INTRODUCTION

Preterm births (< 37 weeks gestation) account for more than 80% of all perinatal complications and deaths with increasing numbers of preterm infants born annually (1). In Canada, preterm birth represented 7.8% of all live births in 2010, compared to 6.6% in 1991 (1). Numbers have been increasing in other countries as well with France reporting a rate of 7.5% of all live births in 2016 compared with 6.0% in 1995 (2). In general, survival of infants born at less than 32 weeks of gestational age (GA) has improved in developed nations because of the widespread use of surfactant treatment for respiratory distress syndrome, antenatal glucocorticoids administration and new ventilator strategies (3–6). However, a review of published data from developed nations suggests that the outcomes of preterm infants can vary greatly between countries especially at the lower gestations (7,8). This is likely related to variations in practice and approach to the management of preterm births. It is extremely difficult to compare these differences via randomized control trials due to ethical concerns. However, many counties have developed large-scale databases/registries to track the birth and outcomes of preterm infants. This often includes in-depth information on maternal and neonatal variables, as well as elements surrounding obstetrical management and delivery. By utilizing these datasets, we are able to compare management approaches and outcomes of preterm infants between countries and determine if practice variations are associated with differences in outcomes. For this study, our primary objective was to compare the obstetrical interventions and rate of neonatal death of preterm deliveries (≤34 weeks) in Ontario and France.

METHODS

Study populations

We compared two population-based birth cohorts: 1) the Better Outcomes Registry & Network (BORN) Information System representing Ontario, Canada, and 2) the Epidemiological Study on low gestational age infants cohort second cycle (EPIPAGE-2) representing France. Both data sources are described in more detail elsewhere (9,10). Relevant to the current study is that EPIPAGE-2 is a population based sample of very preterm infants (≤34 completed gestational weeks) born between March and November 2011, whereas BORN Ontario is an ongoing birth registry that captures all births in the province of Ontario. Since the population of France is larger than Ontario, EPIPAGE-2 recruited a greater number of very preterm infants over a shorter period of time. For this reason, in creating the BORN Ontario cohort we included very preterm births over an 18-month period (April 2012 and December 2013). This period was chosen to provide sufficient statistical power, ensuring a minimum of 200 records per gestational week category. Any live born very preterm infant, born within the study periods were eligible for inclusion. Excluded were any infants with identified congenital anomalies.

Comorbidities and covariates

We compared maternal characteristics such as age, BMI, morbidity (any chronic medical condition diagnosed prior to pregnancy such as psychiatric conditions, kidney disease, cardiac disease etc.), pregnancy related complications such as gestational diabetes and gestational hypertension, obstetrical characteristics such as multi-fetal gestation and delivery in an institution with a level of care 3 NICU, obstetrical interventions such as assisted reproductive therapy, caesarean section, induction of labor

and use of antenatal steroids, and neonatal characteristics such as birth weight and infant sex for women/infants who delivered at ≤ 34 weeks gestation. Gestational age was categorized into 3 discrete groups: 1) 22-26 weeks, 2) 27-31 weeks and 3) 32-34 weeks for ease of comparison of BORN Ontario to the EPIPAGE-2 cohort. To ensure complete capture of all neonatal deaths at lower gestational ages in BORN, information on neonatal deaths was supplemented with data from the Canadian Institute for Health Information (11), a Canada-wide institute that independently collects health administrative data. Only live born infants were used for descriptive characteristics and as the denominator for analyzing neonatal deaths.

Statistical Analysis

To facilitate data analysis, EPIPAGE-2 data was securely transferred directly from EPIPAGE-2 to BORN Ontario servers. Live births, still births and neonatal deaths were stratified by gestational age, and summary statistics were used to represent covariates stratified by gestational age groups between Ontario and France. Statistical significance was determined using student's t-test or chi-square test of homogeneity. For comparing the population based sample approach used by EPIPAGE-2 to BORN Ontario, sample weighting was not necessary, as the comparisons are within gestational age groups. As such the summary estimates are unbiased. However, for overall analyses that combine gestational age groups, sample weightings are used. Neonatal death for all live births was compared between EPIPAGE-2 and BORN using a sample-weighted crude and multi-variable logistic regression models. Models were adjusted for clinically important co-variates based on clinical rational and results of the uni-variate analysis. Data was adjusted in two stages, first for non-modifiable intrinsic characteristics,

including maternal age, maternal BMI, gestational hypertension, assisted reproductive technology, infant birth weight and muti-fetal pregnancy; and secondly, for variables related to obstetrical and neonatal care, including birth in a center with a level 3 NICU, antenatal corticosteroids and cesarean section for delivery. Un-weighted models were repeated within each gestational age group and for neonatal deaths occurring within 1 and 5 months of birth.

Data management and analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC) and statistical significance was evaluated with a two-sided p-value of 0.05. The STROBE cohort reporting guidelines was used (9). This study was approved by the Research Ethics Boards of the University of Ottawa, and the Children's Hospital of Eastern Ontario. EPIPAGE-2 was approved by the National Data Protection Authority (CNIL no.911009) and by appropriate ethics committees. Funding was provided by a joint partnership between the University of Ottawa and the University of Paris Rene Descartes.

RESULTS

A total of 14,760 records were included in the study (8,278 from BORN and 6,482 from EPIPAGE-2), consisting of 1,067 neonatal deaths (365 from BORN and 702 from EPIPAGE-2), see Tables 1 and 2. Univariate comparisons of maternal/obstetrical and neonatal characteristics are shown in Table 3 and Table 4, respectively, stratified by gestational age. On average, mothers in the BORN cohort were older with higher BMI, but less likely to have gestational hypertension. Infants from EPIPAGE-2 had lower birth weights. There are also differences in other baseline characteristics such as multifetal

pregnancies and assisted reproductive therapy (ART) use especially at certain gestational age groups.

In terms of obstetrical management, more women in France received completed courses of antenatal steroids for infants born 27-34 weeks gestation. A greater number of preterm infants were also born in hospitals with level 3 NICU care in France compared with Ontario across all gestational ages. There were also differences in obstetrical management of preterm births at certain gestational age groups. For example, France had a higher rate of C-section above 27 weeks and Ontario had a higher rate of labour induction below 32 weeks.

The most important difference was the number of neonatal deaths as a proportion of live births in Ontario and France. Figure 1 illustrates the proportion of neonatal death per live birth at each gestational age in France as compared to Ontario. The figure suggests that there is a higher proportion of neonatal death in France until 28 weeks gestation, after which the numbers become similar. Table 5 demonstrates the crude and adjusted odds ratios for neonatal death in EPIPAGE-2 as compared to BORN within 1 month and 5 months. After adjusting for intrinsic factors which were found to be different between the two groups and may impact the rate of this outcome, there was a significantly higher rate of neonatal death in France compared to Ontario from 22 weeks to 31 completed weeks gestation with the difference being most pronounced at 22-26 weeks gestation despite adjustment for intrinsic population differences (aOR: 2.17; 95%CI: 1.59,2.94; p =<0.001). This disparity became even more marked with further adjustment for management variations including rate of cesarean section, birth in a center with a level 3 NICU and rate of corticosteroid use (aOR: 2.51; 95% CI: 1.79, 3.51; p

=<0.001). The majority of the deaths appear to have occurred within the first month. There was also increased likelihood of death in the 27-31 week gestation infants, however this is less pronounced and only after adjustment for both intrinsic factors and management differences (aOR: 1.54; 95%CI: 1.01, 2.35; p<0.05). The deaths in the 27-31 weeks age group appear to be more temporally spread out and do not reach significance until all deaths occurring <5 month were included.

INTERPRETATION

We found statistically significant differences in certain maternal and neonatal baseline characteristics across all gestational ages, including mean maternal age, BMI and infant birth weight. The higher birth weight in the Ontario cohort is likely related to higher maternal BMI. This, along with the greater average maternal age, is likely a reflection of intrinsic cultural/social difference between the populations. There were also some differences in the rates of gestational hypertension, ART use and multifetal pregnancy with France having higher rates. At the time of the two cohorts, France appears to have had better insurance coverage for patients seeking ART treatments. The higher proportion of ART could explain the higher rates of multifetal pregnancies. Both IVF and mutifetal pregnancies are associated with higher pregnancy related complications such as gestational hypertension (10,11). There were also a greater number of deliveries occurring in centers with level 3 NICUs in France. Ontario has nearly twice the land area of France with the majority of level 3 NICUs located in the southern part of the province. This large geographic area can make transport of laboring mothers to a level 3 NICU more challenging.

The most interesting finding is the increased number of neonatal deaths especially at the lowest gestational ages despite adjustments. To verify the data we also compared our BORN Ontario cohort to the 2014 Canadian Neonatal Network (CNN) annual report which is a database of preterm infants admitted to level 3 centers across Canada (12). While Ontario NICUs make up a larger number of the sites included in the CNN data, the data is collected separately from the BORN data (14). We also verified the EPIPAGE-2 numbers with the literature (13). This is supported our findings that the French and

Ontario cohorts do not approach similar survival rates until 28 weeks gestation (Figure 1).

Previous studies have compared the morbidity and mortality of preterm infants in developed nations and found significant variations despite similar access to available technology and expertise (14–16). A recently published article by Helenius et al. comparing the survival rates of 10 neonatal networks found marked differences in mortality at the lower gestational ages with the difference diminishing as the gestational age increased (8). One possible explanation for the significant disparity in survival at the lower gestational ages, despite adjustments for intrinsic population differences followed by differences in management may be related to differing beliefs regarding the "survivability" of extreme preterm infants (17). In a previous publication using EPIPAGE-2 data, intensive care was withheld or withdrawn for > 90% of live-born infants between 22-23 weeks gestation, 38% at 24 weeks, 8% at 25 weeks and 3% at 26 weeks (18). While we do not have specific data for the Ontario cohort, the 2014 CNN annual report indicated that only 43.9% of babies born at 22-23 weeks received palliative care, 4.9% of babies born at 24 weeks, 1.2% at 25 weeks and 0.6% at 26 weeks (12). Thus, there is a potential difference in approach to the resuscitation and early management of extreme preterm infants between France and Canada. Smith et. al. evaluated if the approach taken by care centers at 22-24 weeks is predictive of outcomes (19). They concluded that a physician's willingness to provide care to extremely low gestation infants is associated with improved outcome. The marker they found to be most indicative of an intention to provide aggressive care is the use of antenatal steroids. However, in our results, there was no difference in the rate of antenatal steroid

administration in the lowest gestation group and higher steroid administration in France for the higher gestations. France also did better in delivering premature babies in a center with a level 3 NICU. Thus the EPIPAGE-2 cohort actually received more aggressive management on average antenatally based on the variables we collected. It is possible the difference in attitudes towards the outcomes of these preterm infants occurs after post-delivery assessment. This may have been reflected in our finding that the majority of the deaths occurred within the first month of life. In the original EPIPAGE-1 cohort, there was a higher probability of death after active withdrawal in France versus the UK (20). In a single center study published in 2005, it was found that majority (> 70%) of newborn death in the center were a result of withdrawal of care in cases deemed "futile" (21).

Through this study, we were able to compare obstetrical management and survival of two very large cohorts of preterm infants born over a similar time period. Limitations include the retrospective nature of the comparison. We were also unable to compare the exact cause of death and major morbidity of the babies during their NICU stay and long term neurodevelopmental outcomes.

In summary, despite controlling for prognostic factors and differences in obstetrical management, there appears to be a significant difference in the survival of infants born ≤31 weeks gestation (in particular those ≤26 weeks) in France and Ontario with a greater proportion of live born infants surviving in Ontario. Further work will need to be done to explore the long-term outcomes of surviving infants and the cause for the difference in survival given that both France and Ontario have access to similar

technologies. We postulate that perhaps this could be in part due to differences in the beliefs of care providers towards the perceived survivability of these infants.

REFERENCES

1. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller A-B, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet [Internet]. 2012;379(9832):2162–72. Available from: http://www.sciencedirect.com/science/article/pii/S0140673612608204
2. Blondel B, Coulm B, Bonnet C, Goffinet F, Le Ray C. Trends in perinatal health in metropolitan France from 1995 to 2016: Results from the French National Perinatal Surveys. J Gynecol Obstet Hum Reprod. 2017;46(10):701–13.
3. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ [Internet]. 2012;345:e7976. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3514472&tool=pmcentrez&rendertype=abstract
4. Fellman V, Hellström-Westas L, Norman M, Westgren M, Källén K, Lagercrantz H, et al. One-year survival of extremely preterm infants after active perinatal care in Sweden. JAMA. 2009;301:2225–33.
5. Zeitlin J, Ancel P-Y, Delmas D, Bréart G, Papiernik E. Changes in care and outcome of very preterm babies in the Parisian region between 1998 and 2003. Arch Dis Child Fetal Neonatal Ed. 2010;95:F188–93.
6. Field DJ, Dorling JS, Manktelow BN, Draper ES. Survival of extremely premature babies in a geographically defined population: prospective cohort study of 1994-9

compared with 2000-5. BMJ. 2008;336:1221–3.

7. Draper ES, Zeitlin J, Fenton AC, Weber T, Gerrits J, Martens G, et al. Investigating the variations in survival rates for very preterm infants in 10 European regions: the MOSAIC birth cohort. Arch Dis Child - Fetal Neonatal Ed [Internet]. 2008;94(3):F158–63. Available from: http://fn.bmj.com/cgi/doi/10.1136/adc.2008.141531

8. Helenius K, Sjörs G, Shah PS, Modi N, Reichman B, Morisaki N, et al. Survival in Very Preterm Infants: An International Comparison of 10 National Neonatal Networks. Pediatrics [Internet]. 2017;140(6):e20171264. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29162660

9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9.

10. Sibai BM, Hauth J, Caritis S, Lindheimer MD, MacPherson C, Klebanoff M, et al. Hypertensive disorders in twin versus singleton gestations. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. Am J Obstet Gynecol. 2000;182(4):938–42.

11. Opdahl S, Henningsen AA, Tiitinen A, Bergh C, Pinborg A, Romundstad PR, et al. Risk of hypertensive disorders in pregnancies following assisted reproductive technology: A cohort study from the CoNARTaS group. Hum Reprod. 2015;30(7):1724–31.

12. Shah, Prakesh S.; Yoon, Eugene W.; Chan PM of the ARRC. The Canadian

Neonatal Network Annual Report [Internet]. 2014. Available from: http://www.canadianneonatalnetwork.org/Portal/LinkClick.aspx?fileticket=eGgxmMubxjk%3D&tabid=39

13. Ancel P-Y, Goffinet F, Kuhn P, Langer B, Matis J, Hernandorena X, et al. Survival and morbidity of preterm children born at 22 through 34 weeks' gestation in France in 2011: results of the EPIPAGE-2 cohort study. JAMA Pediatr [Internet]. 2015;169(3):230–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25621457

14. Isayama T, Lee SK, Mori R, Kusuda S, Fujimura M, Ye XY, et al. Comparison of Mortality and Morbidity of Very Low Birth Weight Infants Between Canada and Japan. Pediatrics [Internet]. 2012;130(4):e957–65. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22966031

15. Shah PS, Lui K, Sjörs G, Mirea L, Reichman B, Adams M, et al. Neonatal Outcomes of Very Low Birth Weight and Very Preterm Neonates: An International Comparison. J Pediatr [Internet]. 2016; Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022347616301937

16. Su BH, Hsieh WS, Hsu CH, Chang JH, Lien R, Lin CH. Neonatal outcomes of extremely preterm infants from Taiwan: Comparison with Canada, Japan, and the USA. Pediatr Neonatol. 2015;56(1):46–52.

17. Gallagher K, Aladangady N, Marlow N. The attitudes of neonatologists towards extremely preterm infants: A Q methodological study. Arch Dis Child Fetal Neonatal Ed. 2016;101(1):F31–6.

18. Perlbarg J, Ancel PY, Khoshnood B, Durox M, Boileau P, Garel M, et al. Delivery

room management of extremely preterm infants: the EPIPAGE-2 study. Arch Dis Child Fetal Neonatal Ed [Internet]. 2016;PubAh:1–8. Available from: http://fn.bmj.com/content/early/2016/02/02/archdischild-2015-308728.abstract%5Cnhttp://fn.bmj.com/lookup/doi/10.1136/archdischild-2015-308728%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/26837310

19. Smith PB, Ambalavanan N, Li L, Cotten CM, Laughon M, Walsh MC, et al. Approach to infants born at 22 to 24 weeks' gestation: relationship to outcomes of more-mature infants. Pediatrics [Internet]. 2012;129(6):e1508-16. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3362905&tool=pmcentrez&rendertype=abstract

20. Pignotti MS, Berni R. Extremely preterm births: end-of-life decisions in European countries. Arch Dis Child Fetal Neonatal Ed. 2010;95(4):F273–6.

21. Barton L, Hodgman JE. The contribution of withholding or withdrawing care to newborn mortality. Pediatrics. 2005;116(6):1487–91.

Table 1: Ontario Births by Gestational Age (April 2012-December 2013)

Gestational Age	Total Births	Still Births*	Live Births	Neonatal Deaths**
22	172	82 (47.6)	90	68 (75.6)
23	195	58 (29.7)	137	89 (65.0)
24	210	40 (19.0)	170	57 (33.5)
25	273	43 (15.7)	230	34 (14.8)
26	270	29 (10.7)	241	26 (10.8)
22-26	1120	252	868	274
27	296	28 (9.5)	268	21 (7.8)
28	298	23 (7.7)	275	7 (2.5)
29	402	48 (11.9)	354	13 (3.7)
30	499	18 (3.6)	481	6 (1.2)
31	731	35 (4.8)	696	10 (1.4)
27-31	2226	152	2074	57
32	1000	39 (3.9)	961	12 (1.2)
33	1474	38 (2.6)	1436	13 (0.9)
34	2458	45 (1.8)	2413	9 (0.4)
32-34	4932	122	4810	34
Total	8278	526	7752	365

* In brackets is percentage of still birth with a denominator of total birth for each gestational age group

** In brackets is percentage of neonatal death with a denominator of live birth for each gestational age group

Table 2: France Births by Gestational Age (March 2011-November 2011)

Gestational Age	Total Births	Still Births*	Live Births	Neonatal Deaths**
22	377	319 (84.6)	58	58 (100.0)
23	371	282 (76.0)	89	88 (98.9)
24	364	178 (48.9)	186	128 (68.8)
25	407	99 (24.3)	308	126 (40.9)
26	498	85 (17.1)	413	102 (24.7)
22-26	2017	963	1054	502
27	467	67 (14.3)	400	71 (17.8)
28	520	63 (12.1)	457	46 (10.1)
29	557	48 (8.6)	509	23 (4.5)
30	756	75 (9.9)	681	21 (3.1)
31	931	69 (7.4)	862	26 (3.0)
27-31	3231	322	2909	187
32	281	10 (3.6)	271	5 (1.8)
33	363	9 (2.5)	354	3 (0.8)
34	590	9 (1.5)	581	5 (0.9)
32-34	1234	28	1206	13
Total	6482	1313	5169	702

* In brackets is percentage of still birth with a denominator of total birth for each gestational age group

** In brackets is percentage of neonatal death with a denominator of live birth for each gestational age group

Table 3: Maternal/Obstetrical Characteristics Stratified by Gestational Age

Mothers who gave birth to live born infants	ONTARIO (N=6,543)	FRANCE (N=4,300)	P value
Maternal Age (mean, sd)			
22-26 week	30.43 (5.98)	29.10 (5.96)	<0.001
27-31 week	31.08 (6.01)	29.67 (6.04)	<0.001
32-34 week	30.67 (5.85)	29.94 (5.54)	<0.001
BMI (mean, sd)			
22-26 week	26.75 (7.48)	24.42 (5.65)	<0.001
27-31 week	26.19 (6.81)	24.44 (5.64)	<0.001
32-34 week	25.71 (6.74)	23.97 (5.49)	<0.001
Morbidity (n, col %*)			
22-26 week	350 (47.36)	436 (49.32)	0.431
27-31 week	770 (46.03)	1114 (45.71)	0.843
32-34 week	1756 (44.74)	447 (45.66)	0.605
Gestational Diabetes (n, col %*)			
22-26 week	21 (3.49)	31 (3.88)	0.702
27-31 week	120 (8.50)	190 (8.45)	0.961
32-34 week	323 (9.13)	88 (9.78)	0.549
Gestational Hypertension (n, col %*)			
22-26 week	52 (8.51)	104 (11.76)	0.043
27-31 week	236 (16.65)	585 (24.00)	<0.001
32-34 week	541 (14.93)	175 (17.88)	0.024
Assisted Reproductive Therapy (n, col %*)			
22-26 week	83 (11.66)	130 (15.40)	0.032
27-31 week	186 (11.50)	266 (11.32)	0.862
32-34 week	388 (10.06)	122 (12.90)	0.011
Cesarean Section (n, col %*)			
22-26 week	285 (37.30)	316 (36.41)	0.707
27-31 week	980 (56.39)	1671 (69.34)	<0.001
32-34 week	1924 (47.61)	523 (53.97)	<0.001
Induction of Labour (n, col %*)			
22-26 week	60 (7.85)	28 (3.24)	<0.001
27-31 week	53 (3.05)	41 (1.75)	0.006
32-34 week	431 (10.67)	94 (9.98)	0.536
Multifetal pregnancy (n, col %*)			
22-26 week	103 (13.48)	167 (18.89)	<0.001
27-31 week	308 (17.72)	455 (18.67)	0.541
32-34 week	743 (18.39)	219 (22.37)	<0.001
Antenatal Steroids (n, col %*)			
22-26 week	444 (60.33)	552 (64.71)	0.070
27-31 week	1292 (78.30)	1987 (83.17)	<0.001
32-34 week	1728 (45.43)	685 (71.58)	<0.001
Level of Care III (n, col %*)			
22-26 week	513 (68.04)	704 (79.64)	<0.001
27-31 week	1112 (64.43)	2064 (84.69)	<0.001
32-34 week	1186 (29.52)	490 (50.05)	<0.001
Birth weight (mean, sd)**			
22-26 week	906 (710)	748 (161)	<0.001
27-31 week	1408 (423)	1275 (326)	<0.001
32-34 week	2123 (458)	1982 (384)	<0.001
Male Gender (n, col %)**			
22-26 week	489 (56.34)	558 (52.99)	0.143
27-31 week	1131 (54.64)	1537 (52.84)	0.209
32-34 week	2666 (55.50)	647 (53.69)	0.261

* Col % = column percentage, calculated with a denominator of mothers within the respective gestational age group.
** Col % = column percentage, calculated with a denominator of infants within the respective gestational age group.

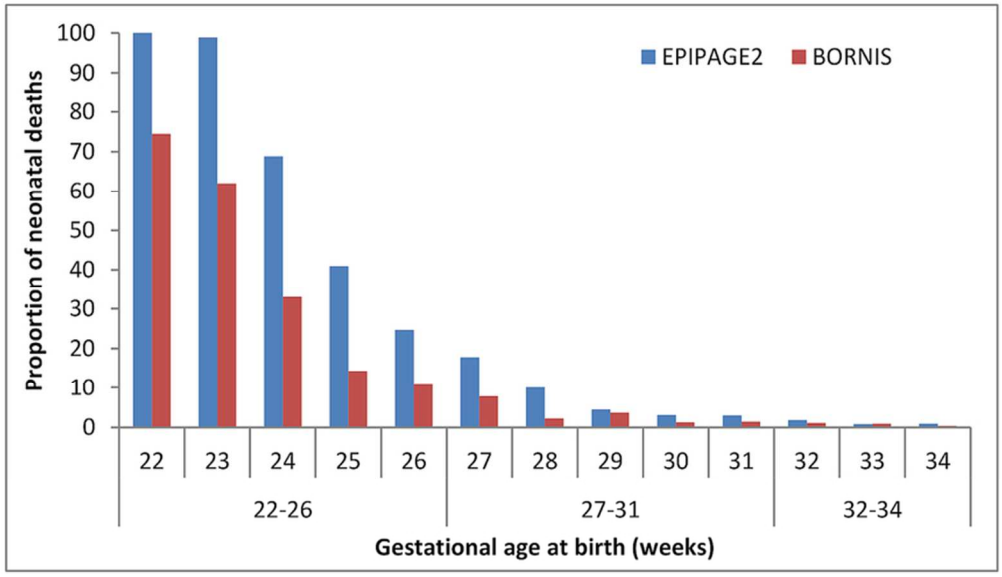

Figure 1: Comparison of crude rates of neonatal death per live born infants at each gestational age.

72x41mm (300 x 300 DPI)

Table 4: Logistic regression model comparing neonatal deaths in France and Ontario.

	Number of neonatal deaths		Unadjusted Odds ratios (95%CI) p value	Adjusted Odds ratios* (95%CI) p value	Adjusted Odds ratios** (95%CI) p value
	Ontario	France			
Any neonatal deaths†	356	702	1.47 (0.94, 2.28) p =0.088	1.31 (0.65, 2.63) p =0.455	1.61 (0.76, 3.42) p =0.215
Neonatal deaths within 1 month†	344	638	1.36 (0.86, 2.13) p =0.185	1.20 (0.59, 2.45) p =0.622	1.54 (0.71, 3.34) p =0.279
Neonatal deaths within 5 months†	356	696	1.46 (0.94, 2.26) p =0.096	1.29 (0.64, 2.60) p =0.472	1.59 (0.75, 3.38) p =0.225
Neonatal deaths for births between 22-26 weeks	267	502	**2.05 (1.09, 3.83) p =0.025**	**2.17 (1.59, 2.94) p =<.0001**	**2.51 (1.79, 3.51) p =<.0001**
Neonatal deaths within 1 month	259	470	**1.89 (1.01, 3.56) p =0.048**	**1.96 (1.44, 2.68) p =<.0001**	**2.28 (1.62, 3.21) p =<.0001**
Neonatal deaths within 5 months	267	497	**2.01 (1.07, 3.76) p =0.029**	**2.12 (1.56, 2.88) p =<.0001**	**2.43 (1.73, 3.41) p =<.0001**
Neonatal deaths for births between 27-31 weeks	56	187	2.48 (0.86, 7.13) p =0.093	1.46 (0.98, 2.18) p =0.064	**1.54 (1.01, 2.35) p =0.047**
Neonatal deaths within 1 month	53	157	2.18 (0.73, 6.49) p =0.164	1.31 (0.86, 1.98) p =0.208	1.43 (0.92, 2.23) p =0.111
Neonatal deaths within 5 months	56	186	2.46 (0.85, 7.09) p =0.096	1.45 (0.97, 2.17) p =0.068	**1.54 (1.01, 2.35) p =0.047**
Neonatal deaths for births between 32-34 weeks	33	13	1.58 (0.39, 6.46) p =0.526	1.40 (0.67, 2.95) p =0.373	0.92 (0.42, 1.99) p =0.823
Neonatal deaths within 1 month	32	11	1.37 (0.32, 5.84) p =0.667	1.21 (0.54, 2.69) p =0.645	0.82 (0.36, 1.87) p =0.631
Neonatal deaths within 5 months	33	13	1.58 (0.39, 6.46) p =0.526	1.40 (0.67, 2.95) p =0.373	0.92 (0.42, 1.99) p =0.823

*Models adjusted for maternal age, maternal BMI, gestational hypertension, assisted reproductive therapy, infant birthweight and multifetal pregnancy.
** Models additionally adjusted for the cesarean section mode of delivery, antenatal steroid use, and delivery in a hospital institute with a level of care III rating
† Regression models weighted to account for stratified sampling methodology used by EPIPAGE in setting up the France cohort.