Neonatal Outcomes of Very Low Birth Weight and Very Preterm Neonates: An International Comparison

Prakesh S. Shah, MD[1], Kei Lui, MD[2], Gunnar Sjörs, MD[3], Lucia Mirea, PhD[1,*], Brian Reichman, MBChB[4], Mark Adams, MSc[5], Neena Modi, MD[6], Brian A. Darlow, MD[7], Satoshi Kusuda, MD[8], Laura San Feliciano, MD[9], Junmin Yang, MSc[1], Stellan Håkansson, MD[10], Rintaro Mori, MD[11], Dirk Bassler, MD[5], Josep Figueras-Aloy, PhD[12], and Shoo K. Lee, MBBS[1], for the investigators of the International Network for Evaluating Outcomes (iNeo) of Neonates[†]

Objective To compare rates of a composite outcome of mortality or major morbidity in very-preterm/very low birth weight infants between 8 members of the International Network for Evaluating Outcomes.

Study design We included 58 004 infants born weighing <1500 g at 24^0–31^6 weeks' gestation from databases in Australia/New Zealand, Canada, Israel, Japan, Spain, Sweden, Switzerland, and the United Kingdom. We compared a composite outcome (mortality or any of grade ≥3 peri-intraventricular hemorrhage, periventricular echodensity/echolucency, bronchopulmonary dysplasia, or treated retinopathy of prematurity) between each country and all others by using standardized ratios and pairwise using logistic regression analyses.

Results Despite differences in population coverage, included neonates were similar at baseline. Composite outcome rates varied from 26% to 42%. The overall mortality rate before discharge was 10% (range: 5% [Japan]-17% [Spain]). The standardized ratio (99% CIs) estimates for the composite outcome were significantly greater for Spain 1.09 (1.04-1.14) and the United Kingdom 1.16 (1.11-1.21), lower for Australia/New Zealand 0.93 (0.89-0.97), Japan 0.89 (0.86-0.93), Sweden 0.81 (0.73-0.90), and Switzerland 0.77 (0.69-0.87), and nonsignificant for Canada 1.04 (0.99-1.09) and Israel 1.00 (0.93-1.07). The adjusted odds of the composite outcome varied significantly in pairwise comparisons.

Conclusions We identified marked variations in neonatal outcomes between countries. Further collaboration and exploration is needed to reduce variations in population coverage, data collection, and case definitions. The goal would be to identify care practices and health care organizational factors, which has the potential to improve neonatal outcomes. *(J Pediatr 2016; ■: ■-■).*

See editorial, p •••

Infants born very preterm (<32 weeks' gestation) and very low birth weight (birth weight <1500 g) are at an increased risk of mortality and multiple morbidities.[1] In high-resourced countries, complications of preterm birth are the leading cause of mortality in children younger than 5.[2] The need to continually improve the care of these infants has led to the establishment of national, population-based and academic/open-membership initiatives to benchmark, identify trends,[3-12] and improve neonatal outcomes, with variable success.[4,13-18]

Understanding international variations in outcomes is very important because all countries aim to provide the best possible health care to their residents without significant impact on budget or other initiatives.[19] This idea underpins the premise that medicine is universal and, thus, advances in biomedical research should span borders and yield similar results regardless of the organization of health care. Potential threats to this concept include the role of quality of care, health care organization, and access to health care. Identifying outcome variations in very preterm/very low birth weight infants across countries can provide impetus for identifying areas of improvement for each country. The International Network for Evaluating Outcomes (iNeo) of Neonates is a multinational

iNeo	International Network for Evaluating Outcomes
NEC	Necrotizing enterocolitis
SR	Standardized ratio
UKNC	United Kingdom Neonatal Collaborative

From the [1]Canadian Neonatal Network, Maternal-Infant Care Research Centre, Mount Sinai Hospital, Toronto, Ontario, Canada; [2]Australian and New Zealand Neonatal Network, Royal Hospital for Women, National Perinatal Epidemiology and Statistic Unit, University of New South Wales, Randwick, Australia; [3]Swedish Neonatal Quality Register, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; [4]Israel Neonatal Network, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Centre, Tel Hashomer, Israel; [5]Swiss Neonatal Network, Department of Neonatology, University Hospital Zurich, University of Zurich, Zürich, Switzerland; [6]UK Neonatal Collaborative, Neonatal Data Analysis Unit, Section of Neonatal Medicine, Department of Medicine, Imperial College London, Chelsea and Westminster Hospital campus, London, United Kingdom; [7]Australia and New Zealand Neonatal Network, Department of Pediatrics, University of Otago, Christchurch, New Zealand; [8]Neonatal Research Network Japan, Maternal and Perinatal Center, Tokyo Women's Medical University, Shinjuku, Tokyo, Japan; [9]Spanish Neonatal Network, Hospital Universitario de Salamanca, Salamanca, Spain; [10]Swedish Neonatal Quality Register, Department of Pediatrics/Neonatal Services, Umeå University Hospital, Umeå, Sweden; [11]Neonatal Research Network Japan, Department of Health Policy, National Center for Child Health and Development, Tokyo, Japan; and [12]Spanish Neonatal Network, Hospital Clínic, Barcelona, Spain

*Current address: Phoenix Children's Hospital, Phoenix, AZ.

†List of additional investigators of iNeo of Neonates is available at www.jpeds.com (**Appendix 1**).

Funding for iNeo of Neonates has been provided by a Canadian Institutes of Health Research (FRN87518) Chair in Reproductive and Child Health Services and Policy Research (to P.S.). Additional funding is available at www.jpeds.com (**Appendix 2**). The authors declare no conflicts of interest.

Portions of the study were presented at the meeting of the Pediatric Academic Societies, Baltimore, MD, April 30-May 3, 2016.

http://dx.doi.org/10.1016/j.jpeds.2016.04.083

collaboration between 9 high-resource countries, including the Australian and New Zealand Neonatal Network,[3] Canadian Neonatal Network,[9] Israel Neonatal Network,[20] Neonatal Research Network of Japan,[8] Spanish Neonatal Network,[10] Swedish Neonatal Quality Register,[5] Swiss Neonatal Network,[6] and United Kingdom Neonatal Collaborative (UKNC).[11] The structure, design, and overall objectives of iNeo of Neonates have been reported elsewhere.[21] Our objective was to compare rates of a composite outcome of mortality or major morbidity in very preterm/very low birth weight infants between the iNeo of Neonates members.

Methods

This retrospective cohort study included infants born weighing <1500 g at 24^0 to 31^6 weeks' gestation and admitted to the contributing neonatal units of participating countries during 2007-2010 (2008-2010 for the UKNC). We excluded infants born at <24 weeks' gestation because culture, practices, and guidelines[22,23] concerning resuscitation differed at lower gestational ages, which was reflected in widely differing rates of neonates born at <24 weeks' gestation admitted to networks. This was a post-hoc deviation from protocol. We excluded neonates born weighing ≥1500 g/at ≥32 weeks' gestation because some networks did not collect data on such infants, neonates with major congenital anomalies,[24] those admitted after 36 weeks' postmenstrual age, and those who died in the delivery room without receiving resuscitation.

Data on infant characteristics and outcomes for this study were extracted by participating networks from their existing databases according to predetermined definitions.[21] For most networks, data for defined data elements were either collected from patient records by designated abstractors according to network policies and sent to coordinating centers or entered directly into a central online database by the participating neonatal units. UKNC data were obtained from the National Neonatal Research Database managed by the Neonatal Data Analysis Unit, which contains a predefined extract from the Electronic Patient Record used in UK neonatal units regardless of designation and is updated quarterly. All iNeo of Neonates collaborators obtained research ethics approval for their primary data collection. For the purpose of iNeo of Neonates, separate data-sharing agreements were obtained from the Executive Committees of each network and the iNeo of Neonates Coordinating Centre.

Table I presents an overview of the organization of perinatal-neonatal health care services obtained by surveying directors of the databases and publicly available perinatal information from country's vital statistics. There were variations in how health services are organized, especially in the United Kingdom, where neonatal services are organized in a networked basis with infants moving to higher or lower designation units according to clinical need.

Outcomes

We defined our primary composite outcome as mortality (all cause after neonatal unit admission until discharge or transfer) or any of grade ≥3 peri-intraventricular hemorrhage,[25] persistent periventricular echodensity/echolucency; bronchopulmonary dysplasia, defined as infants receiving oxygen at 36 weeks postmenstrual age[26]; or retinopathy of prematurity[27] requiring treatment by laser or cryotherapy. Necrotizing enterocolitis (NEC) was included in the composite outcome in the protocol but was later excluded because data from one of the networks were not available.

Covariate Definitions

Gestational age was determined by the best estimate based on early prenatal ultrasound, last menstrual period, or physical examination of infants at birth, in that order. Prenatal steroid use was defined as any administration before birth, regardless of the time interval. Birth weight z scores were calculated relative to population- and sex-specific birth weight for gestational age references selected by each network as most appropriate for the comparison.

With respect to specific practices, the majority of women in the participating countries (>90%) received prenatal care. Resuscitation and management of infants at each site was according to local unit guidelines. No data were available regarding artificial reproductive technology. None of the neonates included in the study period received injection treatment for retinopathy. The frequency of head ultrasound examination, eye examination, threshold stage of retinopathy used for treatment, and oxygen saturation targets were according to local guidelines and not available for comparison.

Statistical Analyses

Infant characteristics were summarized and compared by the use of either the Pearson χ^2 test or the ANOVA F test for categorical variables and continuous measures, respectively. Standardized ratios (SRs) were computed by use of the "indirect standardization" approach.[28] For each country, the SR was calculated as the observed number of infants with the composite outcome divided by the number of infants expected to develop this outcome, computed as the sum of predicted probabilities from a multivariable logistic regression model, with adjustment for gestational age (linear), birth weight z score (linear and quadratic), multiple birth, sex, antenatal steroids, cesarean delivery, and the interaction between birth weight z score and multiple birth, derived with the use of data from all other countries. SR estimates were displayed graphically to identify countries with outcome rates above and below the average rate of all others at the 99% confidence level. Because the SR estimate is calculated in relation to all other countries combined, it is not directly comparable between contributors.[29]

Using multivariable logistic regression including country-specific fixed effects, we compared the composite outcome for all countries simultaneously (using same variables as mentioned previously except cesarean delivery; variables were selected based on $P < .1$ in univariate analyses). Hosmer-Lemeshow test and c-statistic were used to check model fit. aORs were estimated for all possible pair-wise comparisons. We evaluated statistical significance by

Table I. Organizational characteristics of perinatal-neonatal health care services in the 8 iNeo of Neonates contributors

Organizational characteristics	ANZNN		CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC
	Australia	New Zealand							
Number of neonatal units in the country providing tertiary neonatal care during study period	23	6	28	23	93	50	7	9	179
Number of tertiary units from which data are included in this collaboration	23	6	28	23	61	50	7	9	34
Number of units from whom data are included in this collaboration (including step-down units)*	23	6	28	27	73	61	28	12	104
Number of total births in the country/y	300 000	60 000	380 863	166 000	1 071 304	497 023	110 000	80 000	687 000
Definition of live birth	>20 wk and 400 g	>20 wk and 400 g	No lower limit	No lower limit	≥22 wk	≥23 wk	≥22 wk	≥22 wk	No lower limit
Proportion of pregnant women who attended antenatal care before 20 weeks' gestation	>90	>90	>90	>90	>90	>90	>90	>90	>90
Proportion of pregnant women who get early ultrasound examinations to estimate gestation	75-95	50-75	75-95	75-95	>95	75-95	>95	>95	75-95
National guidelines for antenatal maternal transfers	<33 wk	<34 wk	<32 wk	No	<34 wk	<32 wk	Regional, No national	<32 wk	<28 wk and as indicated
Designated neonatal transport teams	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Percentage of infants managed exclusively at "step-down" neonatal units	<10	<10	10-50	<10	10-50	None	10-50	<10	10-50
Percentage of infants retro- transferred to "step-down" neonatal units	10-50	10-50	10-50	<10	<10	10-50	>75	10-50	10-50
Delivery room deaths recorded in database	No	No	Partial	Yes	Yes	Yes	Yes	Yes	Partial

ANZNN, Australian and New Zealand Neonatal Network; *CNN*, Canadian Neonatal Network; *INN*, Israel Neonatal Network; *NRNJ*, Neonatal Research Network of Japan; *SEN1500*, Spanish Neonatal Network; *SNQ*, Swedish Neonatal Quality Register; *SwissNeoNet*, Swiss Neonatal Network.

*The number of units included in these data may be higher or lower based on how many tertiary units contributed to data and how many step-down units contributed to data.

applying a stringent Bonferroni multiple testing adjustment to account for 28 independent pairwise comparisons with a significance threshold of $P < .0018$ (corresponding to 99.8% CI for OR estimates). Missing data were not imputed. Data management and all statistical analyses were performed at the iNeo of Neonates Coordinating Centre in Toronto, Toronto, Canada with SAS version 9.2 (SAS Institute, Inc, Cary, North Carolina) and R version 2.2.

Results

Of the registered total 75 578 neonates in these databases, after exclusions, the final study sample comprised 58 004 (77%) of the 75 578 very low birth weight infants (**Table II**). Infant characteristics are presented in **Table III**, with significant differences detected between countries for all characteristics except sex. Notably, the rate of multiple births was greatest in Israel (42%) and lowest in Japan (24%), which also had the lowest rate of antenatal steroid use (49%). The rate of cesarean births was greatest in Switzerland (84%) and lowest in the UKNC (47%). Missing data for each characteristic are reported in **Table IV** (available at www.jpeds.com).

The composite outcome rate varied from 26% to 42% between countries (**Table III**). Unadjusted analyses of the individual components of the composite outcome showed that the mortality rate was 5% in Japan; between 6% and 10% in Canada, Australia/New Zealand, Sweden, Switzerland, and the UKNC; 14% in Israel; and 17% in Spain. Rates of bronchopulmonary dysplasia were ≤15% in Israel, Spain, and Switzerland; 32% in the UKNC; and between 16% and 25% in the remaining countries. The rate of neurologic injury was >10% for Canada, Israel, and Spain but <10% in the remaining countries. The rate of treated retinopathy was lowest in Switzerland and the UKNC (2%) and greatest in Japan (16%).

The estimated SR and 99% CI for the composite outcome comparing each country to all other countries was significantly greater in Spain (SR 1.09; 99% CI 1.04-1.14) and the UKNC (SR 1.16; 99% CI 1.11-1.21); lower in Australia/New Zealand (SR 0.93; 99% CI 0.89-0.97), Japan (SR 0.89; 99% CI 0.86-0.93), Sweden (SR 0.81; 99% CI 0.73-0.90), and Switzerland (SR 0.77; 99% CI 0.69-0.87); and nonsignificant for Canada (SR 1.04; 99% CI 0.99-1.09) and Israel (SR 1.00; 99% CI 0.93-1.07) (**Figure**).

Results of the multivariable logistic regression analyses confirmed variation in the composite outcome across countries (overall likelihood ratio test $P < .0001$). Pairwise comparisons revealed that the UKNC had greater odds of the composite outcome than each of the other countries and that Spain had greater odds compared with all other countries except the UKNC and Canada (**Table V**). In contrast, the odds of the composite outcome were lowest for Sweden and Switzerland. Model characteristics are reported in **Table VI** (available at www.jpeds.com).

Discussion

In this large, multicenter, multinational cohort of very preterm and very low birth weight infants born weighing <1500 g at 24^0 to 31^6 weeks' gestation, we identified marked variation in the composite outcome, as well as mortality and each morbidity across countries. For example, Japan had the lowest mortality but the greatest rate of treatment for retinopathy of prematurity, whereas Spain had the greatest mortality but a relatively lower rate of bronchopulmonary dysplasia. These variations could be the result of differences in population coverage, organization of perinatal health care delivery,

Table II. Study population of infants born weighing <1500 g at 24^0-31^6 weeks' gestation from the 8 iNeo of Neonates contributors

	ANZNN*	CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC*	Total
Population coverage (estimated from national birth data)†									
For 24^0-31^6 weeks' gestation, %	89.2	84.6	77.9	43.9	53.5	83.5	95.8	59.7	
For <1500 g birth weight, %	77.9	72.7	97.0	52.7	64.8	80.7	84.3	58.2	
Estimated infants of <32 weeks‡ or <1500 g§ born in the country (estimated from national birth data),†n	12 925‡	12 894‡	6270§	30 094§	17 518§	3195‡	2595§	21 606‡	107 097
Infants with birth weight <1500 g registered in database, n	11 529	10 909	6082	17 653	11 352	2668	2486	12 899	75 578
Infants excluded									
Major congenital anomalies, n (%)	482 (4.2)	817 (7.5)	184 (3)	1174 (6.7)	759 (6.7)	74 (2.8)	70 (2.8)	232 (1.8)	3792 (5)
Admitted at >36 weeks' gestation, n (%)	21 (0.2)	114 (1)	11 (0.2)	75 (0.4)	258 (2.3)	3 (0.1)	6 (0.2)	31 (0.2)	519 (0.7)
Gestational age <24^0 weeks, n (%)	215 (1.9)	216 (2)	178 (2.9)	992 (5.6)	177 (1.6)	162 (6.1)	9 (0.4)	435 (3.4)	2384 (3.2)
Gestational age >31^6 weeks, n (%)	1168 (10.1)	1096 (10)	1228 (20.2)	2804 (15.9)	2095 (18.5)	245 (9.2)	367 (14.8)	1876 (14.5)	10 879 (14.4)
Study infants, n (%)	9643 (84)	8666 (79)	4481 (74)	12 608 (71)	8063 (71)	2184 (82)	2034 (82)	10 325 (80)	58 004 (77)

*Data from 2008 to 2010.
†Data estimated from national birth registries.
‡For networks that collected data on all preterm neonates.
§For networks that collected data based on birth weight <1500 g.

Table III. Characteristics of study infants and outcomes from the 8 iNeo of Neonates contributors

Population	ANZNN	CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC	Total
Country(ies)	Australia and New Zealand	Canada	Israel	Japan	Spain	Sweden	Switzerland	United Kingdom	
Study infants, N	9643	8666	4481	12 608	8063	2184	2034	10 325	58 004
Characteristics*									
Gestational age, wk†	27.8 (2.1)	27.7 (2.0)	28.1 (2.1)	27.8 (2.1)	28.1 (2.1)	27.8 (2.1)	28.0 (2.0)	27.8 (2.1)	27.9 (2.1)
Birth weight, g†	1062 (263)	1049 (259)	1066 (264)	1008 (279)	1061 (263)	1059 (274)	1052 (271)	1046 (260)	1045 (267)
Birth weight z score† (missing data = 36)	−0.18 (0.95)	−0.26 (0.84)	−0.26 (0.78)	−0.26 (0.94)	−0.32 (0.99)	−0.27 (0.85)	−0.30 (0.81)	−0.30 (0.92)	−0.27 (0.91)
Multiple birth‡ (missing data = 24)	2964 (31)	2656 (31)	1891 (42)	3013 (24)	2692 (33)	641 (29)	685 (34)	2912 (28)	17 454 (30)
Male sex (missing data = 35)	4951 (51)	4519 (52)	2332 (52)	6592 (52)	4210 (52)	1177 (54)	1051 (52)	5313 (52)	30 145 (52)
Antenatal steroid use‡ (missing data = 1523)	8635 (90)	7310 (84)	3382 (76)	6233 (49)	6802 (84)	1782 (82)	1812 (89)	8461 (82)	44 417 (77)
Cesarean birth‡ (missing data = 213)	6135 (64)	5407 (62)	3285 (73)	9660 (77)	5399 (67)	1564 (72)	1717 (84)	4838 (47)	38 005 (66)
Outcomes									
Composite outcome‡ (missing data = 2111)	3193 (34)	3139 (40)	1462 (33)	4575 (37)	2877 (38)	663 (30)	532 (26)	4241 (42)	20 682 (37)
Mortality‡ (missing data = 0)	820 (9)	832 (10)	622 (14)	635 (5)	1366 (17)	167 (8)	208 (10)	1065 (10)	5715 (10)
Bronchopulmonary dysplasia‡,§ (missing data = 5938)	2096 (24)	1893 (25)	546 (14)	2293 (19)	971 (15)	409 (20)	231 (13)	2999 (32)	11 438 (22)
Grade ≥3 peri-Intraventricular hemorrhage‡,¶ (missing data = 2782)	525 (6)	801 (10)	531 (12)	534 (4)	764 (10)	115 (5)	152 (8)	578 (6)	4000 (7)
Cystic periventricular leukomalacia‡,¶(missing data = 2215)	239 (3)	469 (6)	218 (5)	487 (4)	487 (6)	54 (2)	49 (2)	157 (2)	2160 (4)
Grade ≥3 peri- Intraventricular hemorrhage/cystic periventricular leukomalacia‡,¶ (missing data = 2760)	654 (7)	872 (11)	649 (15)	956 (8)	1103 (15)	154 (7)	187 (9)	692 (7)	5267 (10)
Retinopathy treatment‡,¶ (missing data = 54)	292 (3)	351 (4)	153 (3)	2044 (16)	332 (4)	86 (4)	34 (2)	229 (2)	3521 (6)

*All numbers are expressed as n (%) except gestational age, birth weight, and birth weight z score, which are expressed as mean (SD).
†*P* value <.0001 evaluated with the ANOVA F-test.
‡*P* value <.0001 evaluated with the Pearson χ^2 test; Number with missing data on composite outcome is lower than individual outcomes because a patient may have developed any of the components of composite outcome and would be counted as composite outcome is ascertained.
§Denominator used to calculate percentages excluded infants who died at <37 weeks postmenstrual age or had missing bronchopulmonary dysplasiadata.
¶Denominator used to calculate percentages excluded infants with missing data for the respective morbidity.

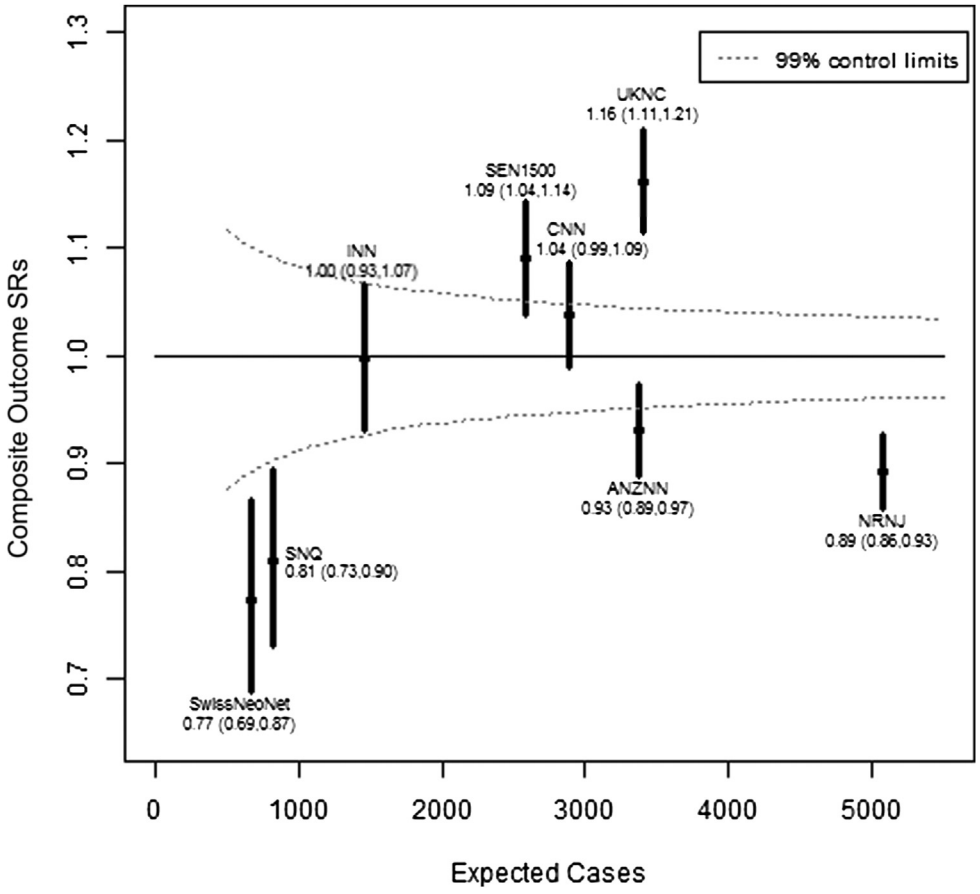

Figure. SRs comparing the composite outcome of each network to all other networks combined. *Vertical bars* are the estimated 99% CIs of the SR. The *dotted curves* represent the 99% control limits expected under the null hypothesis of similar outcome rates (SR = 1). *ANZNN*, Australian and New Zealand Neonatal Network; *CNN*, Canadian Neonatal Network; *INN*, Israel Neonatal Network; *NRNJ*, Neonatal Research Network of Japan; *SEN1500*, Spanish Neonatal Network; *SNQ*, Swedish Neonatal Quality Register; *SwissNeoNet*, Swiss Neonatal Network.

population characteristics, case definitions, ascertainment, data quality and reliability, and care processes.

The main strength of the iNeo of Neonates collaboration is that it contains the largest geographical cohort of very preterm and very low birth weight neonates with individual patient data. Data spanning a 4-year time frame provided a robust sample and minimized fluctuations as the result of annual variations. The large sample size allowed us to perform both pairwise and general (1 network vs entire sample) comparisons. These results may provide a platform for planning activities targeted to further improve data collection systems, standardize neonatal-perinatal terminology,

Table V. aORs (99.8% CI after Bonferroni correction for multiple testing) comparing the composite outcome pairwise between the 8 iNeo of Neonates contributors (row odds vs column odds)*

Networks	ANZNN	CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC
ANZNN	1.00	0.83 (0.74-0.93)	0.90 (0.78-1.04)	1.04 (0.93-1.16)	0.76 (0.67-0.85)	1.37 (1.14-1.65)	1.44 (1.18-1.77)	0.67 (0.60-0.75)
CNN	1.20 (1.07-1.35)	1.00	1.09 (0.94-1.26)	1.26 (1.12-1.41)	0.91 (0.81-1.03)	1.65 (1.37-1.99)	1.74 (1.42-2.13)	0.81 (0.72-0.91)
INN	1.11 (0.96-1.28)	0.92 (0.80-1.06)	1.00	1.16 (1.01-1.33)	0.84 (0.72-0.97)	1.52 (1.24-1.87)	1.60 (1.28-1.99)	0.75 (0.65-0.86)
NRNJ	0.96 (0.86-1.07)	0.80 (0.71-0.89)	0.87 (0.75-0.99)	1.00	0.73 (0.65-0.82)	1.32 (1.10-1.58)	1.39 (1.13-1.69)	0.65 (0.58-0.72)
SEN1500	1.32 (1.17-1.48)	1.10 (0.97-1.24)	1.19 (1.03-1.38)	1.38 (1.23-1.54)	1.00	1.81 (1.50-2.19)	1.91 (1.55-2.34)	0.89 (0.79-0.997)
SNQ	0.73 (0.61-0.88)	0.61 (0.50-0.73)	0.66 (0.54-0.81)	0.76 (0.63-0.91)	0.55 (0.46-0.67)	1.00	1.05 (0.82-1.35)	0.49 (0.41-0.59)
SwissNeoNet	0.69 (0.57-0.85)	0.58 (0.47-0.71)	0.63 (0.50-0.78)	0.72 (0.59-0.88)	0.53 (0.43-0.64)	0.95 (0.74-1.22)	1.00	0.47 (0.38-0.57)
UKNC	1.49 (1.33-1.66)	1.24 (1.10-1.38)	1.34 (1.17-1.55)	1.55 (1.39-1.73)	1.13 (1.00-1.26)	2.04 (1.69-2.45)	2.15 (1.76-2.62)	1.00

*Multivariable logistic regression analyses included country-specific fixed effects and were adjusted for: gestational age (linear), birth weight z score (linear and quadratic), multiple birth, sex, antenatal steroids, and the interaction between birth weight z score and multiple birth.

and explore practice variations between participating countries.

We acknowledge the limitations of our study. Each country was considered as a single entity, but countries provided data from between 12 and 104 different neonatal units. In some countries (Israel, Sweden, Switzerland, and the United Kingdom) data from all levels of neonatal units regardless of designation were included, whereas for the remaining countries, only data from tertiary units were included. We would like to indicate that the participating sites were an unbiased sample of the total units in the country (eg, included based on consent for participation [United Kingdom], and unselected based on type of care provision [Japan for treatment of retinopathy of prematurity]). The number of infants admitted to sites participating in iNeo of Neonates represented 53.5%-95.8% of those born at 24^0 to 31^6 weeks' gestation and 52.7%-84.3% of those weighing <1500 g at birth in included collaborators (**Table I**). Note that some of the infants are missing because of the combined study cut-off at 31^6 weeks' gestation and 1500 g birth weight. However, the population studied was a relatively homogeneous sample as evident from mean birth weight, gestational age, and Z scores for birth weight, which are very similar between participants. In some countries (Australia/New Zealand and Canada), infants who died before transfer or during resuscitation or who were not resuscitated were not captured. Some of the variation also may be attributable to differences in guidelines for resuscitation and ongoing management of extremely low-gestational age neonates. To avoid variations in outcome resulting from differing practices for infants born at <24 weeks' gestation,[30] these neonates were excluded. Despite these efforts, it is possible that selection bias may have been introduced. Variation at greater gestations reflects that a larger proportion of these neonates were managed in neonatal units that provide step-down care. Thus the variation in population coverage may have influenced the study results; however, included units were a representative sample for each participant.

Inconsistency in the definitions of morbidity in the composite outcome also may have contributed to variations. Minor differences in outcome definitions and data collection were solved by generalizing classifications; however, this difficulty highlights the need for standardized terminology in perinatology. Although all outcomes included in the composite outcome may be influenced by practices, bronchopulmonary dysplasia arguably has a high level of subjectivity and is influenced by both care practices and case definitions, data on which were not available. In some countries, neonates were transferred to step-down units before being discharged home, which may affect mortality rate. In addition, all morbidity outcomes interact with mortality; therefore, we elected to use a composite outcome to reduce competing outcomes bias. The high rate of retinopathy treatment in Japan reflects earlier treatment at a lower threshold. We did not include infants with NEC who received surgery in our composite outcome as the distinction of NEC from spontaneous intestinal perforation was not possible from the data we had available. We also did not include sepsis, because practice varied with regard to designation of early and late onset sepsis, and case-definitions.

To some extent, the observed variations also may be attributable to differences in population characteristics. In Japan, the use of prenatal steroids is increasing gradually but remained low during the study period because it was not approved in Japan until 2009.[31] A further possible confounding factor that often is cited is ethnicity or genetic background. However, ethnicity is a term that is poorly defined and for legal, ethical, and practical reasons, data were not available for all networks. The relative homogeneity of the population in countries like Japan may influence some of the outcomes studied, and this will need to be examined further.

In addition to issues related to data quality, validity, and reliability, data comparability is of concern when independent databases are combined. All participating networks have ongoing data validation and reliability control methods. Thus, amalgamating data in the larger context of iNeo of Neonates could be viewed with similar scrutiny.

Internationally, there are well-known variations in processes of neonatal care. For example, noninvasive respiratory support is used more frequently in Europe and Australia/New Zealand; human milk ingestion is greater and commencement of enteral feeding is earlier in Japan, Scandinavia, and the United Kingdom; and the use of echocardiography for management of hemodynamic status is routine in Japan.[32] Marked variations in health service delivery also are present. For example, the proportion of outborn infants is lower in Australia compared with Canada and the use of respiratory therapists is practically nonexistent in Europe and Australia/New Zealand. The variable experience of staff across work shifts also may be influential.[33] Furthermore, the characteristics of neonatal units (size, bed capacity; nurse: patient; occupancy rates) are likely to differ with different impacts,[34,35] although this remains to be quantified. We acknowledge that variation between units within a network may be similar, if not greater than that we identified between networks. In addition, there are differences both in the types and methods of administration of interventions possibly due to different interpretations of evidence or lack of local evidence to change practice,[36] as well as practitioner preferences.

Our results are in some aspects similar, but also novel and different from previous reports. Draper et al[37] reported variation (75%-92%) in the survival of preterm infants in 10 regions in Europe. Similarly, in the European Health Care Outcomes, Performance and Efficiency (EuroHOPE) study,[38] variation in mortality and length of stay were reported in 7 European countries; however, mortality, considered a robust measure of care delivery in other situations, is not a straightforward measure in neonatology because it may be influenced by fetal death rate, death in delivery room, guidelines of unit, region, and nation, as well as by cultural and ethical considerations. Draper et al[39] highlighted the importance of the denominator by identifying discrepancy

in the recording of live births, especially at very low gestation. Previous studies have not compared neonatal morbidities between such a large set of nationally representative samples.

Most of the countries in this collaboration have publicly funded national health systems. Similar comparisons with the country/state level data from the US and other countries without such systems will need to be conducted with extreme caution as differences are likely in the baseline population, access to care, availability and access to prenatal ultrasound scan, and receipt of antenatal care including steroids in addition to the organization of between and within hospital care provision. Such comparisons, however, are of value because differences in the care of pregnant women, neonatal transport systems, and regionalization of care, and postnatal management are key avenues for collaborative learning and improvement.[40]

Notwithstanding the limitations, our results have implications for physicians, policy-makers, administrators, communities, and the public at large. Participation in international multicenter clinical trials and international benchmarking/quality improvement activities is increasingly considered an index of quality of care. Advancement in the latter requires that health care providers, regulators, and the public embrace a culture of openness and willingness to learn, and that sufficient care and attention is paid to capturing reliable data. Finally, detailed mapping of management practices in different units and childhood follow-up of these infants will provide important insights into the impact of neonatal outcome variation on later life. ■

We thank Ruth Warre, PhD, and Lisa Martin, PhD (Maternal-Infant Care Research Centre, supported by the Canadian Institutes of Health Research and Mount Sinai Hospital, Toronto, Ontario, Canada), for editorial assistance. We also acknowledge Shalini Santhakumaran, MSc, and Eugene Statnikov, MSc (Neonatal Data Analysis Unit, United Kingdom), for their help in the planning stages of analyses and in data extraction.

Submitted for publication Jan 4, 2016; last revision received Apr 5, 2016; accepted Apr 25, 2016.

Reprint requests: Prakesh S. Shah, MD, Professor, Department of Paediatrics, Mount Sinai Hospital, Rm 19-231F, 600 University Ave, Toronto, Ontario, Canada M5G 1X5. E-mail: pshah@mtsinai.on.ca

References

1. Patel RM, Kandefer S, Walsh MC, Bell EF, Carlo WA, Laptook AR, et al. Causes and timing of death in extremely premature infants from 2000 through 2011. N Engl J Med 2015;372:331-40.
2. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2014;385:430-40.
3. Cust AE, Darlow BA, Donoghue DA. Outcomes for high risk New Zealand newborn infants in 1998-1999: a population based, national study. Arch Dis Child Fetal Neonatal Ed 2003;88:F15-22.
4. Fanaroff AA, Hack M, Walsh MC. The NICHD neonatal research network: changes in practice and outcomes during the first 15 years. Semin Perinatol 2003;27:281-7.
5. Fellman V, Hellstrom-Westas L, Norman M, Westgren M, Kallen K, Lagercrantz H, et al. One-year survival of extremely preterm infants after active perinatal care in Sweden. JAMA 2009;301:2225-33.
6. Ruegger C, Hegglin M, Adams M, Bucher HU. Population based trends in mortality, morbidity and treatment for very preterm- and very low birth weight infants over 12 years. BMC Pediatr 2012;12:17.
7. Horbar JD. The Vermont Oxford Network: evidence-based quality improvement for neonatology. Pediatrics 1999;103:350-9.
8. Kusuda S, Fujimura M, Sakuma I, Aotani H, Kabe K, Itani Y, et al. Morbidity and mortality of infants with very low birth weight in Japan: center variation. Pediatrics 2006;118:e1130-8.
9. Lee SK, McMillan DD, Ohlsson A, Pendray M, Synnes A, Whyte R, et al. Variations in practice and outcomes in the Canadian NICU network: 1996-1997. Pediatrics 2000;106:1070-9.
10. Moro M, Perez-Rodriguez J, Figueras-Aloy J, Fernandez C, Domenech E, Jimenez R, et al. Predischarge morbidities in extremely and very low-birth-weight infants in Spanish neonatal units. Am J Perinatol 2009;26:335-43.
11. Wong HS, Santhakumaran S, Statnikov Y, Gray D, Watkinson M, Modi N. Retinopathy of prematurity in English neonatal units: a national population-based analysis using NHS operational data. Arch Dis Child Fetal Neonatal Ed 2014;99:F196-202.
12. Grisaru-Granovsky S, Reichman B, Lerner-Geva L, Boyko V, Hammerman C, Samueloff A, et al. Population-based trends in mortality and neonatal morbidities among singleton, very preterm, very low birth weight infants over 16 years. Early Hum Dev 2014;90:821-7.
13. Hack M, Wright LL, Shankaran S, Tyson JE, Horbar JD, Bauer CR, et al. Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Network, November 1989 to October 1990. Am J Obstet Gynecol 1995;172:457-64.
14. Horwood SP, Boyle MH, Torrance GW, Sinclair JC. Mortality and morbidity of 500- to 1,499-gram birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. Pediatrics 1982;69:613-20.
15. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics 2001;107:E1.
16. Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. Am J Obstet Gynecol 2007;196:147-8.
17. Horbar JD, Carpenter JH, Badger GJ, Kenny MJ, Soll RF, Morrow KA, et al. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. Pediatrics 2012;129:1019-26.
18. Shah PS, Sankaran K, Aziz K, Allen AC, Seshia M, Ohlsson A, et al. Outcomes of preterm infants <29 weeks gestation over 10-year period in Canada: a cause for concern? J Perinatol 2012;32:132-8.
19. Morrissey S, Blumenthal D, Osborn R, Curfman GD, Malina D. International Health Care Systems [editorial]. N Engl J Med 2015;273:75-6.
20. Bader D, Kugelman A, Boyko V, Levitzki O, Lerner-Geva L, Riskin A, et al. Risk factors and estimation tool for death among extremely premature infants: a national study. Pediatrics 2010;125:696-703.
21. Shah PS, Lee SK, Lui K, Sjors G, Mori R, Reichman B, et al. The International Network for Evaluating Outcomes of very low birth weight, very preterm neonates (iNeo): a protocol for collaborative comparisons of international health services for quality improvement in neonatal care. BMC Pediatr 2014;14:110.
22. Guillen U, Weiss EM, Munson D, Maton P, Jefferies A, Norman M, et al. Guidelines for the management of extremely premature deliveries: a systematic review. Pediatrics 2015;136:343-50.
23. Rysavy MA, Li L, Bell EF, Das A, Hintz SR, Stoll BJ, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. N Engl J Med 2015;372:1801-11.
24. Kirtsman M, Yoon EW, Ojah C, Cieslak Z, Lee SK, Shah PS. Nil-per-os days and necrotizing enterocolitis in extremely preterm infants. Am J Perinatol 2015;32:785-94.

25. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr 1978;92:529-34.
26. Shennan AT, Dunn MS, Ohlsson A, Lennox K, Hoskins EM. Abnormal pulmonary outcomes in premature infants: prediction from oxygen requirement in the neonatal period. Pediatrics 1988;82:527-32.
27. International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 2005;123:991-9.
28. Keiding N. Standardized mortality ratio and statistical analysis: Historical perspective. Biometrics 1985;41:109.
29. Evans TA, Seaton SE, Manktelow BN. Quantifying the potential bias when directly comparing standardised mortality ratios for in-unit neonatal mortality. PLoS One 2013;8:e61237.
30. Marlow N. The elephant in the delivery room. N Engl J Med 2015;372:1856-7.
31. Ishikawa H, Miyazaki K, Ikeda T, Murabayashi N, Hayashi K, Kai A, et al. The effects of antenatal corticosteroids on short- and long-term outcomes in small-for-gestational-age infants. Int J Med Sci 2015;12:295-300.
32. Isayama T, Mirea L, Mori R, Kusuda S, Fujimura M, Lee SK, et al. Patent ductus arteriosus management and outcomes in Japan and Canada: comparison of proactive and selective approaches. Am J Perinatol 2015;32:1087-94.
33. Abdel-Latif ME, Bajuk B, Oei J, Lui K. Mortality and morbidities among very premature infants admitted after hours in an Australian neonatal intensive care unit network. Pediatrics 2006;117:1632-9.
34. Shah PS, Mirea L, Ng E, Solimano A, Lee SK. Association of unit size, resource utilization and occupancy with outcomes of preterm infants. J Perinatol 2015;35:522-9.
35. Watson SI, Arulampalam W, Petrou S, Marlow N, Morgan AS, Draper ES, et al. The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: retrospective population-based cohort study. BMJ Open 2014;4:e004856.
36. Abrahamsson TR, Rautava S, Moore AM, Neu J, Sherman PM. The time for a confirmative necrotizing enterocolitis probiotics prevention trial in the extremely low birth weight infant in North America is now!. J Pediatr 2014;165:389-94.
37. 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 2009;94:F158-63.
38. Numerato D, Fattore G, Tediosi F, Zanini R, Peltola M, Banks H, et al. Mortality and length of stay of very low birth weight and very preterm infants: A EuroHOPE Study. PLoS One 2015;10:e0131685.
39. Draper ES, Zeitlin J, Field DJ, Manktelow BN, Truffert P. Mortality patterns among very preterm babies: a comparative analysis of two European regions in France and England. Arch Dis Child Fetal Neonatal Ed 2007;92:F356-60.
40. Ohlsson A, Fohlin L. Reproductive medical care in Sweden and the Province of Ontario, Canada. A comparative study. Acta Paediatr Scand Suppl 1983;306:1-15.

Appendix 1

Additional investigators of iNeo of Neonates include (Director or Clinical Lead):

Australian and New Zealand Neonatal Network (ANZNN):

Australia—Nadia Badawi, MD, The Children's Hospital at Westmead, Sydney, New South Wales; Peter Marshall, MD, Flinders Medical Centre, Adelaide, South Australia; Paul Craven, MD, John Hunter Hospital, New Castle, New South Wales; Karen Simmer, MD, King Edward Memorial Hospital and Princess Margaret Hospital, Perth, Western Australia; Jacqueline Stack, MD, Liverpool Hospital, Liverpool, New South Wales; Dan Casalaz, MD, Mercy Hospital for Women, Melbourne, Victoria; Elizabeth Carse, MD, Monash Medical Centre, Melbourne, Victoria; Lucy Cooke, MD, Mater Mothers' Hospital, Brisbane Queensland; Vijay Shingde, MD, Nepean Hospital, Sydney, New South Wales; David Cartwright, MD, Royal Brisbane & Women's Hospital, Brisbane, Queensland; Rod Hunt, MD, The Royal Children's Hospital, Melbourne, Victoria; Charles Kilburn, MD, Royal Darwin Hospital, Darwin, Northern Territory; Peter Dargaville, MD, Royal Hobart Hospital, Hobart, Tasmania; Kei Lui, MD, Royal Hospital for Women, Sydney, New South Wales; Mary Paradisis, MD, Royal North Shore Hospital, Sydney, New South Wales; Ingrid Rieger, MD, Royal Prince Alfred Hospital, Sydney, New South Wales; Carl Kuschel, MD, The Royal Women's Hospital, Melbourne, Victoria; Andrew Numa, MD, Sydney Children's Hospital, Sydney, New South Wales; Hazel Carlisle, MD, The Canberra Hospital, Canberra, Australian Capital Territory; Guan Koh, MD, The Townsville Hospital, Townsville, Queensland; Chad Andersen, MD, Women's and Children's Hospital, Adelaide, South Australia; Melissa Luig, MD, Westmead Hospital, Sydney, New South Wales.

New Zealand—Nicola Austin, MD, Christchurch Women's Hospital, Christchurch, Canterbury; Roland Broadbent, MD, Dunedin Hospital, Dunedin, Otago; Lindsay Mildenhall, MD, Middlemore Hospital, Auckland City, Auckland; Malcolm Battin, MD, Auckland City Hospital, Auckland City, Auckland; David Bourchier, MD, Waikato Hospital, Hamilton, Waikato; Vaughan Richardson, MD, Wellington Women's Hospital, Wellington City, Wellington.

Canadian Neonatal Network (CNN):

Anne Synnes, MD, Children's & Women's Health Centre of BC, Vancouver, British Columbia; Nicole Rouvinez-Bouali, MD, Children's Hospital of Eastern Ontario, Ottawa, Ontario; Bruno Piedboeuf, MD, Centre Hospitalier Universitaire de Quebec, Sainte Foy, Quebec; Barbara Bulleid, MD, Dr Everett Chalmers Hospital, Fredericton, New Brunswick; Wendy Yee, MD, and Nalini Singhal, MD, Foothills Medical Centre, Calgary, Alberta; Adele Harrison, MD, and Cherrie Tan-Dy, MD, Victoria General Hospital, Victoria, British Columbia; Sandesh Shivananda, MD, and Kenneth Tan, MD, Hamilton Health Sciences Centre, Hamilton, Ontario; Andrew James, MD, Hospital for Sick Children, Toronto, Ontario; Molly Seshia, MD, Health Sciences Centre, Winnipeg, Manitoba; Keith Barrington, MD, and Francine Lefebvre, MD, Hôpital Sainte-Justine, Montreal, Quebec; Doug McMillan, MD, IWK Health Centre, Halifax, Nova Scotia; Wayne Andrews, MD, Janeway Children's Health and Rehabilitation Centre, St. John's, Newfoundland; Lajos Kovacs, MD, Jewish General Hospital, Montreal, Quebec; Kimberly Dow, MD, and Maxine Clarke, MD, Kingston General Hospital, London, Ontario; Patricia Riley, MD, Montreal Children's Hospital, Montreal, Quebec; Prakesh Shah, MD, and Arne Ohlsson, MD, Mount Sinai Hospital, Toronto, Ontario; Khalid Aziz, MD, and Abraham Peliowski, MD, Royal Alexandra Hospital & Stollery Children's Hospital, Edmonton, Alberta; Zenon Cieslak, MD, and Todd Sorokan, MD, Royal Columbian Hospital, New Westminster, British Columbia; Zarin Kalapesi, MD, and Abraham Ninan, MD, Regina General Hospital, Regina, Saskatchewan; Koravangattu Sankaran, MD, Royal University Hospital, Saskatoon, Saskatchewan; Daniel Faucher, MD, and Keith Barrington, MD, Royal Victoria Hospital, Barrie, Ontario; Gerarda Cronin, MD, St. Boniface General Hospital, Winnipeg, Manitoba; Roderick Canning, MD, The Moncton Hospital, Moncton, New Brunswick; Orlando da Silva, MD, and David Lee, MD, London Health Sciences Centre, London, Ontario; Cecil Ojah, MD, Saint John Regional Hospital, St. John, New Brunswick; Michael Dunn, MD, Sunnybrook Health Sciences Centre, Toronto, Ontario; Todd Sorokan, Surrey Memorial Hospital, Surrey, British Columbia.

Israel Neonatal Network (INN):

Eli Heymann, MD, Assaf Harofeh Medical Center, Tzrifin; Shmuel Zangen, MD, Barzilai Medical Center, Ashkelon; Amir Kushnir, MD, Baruch Padeh Medical Center, Poriya; Francis Mimouni, MD, Bikur Cholim Hospital, Jerusalem; David Bader, MD, Bnai Zion Medical Center, Haifa; Avi Rothschild, MD, Carmel Medical Center, Haifa; Zipora Strauss, Chaim Sheba Medical Center, Ramat Gan; Clari Felszer, MD, Emek Medical Center, Afula; Jamalia Jeryes, MD, French Saint Vincent de Paul Hospital, Nazareth; Smadar Even Tov-Friedman, MD, Hadassah University Hospital-Ein Karem, Jerusalem; Benjamin Bar-Oz, MD, Hadassah University Hospital-Har Hazofim, Jerusalem; Michael Feldman, MD, Hillel Yaffe Medical Center, Hadera; Nizar Saad, MD, Holy Family (Italian) Hospital, Nazareth; Orna Flidel-Rimon, MD, Kaplan Medical Center, Rehovot; Meir Weisbrod, MD, Laniado Hospital, Netanya; Daniel Lubin, MD, Mayanei Hayeshua Medical Center, Bnei Brak; Ita Litmanovitz, MD, Meir Medical Center, Kfar Saba; Shraga Blazer, MD, Rambam Medical Center, Haifa; Eric Shinwell, MD, Rivka Ziv Medical Center, Safed; Gil Klinger, MD, Schneider Children's Medical Center of Israel, Rabin Medical Center (Beilinson Campus), Petah Tikva; Yousif Nijim, MD, Scottish (EMMS) Hospital, Nazareth; Francis Mimouni, MD, Shaare-Zedek Medical Center, Jerusalem; Agneta Golan, MD, Soroka Medical Center, Beersheba; Dror Mandel, MD, Sourasky Medical Center, Tel Aviv; Vered Fleisher-Sheffer, MD, Western Galilee Medical Center, Nahariya; David Kohelet, MD, Wolfson Medical Center, Holon; Lev Bakhrakh, MD, Yoseftal Hospital, Eilat.

Neonatal Research Network Japan (NRNJ):

Satoshi Hattori, MD, Sapporo City Hospital, Sapporo, Hokkaido; Shohei Konishi, MD, Kushiro Red Cross Hospital, Kushiro, Hokkaido; Takasuke Amizuka, MD, Aomori Prefectural Central Hospital, Aomori, Aomori; Takeo Kasai, MD, Iwate Medical University, Morioka, Iwate; Ritsuko Takahasi, MD, Sendai Red Cross Hospital, Sendai, Miyagi; Hirokazu Arai, MD, Akita Red Cross Hospital, Akita, Akita; Maki Sato, MD, Fukushima Medical University, Fukushima, Fukushima; Yayoi Miyazono, MD, Tsukuba University, Tsukuba, Ibaraki; Junichi Shimizu, MD, Tsuchiura Kyodo Hospital, Tsuchiura, Ibaraki; Hiroshi Suzumura, MD, Dokkyo Medical University, Shimotsuga, Tochigi; Yumi Kono, MD, Jichi Medical University, Shimotsuke, Tochigi; Takahiro Inoue, MD, Gunma Children's Medical Center, Shibukawa, Gunma; Hiroshi Miyabayashi, MD, Saitama Children's Medical Center, Saitama, Saitama; Hisanori Sobajima, Saitama Medical University, Iruma, Saitama; Rika Ishiguro, Kawaguchi Municipal Medical Center, Kawaguchi, Saitama; Hiroyuki Sato, MD, Kameda General Hospital, Chiba, Kamogawa; Satsuki Totsu, MD, Tokyo Women's Medical University, Shinjuku, Tokyo; Nozomi Ishii, MD, Aiiku Hospital, Minato, Tokyo; Shigeharu Hosono, MD, Nihon University Itabashi Hospital, Itabashi, Tokyo; Mika Shiraishi, MD, Teikyo University, Itabashi, Tokyo; Humihiro Miura, MD, Showa University, Shinagawa, Tokyo; Atsushi Nakao, MD, Japan Red Cross Medical Center, Shibuya, Tokyo; Hitoshi Yoda, MD, Toho University, Ota, Tokyo; Mitsumasa Shimizu, MD, Tokyo Metropolitan Bokuto Hospital, Sumida, Tokyo; Kazuo Seki, MD, Yokohama City University Medical Center, Yokohama, Kanagawa; Yasuhumi Itani, MD, Kanagawa Children's Medical Center, Yokohama, Kanagawa; Keiji Suzuki, MD, Tokai University, Isehara, Kanagawa; Atsushi Nemoto, MD, Yamanashi Prefectural Central Hospital, Kofu, Yamanashi; Tomohiko Nakamura, MD, Nagano Children's Hospital, Azumino, Nagano; Masaki Wada, MD, Niigata University, Niigata, Niigata; Yoshihisa Nagayama, MD, Niigata City Hospital, Niigata, Niigata; Osamu Numata, MD, Nagaoka Red Cross Hospital, Nagaoka, Niigata; Takeshi Futatani, MD, Toyama Prefectural Central Hospital, Toyama, Toyama; Yasuhisa Ueno, MD, Ishikawa Prefectural Central Hospital, Kanazawa, Ishikawa; Kazuyuki Iwai, MD, Fukui Prefectural Hospital, Fukui, Fukui; Yoshinori Kono, MD, Gifu Prefectural Medical Center, Gifu, Gifu; Shigeru Ooki, MD, Seirei Hamamatsu General Hospital, Hamamatsu, Shizuoka; Yusuke Nakazawa, MD, Shizuoka Prefectural Children's Hospital, Shizuoka, Shizuoka; Chizuko Suzuki, MD, Nagoya Red Cross First Hospital, Nagoya, Aichi; Taihei Tanaka, MD, Nagoya Red Cross Second Hospital, Nagoya, Aichi; Motoki Bonno, MD, Mie Central Medical Center, Tsu, Mie; Kenji Nakamura, MD, Ohtsu Red Cross Hospital, Otsu, Shiga; Minako Kihara, MD, Kyoto Red Cross First Hospital, Kyoto, Kyoto; Hiroyuki Sano, MD, Yodogawa Christian Hospital, Osaka, Osaka; Atsushi Shiraishi, MD, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Izumi; Atsushi Ohashi, MD, Kansai Medical University Hirakata Hospital, Hirakata, Osaka; Hiroyuki Ichiba, MD, Osaka City General Hospital, Osaka, Osaka; Kiyoaki Sumi, MD, Aizenbashi Hospital, Osaka, Osaka; Seiji Yoshimoto, MD, Kobe Children's Hospital, Kobe, Hyogo; Yukihiro Takahashi, MD, Nara Medical University, Nara, Nara; Takahiro Okutani, MD, Wakayama Medical University, Wakayama, Wakayama; Masumi Miura, MD, Tottori University, Yonago, Tottori; Fumihide Kato, MD, Shimane Prefectural Central Hospital, Izumo, Shimane; Shinichi Watabe, MD, Kurashiki Central Hospital, Kurashiki, Okayama; Misao Kageyama, MD, Okayama Medical Center, Okayama, Okayama; Rie Fukuhara, MD, Hiroshima Prefectural Hospital, Hiroshima, Hiroshima; Michiko Hayashitani, MD, Hiroshima City Hospital, Hiroshima, Hiroshima; Keiko Hasegawa, MD, Yamaguchi Prefectural Medical Center, Hofu, Yamaguchi; Kosuke Koyano, MD, Kagawa University, Kita, Kagawa; Shoko Kobayashi, MD, Shikoku Medical Center for Children and Adults, Zentsuji, Kagawa; Shinosuke Akiyoshi, MD, Ehime Prefectural Central Hospital, Matsuyama, Ehime; Yusei Nakata, MD, Kochi Health Sciences Center, Kochi, Kochi; Takeshi Kanda, MD, National Kyushu Medical Center, Fukuoka, Fukuoka; Hisano Tadashi, MD, St Mary's Hospital, Kurume, Fukuoka; Hiroshi Kanda, MD, Kurume University, Kurume, Fukuoka; Masaki Nakamura, Fukuoka University, Fukuoka, Fukuoka; Naoko Matsumoto, MD, Kitakyushu City Medical Center, Kitakyushu, Fukuoka; Masayuki Ochiai, MD, Kyushu University, Fukuoka, Fukuoka; Mikihiro Aoki, MD, Nagasaki Medical Center, Omura, Nagasaki; Akihiko Kawase, MD, Kumamoto City Hospital, Kumamoto, Kumamoto; Koichi Iida, MD, Oita Prefectural Center Hospital, Oita, Oita; Chie Ishihara, MD, Kagoshima City Hospital, Kagoshima, Kagoshima; Moriyasu Kohama, MD, Okinawa Prefectural Chubu Hospital, Okinawa, Okinawa.

Spanish Neonatal Network (SEN1500):

Mª José Fernández Seara, MD, and José Mª Fraga Bermúdez, MD, Hospital Clinico Universitario Santiago, A Coruña, Galicia; Andrés Martínez Gutiérrez, MD, Complejo Hospitalario De Albacete, Albacete, Albacete; María Mercedes Martínez Ayúcar, MD, Hospital de Txagorritxu, Vitoria-Gasteiz, Araba; Carolina Vizcaíno Díaz, MD, and José Luis Quiles Durá, MD, Hospital General Universitario de Elche, Alicante, Alicante; María González Santacruz, MD, and Mª Anne Feret Siguile, MD, Hospital General Universitario de Alicante, Alicant, Alicante; Adela Rodríguez Fernández, MD, Hospital de Cabueñes, Gijon, Asturias; Belén Fernández Colomer, MD, and Enrique García López, MD, Hospital Universitario Central de Asturias, Oviedo, Asturias; Josep Figuera Aloy, MD, and Francesc Botet Mussons, MD, Hospital Clínic de Barcelona, Barcelona, Catalonia; Israel Anquela Sanz, MD, Hospitalario De Granollers, Granollers, Barcellona; Gemma Ginovart Galiana, MD, and Elisenda Moliner Calderon, MD, Hospital De Sant Pau, Barcelona, Catalonia; Antonio Natal Pujol, MD, Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona; Alicia Mirada Vives, MD, Hospital Universitari Mutua De Terrassa, Barcelona, Catalonia; Martín Iriondo Sanz, MD, Hospital San Juan De Deu, Barcelona, Catalonia; Roser Porta, MD, and Eva Capdevila Cogul, MD, I. Dexeus, Barcelona, Catalonia; Laura Castells Vilella, MD,

Hospital General de Cataluñá, Barcelona, Catalonia; Bruno Alonso Álvarez, MD, and José María Montero Macarro, MD, Hospital General Yagüe, Burgos, Castile; Ana R. Barrio Sacristán, MD, and Mª Jesús López Cuesta, MD, H. San Pedro de Alcántara, Caceres, Caceres; Ortiz Tardío, MD, and Eugenia Valls Sánchez Puerta, MD, Hospital Jerez, Cádiz, Cádiz; Isabel Benavente Fernández, MD, and Juan Mena Romero, MD, Hospital Universitario Puerta Del Mar, Cádiz, Cádiz; María Dolores Martinez Gimenez, MD, Hospital General Universitario de Ciudad Real, Ciudad Real, Castile; Ramón Aguilera Olmos, MD, and Ricardo Tosca Segura, MD, Hospital General de Castelló, Castelló, Castelló; Juana Mª Guzmán Cabañas, MD, and Mª Dolores Huertas Muñoz, MD, Hospital Universitario Reina Sofía, Cordoba, Andalusia; Alberto Trujillo, MD, Hospital Universitari de Josep Trueta, Girona, Catalonia; Luis Fidel Moltó Ripoll, MD, and José Antonio Hurtado Suazo, MD, Hospital Universitario Virgen De Las Nieves, Granada, Granada; Ana Elena Aldea Romero, MD, María Pangua Gómez, MD, Hospital Universitario de Guadalajara, Guadalajara, Castile; Luis Paisán Grisolía, MD, Hospital Donostia, Donostia, Gipuzkoa; Ana Isabel Garrido Ocana, MD, and Eduardo Garcia Soblechero, MD, Hospital Juan Ramón Jiménez, Huelva, Huelva; Mª Yolanda Ruiz del Prado, MD, and Inés Esteba Díez, MD, Hospital San Pedro, Logroño, La Rioja; Gema E. González-Luis, MD, and Fermín García-Muñoz Rodrigo, MD, Hospital Universitario De Canarias, San Cristóbal de La Laguna, Santa Cruz de Tenerife; Emilio Álvaro Iglesias, MD, and Fernando Fernandez Calvo, MD, Hospital Universitario de León, León, León; Eduard Solé Mir, MD, and Jordi Garcia Martí, MD, University Hospital Arnau De Vilanova, Lleida, Catalonia; Roberto Ortiz Movilla, MD, and Lucía Cabanillas Vilaplana, MD, Hospital Universitario de Getafe, Madrid, Madrid; Marta García San Miguel, MD, Hospital Universitario Montepríncipe, Madrid, Madrid; Isabel Llana Martín, MD, and María Fernández Díaz, MD, Hospital Universiatrio Torrelodonesm Madrid, Madrid; Jesús Pérez Rodríguez, MD, and Sofía Salas, MD, Hospital Universitario La Paz, Madrid, Madrid; Carmen Muñoz Labian, MD, and Carmen González Armengod, MD, Hospital Universitario Puerta De Hierro, Majadahonda, Madrid; Laura Domingo Comeche, MD, Hospital Universitario de Fuenlabrada, Feunlabrada, Madrid; Tomás Sánchez Tamayo, MD, and Manuel García del Río, MD, Hospital Carlos Haya, Málaga, Málaga; José Ángel Alonso Gallego, MD, and José María Lloreda Garcia, MD, Hospital Santa María De Rosell, Caragena, Murcia; Javier Vilas González, MD, Complexo Hospitalario Pontevedra, Pontevedra, Pontevedra; Ocampo, MD, and Nieves Balado Insunza, MD, Hospital Xeral, Vigo, Pontevedra; Pilar García González, MD, Hospital Universitario de Salamanca, Salamanca, Castile; Mercedes Granero Asencio, MD, and Antonia López Sanz, MD, Hospital Virgen De La Macarena, Sevilla, Seville; Carmen Macías Díaz, MD, and Araceli Ferrari Cortés, MD, Hospital Universitario Virgen Del Rocío, Sevilla, Seville; Pedro Amadeo Fuster Jorge, MD, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Santa Cruz de Tenerife; Santiago López Mendoza, MD, and Sabina Romero Ramírez, MD, Hospital Universitario Nuestra Señora De Candelaria, Santa Cruz de Tenerife, Santa Cruz de Tenerife; Mª del Mar Albújar Font, MD, Hospital Universitari Joan XXIII, Tarragona, Tarragona; Alicia de Ureta Huertas, MD, and Antonio Arroyos Plana, MD, Hospital Virgen De La Salud, Toledo, Toledo; Javier Estañ Capell, MD, Hospital Clinico Universitario De Valencia, Valencia, Valencia; Vicente Roqués, MD, and F. Morcillo, MD, Hospital Universitari La Fe, Valencia, Valencia; Sara Marín, MD, and María Fernanda Omaña, MD, Hospital Universiatario Río Hortega, Valladolid, Castile and Leon; Gabriel Saitua Iturriaga, MD, Hospital de Basurto, Bilbao, Vizcaya, Bizkaia.

Swedish Neonatal Quality Register (SNQ):

Jiri Kofron, MD, Södra Älvsborgs Sjukhus, Borås; Katarina Strand Brodd, MD, Mälarsjukhuset, Eskilstuna; Andreas Odlind, MD, Falu Lasarett, Falun; Lars Alberg, MD, Gällivare Sjukhus, Gällivare; Sofia Arwehed, MD, Gävle Sjukhus, Gävle; Eva Engström, MD, SU/Östra, Göteborg; Anna Kasemo, MD, Länssjukhuset, Halmstad; Charlotte Ekelund, MD, Helsingborgs Lasarett, Helsingborg; Lars Åhman, MD, Hudiksvalls Sjukhus, Hudiksvall; Fredrik Ingemarsson, MD, Länssjukhuset Ryhov, Jönköping; Laura Österdahl, MD, Länssjukhuset, Kalmar; Pernilla Thurn, MD, Blekingesjukhuset, Karlskrona; Eva Albinsson, MD, Centralsjukhuset, Karlstad; Bo Selander, MD, Centralsjukhuset, Kristianstad; Fredrik Lundberg, MD, Universitetssjukhuset, Linköping; Ingela Heimdahl, MD, Sunderby Sjukhus, Luleå; Ola Hafström, MD, Skånes Universitetssjukhus, Malmö/Lund; Erik Wejryd, MD, Vrinnevisjukhuset, Norrköping; Johanna Kuusima-Löfbom, MD, Skellefteå Lasarett, Skellefteå; Ellen-Elisabeth Lund, MD, Kärnsjukhuset Skaraborg, Skövde; Annelie Thorén, MD, Sollefteå Sjukhus, Sollefteå; Boubou Hallberg, MD, Karolinska Sjukhuset, Stockholm; Eva Berggren Broström, MD, Södersjuhuset, Stockholm; Torbjörn Hertzberg, MD, Sophiahemmet, Stockholm; Björn Stjernstedt, MD, Länssjukhuset, Sundsvall; Johan Robinson, MD, Norra Älvsborgs Länssjukhus, Trollhättan; Aijaz Farooqi, MD, Norrlands Universitetssjukhus, Umeå; Erik Normann, MD, Akademiska Barnsjukhuset, Uppsala; Magnus Fredriksson, MD, Visby Lasarett, Visby; Anders Palm, MD, Västerviks Sjukhus, Västervik; Åsa Hedblom, MD, Centrallasarettet, Västerås; Kenneth Sjöberg, MD, Centrallasarettet, Växjö; Leif Thorbjörnsson, MD, Lasarettet, Ystad; Andreas Ohlin, MD, Universitetssjukhuset, Örebro; Rein Florell, MD, Örnsköldsviks Sjukhus, Örnsköldsvik; Agneta Smedsaas-Löfvenberg, MD, Östersunds Sjukhus, Östersund.

Switzerland Neonatal Network (Swiss NeoNet):

Philipp Meyer, MD, and Claudia Anderegg, MD, Cantonal Hospital, Children's Clinic, Aarau; Sven Schulzke, MD, University Children's Hospital, Basel; Mathias Nelle, MD, University Hospital, Berne; Bendicht Wagner, MD, University Hospital, Berne; Walter Bär, MD, Children's Hospital, Chur; Grégoire Kaczala, MD, Cantonal Hospital, Fribourg; Riccardo E. Pfister, MD, University Hospital (HUG), Geneva; Jean-François Tolsa, MD, and Matthias Roth, MD, University Hospital (CHUV), Lausanne; Thomas M. Berger, MD, Children's Hospital, Lucerne; Bernhard Laubscher, MD, Cantonal Hospital, Neuchatel; Andreas Malzacher, MD,

Cantonal Hospital, St. Gallen; John P. Micallef, MD, Children's Hospital, St. Gallen; Lukas Hegi, MD, Cantonal Hospital, Winterthur; Dirk Bassler, MD, and Romaine Arlettaz, MD, University Hospital (USZ), Zurich; Vera Bernet, MD, University Children's Hospital, Zurich.

UK Neonatal Collaborative (UKNC):

Santanu Bag, MD, Bedford Hospital, Bedford, Bedfordshire; Jonathan Kefas, MD, Lister Hospital, Stevenage, Hertfordshire; Oliver Rackham, MD, Arrowe Park Hospital, Wirral, Merseyside; Arumugavelu Thirumurgan, MD, Leighton Hospital, Crewe, Cheshire; Bill Yoxall, MD, Liverpool Women's Hospital, Liverpool, Merseyside; Tim McBride, MD, Ormskirk District General Hospital, Ormskirk, Lancashire; Delyth Webb, MD, Warrington Hospital, Warrington, Cheshire; Laweh Amegavie, MD, Whiston Hospital, Prescot, Merseyside; Ahmed Hassan, MD, Broomfield Hospital, Chelmsford, Essex; Priyadarshan Ambadkar, MD, James Paget Hospital, Gorleston, Norfolk; Mark Dyke, MD, Norfolk & Norwich University Hospital, Norwich, Norfolk; Seif Babiker, MD, Peterborough City Hospital, Peterborough, Cambridgeshire; Susan Rubin, MD, Queen Elizabeth Hospital, King's Lynn, Birmingham, West Midlands; Amanda Ogilvy-Stuart, MD, Rosie Maternity Hospital, Addenbrookes, Cambridge, Cambridgeshire; Nagesh Panasa, MD, North Manchester General Hospital, Manchester, Greater Manchester; Paul Settle, MD, Royal Bolton Hospital, Bolton, Lancashire; Jonathan Moise, MD, Royal Oldham Hospital, Manchester, Greater Manchester; Ngozi Edi-Osagie, MD, St Mary's Hospital, Manchester, Greater Manchester; Carrie Heal, MD, Stepping Hill Hospital, Stockport, Cheshire; Jacqeline Birch, MD, Tameside General Hospital, Ashton-under-Lyne, Lancashire; Abdul Hasib, MD, Darent Valley Hospital, Dartford, Kent; Aung Soe, MD, Medway Maritime Hospital, Gillingham, Kent; Niraj Kumar, MD, Queen Elizabeth The Queen Mother Hospital, Margate, Kent; Hamudi Kisat, MD, Tunbridge Wells Hospital, Tunbridge Wells, Kent; Vimal Vasu, MD, William Harvey Hospital, Ashford, Kent; Meera Lama, MD, Lancashire Women & Newborn Centre, Burnley, Lancashire; Richa Gupta, MD, Royal Preston Hospital, Preston, Lancashire; Chris Rawlingson, MD, Victoria Hospital, Blackpool, Blackpool, Lancashire; Tim Wickham, MD, Barnet Hospital, Barnet, Hertfordshire; Karin Schwarz, MD, Chase Farm Hospital, Enfield, Middlesex; Van Sommen, MD, The Royal Free Hospital, Hampstead, London; Sara Watkin, MD, University College Hospital, Fitzrovia, London; Aashish Gupta, MD, Basildon Hospital, Basildon, Essex; Narendra Aladangady, MD, Homerton Hospital, Hackney, London; Imdad Ali, MD, Newham General Hospital, Newham, London; Lesley Alsford, MD, North Middlesex University Hospital, Edmonton, London; Khalid Mannan, MD, Queen's Hospital, Romford, Essex; Ebel Rainer, MD, The Royal London Hospital, Whitechapel, London; Nicholas Wilson, MD, Whipps Cross University Hospital, Whipps Cross, London; Mark Thomas, MD, Chelsea & Westminster Hospital, Chelsea, London; Ramnik Mathur, MD, Ealing Hospital, Southall London; Michele Cruwys, MD, Hillingdon Hospital, Hillingdon, London; Sunit Godambe, MD, Queen Charlotte's Hospital, East Acton, London; Sunit Godambe, MD, St Mary's Hospital, Westminster, London; Timothy Watts, MD, Guy's & St Thomas' Hospital, Lambeth, London; Jauro Kuna, MD, University Hospital Lewisham, Lewisham, London; John Chang, MD, Croydon University Hospital, Croydon, Surrey; Jon Filkin, MD, Kingston Hospital, Kingston, London; Charlotte Huddy, MD, St George's Hospital, Wandsworth, London; Ruth Shephard, MD, St. Helier Hospital, Merton, London; Krzystof Zieba, MD, Northwick Park Hospital, Brent, London; Patti Rao, MD, Kettering General Hospital, Kettering, Northamptonshire; Andrew Currie, MD, Leicester General Hospital, Leicester, Leicestershire; Andrew Currie, MD, Leicester Royal Infirmary, Leicester, Leicestershire; Azhar Manzoor, MD, Queen's Hospital, Burton On Trent, Burton-on-Trent, Staffordshire; Munir Ahmed, MD, Alexandra Hospital, Redditch, Worcestershire; Phil Simmons, MD, Birmingham Heartlands Hospital, Birmingham, West Midlands; Julie Nycyk, MD, City Hospital, Birmingham, West Midlands; Phil Simmons, MD, Good Hope Hospital, Birmingham, West Midlands; Andrew Gallagher, MD, Worcestershire Royal Hospital, Worcester, Worcestershire; Chrisantha Halahakoon, MD, New Cross Hospital, Wolverhampton, West Midlands; Sanjeev Deshpande, MD, Royal Shrewsbury Hospital, Shrewsbury, Shropshire; Anand Mohite, MD, Russells Hall Hospital, Dudley, West Midlands; Kate Palmer, MD, University Hospital of North Staffordshire, Hartshill, Staffordshire; Alan Gibson, MD, Jessop Hospital, Sheffield, South Yorkshire; Mehdi Garbash, MD, Darlington Memorial Hospital, Darlington, County Durham; Mithilesh Lal, MD, James Cook University Hospital, Middlesbrough, North Yorkshire; Majd Abu-Harb, MD, Sunderland Royal Hospital, Sunderland, Tyne and Wear; Mehdi Garbash, MD, University Hospital Of North Durham, Durham, Durham; Róisín McKeon-Carter, MD, Derriford Hospital, Plymouth, Devon; Michael Selter, MD, North Devon District Hospital, Barnstaple, Devon; Paul Munyard, MD, Royal Cornwall Hospital, Truro, Cornwall; Vaughan Lewis, MD, Royal Devon & Exeter Hospital, Exeter, Devon; Mala Raman, MD, Torbay Hospital, Torquay, Devon; Graham Whincup, MD, Conquest Hospital, St.Leonards-on-sea, East Sussex; Abdus Mallik, MD, Frimley Park Hospital, Frimley, Surrey; Philip Amess, MD, Princess Royal Hospital, Telford, Shropshire; Charles Godden, MD, Royal Surrey County Hospital, Guildford, Surrey; Philip Amess, MD, Royal Sussex County Hospital, Brighton, East Sussex; Peter Reynolds, MD, St Peter's Hospital, Chertsey, Surrey; Indranil Misra, MD, Milton Keynes Foundation Trust Hospital, Milton Keynes, Buckinghamshire; Naveen Shettihalli, MD, Oxford University Hospitals, Horton Hospital, Oxford, Oxfordshire; Peter De Halpert, MD, Royal Berkshire Hospital, Reading, Berkshire; Sanjay Salgia, MD, Stoke Mandeville Hospital, Aylesbury, Buckinghamshire; Rekha Sanghavi, MD, Wexham Park Hospital, Slough, Berkshire; Ruth Wigfield, MD, Basingstoke & North Hampshire Hospital, Basingstoke, Hampshire; Abby Deketelaere, MD, Dorset County Hospital, Dorchester, Dorset; Minesh Khashu, MD, Poole

Hospital NHS Foundation Trust, Poole, Dorset; Michael Hall, MD, Princess Anne Hospital, Southampton, Hampshire; Charlotte Groves, MD, Queen Alexandra Hospital, Portsmouth, Hampshire; Nick Brown, MD, Salisbury District Hospital, Salisbury, Wiltshire; Nick Brennan, MD, St Richard's Hospital, Chichester, West Sussex; Katia Vamvakiti, MD, Worthing Hospital, Worthing, West Sussex; Mal Ratnayaka, MD, Royal Derby Hospital, Derby, Derbyshire; Simon Pirie, MD, Gloucestershire Royal Hospital, Gloucester, Gloucestershire; Stephen Jones, MD, Royal United Hospital, Avon, Somerset; Paul Mannix, MD, Southmead Hospital, Westbury-on-Trym, Bristol; David Harding, MD, St Michael's Hospital, Bristol, Bristol; Megan Eaton, MD, Yeovil District Hospital, Yeovil, Somerset; Karin Schwarz, MD, Calderdale Royal Hospital, Halifax, West Yorkshire; David Gibson, MD, Dewsbury & District Hospital, Dewsbury, West Yorkshire; Lawrence Miall, MD, Leeds Neonatal Service, Leeds, Yorkshire; David Gibson, MD, Pinderfields General Hospital, Wakefield, West Yorkshire.

Appendix 2

The Canadian Neonatal Network is funded by the Canadian Institutes of Health Research and individual participating centers. The Australian and New Zealand Neonatal Network is funded predominantly by membership contributions from participating centers. The Israel Neonatal Network very low birth weight infant database is partially funded by the Israel Center for Disease Control and the Ministry of Health. The Neonatal Research Network of Japan is partly funded by a Health Labour Sciences Research Grant from the Ministry of Health, Labour and Welfare of Japan. SEN1500 is supported by funds from the Spanish Neonatal Society. The Swedish Neonatal Quality Register is funded by the Swedish Government (Ministry of Health and Social Affairs) and the body of regional health care providers (County Councils). SwissNeoNet is partially funded by participating units in the form of membership fees. The UKNC receives no core funding.

Table IV. Number of missing data for characteristics and outcomes

Population characteristics and outcome		ANZNN	CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC	Total
Study infants, N		9643	8666	4481	12 608	8063	2184	2034	10 325	58 004
Characteristics*										
Birth weight z score†	Missing	9	15	0	3	0	2	0	7	36
Multiple birth‡	Missing	9	12	0	0	0	0	0	3	24
Male sex	Missing	9	15	0	3	0	0	1	7	35
Antenatal steroid use‡	Missing	124	327	3	126	171	0	56	716	1523
Cesarean birth‡	Missing	47	89	0	77	0	0	0	0	213
Outcomes										
Composite outcome‡	Missing	362	832	83	123	396	2	24	290	2112
Bronchopulmonary dysplasia‡,§	Missing	826	1020	575	656	1500	155	206	1000	5938
Grade ≥3 peri- intraventricular hemorrhage/cystic periventricular leukomalacia‡,¶	Missing	440	959	201	110	571	2	18	459	2760
Retinopathy treatment‡,¶	Missing	0	0	0	0	0	0	20	34	54

ANZNN, Australian and New Zealand Neonatal Network; *CNN*, Canadian Neonatal Network; *INN*, Israel Neonatal Network; *NRNJ*, Neonatal Research Network of Japan; *SEN1500*, Spanish Neonatal Network; *SNQ*, Swedish Neonatal Quality Register; *SwissNeoNet*, Swiss Neonatal Network.

*All numbers are expressed as n (%) except gestational age, birth weight, and birth weight z score, which are expressed as mean (SD).

†*P* value <.0001 evaluated with the ANOVA F-test.

‡*P* value <.0001 evaluated with the Pearson χ^2 test; Number with missing data on composite outcome is lower than individual outcomes because a patient may have developed any of the components of composite outcome and would be counted as composite outcome is ascertained.

§Denominator used to calculate percentages excluded infants who died at <37 weeks postmenstrual age or had missing bronchopulmonary dysplasia data.

¶Denominator used to calculate percentages excluded infants with missing data for the respective morbidity.

Table VI. Parameter (SE estimates) predictors included in multivariable logistic models for the composite outcome, derived by excluding each contributor country, and subsequently used to compute the expected number of events for that contributor country

Model parameters	ANZNN	CNN	INN	NRNJ	SEN1500	SNQ	SwissNeoNet	UKNC
Predictors, estimate (SD)								
Gestational age	−0.60 (0.01)	−0.59 (0.01)	−0.58 (0.01)	−0.64 (0.01)	−0.61 (0.01)	−0.60 (0.01)	−0.59 (0.01)	−0.59 (0.01)
BW z score								
Linear	0.57 (0.25)	0.36 (0.24)	0.37 (0.24)	0.26 (0.27)	0.57 (0.26)	0.44 (0.23)	0.39 (0.23)	0.33 (0.25)
Quadratic	0.12 (0.01)	0.12 (0.01)	0.12 (0.01)	0.12 (0.01)	0.13 (0.01)	0.11 (0.01)	0.12 (0.01)	0.12 (0.01)
Multiple birth	0.29 (0.04)	0.26 (0.04)	0.18 (0.04)	0.14 (0.04)	0.20 (0.04)	0.22 (0.04)	0.21 (0.04)	0.23 (0.04)
Sex (male vs female)	0.15 (0.03)	0.17 (0.03)	0.18 (0.03)	0.19 (0.03)	0.22 (0.04)	0.18 (0.03)	0.18 (0.03)	0.18 (0.03)
Antenatal steroids	0.17 (0.04)	0.15 (0.04)	0.18 (0.04)	0.76 (0.04)	0.24 (0.04)	0.22 (0.04)	0.24 (0.04)	0.20 (0.04)
Cesarean delivery	−0.24 (0.04)	−0.23 (0.04)	−0.26 (0.03)	−0.02 (0.04)	−0.24 (0.04)	−0.23 (0.03)	−0.23 (0.03)	−0.23 (0.04)
BW z score × multiple birth interaction	−0.08 (0.04)	−0.07 (0.04)	−0.09 (0.04)	−0.10 (0.04)	−0.07 (0.04)	−0.08 (0.03)	−0.09 (0.03)	−0.09 (0.04)
BW z score × GA interaction	−0.03 (0.01)	−0.02 (0.01)	−0.02 (0.01)	−0.02 (0.01)	−0.03 (0.01)	−0.03 (0.01)	−0.02 (0.01)	−0.02 (0.01)
Model fit statistics								
C-statistic								
Development data*	0.81	0.81	0.80	0.82	0.85	0.81	0.85	0.81
Prediction data†	0.82	0.82	0.86	0.80	0.83	0.80	0.85	0.81
R^2								
Development data*	0.24	0.23	0.22	0.27	0.23	0.24	0.23	0.23
Prediction data†	0.24	0.26	0.38	0.19	0.33	0.21	0.32	0.24
H-L test (*P* value)								
Development data*	0.04	0.27	0.14	0.01	0.06	0.06	0.02	0.02
Prediction data†	0.19	0.17	<0.01	0.18	0.75	0.31	0.03	0.50

BW, birth weight; *GA*, gestational age; *H-L*, Hosmer-Lemeshow.

*The development data included all other contributor countries except for the country for which the model was used to estimate the expected number of events.

†The prediction data included only the one contributor country that was excluded from model development.