Variation in very preterm extrauterine growth in a European multicountry cohort

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Abstract

Objective: Extrauterine growth restriction (EUGR) among very preterm infants is related to poor neurodevelopment, but lack of consensus on EUGR measurement constrains international research. Our aim was to compare EUGR prevalence in a European very preterm cohort using commonly-used measures.

Design: Population-based observational study.

Setting: 19 regions in 11 European countries.

Patients: 6,792 very preterm infants born before 32 weeks' gestational age (GA) surviving to discharge.

Main outcome measures: We investigated two measures based on discharge-weight percentiles with (1) Fenton and (2) Intergrowth (IG) charts and two based on growth velocity (1) Birthweight and discharge-weight Z-score differences using Fenton charts (2) Weight-gain velocity using Patel's model. We estimated country-level relative risks of EUGR adjusting for maternal and neonatal characteristics and associations with population differences in healthy newborn size, measured by mean national birthweight at 40 weeks' GA.

Results: About two-fold differences in EUGR prevalence were observed between countries for all indicators and these persisted after case-mix adjustment. Discharge weight <10th percentile using Fenton charts varied from 24% (Sweden) to 60% (Portugal) and using IG from 13% (Sweden) to 43% (Portugal), while low weight-gain velocity ranged from 35% (Germany) to 62% (UK). Mean term birthweight was strongly correlated with both percentile-based measures (Spearman's rho = -0.90 Fenton, -0.84 IG, P<0.01), but not Patel's weight-gain velocity (rho: -0.38, P=0.25).

Conclusions: Very preterm infants have a high prevalence of EUGR, with wide variations between countries in Europe. Variability associated with mean term

birthweight when using common postnatal growth charts complicates international benchmarking.

Key words: Extrauterine growth restriction, suboptimal growth, very preterm infants, growth velocity, delta Z-scores, percentile norms.

Introduction

Despite progress in the survival of very preterm infants, they remain at significantly higher risk of health and developmental problems than term infants[1]. One promising area to enhance their prognosis is postnatal nutrition and growth as poor postnatal growth is prevalent in this population.[2,3] Studies have related extrauterine growth restriction (EUGR) to neurodevelopmental impairment, and pulmonary and metabolic morbidity in childhood and adulthood[4-8].

International comparisons could provide important benchmarks for evaluating postnatal growth and generate hypotheses to improve nutrition in the neonatal unit. For instance, unit variations in nutritional protocols[9] or in neonatal morbidities impacting growth may affect EUGR prevalence. A growing number of international collaborations, such as the International Network for Evaluating Outcomes of Neonates[10] and the Effective Perinatal Intensive Care in Europe project[11], have raised questions about between-country practice differences related to neonatal mortality and morbidity[10-12], but few have focused on postnatal growth.

One difficulty for international research is the absence of consensual measures of postnatal growth for use in multiple settings. Growth indicators can be point measures, describing whether the child is growth restricted at discharge or at another time point, or capture growth velocity, either in absolute terms (grams per kilogram per day) or as the difference in normalised weight for gestational age (GA)/post menstrual age (PMA). However, to construct measures based on percentiles or Z-scores, agreement is required on appropriate norms[13]. There is an on-going debate regarding whether growth after very preterm birth should mirror the normal growth in-utero, as suggested by the American Academy of Pediatrics or whether healthy postnatal growth among

very preterm infants is different[14]. Another debate centres on whether growth charts should be country specific or whether universal prescriptive standards such as the WHO 2006[15] child growth standards are more suitable[16,17].

Our aim was to compare EUGR prevalence among very preterm neonates in European countries based on currently used measures and to assess how the choice of measure affects prevalence estimates and between-country variation. We also investigated whether these measures are associated with population differences in infant size at birth, determined by the country's mean birthweight at 40 weeks of gestation.

Methods

Data source and population

Data are from the population-based EPICE cohort of births before 32 weeks of gestation in 2011/2012 from 19 regions in 11 countries[11]. Data were abstracted from obstetrical and neonatal medical records and infants were followed up until death or discharge home from the hospital.

Our study population included infants discharged home or to domiciliary care before 50 weeks PMA[18]. The 50 week cut-off was selected because the Fenton growth charts used in two indicators are truncated at 50 weeks. From 6792 infants surviving to discharge, exclusions were: discharge to institutional care (N=219), PMA ≥50 weeks (N=99), missing weight at discharge (N=121) or PMA (N=15), severe congenital anomalies (N=61) as defined previously[18], unrealistic growth velocity, ±4 SD from the mean (N=18). Our final sample included 6259 infants (Supplementary figure 1).

Measures of postnatal growth

We selected four indicators applicable to discharge weight that were commonly used or recently suggested approaches in the literature. Two measures are based on discharge-weight percentiles and two on growth velocity between birth and discharge (Table 1). The percentile measures are derived from Fenton's postnatal growth charts[19] and the Intergrowth-21st (IG) prescriptive charts[20]. Measures of velocity are Z-score differences between discharge weight and birthweight using Fenton charts (Fenton delta Z-score)[19] and average growth velocity in grams per kg of weight per day based on birthweight, discharge weight and number of days of hospitalization proposed by Patel (Patel's weight-gain velocity)[21].

Because there is no consensus for the thresholds to define EUGR, we selected the most commonly used thresholds to permit comparison with previous research: <10th percentile for discharge-weight percentiles, <-1 SD change for Fenton delta Z-score. Severe EUGR thresholds of <3rd percentile were used for discharge-weight percentiles and <-2 SD change for Fenton delta Z-score. For Patel's weight-gain velocity, we defined EUGR as a velocity less than the median in our sample following the convention used by the Vermont Oxford Network(VON)[22] to construct a composite quality indicator[23]. For severe EUGR, we selected a threshold based on the first quartile. To assess consistency across measures, we classified infants as having no EUGR by all measures, EUGR by some measures and EUGR by all measures.

Analysis strategy

We first described maternal and newborn characteristics and the four postnatal growth indicators overall and by country. We then used generalized linear regression models with a Poisson distribution and robust standard errors to estimate unadjusted and adjusted relative risks (RR) of EUGR by country using the mean of all countries as the

reference. Clustering within multiple pairs was accounted for. The aim was to assess whether variation between countries could be explained by differences in population characteristics.

Co-variables were maternal and newborn characteristics hypothesized to affect growth and that differed across countries: maternal age, parity, foreign-born mothers, GA in exact weeks, small for GA (SGA), sex, severe neonatal morbidity (composite of intraventricular hemorrhage grade III or IV, cystic periventricular leukomalacia, retinopathy of prematurity stages III–V), surgery for necrotizing enterocolitis or patent ductus arteriosus (PDA), confirmed late onset sepsis and bronchopulmonary dysplasia (BPD) (respiratory assistance or oxygen at 36 weeks PMA). SGA was defined using intrauterine European references developed for the EPICE population[24]. We used these references to ensure consistency across models for all dependent variables, but we carried out sensitivity analyses using Fenton and IG references (see below). Missing data were under 2%, except for breastfeeding (2.9%) and mother's country of birth or ethnicity (6.9%).

We then assessed correlations between unadjusted and adjusted RR for countries with the birthweight of healthy newborns. Country-level birthweight at 40 weeks of gestation was used as a proxy for healthy newborn size. These data come from the Euro-Peristat project which monitors perinatal indicators in Europe[25] and were used previously to analysis SGA in participating countries[24]. We used scatter plots and Spearman's rank test to assess correlations.

We conducted analyses to assess the sensitivity of the adjusted country RR to model specification by (1) adding two variables which depend on hospital policies and were therefore not included in case-mix models: breastfeeding at discharge and PMA at

discharge; (2) removing foreign-born women and (3) using Fenton and IG references to define SGA when analysing indicators constructed with these norms.

Ethical approval was obtained in each country; the European database was approved by the French Advisory Committee on Use of Health Data in Medical Research (CCTIRSN°13.020) and the French National Commission for Data Protection and Liberties (CNILN°DR-2013–194).

Results

Infants had a mean GA of 29.4 weeks and PMA at discharge of 37.9 weeks (Table 2). Average weight was 1260 grams at birth and 2500 grams at discharge. About 10% had at least one severe neonatal morbidity, not including BPD, 13% had BPD and 20% were SGA (<3rd centile); about 60% were receiving some breastmilk at discharge. All characteristics, except infant sex, differed significantly by country.

Table 3 presents the postnatal growth indicators overall and by country. Fenton charts classified 45% of infants below the 10th percentile versus 30% using IG charts. For velocity measures, 59% infants had a Fenton delta Z-score more than 1 SD lower at discharge than at birth. For Patel's weight-gain velocity, the median, representing the threshold for EUGR was 11.9 g/kg/day (SD 2.9). Overall, 23% of infants were not EUGR by any indicator and 17% were EUGR by all four indicators. EUGR ranged from 24% to 60% across countries using Fenton percentiles, from 13% to 43% using IG percentiles, from 39% to 72% for the Fenton delta Z-score and from 35% to 62% for Patel's weight-gain velocity. Infants from the UK and Portugal tended to be more growth restricted for all indicators, while Swedish and German infants had lower EUGR

prevalence based on velocity measures. Classification as EUGR by all indicators ranged from 2% (Sweden) to 26% (UK).

Figures 1 and 2 plot the association of unadjusted and adjusted country RR for EUGR with the country's mean birthweight at 40 weeks of GA. Adjustment for case-mix had a modest impact on country differences, despite associations with maternal and neonatal characteristics (risk adjustment models in supplementary tables 1 to 4). Measures of EUGR were negatively associated with severe neonatal morbidity and lower GA (except for Patel's weight-gain velocity). Being SGA at birth had a negative association with percentile measures, but a positive association with velocity measures. Being foreign born was not associated with any EUGR measure.

After adjustment, country RRs of being EUGR defined by Fenton and IG percentiles, compared to the sample average, varied from lows of 0.6 (95%CI 0.5–0.7) and 0.5 (95%CI 0.4–0.7), respectively, in Sweden to highs of 1.5 (95%CI 1.4–1.6) and 1.7 (95%CI 1.5–1.8) in Portugal. For the two velocity indicators, RR varied from lows of 0.7 (95%CI 0.7–0.8) and 0.9 (95%CI 0.7 –0.9), respectively, in Germany to highs of 1.3 (95%CI 1.3–1.4) and 1.3 (95%CI 1.3 –1.4) in the UK.

Adjusted RR, based on discharge percentiles, were strongly correlated with national mean birthweight at 40 weeks of GA for both Fenton and IG charts (Spearman's ρ =-0.90, P<0.01 and -0.84, P<0.01, respectively). An attenuated negative correlation was obtained for EUGR defined by the Fenton delta Z-score (ρ=-0.54, P=0.09) and the association was not significant for Patel's weight-gain velocity (ρ= 0.38, P=0.25). Results were similar for severe EUGR, although the correlation coefficient was higher for Fenton delta Z-score (Supplemental Figures 2, 3). Sensitivity analyses using adjusted RR from models including breastfeeding and PMA with alternative SGA

measures and removing foreign-born women yielded similar correlation coefficients (Supplemental Table 5).

Discussion

This study found high EUGR prevalence at discharge from hospital for very preterm infants based on four commonly-used indicators with wide variation across regions in 11 European countries. Variation between countries was strongly associated with average country birthweight at 40 weeks' GA when prevalence was based on discharge percentiles: from 60% in Portugal (average birthweight of 3370 grams) to 24% in Sweden (3658 grams) using Fenton's charts and 43% to 13% using IG charts. These associations persisted after adjustment for population case-mix. National birthweight was not significantly correlated with Patel's weight-gain velocity measure, but high variation remained in EUGR prevalence from 35% in Germany to 62% in the UK. These results support the use of country-specific rather than international references for identifying infants with EUGR and reveal substantial unexplained variation between countries that raises questions for clinical practice and research.

Strengths and limitations

This study provides novel data on postnatal growth in very preterm infants in Europe from a large, population-based sample. A common pretested protocol ensured consistency in inclusion criteria and standardized case-mix variables[26]. Limitations are the assessment of weight only at birth and at discharge. More measurements during the neonatal period taken at the same time points, such as 36 weeks PMA, would be needed for exploration of growth patterns. Reassuringly, although discharge timing varied between countries[27], sensitivity analyses adjusting for PMA at discharge did not

affect results. Another limitation is that our focus on weight means that our results do not apply to other growth parameters, including length and head circumference, and this constitutes an area for further research[6,28]. Finally, we could not provide data on unit policies, such as milk fortification, and nutritional intake, required for further investigation of between country differences.

Our study results are consistent with previous studies, which also document high variation across settings. EUGR prevalence based on Fenton percentiles varied from 26.3% among infants with GA <31 weeks in 18 centres in New York to 50% in the VON very low birthweight population[22,29]. EUGR estimates based on IG percentiles ranged between 18% in Victoria, Australia[2] to 45% in an Indian tertiary centre[30]. Studies using Fenton delta Z-scores have reported means between -0.5 and -1.2[4,28,29,31-35], whereas for Patel's weight-gain velocity, means varied from 11.4 to 13.1 g/kg/day[22,31,32,35,36].

By including all four indicators, we were able to document inconsistency in EUGR classifications which affected 60% of the sample. A recent UK study similarly noted large differences when comparing EUGR based on national versus IG charts, concluding for more research to justify the choice of one measure over another[33]. Fenton charts yields higher EUGR rates because norms for PMA at discharge are derived principally from children born at term, whereas the IG charts model growth in a healthy preterm population. Although IG curves have been criticized because they were constructed on a small sample of 201 preterm infants[37], when followed up at two years, they had a median weight similar to the WHO charts (53rd percentile)[38]. However, studies have not evaluated outcomes of children classified as non-EUGR by the IG charts. In two studies comparing velocity indicators, authors concluded in favour

of delta Z-scores, because they take into consideration sex and PMA[36,39]. However, for the VON NICU quality score, Patel's weight gain velocity was chosen. Our results illustrate the importance of further research to identify which measure best captures health risks associated with poor growth.

Our study revealed strong correlations between percentile indicators and mean country term birthweight. These results are relevant to the on-going debate about the use of common versus country-specific norms[37,40] as it is highly unlikely that these variations reflect true differences in EUGR. As others have suggested, local curves may be more suitable for postnatal growth monitoring and comparisons because of population anthropometric variation[33,37,40]. In contrast, velocity measures were less associated with mean term birthweight, making their use in cross-national settings more straightforward.

Variability exists in Europe in NICU nutritional and other management protocols for enteral feeding, parenteral nutrient supply, management of fresh mother's milk or milk bank availability, fortification of breastmilk[41] and parental presence in the NICU[42]. In addition to their impact on growth, different protocols may affect risks of neonatal morbidities which interfere with growth, such as necrotizing enterocolitis, BPD and late-onset sepsis[43]. Reinforcing knowledge about feeding strategies that promote healthy growth is a priority; recent studies have identified nutritional practices and interventions associated with better postnatal growth and respiratory outcomes, including high volume feeding, protein enriched diets, early initiation of parental nutrition, greater use of breastmilk and not withholding feeding in patients with morbidities[2,29,44-47]. Observational studies show the potential for improvement. In

the New York study cited above, EUGR prevalence declined after an intervention from 33% in 2010 to 26% in 2013[29], while Patel's growth-velocity measure improved by 14% from 2000 to 2013 in the VON Network[22] and Fenton's delta Z-score <-1SD declined from 47% to 38% in California between 2005 and 2012[35].

Conclusion

Our study reveals high EUGR prevalence among very preterm infants and wide variations between European countries regardless of the indicator used. The strong correlations with birthweight at term suggest that part of this variation arises from population anthropometric differences. However, variation also exists in velocity measures that are independent of term birthweight. These wide differences between countries provide an incentive to understand how nutritional and other policies in the neonatal unit affect growth and can be improved to reduce EUGR in this high-risk population.

“What is already known on this topic**”**

- Very preterm neonates have high prevalence of postnatal growth restriction following discharge from the hospital.

- Very preterm neonates are at significantly higher risk of neurodevelopmental impairment and respiratory and metabolic complications than term infants.

- There are no consensual measures to identify very preterm neonates with postnatal growth restriction for use in multiple settings.

“What this study adds”

- Extrauterine growth restriction is highly prevalent among preterm infants in Europe with wide variation between countries.

- Some between country-variation reflects mean term birthweight as shown by strong correlations between the prevalence of extrauterine growth restriction and the birthweight of term newborns.

- Discordance between commonly-used postnatal growth measures is high, with 60% of children classified as growth restricted by at least one, but not all measures.

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Table 1. Measures of postnatal growth

Measure	Definition	Methods	EUGR thresholds
Fenton percentile	Percentiles computed from discharge weight by postmenstrual age and sex using Fenton postnatal growth charts [19].	Charts were derived from a meta-analysis of 6 population-based birthweight charts - Voight 2010 (Germany), Olsen 2010 (US), Kramer 2001 (Canada), Roberts 1999 (Australia), Bonellie 2008 (Scotland), Bertino 2010 (Italy)- and the WHO postnatal growth standards. References span postmenstrual GA from 22 to 50 weeks and are calculated using GA in weeks and days.	< 10th percentile < 3rd percentile
Intergrowth percentile	Percentiles computed from discharge weight by postmenstrual age and sex using Intergrowth 21st postnatal growth charts[20].	Curves were constructed from 201 healthy preterm singleton births enrolled into the Intergrowth preterm postnatal study from Brazil, Italy, Oman, UK, USA, China, India and Kenya. Growth measurements were collected at different time points per neonate. References span postmenstrual age from 27 to 64 weeks and are calculated using postnatal weeks and days.	< 10th percentile < 3rd percentile
Fenton delta Z-score	Growth velocity is calculated as the difference between the Z-score of discharge weight minus birthweight computed using Fenton's charts.	Fenton charts are used for birthweight and discharge weight.	< -1 SD < -2 SD
Patel's weight-gain velocity	Growth velocity is calculated as the average grams per kilogram per day calculated using an exponential model[21].	The Patel measure is calculated as (g/kg/day) = $\frac{1000\ x\ Ln\frac{(discharge\ weight)}{Birthweight}}{Number\ of\ hospital\ days}$ This model assumes that growth occurs at a constant fraction of previous weight.	< Median < 1st quartile

Table 2. . Maternal and neonatal characteristics of the overall sample and by country

	Total (N=6259)	Belgium (N=620)	Denmark (N=259)	Estonia (N=135)	France (N=1068)	Germany (N=612)	Italy (N=917)	Nether-lands (N=311)	Poland (N=226)	Portugal (N=594)	UK (N=1286)	Sweden (N=231)
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD
Mother's age (years)	30.6 (6.0)	29.9 (5.1)	30.4 (5.2)	31.7 (5.9)	29.9 (5.9)	31.4 (5.7)	33.3 (6.1)	30.8 (5.0)	29.2 (5.9)	30.8 (6.0)	28.8 (6.3)	32.5 (5.9)
GA (weeks)	29.4 (2.0)	29.6 (1.9)	29.1 (2.0)	29.3 (2.1)	29.4 (1.9)	29.2 (2.1)	29.4 (2.0)	29.4 (2.1)	29.2 (2.2)	29.4 (1.9)	29.4 (2.0)	29.0 (2.1)
Birthweight (g)	1260 (365)	1332 (372)	1232 (345)	1309 (355)	1236 (348)	1237 (381)	1256 (362)	1278 (382)	1324 (394)	1203 (342)	1266 (361)	1278 (403)
PMA at discharge(wks)	37.9 (2.7)	38.4 (2.5)	37.7 (2.3)	37.1 (2.2)	38.7 (2.4)	38.5 (2.8)	37.3 (2.8)	38.5 (2.5)	37.0 (2.8)	37.4 (2.6)	37.5 (2.7)	36.6 (2.3)
Discharge weight(g)	2500 (509)	2689 (414)	2538 (481)	2482 (496)	2671 (451)	2752 (501)	2306 (461)	2772 (542)	2395 (392)	2277 (419)	2351 (523)	2418 (532)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Foreign born mothers	1238 (21)	113 (19)	41 (17)	1 (1)	345 (34)	64 (16)	285 (31)	54 (18)	2 (1)	96 (17)	162 (14)	75 (33)
Nulliparous	3546 (57)	367 (60)	163 (63)	58 (43)	562 (54)	373 (62)	578 (64)	197 (63)	104 (47)	369 (62)	646 (51)	129 (56)
Multiples	1995	247	110	33	350	230	304	90	48	184	328	71

	(32)	(40)	(43)	(24)	(33)	(38)	(33)	(29)	(21)	(31)	(26)	(31)
Boys	3361	345	139	71	565	333	452	155	125	335	717	124
	(54)	(56)	(54)	(53)	(53)	(54)	(49)	(50)	(55)	(57)	(56)	(54)
SGA												
< 3 centile	1272	102	62	21	240	149	171	73	30	132	242	50
	(20)	(17)	(24)	(16)	(23)	(24)	(19)	(24)	(13)	(22)	(19)	(22)
3-9 centile	737	71	31	23	118	81	113	26	28	78	146	22
	(12)	(12)	(12)	(17)	(11)	(13)	(12)	(8)	(12)	(13)	(11)	(10)
≥ 10th centile	4250	447	166	91	710	382	633	212	168	384	898	159
	(68)	(72)	(64)	(67)	(67)	(62)	(69)	(68)	(74)	(65)	(70)	(69)
Any severe morbidity	592	53	21	18	61	53	92	27	52	61	138	16
	(10)	(9)	(8)	(13)	(6)	(9)	(10)	(9)	(23)	(10)	(11)	(7)
Surgery for PDA	215	11	5	15	45	27	26	10	21	16	26	10
	(3)	(2)	(2)	(11)	(4)	(4)	(3)	(3)	(9)	(3)	(2)	(4)
BPD	799	63	22	16	97	55	74	41	20	67	315	29
	(13)	(10)	(9)	(12)	(10)	(9)	(8)	(13)	(9)	(11)	(25)	(13)
Late onset infection	1713	134	89	33	396	154	154	92	68	219	331	43
	(27)	(22)	(34)	(24)	(37)	(25)	(17)	(30)	(30)	(37)	(26)	(19)
Feeding at discharge												
Exclusive human milk	1668	212	97	64	259	88	164	163	44	146	339	92
	(28)	(35)	(43)	(47)	(24)	(17)	(18)	(53)	(20)	(25)	(27)	(41)
Mix feeding	1899	122	86	36	248	210	409	45	62	246	354	81
	(31)	(20)	(38)	(27)	(23)	(41)	(45)	(15)	(29)	(42)	(28)	(36)

Exclusive formula	2508 (41)	275 (45)	45 (20)	35 (26)	561 (53)	218 (42)	333 (37)	100 (33)	111 (52)	197 (34)	582 (46)	51 (23)

Note: the differences between countries were statistically significantly at the P<.05 level with the exception of infant sex (P=0.1).

Table 3. Comparison of postnatal growth indicators by country

	Total (N=6259)	Belgium (N=620)	Denmark (N=259)	Estonia (N=135)	France (N=1068)	Germany (N=612)	Italy (N=917)	Netherlands (N=311)	Poland (N=226)	Portugal (N=594)	UK (N=1286)	Sweden (N=231)
Fenton Percentile (discharge weight)												
Mean	18.2	21.8	19.5	24.7	17.5	23.3	15.5	24.9	22.6	12.3	14.6	25.0
SD	(18.8)	(20.1)	(18.0)	(21.9)	(18.1)	(20.8)	(17.4)	(21.2)	(20.7)	(15.1)	(16.8)	(19.2)
% <3rd percentile	24	18	18	14	22	15	29	16	19	34	31	11
% <10th percentile	45	37	41	32	47	34	52	31	34	60	54	24
IG Percentile (discharge weight)												
Mean	30.7	36.1	32.9	40.0	29.9	37.7	27.2	39.8	37.5	21.9	25.2	41.4
SD	(26.3)	(27.3)	(25.3)	(28.5)	(25.4)	(27.1)	(25.6)	(27.6)	(27.9)	(22.9)	(24.5)	(25.8)
% <3rd percentile	17	12	12	11	15	10	22	8	12	25	23	6
% <10th percentile	30	22	22	19	30	19	36	18	21	43	38	13
Fenton delta Z-score												
Mean	-1.2	-1.2	-1.1	-1.2	-1.1	-0.9	-1.4	-1.0	-1.4	-1.4	-1.5	-1.0
SD	(0.8)	(0.8)	(0.8)	(0.7)	(0.7)	(0.8)	(0.8)	(0.7)	(0.9)	(0.8)	(0.8)	(0.6)
% <-2 SD	14	11	11	10	10	8	18	8	17	18	22	5
% <-1 SD	59	55	53	61	56	39	65	43	61	66	72	53
Patel's weight-gain velocity, g/kg/day												

Mean	11.7	11.9	12.1	11.6	12.3	12.8	11.2	12.5	11.1	11.5	10.7	12.0
SD	(2.9)	(2.6)	(3.0)	(2.9)	(2.1)	(2.4)	(3.3)	(2.3)	(3.2)	(2.9)	(3.3)	(2.9)
%< median*	25	21	23	24	14	11	33	12	32	27	38	24
% < 1st quartile*	50	48	47	53	43	35	55	39	53	52	62	45
% Cumulative indicator												
Not EUGR by any indicator	23	28	27	25	24	36	19	32	22	17	16	29
EUGR by at least one, but not all indicators	60	61	61	64	62	55	60	61	65	59	59	69
EUGR by all indicators	17	11	12	11	14	9	22	7	13	24	26	2

* Median value of 10.1, 1st quartile value of 11.9

Figure 1. RR of EUGR (percentiles) by country birthweight

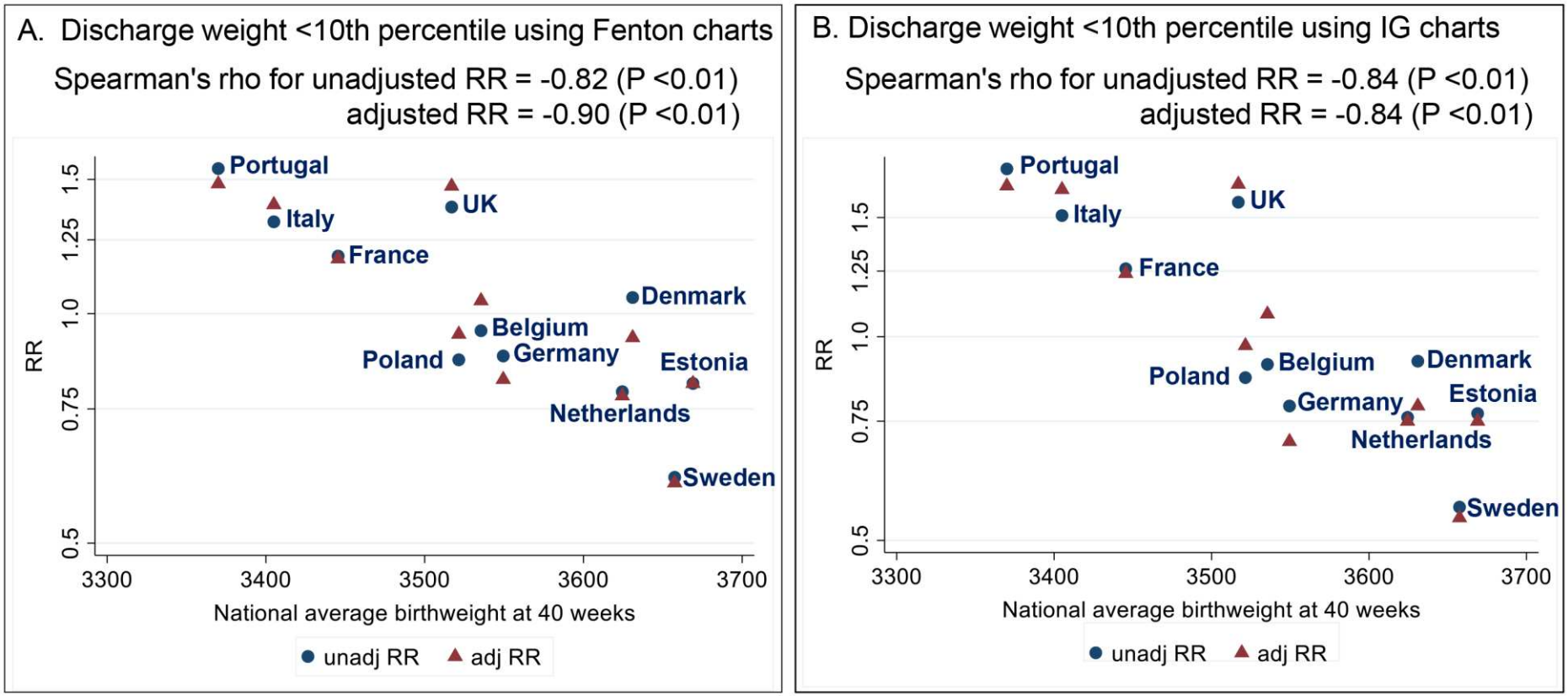
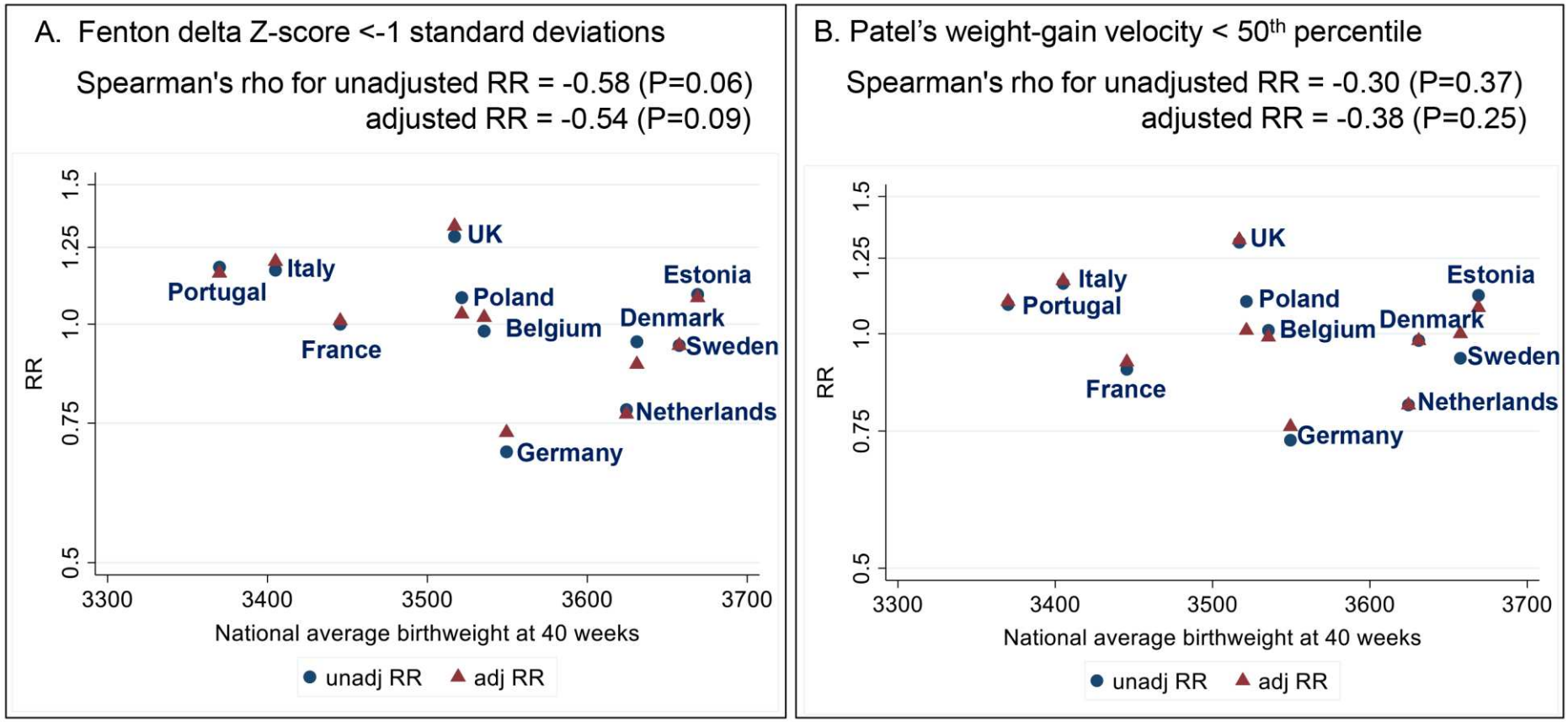


Figure 2. RR of EUGR (velocity) by country birthweight



Supplemental material

Figure 1. Study flow chart; web only

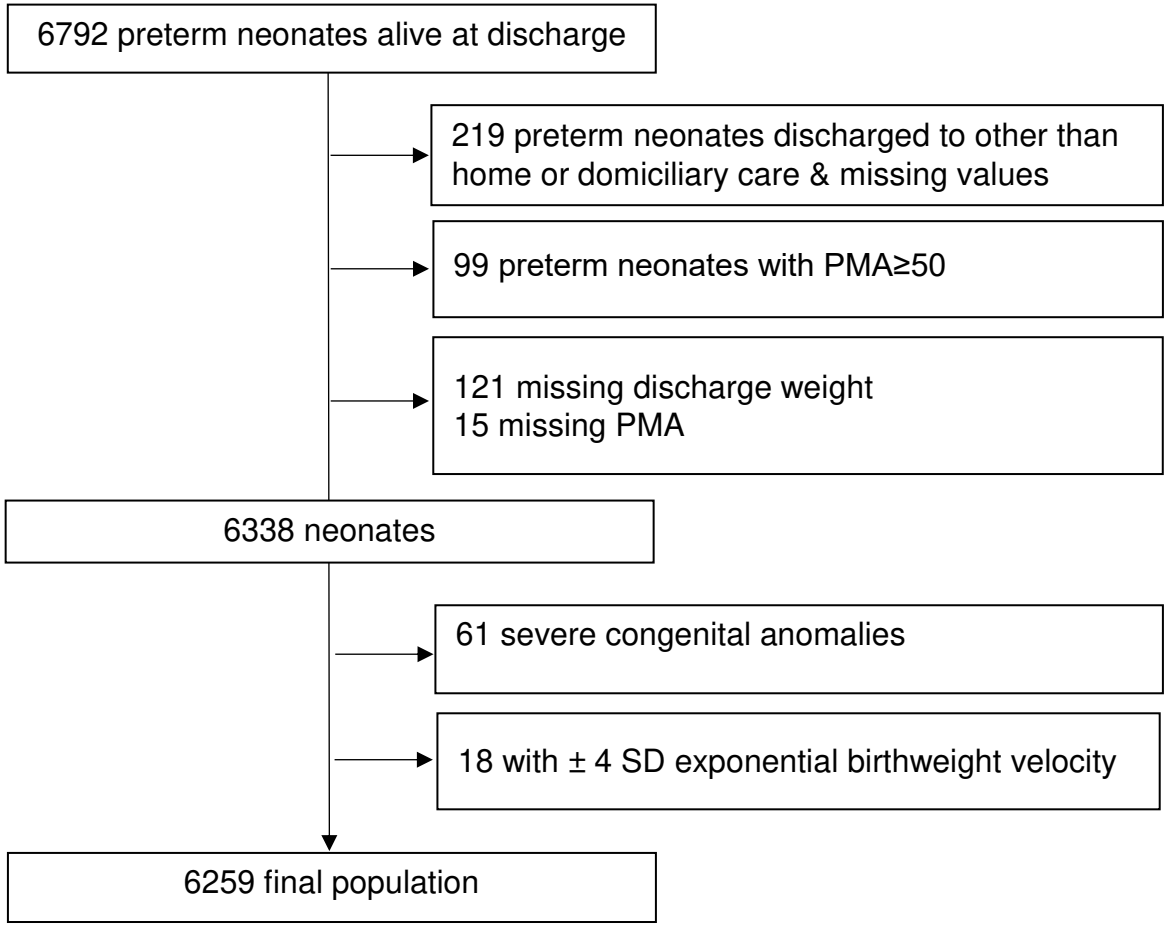
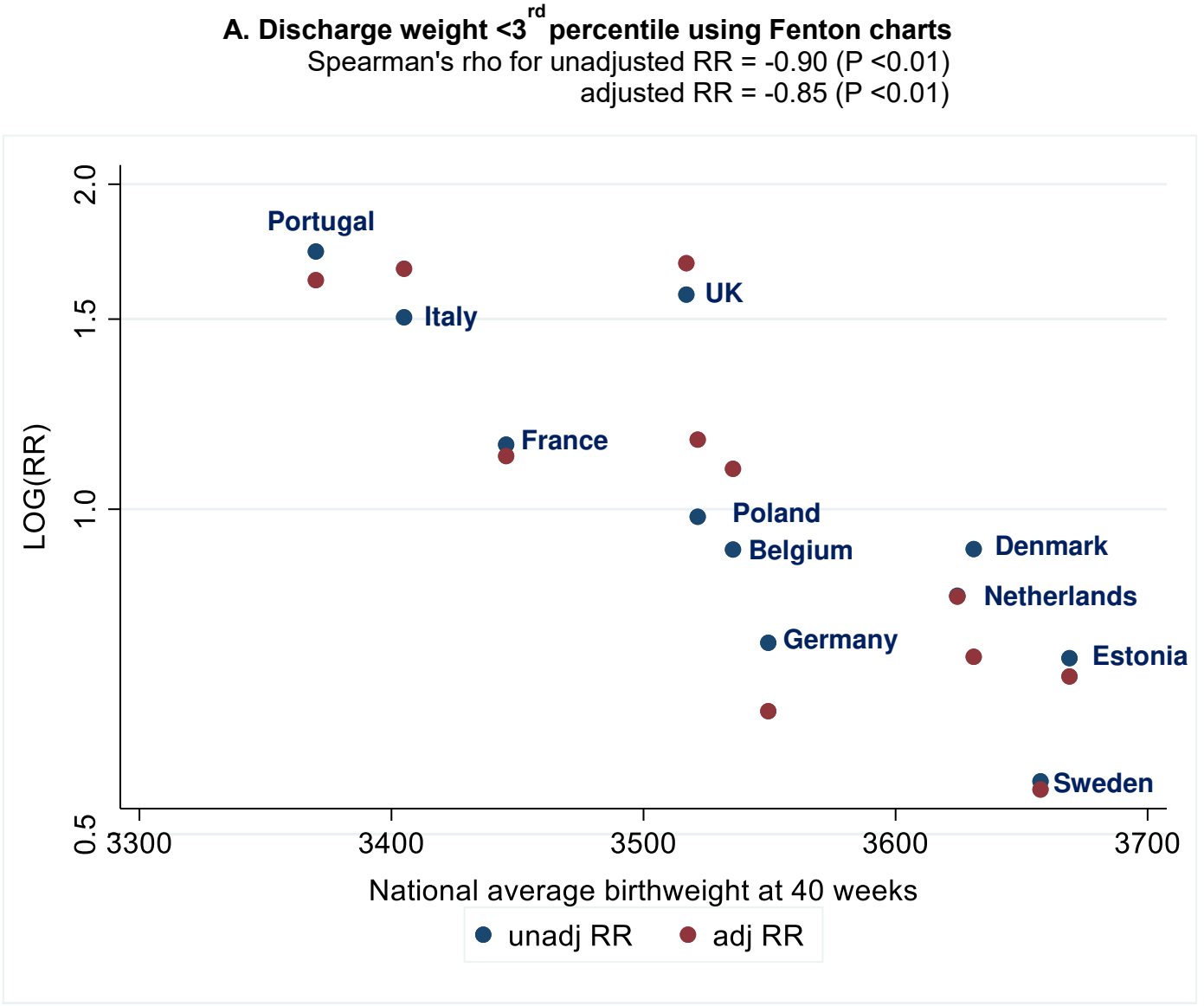


Figure 2. Association of relative risks (RR) of severe EUGR by country with mean national birthweight at 40 weeks' GA for postnatal growth measures based on discharge-weight percentiles; Web only



B. Discharge weight <3rd percentile using IG charts

Spearman's rho for unadjusted RR = -0.87 (P <0.01)

adjusted RR = -0.83 (P <0.01)

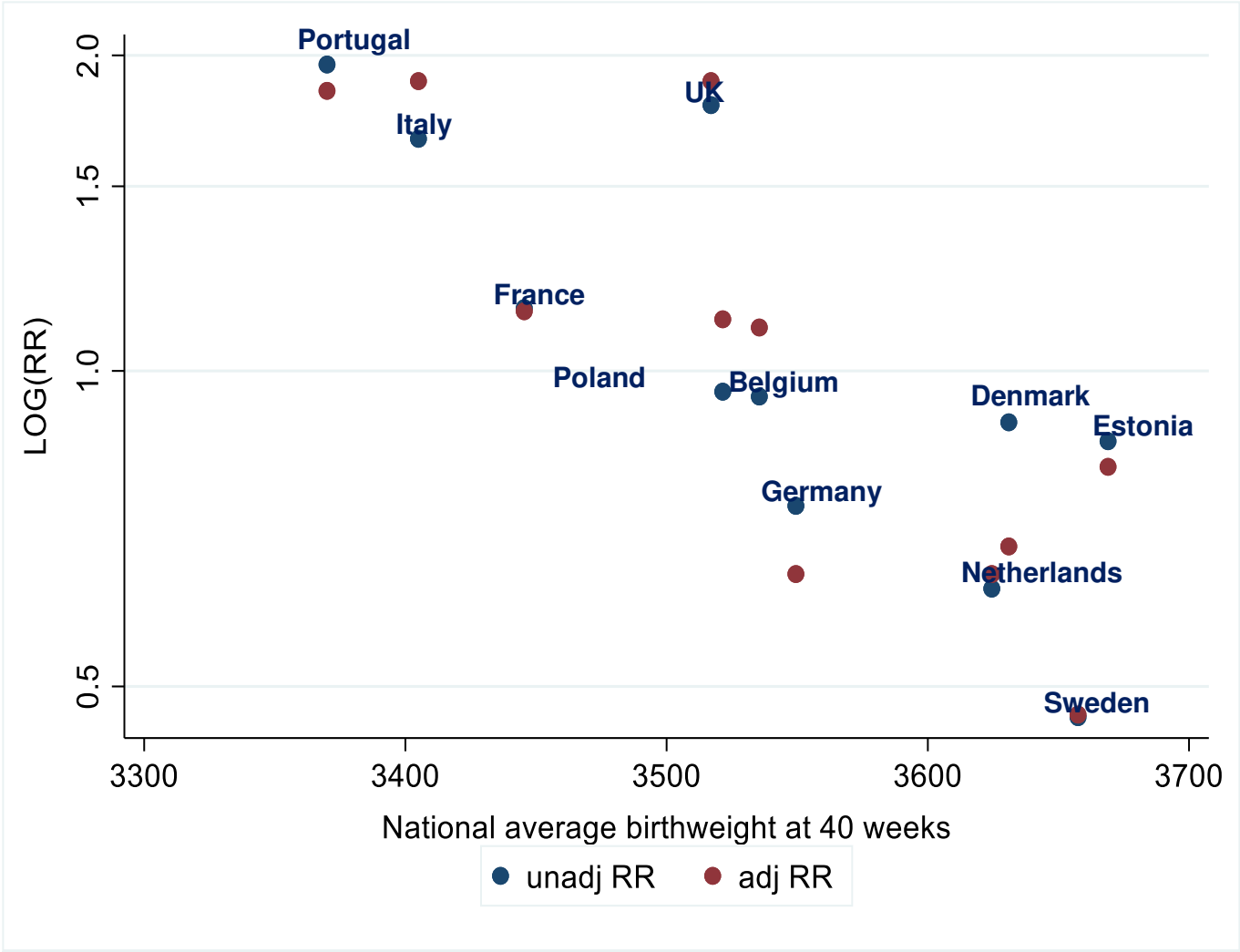
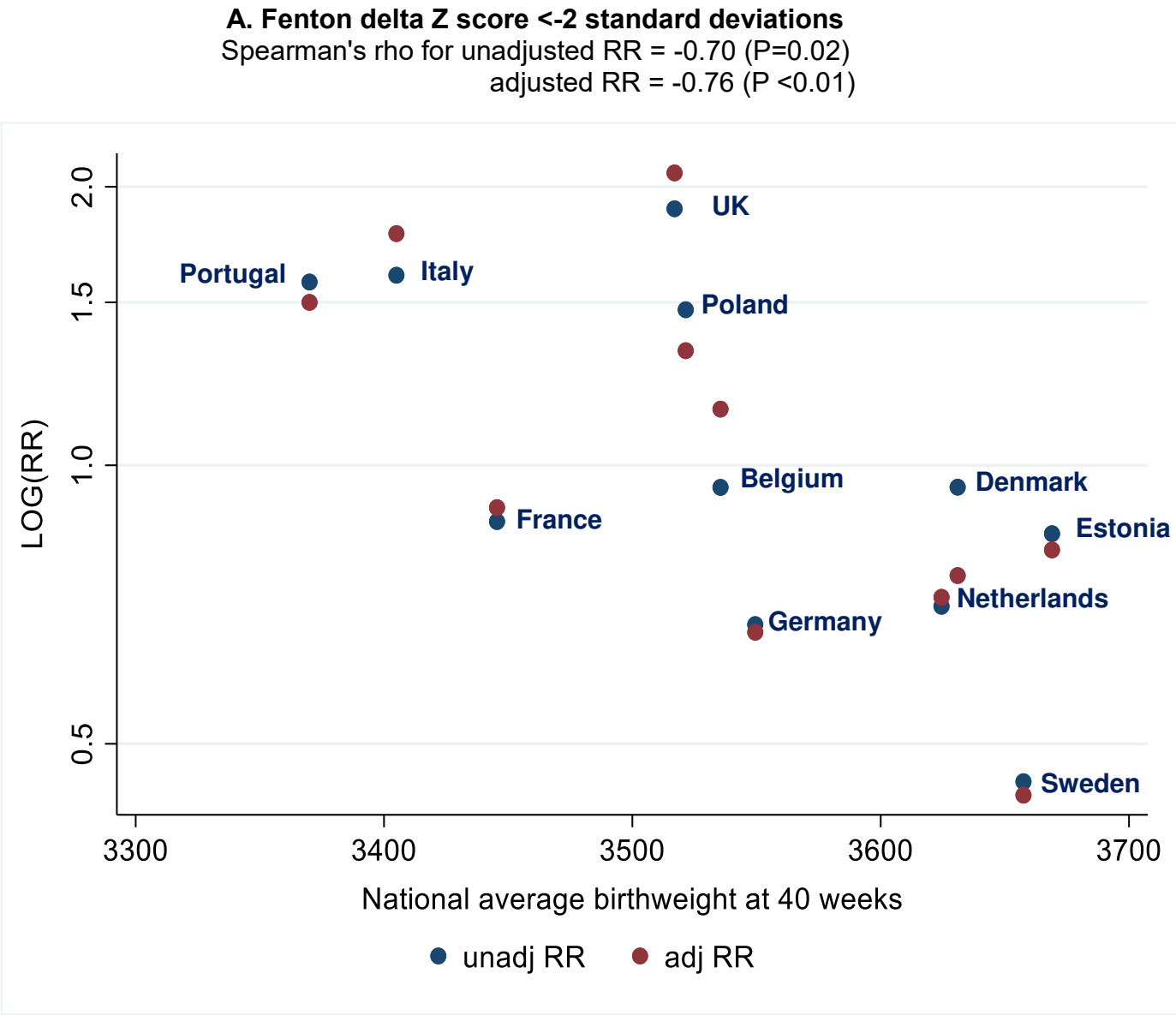


Figure 3. Association of relative risks (RR) of severe EUGR by country with mean national birthweight at 40 weeks' GA for two postnatal growth measures based on velocity; web only



B. Patel's weight-gain velocity <25th percentile (<10.1 g/kg/day)

Spearman's rho for unadjusted RR = -0.38 (P=0.25)

adjusted RR = -0.42 (P=0.20)

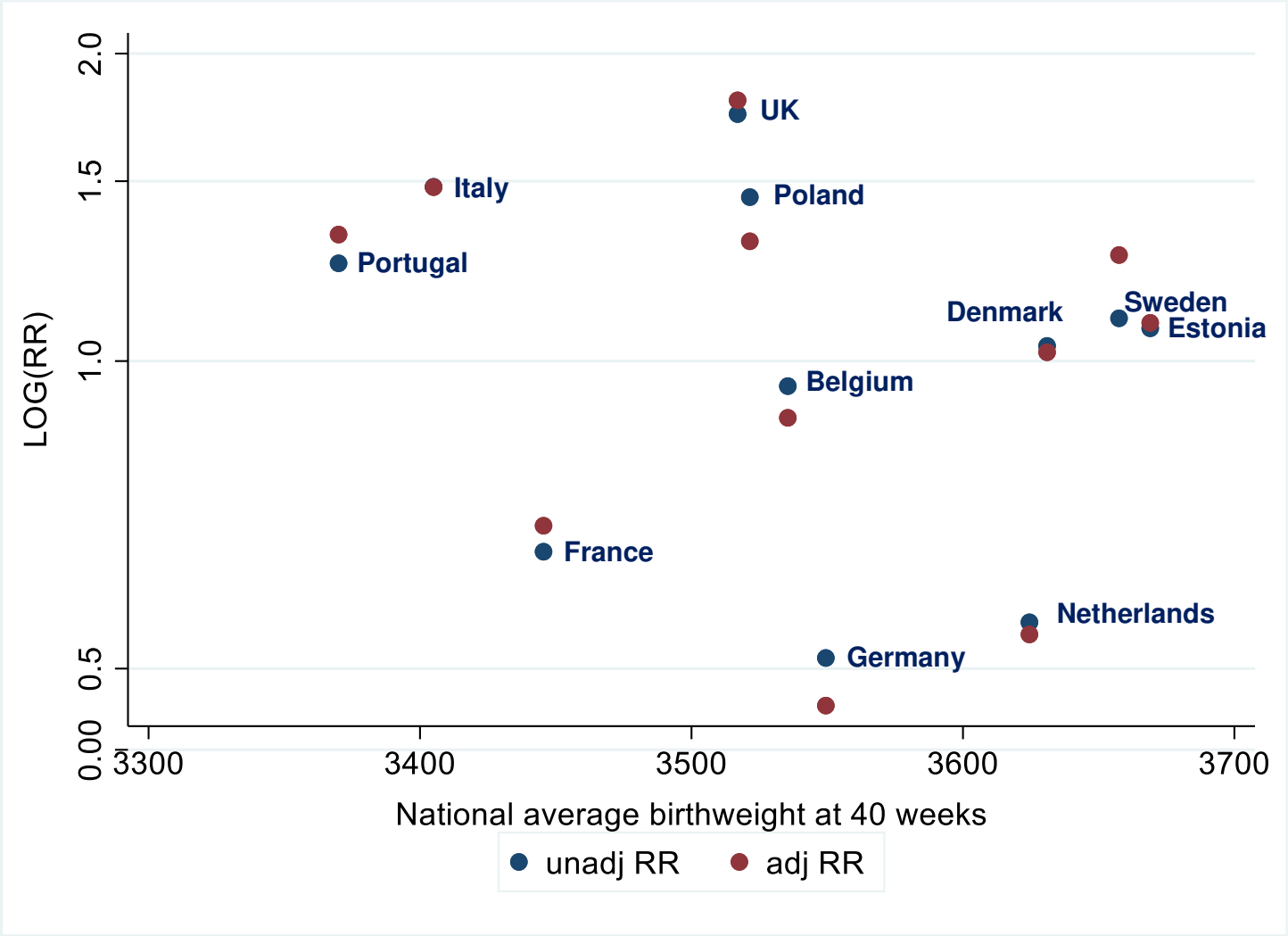


Table 1: Risk adjustment models for EUGR defined by Fenton (moderate); web only

			Unadjusted estimates			Adjusted final model used for the figures			Sensitivity analysis changing SGA measure			Sensitivity analysis adding breastfeeding and PMA at discharge		
	N	% EUGR	Unadj RR	95% CI		Adj[1] RR	95% CI		Adj[2] RR	95% CI		Adj[3] RR	95% CI	
Country (ref. mean)														
Belgium	230	37.1	0.95	0.85	1.06	1.04	0.95	1.15	1.00	0.90	1.12	0.98	0.89	1.08
Denmark	106	40.9	1.05	0.91	1.21	0.93	0.81	1.07	1.04	0.89	1.22	0.85	0.72	0.99
Estonia	43	31.9	0.81	0.63	1.05	0.81	0.66	1.00	0.84	0.66	1.06	0.81	0.66	1.00
France	497	46.5	1.19	1.10	1.29	1.18	1.10	1.26	1.17	1.08	1.26	1.12	1.04	1.20
Germany	210	34.3	0.88	0.78	0.99	0.82	0.73	0.91	0.87	0.77	0.98	0.80	0.71	0.90
Italy	473	51.6	1.32	1.22	1.42	1.39	1.30	1.49	1.32	1.22	1.42	1.46	1.36	1.56
Netherlands	96	30.9	0.79	0.67	0.93	0.78	0.69	0.89	0.76	0.66	0.88	0.72	0.64	0.83
Poland	77	34.1	0.87	0.74	1.03	0.94	0.81	1.08	0.89	0.76	1.04	1.00	0.87	1.16
Portugal	359	60.4	1.55	1.43	1.67	1.48	1.38	1.59	1.47	1.36	1.58	1.55	1.45	1.67
United Kingdom	695	54.0	1.38	1.29	1.48	1.47	1.38	1.56	1.41	1.32	1.51	1.55	1.46	1.66
Sweden	55	23.8	0.61	0.49	0.75	0.60	0.50	0.72	0.61	0.49	0.75	0.65	0.53	0.79
Mother origin *(ref. native)*														
Native	2085	45.4												
Foreign	576	46.5	1.02	0.95	1.10	0.99	0.93	1.06	1.05	0.98	1.12	1.01	0.94	1.07
Maternal age, years *(ref. <25)*														
<25	455	44.6												
25-34	1605	45.3	1.01	0.94	1.10	1.04	0.96	1.12	1.07	0.99	1.15	0.99	0.91	1.06
35+	772	46.2	1.04	0.95	1.13	1.06	0.98	1.15	1.12	1.02	1.22	1.00	0.92	1.09
Gestational age, weeks (ref. 30-31)														
23	16	66.7	1.64	1.24	2.15	2.07	1.56	2.73	1.26	0.95	1.67	1.73	1.31	2.27
24 -25	263	59.2	1.45	1.33	1.59	1.64	1.46	1.84	1.18	1.06	1.32	1.46	1.29	1.65
26-27	551	53.4	1.31	1.22	1.41	1.33	1.23	1.44	1.14	1.05	1.23	1.24	1.14	1.34

28-29	763	45.0	1.11	1.03	1.19	1.03	0.97	1.10	1.04	0.97	1.12	1.02	0.96	1.09
30-31	1248	40.7												
Any severe morbidity (ref.No)	378	63.9	1.46	1.36	1.57	1.24	1.15	1.34	1.24	1.15	1.34	1.16	1.07	1.25
No	2418	43.7												
Surery for PDA *(ref.No)*	146	67.9	1.52	1.38	1.68	1.22	1.09	1.38	1.22	1.09	1.37	1.17	1.05	1.32
No	2,695	44.6												
Late onset sepsis *(ref.No)*	1,026	59.9	1.50	1.42	1.58	1.26	1.19	1.33	1.28	1.20	1.36	1.20	1.13	1.27
No	1,815	39.9												
Sex (ref.girls)														
Boys	1501	44.7	0.97	0.91	1.02	1.04	0.99	1.09	0.96	0.91	1.01	1.03	0.98	1.08
Girls	1340	46.2												
BPD at 36 wks (ref.No)	523	65.5	1.55	1.46	1.65	0.95	0.88	1.02	1.09	1.01	1.18	0.85	0.79	0.92
No	2255	42.2												
Parity (ref. multiparous)														
Nulliparous	1721	48.5	1.18	1.11	1.25	1.10	1.04	1.16	1.18	1.11	1.25	1.06	1.00	1.12
Multiparous	1093	41.2												
SGA (ref. SGA>10)														
<3	1120	88.1	3.03	2.88	3.20	3.24	3.06	3.44	2.15	1.98	2.32	2.84	2.66	3.02
3-10	487	66.1	2.28	2.12	2.44	2.42	2.25	2.60	2.20	2.09	2.32	2.27	2.11	2.45
> 10	1234	29.0												
Postmenstrual age (ref.32 - 36)														
32 - 36	736	27.9												
37 to 39	1,314	52.8	1.89	1.75	2.04							1.54	1.43	1.66
40+	745	70.2	2.51	2.33	2.71							1.73	1.57	1.89
Feeding at discharge (ref. exclusive formula)														
Exclusive human milk	771	46.2	1.08	1.01	1.16							1.03	0.97	1.10
Mix feeding	929	48.9	1.15	1.07	1.23							0.82	0.77	0.87

Exclusive formula	1069	42.6												

[1] Model 1 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (intrauterine European reference) and parity
[2] Model 2 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (Fenton reference) and parity
[3] Model 3 adjusted for model 1 & breastfeeding at discharge and postmenstrual age

Table 2: Risk adjustment models for EUGR defined by IG (moderate); web only

			Unadjusted estimates			**Adjusted final model used for the figures**			**Sensitivity analysis changing SGA measure**			**Sensitivity analysis adding breastfeeding and PMA at discharge**		
	N	**% EUGR**	**Unadj RR**	**95% CI**		**Adj[1] RR**	**95% CI**		**Adj[2] RR**	**95% CI**		**Adj[3] RR**	**95% CI**	
Country (ref. mean)														
Belgium	136	21.9	0.91	0.78	1.07	1.08	0.94	1.24	1.04	0.90	1.19	0.95	0.82	1.09
Denmark	57	22.0	0.92	0.73	1.15	0.79	0.63	0.99	0.89	0.71	1.12	0.74	0.58	0.93
Estonia	25	18.5	0.77	0.54	1.11	0.75	0.54	1.03	0.82	0.58	1.15	0.77	0.57	1.04
France	324	30.3	1.26	1.13	1.41	1.24	1.12	1.36	1.19	1.07	1.32	1.12	1.01	1.23
Germany	116	19.0	0.79	0.67	0.93	0.70	0.59	0.82	0.75	0.64	0.89	0.65	0.54	0.77
Italy	332	36.2	1.51	1.36	1.67	1.65	1.50	1.82	1.53	1.39	1.69	1.74	1.59	1.91
Netherlands	57	18.3	0.76	0.61	0.96	0.75	0.62	0.91	0.71	0.59	0.86	0.66	0.54	0.81
Poland	47	20.8	0.87	0.68	1.10	0.97	0.79	1.19	0.92	0.75	1.14	1.09	0.89	1.33
Portugal	253	42.6	1.77	1.60	1.98	1.67	1.51	1.84	1.56	1.41	1.73	1.80	1.63	1.99
United Kingdom	488	38.0	1.58	1.44	1.73	1.68	1.54	1.84	1.64	1.49	1.80	1.83	1.67	2.00
Sweden	31	13.4	0.56	0.41	0.75	0.54	0.41	0.70	0.57	0.43	0.76	0.63	0.47	0.84
Mother origin *(ref. native)*														
Native	1375	30.0												
Foreign	377	30.5	1.02	0.92	1.12	0.98	0.90	1.07	1.05	0.95	1.15	1.01	0.92	1.10

Maternal age, years *(ref. <25)*														
<25	291	28.5												
25-34	1055	29.7	1.04	0.93	1.17	1.14	1.02	1.26	1.17	1.05	1.31	1.08	0.97	1.20
35+	517	30.9	1.08	0.96	1.23	1.15	1.02	1.29	1.20	1.06	1.35	1.08	0.96	1.21
Gestational age, weeks (ref. 30-31)														
23	12	50.0	2.00	1.36	2.95	2.56	1.59	4.12	0.38	0.23	0.61	2.09	1.37	3.20
24 -25	187	42.1	1.69	1.48	1.92	1.99	1.69	2.35	1.54	1.31	1.80	1.66	1.41	1.96
26-27	388	37.6	1.51	1.36	1.67	1.53	1.37	1.71	1.32	1.18	1.47	1.34	1.21	1.50
28-29	514	30.3	1.22	1.10	1.34	1.09	1.00	1.19	1.09	0.99	1.20	1.06	0.97	1.15
30-31	765	25.0												
Any severe morbidity (ref.No)	285	48.1	1.72	1.56	1.89	1.34	1.20	1.49	1.34	1.20	1.49	1.16	1.05	1.29
No	1553	28.1												
Surery for PDA *(ref.No)*	117	54.4	1.88	1.65	2.14	1.37	1.17	1.60	1.34	1.15	1.56	1.29	1.11	1.50
No	1,749	28.9												
Late onset sepsis *(ref.No)*	749	43.7	1.78	1.65	1.92	1.37	1.26	1.48	1.36	1.25	1.48	1.23	1.14	1.33
No	1,866	29.81												
Sex (ref.girls)														
Boys	1501	44.7	1.31	1.21	1.42	1.43	1.34	1.54	1.36	1.27	1.46	1.42	1.33	1.52
Girls	1340	46.2												
BPD at 36 wks (ref.No)	523	65.5	1.96	1.80	2.12	0.97	0.88	1.07	1.04	0.94	1.14	0.79	0.72	0.88
No	2255	42.2												
Parity (ref. multiparous)														
Nulliparous	1721	48.5	1.25	1.15	1.36	1.14	1.06	1.23	1.20	1.11	1.30	1.07	0.99	1.16
Multiparous	1093	41.2												
SGA (ref. SGA>10)														
<3	1120	88.1	4.60	4.24	5.00	5.25	4.82	5.72	4.07	3.76	4.39	4.17	3.79	4.58
3-10	487	66.1	2.87	2.57	3.20	3.24	2.91	3.60	3.49	3.21	3.81	2.90	2.60	3.24
> 10	1234	29.0												

Postmenstrual age (ref.32 - 36)														
32 - 36	349	13.2												
37 to 39	853	34.3	2.59	2.31	2.91							2.07	1.85	2.32
40+	633	59.6	4.50	4.02	5.04							2.84	2.48	3.24
Feeding at discharge (ref. exclusive formula)														
Exclusive human milk	771	46.2	1.07	0.97	1.18							1.06	0.97	1.16
Mix feeding	929	48.9	1.16	1.06	1.27							0.79	0.73	0.86
Exclusive formula	1069	42.6												

[1] Model 1 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (intrauterine European reference) and parity

[2] Model 2 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (Fenton reference) and parity

[3] Model 3 adjusted for model 1 & breastfeeding at discharge and postmenstrual age

Table 3: Risk adjustment models for EUGR defined by delta Fenton delta Z scores (moderate); web only

			Unadjusted estimates			**Adjusted final model used for the figures**			**Sensitivity analysis changing SGA measure**			**Sensitivity analysis adding breastfeeding and PMA at discharge**		
	N	**% EUGR**	**Unadj RR**	**95% CI**		**Adj[1] RR**	**95% CI**		**Adj[2] RR**	**95% CI**		**Adj[3] RR**	**95% CI**	
Country (ref. mean)														
Belgium	341	55.0	0.98	0.91	1.06	1.02	0.94	1.10	1.03	0.95	1.11	0.98	0.90	1.06
Denmark	138	53.3	0.95	0.85	1.07	0.89	0.79	1.01	0.88	0.77	1.00	0.83	0.72	0.95
Estonia	82	60.7	1.09	0.94	1.25	1.08	0.94	1.25	1.08	0.93	1.24	1.07	0.93	1.22
France	599	56.1	1.00	0.95	1.06	1.01	0.95	1.08	1.01	0.95	1.08	0.99	0.93	1.05
Germany	237	38.7	0.69	0.63	0.77	0.73	0.65	0.81	0.71	0.64	0.80	0.72	0.64	0.80
Italy	600	65.4	1.17	1.11	1.24	1.20	1.13	1.27	1.21	1.14	1.28	1.25	1.19	1.33
Netherlands	135	43.4	0.78	0.68	0.88	0.77	0.68	0.87	0.77	0.68	0.87	0.71	0.63	0.81

Poland	137	60.6	1.08	0.98	1.20	1.03	0.94	1.14	1.05	0.94	1.16	1.12	1.01	1.24
Portugal	392	66.0	1.18	1.11	1.26	1.16	1.09	1.24	1.16	1.09	1.24	1.22	1.15	1.30
United Kingdom	924	71.9	1.29	1.23	1.34	1.33	1.27	1.40	1.35	1.28	1.41	1.39	1.32	1.46
Sweden	122	52.8	0.94	0.84	1.07	0.94	0.83	1.07	0.94	0.83	1.07	0.96	0.85	1.09
Mother origin *(ref. native)*														
Native	2779	60.6												
Foreign	700	56.5	0.93	0.88	0.99	0.94	0.89	0.99	0.93	0.88	0.98	0.95	0.89	1.00
Maternal age, years *(ref. <25)*														
<25	591	57.9												
25-34	2122	59.8	1.03	0.97	1.10	1.08	1.02	1.15	1.08	1.01	1.15	1.02	0.96	1.08
35+	986	59.0	1.02	0.95	1.09	1.08	1.00	1.16	1.07	0.99	1.14	1.02	0.95	1.09
Gestational age, weeks (ref. 30-31)														
23	21	87.5	1.70	1.46	1.97	1.30	1.13	1.50	1.45	1.26	1.67	1.21	1.03	1.41
24 -25	337	75.9	1.47	1.38	1.57	1.25	1.15	1.35	1.35	1.24	1.46	1.18	1.08	1.29
26-27	738	71.5	1.39	1.31	1.47	1.31	1.23	1.39	1.36	1.28	1.45	1.26	1.18	1.34
28-29	1031	60.9	1.18	1.12	1.25	1.15	1.09	1.22	1.16	1.10	1.23	1.14	1.08	1.21
30-31	1580	51.6												
Any severe morbidity (ref.No)	445	75.2	1.30	1.23	1.37	1.11	1.05	1.18	1.11	1.05	1.18	1.07	1.01	1.14
No	3201	57.8												
Surery for PDA *(ref.No)*	109	50.7	1.37	1.27	1.47	1.17	1.08	1.27	1.17	1.08	1.27	1.11	1.02	1.21
No	3020	50.0												
Late onset sepsis *(ref.No)*	851	49.7	1.29	1.24	1.35	1.18	1.13	1.24	1.17	1.12	1.23	1.15	1.09	1.20
No	2278	50.1												
Sex (ref.girls)														
Boys	1987	59.1	1.00	0.95	1.04	0.99	0.94	1.03	1.00	0.96	1.04	0.98	0.94	1.02
Girls	1720	59.4												
BPD at 36 wks (ref.No)	539	67.5	1.16	1.10	1.23	0.91	0.86	0.97	0.87	0.81	0.92	0.82	0.77	0.88

No	3095	58.0												
Parity (ref. multiparous)														
Nulliparous	2088	58.9	0.99	0.94	1.03	1.02	0.97	1.06	1.00	0.96	1.05	0.98	0.94	1.03
Multiparous	1584	59.7												
SGA (ref. SGA>10)														
<3	586	46.1	0.71	0.67	0.76	0.76	0.71	0.81	1.16	1.00	1.35	0.72	0.67	0.76
3-10	380	51.6	0.80	0.74	0.86	0.82	0.76	0.89	0.92	0.83	1.01	0.80	0.74	0.86
> 10	2741	64.5												
Postmenstrual age (ref.32 - 36)														
32 - 36	1526	57.9												
37 to 39	1042	41.9	1.07	1.02	1.13							1.22	1.16	1.29
40+	538	50.7	1.28	1.21	1.35							1.48	1.37	1.59
Feeding at discharge (ref. exclusive formula)														
Exclusive human milk	1113	66.7	1.27	1.20	1.34							1.12	1.06	1.18
Mix feeding	1192	62.8	1.19	1.13	1.26							0.82	0.78	0.87
Exclusive formula	1320	52.6												

[1] Model 1 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (intrauterine European reference) and parity

[2] Model 2 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (Fenton reference) and parity

[3] Model 3 adjusted for model 1 & breastfeeding at discharge and postmenstrual age

Table 4: Risk adjustment models for EUGR defined by Patel's weight-gain velocity (moderate); web only

			Unadjusted estimates	**Adjusted final model used for the figures**	**Sensitivity analysis adding breastfeeding and PMA at discharge**

	N	% EUGR	Unadj RR	95% CI		Adj[1] RR	95% CI		Adj[2] RR	95% CI	
Country (ref. mean)											
Belgium	300	48.4	1.01	0.93	1.10	0.99	0.91	1.07	0.97	0.90	1.06
Denmark	121	46.7	0.98	0.86	1.12	0.98	0.85	1.12	0.89	0.76	1.04
Estonia	72	53.3	1.12	0.95	1.32	1.08	0.92	1.26	1.07	0.92	1.24
France	461	43.2	0.90	0.84	0.97	0.92	0.85	0.99	0.92	0.85	0.99
Germany	213	34.8	0.73	0.65	0.81	0.76	0.68	0.86	0.75	0.66	0.85
Italy	508	55.4	1.16	1.09	1.24	1.17	1.10	1.24	1.19	1.12	1.27
Netherlands	120	38.6	0.81	0.70	0.93	0.81	0.71	0.91	0.77	0.68	0.88
Poland	119	52.7	1.10	0.98	1.24	1.01	0.90	1.12	1.08	0.97	1.21
Portugal	309	52.0	1.09	1.00	1.18	1.10	1.03	1.19	1.14	1.06	1.23
United Kingdom	803	62.4	1.31	1.24	1.38	1.32	1.25	1.39	1.39	1.32	1.46
Sweden	103	44.6	0.93	0.81	1.08	1.00	0.88	1.13	0.99	0.88	1.12
Mother origin *(ref. native)*											
Native	2353	51.3									
Foreign	575	46.5	0.91	0.85	0.97	0.96	0.90	1.02	0.96	0.91	1.03
Maternal age, years *(ref. <25)*											
<25	511	50.1									
25-34	1,792	50.5	1.01	0.94	1.08	1.08	1.01	1.16	1.03	0.96	1.10
35+	818	48.9	0.98	0.90	1.06	1.06	0.98	1.14	1.02	0.94	1.10
Gestational age, weeks (ref. 30-31)											
23	9	37.5	0.62	0.36	1.05	0.30	0.17	0.52	0.29	0.18	0.49
24 -25	153	34.5	0.57	0.49	0.65	0.37	0.32	0.43	0.34	0.29	0.40
26-27	398	38.6	0.63	0.58	0.69	0.53	0.49	0.59	0.52	0.48	0.57
28-29	704	41.6	0.68	0.64	0.73	0.66	0.61	0.70	0.66	0.62	0.70
30-31	1866	60.9									
Any severe morbidity (ref.No)	316	53.4	1.07	0.99	1.16	1.28	1.18	1.40	1.18	1.09	1.29

No	2749	49.7									
Surery for PDA *(ref.No)*	109	50.7	1.01	0.89	1.16	1.45	1.25	1.67	1.31	1.14	1.51
No	3,020	50.0									
Late onset sepsis *(ref.No)*	851	49.7	0.99	0.94	1.05	1.25	1.18	1.33	1.20	1.13	1.27
No	2,278	50.1									
Sex (ref.girls)											
Boys	1764	52.5	1.11	1.06	1.17	1.05	1.00	1.10	1.05	1.00	1.10
Girls	1365	47.1									
BPD at 36 wks (ref.No)	322	40.3	0.78	0.72	0.86	1.02	0.92	1.13	0.86	0.77	0.95
No	2742	51.4									
Parity (ref. multiparous)											
Nulliparous	1734	48.9	0.95	0.90	1.00	1.01	0.96	1.06	0.99	0.94	1.04
Multiparous	1366	51.5									
SGA (ref. SGA>10)											
<3	228	17.9	0.30	0.26	0.33	0.28	0.24	0.31	0.26	0.23	0.29
3-10	319	43.3	0.71	0.65	0.78	0.68	0.62	0.74	0.66	0.61	0.72
> 10	2582	60.8									
Postmenstrual age (ref.32 - 36)											
32 - 36	1,526	57.9									
37 to 39	1,042	41.9	0.72	0.68	0.77				1.06	1.00	1.13
40+	538	50.7	0.88	0.82	0.94				1.72	1.58	1.88
Feeding at discharge (ref. exclusive formula)											
Exclusive human milk	962	57.7	1.37	1.29	1.46				1.07	1.01	1.14
Mix feeding	1028	54.1	1.29	1.21	1.37				0.78	0.74	0.83
Exclusive formula	1453	42.1									

[1] Model 1 adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (intrauterine European reference) and parity

[2] Model 3 adjusted for model 1 & breastfeeding at discharge and postmenstrual age

Table 5: Spearman rho coefficients for the association of adjusted relative risks of moderate EUGR by country with mean national birthweight at 40 weeks' GA for four postnatal growth measures using 3 sensitivity models; web only

	Fenton		**IG**		**Fenton delta Z scores**		**Patel's weight-gain velocity**	
	adj rho	**P-value**	**adj rho**	**P-value**	**adj rho**	**P-value**	**adj rho**	**P-value**
Principal analysis	-0.90	<0.01	-0.84	<0.01	-0.54	0.09	-0.38	0.25
Sensitivity analysis 1	-0.86	<0.01	-0.82	<0.01	-0.63	0.04	-0.49	0.13
Sensitivity analysis 2	-0.79	<0.01	-0.79	<0.01	-0.51	0.11	-0.26	0.43
Sensitivity analysis 3	-0.84	<0.01	-0.84	<0.01	-0.54	0.09	-0.45	0.17

Sensitivity 1: using principal analysis adjusted for breastfeeding at discharge and postmenstrual age
Sensitivity 2: using principal analysis only on native mothers natives
Sensitivity 3: adjusted for maternal origin, mother age, gestational age, any morbidity, sugery for PDA, late onset infection, sex, bpd, SGA (defined by Fenton with Fenton EUGR measures & velocity and IG with the IG measure) and parity