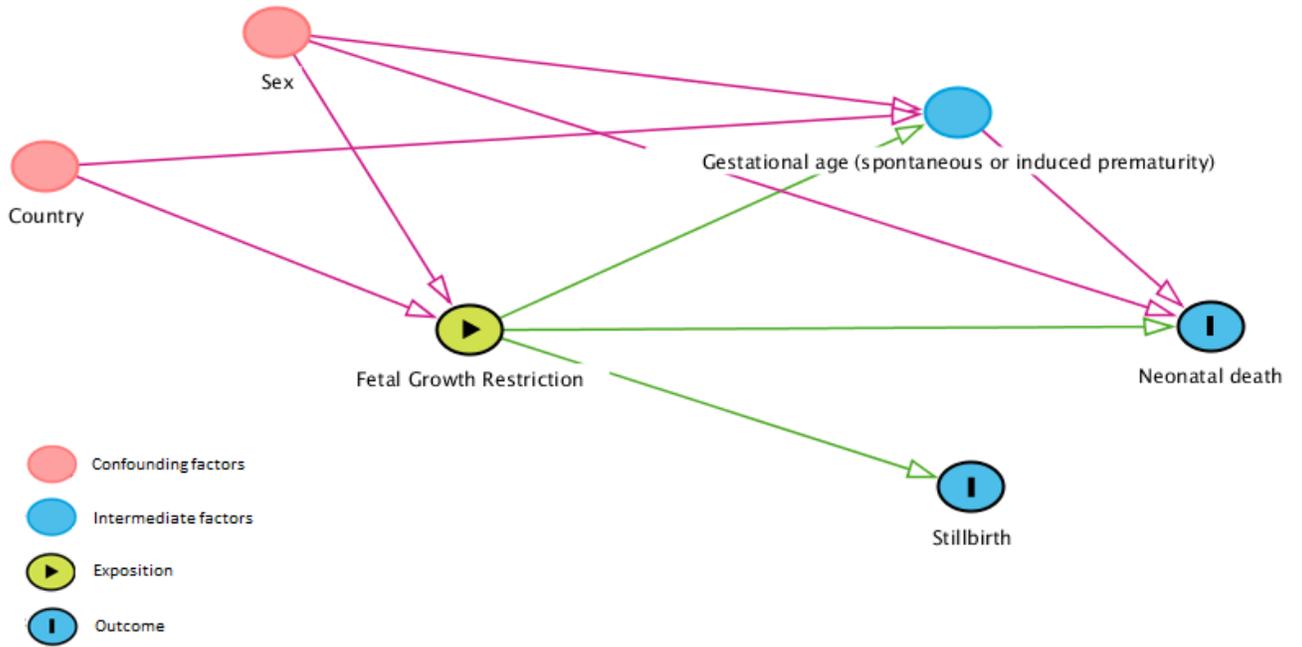
588 *Table 3: Risk of stillbirth, neonatal and perinatal death by birthweight (BW) classification for all births ≥ 33 weeks and term births*

589 *NOTE: (1) ≥ 33 to ≤42 completed weeks of gestation (2) Model adjusted on fetal sex and with a supplementary level for the country (3) Births with data on perinatal death*

590 Supplementary materials

591 **Supplementary Figure 1 : Directed acyclic graph of the relationship between fetal growth restriction and**
592 **perinatal death**

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598 **Supplementary Table 1: Countries' mean birthweight and coefficient of variation at 40 weeks of gestation**
599 **used to create national charts**

Country	Boys		Girls	
	Mean birthweight at 40 weeks of gestation (m _c)	Coefficient of variation at 40 weeks of gestation (s _c)	Mean birthweight at 40 weeks of gestation (m _c)	Coefficient of variation at 40 weeks of gestation (s _c)
AUSTRIA	3594	11.5	3443	11.7
BELGIUM	3532	11.7	3388	12.0
CYPRUS	3495	11.8	3346	11.6
ESTONIA	3752	11.4	3596	11.7
FINLAND	3698	11.5	3559	11.6
FRANCE ENP	3511	11.7	3378	11.7
LATVIA	3734	12.0	3570	11.9
LUXEMBOURG	3552	11.1	3409	11.7
MALTA	3492	11.5	3341	11.2
NORWAY	3704	11.6	3583	11.7
POLAND	3604	12.3	3441	12.3
PORTUGAL	3439	11.9	3310	11.7
SCOTLAND	3622	12.2	3478	12.3
SWITZERLAND	3571	11.5	3416	11.5
LITHUANIA	3690	11.8	3537	11.8

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603 **Supplementary Table 2: SGA, AGA and LGA distribution according to both national and international**
604 **charts in each country**

		SGA both	SGA international only	SGA national only	AGA both	LGA national only	LGA international only	LGA both	Total
AUSTRIA	n	9031	0	6282	115579	865	4713	16940	153410
	%	5.9	0.0	4.1	75.3	0.6	3.1	11.0	100.0
BELGIUM	n	5905	0	1339	55292	1000	741	7711	71988
	%	8.2	0.0	1.9	76.8	1.4	1.0	10.7	100.0
CYPRUS	n	1556	13	164	15625	737	74	2121	20290
	%	7.7	0.1	0.8	77.0	3.6	0.4	10.5	100.0
ESTONIA	n	855	0	1901	18476	3	4061	2988	28284
	%	3.0	0.0	6.6	65.3	0.0	14.4	10.6	100.0
FINLAND	n	4514	0	7090	76563	40	12795	13608	114610
	%	3.9	0.0	6.2	66.8	0.0	11.2	11.9	100.0
FRANCE	n	1284	0	253	11223	227	157	1395	14539
	%	8.8	0.0	1.6	77.2	1.6	1.1	9.6	100.0
LATVIA	n	1583	0	2357	26138	1	5040	4047	39166
	%	4.0	0.0	6.0	66.7	0.0	12.9	10.3	100.0
LITHUANIA	n	2490	0	3069	39762	23	5440	6240	57024
	%	4.4	0.0	5.4	69.7	0.0	9.5	10.9	100.0
LUXEMBOURG	n	830	0	382	9852	180	147	1463	12854
	%	6.5	0.0	3.0	76.7	1.4	1.1	11.4	100.0
MALTA	n	687	0	82	6032	337	1	845	7984
	%	8.6	0.0	1.0	75.6	4.2	0.0	10.6	100.0
NORWAY	n	4562	0	7537	77309	19	14239	12937	116603
	%	3.9	0.0	6.5	66.3	0.0	12.2	11.1	100.0
POLAND	n	26685	0	10556	295488	1040	20559	44436	398764
	%	6.7	0.0	2.7	74.1	0.3	5.2	11.1	100.0
PORTUGAL	n	15707	2175	284	136807	7803	44	14193	177013
	%	8.9	1.2	0.2	77.3	4.4	0.0	8.0	100.0
SCOTLAND	n	7018	0	3903	76944	92	7746	12088	107791
	%	6.5	0.0	3.6	71.4	0.1	7.2	11.2	100.0
SWITZERLAND	n	9852	0	5046	118234	1518	3494	16993	155137
	%	6.4	0.0	3.3	76.2	1.0	2.3	11.0	100.0
Total	n	93512	2188	51784	1096494	13890	82070	160738	1500676
	%	6.2	0.2	3.5	73.1	0.9	5.5	10.7	100.0

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607 **Appendix A: list of data sources**

Country	Data source
Austria	Vital Statistics
Belgium	Fédération Wallonie-Bruxelles / Région wallonne
Cyprus	Medical Birth Register of Public Maternity Units
Estonia	Estonian Medical Birth Registry; Estonian Registry on Causes of Death
Finland	THL Medical Birth Register
France	National Perinatal Survey
Latvia	Medical Birth Register
Lithuania	Medical Date of Births
Luxembourg	Système de Surveillance de la Santé
Malta	National Obstetrics Information System. Directorate for Health Information and Research
Norway	Medical Birth Registry of Norway
Poland	Central Statistical Office
Portugal	National Statistics (INE - Instituto Nacional de Estatística)
Scotland	National Records for Scotland and Public Health Scotland: vital event and maternal hospital discharge data
Switzerland	BEVNAT. statistics of natural population change

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