

# Rapid #: -22820483

CROSS REF ID: 23010610310004336

LENDER: TFH (Tufts Univ, Hirsh Health Sciences Lib.) :: Ejournals

BORROWER: UAU (University of Calgary) :: Taylor Family Digital Library

TYPE: Article CC:CCG

JOURNAL TITLE: American journal of perinatology

USER JOURNAL TITLE: American Journal of Perinatology

ARTICLE TITLE: Association of 24-Hour In-house Neonatologist Coverage with Outcomes of Extremely Preterm

Infants

ARTICLE AUTHOR: Debay, Anthony; Shah, Prakesh; Lodha, Abhay; Sh

VOLUME: 41

ISSUE: 6

MONTH:

YEAR: 2024

PAGES: 747 - 755

ISSN: 0735-1631

OCLC #: 38921283

Processed by RapidX: 7/10/2024 9:34:54 AM

This material may be protected by copyright law (Title 17 U.S. Code)

# Association of 24-Hour In-house Neonatologist Coverage with Outcomes of Extremely Preterm Infants

Anthony Debay<sup>1</sup> Prakesh Shah, MD<sup>2</sup> Abhay Lodha, MD<sup>3</sup> Sandesh Shivananda, MD<sup>4</sup> Stephanie Redpath, MBChB, FRCPCH<sup>5</sup> Mary Seshia, MBChB<sup>6</sup> Jon Dorling, MD<sup>7</sup> Anie Lapointe, MD<sup>8</sup> Rody Canning, MD<sup>9</sup> Lannae Strueby, MD<sup>10</sup> Marc Beltempo, MD<sup>1</sup> and on behalf of the Canadian Neonatal Network Investigators

- <sup>1</sup> Department of Pediatrics, Montreal Children's Hospital, McGill University, Montreal, Quebec, Canada
- <sup>2</sup> Departement of Pediatrics, Toronto University, Toronto, Ontario, Canada
- <sup>3</sup> Departement of Pediatrics, University of Calgary, Calgary, Alberta, Canada
- <sup>4</sup> Departement of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada
- <sup>5</sup> Departement of Pediatrics, University of Ottawa, Ottawa, Ontario, Canada
- <sup>6</sup> Departement of Pediatrics, University of Manitoba, Winnipeg, Manitoba, Canada

Am | Perinatol 2024;41:747-755.

Address for correspondence Marc Beltempo, MD, Department of Pediatrics, Montreal Children's Hospital, McGill University Health Centre, 1001 Boul Décarie, Montreal, H3J 2W8, Canada (e-mail: marc.beltempo@mcgill.ca).

- <sup>7</sup>Departement of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada
- <sup>8</sup> Departement of Pediatrics, Université de Montréal, Montreal, Quebec, Canada
- <sup>9</sup> Departement of Pediatrics, Moncton Hospital, Moncton, Alberta, Canada
- <sup>10</sup>Departement of Pediatrics, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

# **Abstract**

 $\label{eq:objective} \textbf{Objective} \quad \text{This study aimed to assess if 24-hour in-house neonatologist (NN) coverage} \\ \text{is associated with delivery room (DR) resuscitation/stabilization and outcomes among} \\ \text{inborn infants $<\!29$ weeks' gestational age (GA).} \\$ 

**Study design** Survey-linked cohort study of 2,476 inborn infants of 23 to 28 weeks' gestation, admitted between 2014 and 2015 to Canadian Neonatal Network Level-3 neonatal intensive care units (NICUs) with a maternity unit. Exposures were classified using survey responses based on the most senior provider offering 24-hour in-house coverage: NN, fellow, and no NN/fellow. Primary outcome was death and/or major morbidity (bronchopulmonary dysplasia, severe neurological injury, late-onset sepsis, necrotizing enterocolitis, and retinopathy of prematurity). Multivariable logistic regression analysis was used to assess the association between exposures and outcomes and adjust for confounders.

**Results** Among the 28 participating NICUs, most senior providers ensuring 24-hour in-house coverage were NN (32%, 9/28), fellows (39%, 11/28), and no NN/fellow (29%, 8/28). No NN/fellow coverage and 24-hour fellow coverage were associated with higher odds of infants receiving DR chest compressions/epinephrine compared with 24-hour NN coverage (adjusted odds ratio [aOR] = 4.72, 95% confidence interval [CI]: 2.12–10.6 and aOR = 3.33, 95% CI: 1.44–7.70, respectively). Rates of mortality/major

#### **Keywords**

- prematurity
- coverage
- neonatal intensive care unit
- resuscitation
- delivery room
- cardiopulmonary resuscitation
- neonatologist

morbidity did not differ significantly among the three groups: NN, 63% (249/395 infants); fellow, 64% (1092/1700 infants); no NN/fellow, 70% (266/381 infants). **Conclusion** 24-hour in-house NN coverage was associated with lower rates of DR chest compressions/epinephrine. There was no difference in neonatal outcomes based on type of coverage; however, further studies are needed as ecological fallacy cannot be ruled out.

# **Key Points**

- Lower rates of DR cardiopulmonary resuscitation with 24h in-house NN coverage
- The type of 24h in-house coverage was not associated with mortality and/or major morbidity.
- High-volume centers more often have 24h in-house neonatal fellow coverage

Advances in Neonatology and the regionalization of neonatal care have significantly improved the outcomes of extremely preterm infants <29 weeks' gestational age (GA).<sup>1–5</sup> Despite this progress, over 65% of extremely preterm infants <29 weeks' GA will either die or develop major neonatal morbidity during initial hospitalization. Centralizing the care of higher risk patients into hospitals with specialized units (level-3 neonatal intensive care units [NICUs]) has allowed the development of clinical expertise and subsequently improved outcomes.<sup>4,6–8</sup> Similar to pediatric and adult ICUs, daytime (8 a.m.–5 p.m.) presence of an attending physician in level-3 NICUs is currently considered a standard of care in most units. Nevertheless, there is still no consensus on 24-hour (h) in-house neonatologist (NN) coverage.<sup>9–12</sup>

The presence of 24-hour in-house NN coverage may contribute to better patient outcomes through the provision of better delivery room (DR) resuscitation (lower intubation rates and lower need for advanced resuscitation) and by improving the coordination of stabilization and subsequent temperature management. 13,14 Additionally, 24-hour NN coverage could help establish early treatment plans, provide uninterrupted provision of complex care, and mitigate patients' deterioriations. 10,12,15–17 Two recent studies showed higher mortality rates in extremely preterm infants born at night compared with daytime, and suggested that staffing patterns may contribute to these differences. 18,19 In contrast, 24-hour NN coverage is resource-intensive and may not be as beneficial in units where senior trainees (such as neonatal fellows) are available at night.<sup>20-22</sup> Studies in adult ICUs have also shown varying impacts of 24-hour in-house intensivist coverage; some reported a reduction in mortality, while others found no impact on mortality. 9-12,20,23 Consequently, we aimed to assess the association of 24hour in-house NN coverage with death and/or major morbidity and care practices among extremely preterm infants <29 weeks' GA born in hospitals with a level-3 NICU.

# **Materials and Methods**

# **Study Population and Eligibility Criteria**

This was a survey-linked cohort study of inborn infants born between 23<sup>0/7</sup> and 28<sup>6/7</sup> weeks' GA from January 1, 2014, to December 31, 2015. We included infants admitted to NICUs with a maternity unit who were part of the Canadian Neonatal Network (CNN) and who completed the 2015 CNN/International Network for Evaluating Outcomes in Neonates (iNeo) survey on resource allocation.<sup>24</sup> We excluded infants with major congenital anomalies and infants who were moribund on admission.

# **Data Collection and Survey Description**

The survey on available resources and staffing in the NICUs was distributed in 2016 and has previously been described.<sup>24</sup> The survey included questions on the type of coverage offered during different times of the day. Sites answered based on staffing patterns of 2015. The survey was circulated among all 30 level-3 NICUs in Canada (28 sites with maternity units were included in this study) and closed after three rounds of reminders. At the time of the survey, all Canadian NICUs consented to linking the survey data to CNN patient data.

Patient characteristics and outcome data were obtained from the CNN database. Trained abstractors collected data for each infant during their NICU stay following standard protocol, with information from patient charts entered electronically into a data-entry program with a built-in error checking system that has shown high reliability and internal consistency.<sup>25</sup> Maternal variables included maternal diabetes, maternal hypertension, rupture of membranes (ROM) >24 hours, antenatal magnesium sulfate (MgSO<sub>4</sub>), antenatal steroids exposure, multiple gestation, and mode of delivery. Infant variables included GA, birth weight, small for GA status (birth weight below 10th percentile), <sup>26</sup> sex, 5-minute Apgar's score, and the Score for Neonatal Acute Physiology, version 2 (SNAP-II).<sup>27</sup> This project was approved by the McGill University Health Centre Research Ethics Board and by the CNN Executive committee.

#### **Variable Definitions**

Exposure for each infant was classified based on the most senior provider offering 24-hour in-house coverage based on survey responses linked to NICU of admission. Exposures were categorized as 24-hour NN in-house coverage, 24-hour fellow in-house coverage (neonatal-perinatal medicine subspecialty residents or clinical assistants), and no 24-hour NN/fellow in-house coverage (residents or neonatal nurse practitioners).

#### **Outcomes**

The primary composite outcome was death prior to NICU discharge and/or major morbidity. Major morbidities included bronchopulmonary dysplasia (BPD; need for supplemental oxygen at 36 weeks postmenstrual age or at time of discharge to a level-2 center if discharged alive prior to 36 weeks),<sup>28</sup> severe neurological injury (SNI; grade ≥3 intraventricular hemorrhage [IVH] according to Papile et al<sup>29</sup> and/or periventricular leukomalacia based on ultrasound findings), severe retinopathy of prematurity (ROP; stage ≥3 ROP in at least one eye according to the international classification<sup>30</sup> or need for treatment with laser or ophthalmologic injection),<sup>31</sup> necrotizing enterocolitis (NEC; stage  $\geq 2$  according to Bell's criteria),<sup>32</sup> and nosocomial infection (NI; positive blood and or cerebrospinal fluid culture in symptomatic neonate after at least 3 days in the NICU). Predefined secondary outcomes included death and the composite outcome of death and/or SNI.

We identified resuscitative measures in the DR and stabilization processes that may be affected by 24-hour NN coverage: DR intubation, DR chest compressions/epinephrine, and the maintenance of optimal admission temperature (temperature between 36.5 and 37.2°C).<sup>13</sup>

# **Statistical Analyses**

Preliminary data indicated a rate of mortality and/or major morbidity of approximately 67% among extremely preterm infants <29 weeks' GA and 30% of CNN NICUs had 24-hour NN coverage. We estimated that a sample size of 369 infants per group would be required to detect a 10% absolute difference in the risk of death and/or major morbidity between two of the exposure groups with a power of 80% and a type-I error of 5% using Fisher's exact test. Approximately 1,200 inborn infants with <29 weeks' GA are admitted in the CNN per year. Consequently, a 2-year study period would provide a sufficient sample size under the assumption that 15 to 30% of infants (~400–800) would be exposed to 24-hour NN coverage (depending on site volume and type of coverage).

Descriptive statistics were used to compare infants' characteristics and outcomes according to exposure groups. Unadjusted comparisons were made using the Chi-square test for categorical variables, and the Mann–Whitney and Kruskal–Wallis tests for continuous variables. Logistic regression models were used to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for the association of exposures with outcomes using 24-hour NN coverage as a

reference group. ORs were adjusted for potential confounders including GA, antenatal steroids exposure, antenatal MgSO<sub>4</sub>, ROM > 24 hours, mode of delivery, multiple birth, and small for GA status. To account for clustering within each site, the Generalized Estimating Equations approach with symmetric covariance structure was used.<sup>33</sup>

We conducted two additional exploratory analyses to assess for additional confounders and interaction. First, we observed high collinearity between the type of coverage and site volume (number of infants <29 weeks' GA admitted per site per year). Consequently, we evaluated the association between type of coverage and outcomes in the subgroups of infants admitted to low-volume NICUs (number of infants <29 weeks' GA < median) and to highvolume NICUs (number of infants <29 weeks' GA > median) and tested for interaction between the type of coverage and the site volume. Second, previous studies have suggested that infants born at nighttime may have worse outcomes than those born during daytime. 18,21 To evaluate this, we compared outcomes of infants born during daytime (8 a.m.-5 p.m.) to those born at nighttime (5 p.m.-8 a.m.) based on the type of coverage and tested for interaction between type of coverage and time of birth (daytime vs. nighttime).

Primary analyses focused on the association between the type of coverage and death and/or major morbidity. Predefined secondary outcomes were death and death and/or SNI. Additional analyses on care practices and individual morbidities were not adjusted for multiple comparisons, as these were conducted to generate hypotheses, and should be interpreted with caution.<sup>34</sup> A two-sided *p*-value of <0.05 was considered statistically significant. Data management and statistical analyses were performed using SAS, version 9.3 (SAS Institute Inc., Cary, NC).

## Results

During the study period, a total of 2,611 inborn infants with <29 weeks' GA were admitted to the 28 eligible NICUs. Of those infants, 135 were excluded for the prespecified reasons (Fig. 1). Of the participating sites, 32% (9/28) had 24-hour NN coverage (395 infants), 39% (11/28) had 24-hour fellow coverage (1,700 infants), and 29% (8/28) had no NN/fellow coverage (381 infants).

Characteristics that differed between groups were rates of ROM >24 hours, use of antenatal MgSO<sub>4</sub>, antenatal steroids exposure, multiple birth, and 5-minute Apgar's score of <7 (¬Table 1). Rates of DR intubation did not differ significantly among the three groups (¬Table 2). Unadjusted rates of DR chest compressions/epinephrine were significantly lower in the 24-hour NN coverage group compared with both 24-hour fellow coverage and no NN/fellow coverage groups. Unadjusted rates of optimal admission temperature significantly differed between the groups: higher rates of optimal admission temperature were reported in the 24-hour fellow coverage group compared with 24-hour NN coverage and no NN/fellow coverage groups. Rates of death and/or major morbidity did not significantly differ among the three

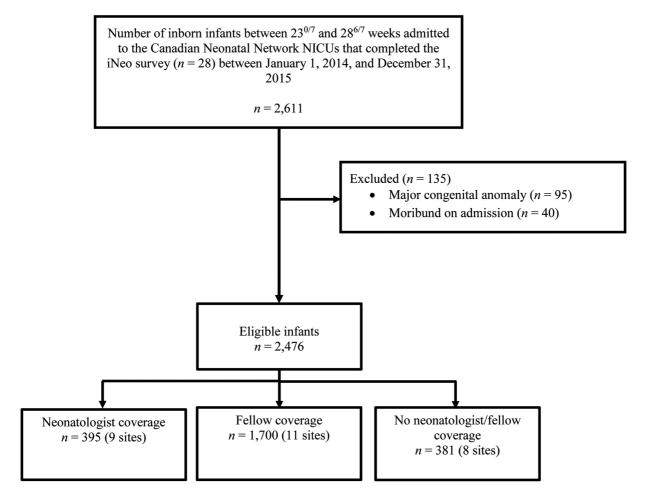


Fig. 1 Infants included in the study sample for the time period between 2014 and 2015. iNeo, International Network for Evaluating Outcomes in Neonates; NICU, neonatal intensive care unit.

groups. However, unadjusted rates of death before discharge significantly differed between the groups. Rates of death and/or SNI did not significantly differ between the three groups.

In the adjusted analyses, both 24-hour fellow coverage and no NN/fellow coverage were associated with higher odds of DR chest compressions/epinephrine administration compared with 24-hour NN coverage ( Table 3). Optimal admission temperature was more likely in 24-hour fellow coverage when compared with 24-hour NN coverage. There was no difference in death and/or major morbidity based on type of coverage. Nevertheless, 24-hour fellow coverage was associated with lower odds of death before discharge when compared with 24-hour NN coverage. There was no association between the type of coverage and death and/or SNI. Primary analyses were repeated in the subgroup of infants <26 weeks' GA and yielded similar results (data not shown).

There was a significant association between site volume and type of coverage: the majority of high-volume sites had 24-hour fellow coverage (10/14, 71%), whereas low-volume sites either had 24-hour NN coverage (7/14, 50%) or no NN/fellow coverage (6/14, 43%; -Supplementary Table S1 [available in the online version]). Among high-volume NICUs, no NN/fellow coverage was associated with higher odds of

mortality/major morbidity compared with 24-hour NN coverage (~Table 4; ~Supplementary Table S2 [available in the online version]). Nonetheless, we report no statistically significant interaction between site volume and type of coverage. In the exploratory analyses looking at the time of birth, we also found no significant interaction between the time of birth and the type of coverage (all *p*-values for interaction  $\geq$ 0.19; ~Supplementary Table S3; available in the online version).

#### Discussion

In this study-linking survey data to outcomes of infants with <29 weeks' GA admitted to 28 level-3 NICUs in Canada, we report no association between 24-hour NN in-house coverage and death and/or major morbidity. The 24-hour NN coverage was associated with lower odds of DR chest compressions/epinephrine compared with 24-hour fellow coverage and no NN/fellow coverage.

There are several possible explanations for the absence of association between the type of coverage and death and/or major morbidity. First, our study was designed to detect a 10% absolute risk difference between groups and was underpowered to detect smaller differences. Second, death and/or

| Table 1 Characteristics of infants acc           | cording to type of coverac               | je                                  |   |                 |
|--|--|-------------------------------------|---|-----------------|
|  | 24-hour neonatologist coverage (n = 395) | 24-hour fellow coverage (n = 1,700) | No neonatologist/ fellow coverage $(n = 381)$ | <i>p</i> -Value |
| Maternal variables                               |  |                                     |   |                 |
| Maternal diabetes                                | 35 (10)                                  | 179 (11)                            | 35 (9)  | 0.77            |
| Maternal hypertension                            | 66 (17)                                  | 287 (17)                            | 63 (17)                                       | 0.99            |
| Rupture of membranes >24 hours                   | 112 (30)                                 | 481 (29)                            | 82 (22)                                       | 0.03            |
| Antenatal MgSO <sub>4</sub>                      | 232 (60)                                 | 1,158 (70)                          | 279 (75)                                      | <0.01           |
| Antenatal steroids exposure                      | 371 (95)                                 | 1,608 (95)                          | 337 (90)                                      | <0.01           |
| Multiple births                                  | 96 (24)                                  | 429 (25)                            | 124 (33)                                      | 0.01            |
| Caesarean birth                                  | 269 (69)                                 | 950 (56)                            | 221 (58)                                      | <0.01           |
| Infant variables                                 |  |                                     |   |                 |
| Gestational age (wk)                             | 26 (2)                                   | 26 (2)                              | 26 (2)  | 0.68            |
| Birth weight (g)                                 | 913 (240)                                | 917 (252)                           | 912 (239)                                     | 0.93            |
| Small for gestational age                        | 45 (11)                                  | 157 (9)                             | 37 (10)                                       | 0.42            |
| Male sex   | 203 (52)                                 | 879 (52)                            | 195 (51)                                      | 0.99            |
| Apgar's score at 5 minute <7                     | 173 (44)                                 | 652 (39)                            | 167 (44)                                      | 0.04            |
| Score for neonatal acute physiology-II score >20 | 109 (28)                                 | 489 (29)                            | 99 (27)                                       | 0.66            |

Abbreviation: MgSO<sub>4</sub>, magnesium sulfate.

Notes: Data presented as n (%) or mean (standard deviation)

p-Value comparing the three groups obtained with the Chi-square test for categorical variables and the Mann–Whitney test for continuous variables. Bold values are statistically significant.

major morbidity is a multifactorial outcome and may not be the most sensitive outcome to evaluate the impact of 24hour NN coverage. A single-center study in a Canadian NICU did not find an association between 24-hour NN coverage

and death and/or major morbidity but reported a reduction in the duration of invasive mechanical ventilation.<sup>22</sup> This suggests that 24-hour NN coverage may be associated with improvement in outcomes that are more closely related to

| Table 2 Care practices and outcomes             | s of infants according to t                  | ype of coverage                         |   |                 |
|---|--|---|---|-----------------|
| Care practices and outcomes                     | 24-hour neonatologist coverage ( $n = 395$ ) | 24-hour fellow coverage ( $n = 1,700$ ) | No neonatologist/ fellow coverage $(n = 381)$ | <i>p</i> -Value |
| Care practices                                  |  |   |   |                 |
| Intubation in delivery room                     | 176 (45)                                     | 738 (44)                                | 160 (42)                                      | 0.72            |
| Chest compressions/epinephrine in delivery room | 7 (2)  | 89 (5)                                  | 27 (7)  | <0.01           |
| Optimal admission temperature                   | 182 (46)                                     | 1,113 (66)                              | 198 (52)                                      | < 0.01          |
| Primary outcome                                 |  |   |   |                 |
| Death/major morbidity                           | 249 (63)                                     | 1,092 (64)                              | 266 (70)                                      | 0.08            |
| Secondary outcomes                              |  |   |   |                 |
| Death before discharge                          | 62 (16)                                      | 198 (12)                                | 60 (16)                                       | 0.02            |
| Death/severe neurological injury                | 87 (22)                                      | 375 (22)                                | 88 (23)                                       | 0.90            |
| Major morbidities                               |  |   |   |                 |
| Bronchopulmonary dysplasia                      | 149 (44)                                     | 721 (48)                                | 158 (48)                                      | 0.47            |
| Severe neurological injury                      | 38 (10)                                      | 233 (14)                                | 43 (12)                                       | 0.08            |
| Late-onset sepsis                               | 109 (28)                                     | 348 (21)                                | 79 (21)                                       | 0.01            |
| Necrotizing enterocolitis                       | 31 (8)                                       | 138 (8)                                 | 28 (7)  | 0.88            |
| Severe retinopathy of prematurity               | 42 (14)                                      | 148 (13)                                | 36 (14)                                       | 0.81            |

Notes: Data presented as n (%).

p-Value comparing the three groups obtained with the Chi-square test. Bold values are statistically significant.

**Table 3** Multivariable logistic regression analysis assessing the association of medical team coverage with care practices and outcomes

| outcomes  |  |                         |  |                                      |
|---|--|-------------------------|--|--------------------------------------|
| Care practices and outcomes                     | 24-hour fellow cover<br>neonatologist covera | _                       | No neonatologist/<br>24-hour neonatolo | fellow coverage vs.<br>gist coverage |
|   | Crude OR (95% CI)                            | Adjusted OR<br>(95% CI) | Crude OR<br>(95% CI)                   | Adjusted OR<br>(95% CI)              |
| Care practices                                  |  |                         |  |                                      |
| Intubation in delivery room                     | 0.94 (0.40, 2.19)                            | 1.04 (0.36, 2.95)       | 0.89 (0.37, 2.13)                      | 0.97 (0.33, 2.89)                    |
| Chest compressions/epinephrine in delivery room | 3.03 (1.37, 6.71)                            | 3.33 (1.44, 7.70)       | 4.20 (1.95, 9.02)                      | 4.72 (2.12, 10.60)                   |
| Optimal admission temperature                   | 2.22 (1.48, 3.34)                            | 2.26 (1.51, 3.37)       | 1.27 (0.65, 2.48)                      | 1.21 (0.60, 2.44)                    |
| Primary outcome                                 |  |                         |  |                                      |
| Death/major morbidity                           | 1.05 (0.60, 1.83)                            | 1.01 (0.56, 1.82)       | 1.36 (0.80, 2.31)                      | 1.43 (0.82, 2.51)                    |
| Secondary outcomes                              |  |                         |  |                                      |
| Death before discharge                          | 0.71 (0.46, 1.10)                            | 0.62 (0.43, 0.88)       | 1.00 (0.52, 1.92)                      | 0.90 (0.51, 1.57)                    |
| Death/severe neurological injury                | 1.00 (0.67, 1.50)                            | 0.97 (0.65, 1.43)       | 1.06 (0.74, 1.52)                      | 1.02 (0.77, 1.36)                    |
| Major morbidities                               |  |                         |  |                                      |
| Bronchopulmonary dysplasia                      | 1.15 (0.59, 2.23)                            | 1.16 (0.55, 2.43)       | 1.19 (0.62, 2.28)                      | 1.35 (0.63, 2.87)                    |
| Severe neurological injury                      | 1.47 (0.87, 2.47)                            | 1.57 (0.93, 2.64)       | 1.19 (0.86, 1.65)                      | 1.29 (0.92, 1.81)                    |
| Late-onset sepsis                               | 0.68 (0.41, 1.12)                            | 0.63 (0.38, 1.03)       | 0.69 (0.40, 1.17)                      | 0.61 (0.35, 1.07)                    |
| Necrotizing enterocolitis                       | 1.02 (0.53, 1.96)                            | 0.98 (0.59, 1.63)       | 0.92 (0.45, 1.89)                      | 0.81 (0.45, 1.48)                    |
| Severe retinopathy of prematurity               | 0.90 (0.51, 1.57)                            | 0.71 (0.38, 1.34)       | 0.98 (0.57, 1.68)                      | 1.00 (0.51, 1.94)                    |

Abbreviations: CI, confidence interval; OR, odds ratio.

Note: ORs adjusted for gestational age, antenatal steroids exposure, antenatal magnesium sulfate (MgSO<sub>4</sub>), rupture of membranes >24 hours, mode of delivery, multiple birth and small for gestational age with the Generalized Estimation Equations approach to account for the clustering within each site

physician decision-making, such as the decision to intubate, timing of extubation, or whether a baby needs to receive DR chest compression/epinephrine or time for transition instead. Third, NNs likely modulate their degree of supervision based on the trainees' level of experience, even when they are not providing systematic 24-hour in-house coverage. Fourth, the effects of 24-hour NN coverage may vary based on the type of daytime organization in the NICU. Wallace et al reported that among adult patients admitted to low-intensity ICUs (defined as units not having a mandatory consultation with an intensivist on admission), 24-hour in-house intensivist coverage was associated with lower mortality; however, such an association was not observed among patients admitted to high-intensity ICUs (defined as units with transfer of care to an intensivist on ICU admission).<sup>12</sup> Although the secondary analyses were limited by small group size, we found higher odds of death and/or major morbidity among high-volume NICUs with no NN/fellow coverage compared with 24-hour NN coverage which may reflect differences in the supervision based on site size.

Overall, 32% (9/28) of NICUs had 24-hour NN in-house coverage. This highlights an important change in practice; in a study conducted in 17 level-3 NICUs in Canada in 1996 to 1997, only 1 unit (6%) had 24-hour in-house NN.<sup>21</sup> Additionally, our study did not find a difference in death and/or major morbidity among inborn infants with <29 weeks' GA in hospitals with level-3 NICUs, whereas the study by Lee

et al showed higher mortality among infants born at nighttime.<sup>21</sup> This suggests that the changes in staffing patterns in level-3 NICUs, in combination with quality improvement initiatives and bundles aimed at improving the care of extremely preterm infants, may have helped harmonize care for infants regardless of their timing of birth.<sup>3</sup>

A recent, Canadian population-based study including all extremely preterm births in the country between 2010 and 2015 (in level-1, -2, and -3 NICUs) showed higher mortality rates among extremely preterm infants born at nighttime compared with daytime but did not report information on the level of care provided by the birth hospital. 18,19 The difference in mortality when comparing daytime and nighttime births in Canada (in all hospitals), in combination with our results, showing no association between timing of birth and death and/or major morbidity in level-3 NICUs, suggesting that the variation in outcomes between daytime and nighttime birth might be driven by infants born in level-1 and -2 NICUs. This is important, since most quality improvement programs and resource allocation studies have so far focused on level-3 NICUs, and little is known on circadian variations in staffing patterns and their impacts on patient outcomes in level-1 and -2 NICUs.

We still observed some differences in care practices that were associated with the type of coverage. First, 24-hour NN coverage was linked to lower odds of DR chest compressions/epinephrine compared with 24-hour fellow

| <b>Table 4</b> The aORs (959)       | Table 4 The aORs (95% CI) for the association between the types of coverage with outcomes stratified by site volume | etween the types           | of coverage wit                      | th outcomes stratifi                 | ed by site volume          |                                      |  |   |
|-------------------------------------|---|----------------------------|--------------------------------------|--------------------------------------|----------------------------|--------------------------------------|--|---|
|                                     | Low-volume NICUs  |                            |                                      | High-volume NICUs                    |                            |                                      | p-Value for interaction term of site volume              |   |
|                                     | No neonatologist/fellow<br>coverage   | 24-hour fellow<br>coverage | 24-hour<br>neonatologist<br>coverage | No neonatologist/<br>fellow coverage | 24-hour fellow<br>coverage | 24-hour<br>neonatologist<br>coverage | No neonatologist/<br>fellow vs.<br>24-hour neonatologist | 24-hour fellow vs.<br>24-hour neonatologist |
| Number of infants                   | 180   | 36                         | 157                                  | 201                                  | 1664                       | 238                                  |  |   |
| Primary outcome                     |   |                            |                                      |                                      |                            |                                      |  |   |
| Death/major morbidity               | 1.18 (0.70, 2.00)   | 1.06 (0.46, 2.46)          | Reference                            | 1.79 (1.12, 2.86)                    | 0.90 (0.65, 1.26)          | Reference                            | 0.20   | 0.76  |
| Secondary outcomes                  |   |                            |                                      |                                      |                            |                                      |  |   |
| Death/severe<br>neurological injury | 0.92 (0.51, 1.66)   | 0.99 (0.37, 2.60)          | Reference                            | 1.12 (0.68, 1.83)                    | 0.98 (0.69, 1.41)          | Reference                            | 0.58   | 0.99  |
| Death before discharge              | 0.89 (0.43, 1.83)   | 1.04 (0.31, 3.51)          | Reference                            | 0.92 (0.51, 1.65)                    | 0.59 (0.39, 0.90)          | Reference                            | 0.95   | 0.44  |
|                                     |   |                            |                                      |                                      |                            |                                      |  |   |

Odds ratios adjusted for gestational age, antenatal steroids exposure, antenatal magnesium sulfate (MgSO<sub>4</sub>), rupture of membranes >24 hours, mode of delivery, multiple birth, and small for gestational age Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; NICU, neonatal intensive care unit. Notes: ORs presented as aOR (95% CI)

coverage and no NN/fellow coverage. Although the event rate was small and was not paralleled with lower death and/or major morbidity, this suggests that having 24-hour NN coverage may provide more effective initial steps of DR resuscitation which could reduce the eventual need for advanced resuscitative measures like chest compressions/epinephrine. This is consistent with results from Bensouda et al who found that 24hour NN coverage was associated with a reduction in chest compressions among infants with >36 weeks' GA.<sup>35</sup> Rates of optimal admission temperature were higher among infants admitted to NICUs with 24-hour fellow coverage compared with NICUs with 24-hour NN coverage. It is possible that temperature management may not be an outcome sensitive to the presence of NN. In addition, 71% (10/14) of high-volume NICUs had 24-hour fellow coverage which suggests that interdisciplinary teams in high-volume NICUs may have developed more expertise for temperature management due to higher volume of infants.

# **Strengths and Limitations**

We leveraged the use of a large national dataset that well reflect the practices of all Canadian level-3 NICUs. Moreover, all sites participated in the survey which helped provide better insight on the type of coverage and improved generalizability.

This study is subject to limitations. First, exposures were based on survey data which prevent us from precisely extracting which type of provider was present at each delivery. Reduced insight into the exact type of coverage at birth or throughout NICU stay for each patient thus reduces the granularity of our investigation and excludes causation between exposure and outcomes. Moreover, exposures were defined by the presence of the most senior provider and do not preclude overlap between different types of providers (i.e., NN and fellows present during shifts). Second, there is the intrinsic possibility of an ecological fallacy, as the exact exposure of an infant cannot be ascertained. Third, the association between the type of medical coverage and the outcomes of preterm infants may also be influenced by other providers, such as nursing staff and respiratory therapists, who were not included in the present study. Fourth, management of patients' deteriorations along with major decisions taken during the night after initial stabilization (e.g., reintubation or extubation) was not assessed in this study.

# Conclusion

In this study-linking survey data to infant outcomes among all level-3 NICUs in Canada with a maternity unit, we found that the majority of NICUs have either 24-hour in-house NN coverage or fellow coverage, and that there was no association between type of coverage and death and/or major morbidity among inborn infants <29 weeks' GA. These results are from a survey-linked cohort, and data on the actual presence of providers were not available. Additional prospective studies describing providers present in the DR and the NICU are required to better understand whether type of coverage is associated with infant outcomes.

#### Note

This study was partly presented at the Canadian Pediatric Socciteoes – June 11th 2021 Annual Conference (Oral Presentation) and Pediatric Academic Societies – May 2nd 2021 (Poster Presentation).

#### **Funding**

M.B. holds an Early Career Investigator Grant from the CIHR Institute of Human Development, Child and Youth Health (IHDCYH), a Research Grant Funding from the FRSQ Clinical Research Scholar Career Award Junior 1, and an Early Career Investigator Grant from the Montreal Children's Hospital Foundation. J.D. holds grants from the Canadian Institutes of Health Research (CIHR), Research Nova Scotia, the National Institutes of Health Research, and the IWK Health Centre. This study was supported by a grant from the CIHR funding the Canadian Preterm Birth Network, Government of Canada (grant no.: PBN 150642).

#### **Conflict of Interest**

None declared.

### Acknowledgments

The authors thank all site investigators and data abstractors of the Canadian Neonatal Network. A list of Network member investigators and their affiliations is provided below:

Prakesh S. Shah, MD, MSc (Director, Canadian Neonatal Network and Site Investigator), Mount Sinai Hospital, Toronto, Ontario; Marc Beltempo, MD, (Associate Director, Canadian Neonatal Network and Site Investigator), Montreal Children's Hospital at McGill University Health Centre, Montréal, Québec; Jaideep Kanungo, MD, Victoria General Hospital, Victoria, British Columbia; Joseph Ting, MD, British Columbia Women's Hospital, Vancouver, British Columbia; Zenon Cieslak, MD, Royal Columbian Hospital, New Westminster, British Columbia; Rebecca Sherlock, MD, Surrey Memorial Hospital, Surrey, British Columbia; Ayman Abou Mehrem, MD, Foothills Medical Centre, Calgary, Alberta; Jennifer Toye, MD, and Khalid Aziz, MBBS, Royal Alexandra Hospital, Edmonton, Alberta; Carlos Fajardo, MD, Alberta Children's Hospital, Calgary, Alberta; Jaya Bodani, MD, Regina General Hospital, Regina, Saskatchewan; Lannae Strueby, MD, Royal University Hospital, Saskatoon, Saskatchewan; Mary Seshia, MBChB, and Deepak Louis, MD, Winnipeg Health Sciences Centre, Winnipeg, Manitoba; Ruben Alvaro, MD, St. Boniface General Hospital, Winnipeg, Manitoba; Amit Mukerji, MD, Hamilton Health Sciences Centre, Hamilton, Ontario; Orlando Da Silva, MD, MSc, London Health Sciences Centre, London, Ontario; Sajit Augustine, MD, Windsor Regional Hospital, Windsor, Ontario; Kyong-Soon Lee, MD, MSc, Hospital for Sick Children, Toronto, Ontario; Eugene Ng, MD, Sunnybrook Health Sciences Centre, Toronto, Ontario; Brigitte Lemyre, MD, The Ottawa Hospital, Ottawa, Ontario; Thierry Daboval, MD, Children's Hospital of Eastern Ontario, Ottawa, Ontario; Faiza Khurshid, MD, Kingston General Hospital, Kingston, Ontario; Victoria Bizgu, MD, Jewish General Hospital, Montréal, Québec; Keith Barrington, MBChB, Anie Lapoint, MD, and Guillaume Ethier, NNP, Hôpital Sainte-Justine, Montréal, Québec; Christine Drolet, MD, and Bruno Piedboeuf, MD, Centre Hospitalier Universitaire de Québec, Sainte Foy, Québec; Martine Claveau, MSc, LLM, NNP, Montreal Children's Hospital at McGill University Health Centre, Montréal, Québec; Marie St-Hilaire, MD, Hôpital Maisonneuve-Rosemont, Montréal, Québec; Valerie Bertelle, MD, and Edith Masse, MD, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Québec; Roderick Canning, MD, Moncton Hospital, Moncton, New Brunswick; Hala Makary, MD, Dr. Everett Chalmers Hospital, Fredericton, New Brunswick; Cecil Ojah, MBBS, and Luis Monterrosa, MD, Saint John Regional Hospital, Saint John, New Brunswick; Julie Emberley, MD, Janeway Children's Health and Rehabilitation Centre, St. John's, Newfoundland; Jehier Afifi, MB BCh, MSc, IWK Health Centre, Halifax, Nova Scotia; Andrzej Kajetanowicz, MD, Cape Breton Regional Hospital, Sydney, Nova Scotia; Shoo K. Lee, MBBS, PhD (Chairman, Canadian Neonatal Network), Mount Sinai Hospital, Toronto, Ontario.

#### References

- 1 Lasswell SM, Barfield WD, Rochat RW, Blackmon L. Perinatal regionalization for very low-birth-weight and very preterm infants: a meta-analysis. JAMA 2010;304(09):992–1000
- 2 Stoll BJ, Hansen NI, Bell EF, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993–2012. JAMA 2015; 314(10):1039–1051
- 3 Lee SK, Beltempo M, McMillan DD, et al; Evidence-based Practice for Improving Quality Investigators. Outcomes and care practices for preterm infants born at less than 33 weeks' gestation: a qualityimprovement study. CMAJ 2020;192(04):E81–E91
- 4 McCormick MC, Shapiro S, Starfield BH. The regionalization of perinatal services. Summary of the evaluation of a national demonstration program. JAMA 1985;253(06):799–804
- 5 Phibbs CS, Bronstein JM, Buxton E, Phibbs RH. The effects of patient volume and level of care at the hospital of birth on neonatal mortality. JAMA 1996;276(13):1054–1059
- 6 Pearson G, Shann F, Barry P, et al. Should paediatric intensive care be centralised? Trent versus Victoria. Lancet 1997;349 (9060):1213–1217
- 7 Pollack MM, Alexander SR, Clarke N, Ruttimann UE, Tesselaar HM, Bachulis AC. Improved outcomes from tertiary center pediatric intensive care: a statewide comparison of tertiary and nontertiary care facilities. Crit Care Med 1991;19(02):150–159
- 8 Gemke RJ, Bonsel GJPediatric Intensive Care Assessment of Outcome (PICASSO) Study Group. Comparative assessment of pediatric intensive care: a national multicenter study. Crit Care Med 1995;23(02):238–245
- 9 Hanson CW III, Deutschman CS, Anderson HL III, et al. Effects of an organized critical care service on outcomes and resource utilization: a cohort study. Crit Care Med 1999;27(02):270–274
- 10 Pronovost PJ, Angus DC, Dorman T, Robinson KA, Dremsizov TT, Young TL. Physician staffing patterns and clinical outcomes in critically ill patients: a systematic review. JAMA 2002;288(17): 2151–2162
- 11 Vincent J-L. Need for intensivists in intensive-care units. Lancet 2000;356(9231):695–696
- 12 Wallace DJ, Angus DC, Barnato AE, Kramer AA, Kahn JM. Nighttime intensivist staffing and mortality among critically ill patients. N Engl J Med 2012;366(22):2093–2101

- 13 Lyu Y, Shah PS, Ye XY, et al; Canadian Neonatal Network. Association between admission temperature and mortality and major morbidity in preterm infants born at fewer than 33 weeks' gestation. JAMA Pediatr 2015;169(04):e150277
- 14 Croop SEW, Thoyre SM, Aliaga S, McCaffrey MJ, Peter-Wohl S. The Golden Hour: a quality improvement initiative for extremely premature infants in the neonatal intensive care unit. J Perinatol 2020;40(03):530-539
- 15 Arabi Y. Pro/Con debate: should 24/7 in-house intensivist coverage be implemented? Crit Care 2008;12(03):216
- 16 Wilcox ME, Chong CA, Niven DJ, et al. Do intensivist staffing patterns influence hospital mortality following ICU admission? A systematic review and meta-analyses. Crit Care Med 2013;41 (10):2253-2274
- 17 Banerjee R, Naessens JM, Seferian EG, et al. Economic implications of nighttime attending intensivist coverage in a medical intensive care unit. Crit Care Med 2011;39(06):1257-1262
- 18 Rizzolo A, Shah PS, Bertelle V, et al; Canadian Neonatal Network (CNN) and Canadian Preterm Birth Network (CPTBN) Investigators. Association of timing of birth with mortality among preterm infants born in Canada. J Perinatol 2021;41(11): 2597-2606
- 19 Jensen EA, Lorch SA. Association between off-peak hour birth and neonatal morbidity and mortality among very low birth weight infants. J Pediatr 2017;186:41-48.e4, e4
- 20 Kerlin MP, Small DS, Cooney E, et al. A randomized trial of nighttime physician staffing in an intensive care unit. N Engl J Med 2013;368(23):2201-2209
- 21 Lee SK, Lee DSC, Andrews WL, Baboolal R, Pendray M, Stewart SCanadian Neonatal Network. Higher mortality rates among inborn infants admitted to neonatal intensive care units at night. J Pediatr 2003;143(05):592-597
- 22 Lodha A, Brown N, Soraisham A, Amin H, Tang S, Singhal N. Twenty-four-hour in-house neonatologist coverage and longterm neurodevelopmental outcomes of preterm infants. Paediatr Child Health 2017;22(05):249-254
- 23 Kerlin MP, Adhikari NK, Rose L, et al; ATS Ad Hoc Committee on ICU Organization. An official American Thoracic Society systematic review: the effect of nighttime intensivist staffing on mortal-

- ity and length of stay among intensive care unit patients. Am I Respir Crit Care Med 2017;195(03):383-393
- Shahroor M, Lehtonen L, Lee SK, et al; on behalf of the International Network for Evaluation of Outcomes (iNeo) of neonates. Unit-level variations in healthcare professionals' availability for preterm neonates < 29 weeks' gestation: an international survey. Neonatology 2019;116(04):347-355
- 25 Canadian Neonatal Network. Abstractor's Manual v2.1.2. 2014 http://www.canadianneonatalnetwork.org/
- 26 Kramer MS, Platt RW, Wen SW, et al; Fetal/Infant Health Study Group of the Canadian Perinatal Surveillance System. A new and improved population-based Canadian reference for birth weight for gestational age. Pediatrics 2001;108(02):E35
- Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II: Simplified newborn illness severity and mortality risk scores. J Pediatr 2001;138(01):92-100
- 28 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(04):527–532
- 29 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(04):529-534
- 30 An international classification of retinopathy of prematurity. Pediatrics 1984;74(01):127-133
- Willinger U, Lenzinger E, Hornik K, et al; European fluvoxamine in alcoholism study group. Anxiety as a predictor of relapse in detoxified alcohol-dependent patients. Alcohol Alcohol 2002;37 (06):609-612
- 32 Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg 1978;187(01):1-7
- 33 Hanley JA, Negassa A, Edwardes MD, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. Am J Epidemiol 2003;157(04):364-375
- Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology 1990;1(01):43-46
- 35 Bensouda B, Boucher J, Mandel R, Lachapelle J, Ali N. 24/7 in house attending staff coverage improves neonatal short-term outcomes: a retrospective study. Resuscitation 2018;122:25-28