4-1-2015

Association between admission temperature and mortality and major morbidity in preterm infants born at fewer than 33weeks' gestation

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Original Investigation

Association Between Admission Temperature and Mortality and Major Morbidity in Preterm Infants Born at Fewer Than 33 Weeks' Gestation

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IMPORTANCE Neonatal hypothermia has been associated with higher mortality and morbidity; therefore, thermal control following delivery is an essential part of neonatal care. Identifying the ideal body temperature in preterm neonates in the first few hours of life may be helpful to reduce the risk for adverse outcomes.

OBJECTIVES To examine the association between admission temperature and neonatal outcomes and estimate the admission temperature associated with lowest rates of adverse outcomes in preterm infants born at fewer than 33 weeks' gestation.

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational study at 29 neonatal intensive care units in the Canadian Neonatal Network. Participants included 9833 inborn infants born at fewer than 33 weeks' gestation who were admitted between January 1, 2010, and December 31, 2012.

EXPOSURE Axillary or rectal body temperature recorded at admission.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite adverse outcome defined as mortality or any of the following: severe neurological injury, severe retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, or nosocomial infection. The relationships between admission temperature and the composite outcome as well as between admission temperature and the components of the composite outcome were evaluated using multivariable analyses.

RESULTS Admission temperatures of the 9833 neonates were distributed as follows: lower than 34.5°C (1%); 34.5°C to 34.9°C (1%); 35.0°C to 35.4°C (3%); 35.5°C to 35.9°C (7%); 36.0°C to 36.4°C (24%); 36.5°C to 36.9°C (38%); 37.0°C to 37.4°C (19%); 37.5°C to 37.9°C (5%); and 38.0°C or higher (2%). After adjustment for maternal and infant characteristics, the rates of the composite outcome, severe neurological injury, severe retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, and nosocomial infection had a U-shaped relationship with admission temperature ($\alpha > 0$ [$P < .05$]). The admission temperature at which the rate of the composite outcome was lowest was 36.8°C (95% CI, 36.7°C-37.0°C). Rates of severe neurological injury, severe retinopathy of prematurity, necrotizing enterocolitis (95% CI, 36.3°C-36.7°C), bronchopulmonary dysplasia, and nosocomial infection (95% CI, 36.9°C-37.3°C) were lowest at admission temperatures ranging from 36.5°C to 37.2°C.

CONCLUSIONS AND RELEVANCE The relationship between admission temperature and adverse neonatal outcomes was U-shaped. The lowest rates of adverse outcomes were associated with admission temperatures between 36.5°C and 37.2°C.

JAMA Pediatr. 2015;169(4):e150277. doi:10.1001/jamapediatrics.2015.0277

Supplemental content at jamapediatrics.com

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Neonates regulate body temperature much less efficiently than adults and both hypothermia and hyperthermia can occur easily. The smaller and more premature the infant, the higher the risk.[1,2] In 1958, it was first demonstrated that maintaining body temperature by controlling the thermal environment during the first 5 days after birth significantly reduced mortality in low-birth-weight infants.[3] Subsequent studies have investigated reducing the incidence of hypothermia or improving temperature at birth or admission to the neonatal intensive care unit (NICU) for low-birth-weight/preterm infants.[4-6] Hypothermia has been reported to be significantly related to in-hospital mortality,[7] respiratory distress syndrome,[8] necrotizing enterocolitis (NEC),[9] and intraventricular hemorrhage[10] in low-birth-weight/preterm infants. Two studies investigated this relationship in very low-birth-weight infants. Laptook et al[11] showed that mortality was inversely related to admission temperature (28% increase per 1°C decrease) as well as late-onset sepsis (11% increase per 1°C decrease) but not intraventricular hemorrhage, NEC, nor duration of conventional ventilation. Miller et al[12] found that moderate hypothermia (32.0°C-35.9°C) was associated with intraventricular hemorrhage and mortality.

The findings from these studies are confounded by lack of consistent definitions of *hypothermia* and *hyperthermia*.[13] Textbooks define the lower range of a healthy body temperature as 35.5°C to 36.5°C and the upper range as 37.0°C to 37.8°C.[14] Researchers have varyingly defined hypothermia as lower than 35.0°C,[15] lower than 35.5°C,[9] lower than 36.0°C,[4,8,10,16] or lower than 36.5°C[12] in studies on admission temperature and in-hospital outcomes. In 2012, the American Academy of Pediatrics/American College of Obstetricians and Gynecologists distributed guidelines recommending an axillary temperature of 36.5°C in the delivery room and an axillary temperature range of 36.5°C to 37.4°C prior to discharge for an infant in an open crib.[17] The World Health Organization classifies 36.0°C to 36.4°C as cold stress or mild hypothermia, 32.0°C to 35.9°C as moderate hypothermia, and lower than 32.0°C as severe hypothermia. The World Health Organization advocates that neonatal body temperature is maintained at 36.5°C to 37.5°C[18]; however, evidence supporting these recommendations is weak.

Pinheiro et al[19] reported that when chemical warming packs were added to routine plastic wrapping and warm blankets, the rate of hypothermia (<36.5°C) on admission decreased from 68% to 39% whereas the rate of hyperthermia (>38.0°C) increased from 1.0% to 1.6%. Other recommendations have also highlighted the need to avoid hyperthermia during neonatal intensive care.[20] However, to our knowledge, there have been no studies describing differences in the risk for adverse neonatal outcomes across a full range of admission temperatures, including hypothermia and hyperthermia. This study aimed to describe the distribution of admission temperatures in preterm infants born at fewer than 33 weeks' gestation in Canadian NICUs, examine the association between admission temperature (both hypothermia and hyperthermia) and neonatal mortality and major morbidities, and identify the admission temperature where the rates of adverse outcomes are the lowest in preterm infants.

At a Glance

- Thermal management following delivery is important to the survival of very preterm neonates but evidence supporting an optimal body temperature is needed.
- This retrospective observational study examined the association between admission temperature and neonatal outcomes.
- Analysis indicated a U-shaped relationship between admission temperature and a composite mortality or morbidity (neurological injury, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, or nosocomial infection) outcome as well as between admission temperature and individual morbidities.
- The lowest rates of the adverse outcomes were associated with admission temperatures between 36.5°C and 37.2°C.

Methods

Study Population

The Canadian Neonatal Network (CNN) maintains a standardized nationwide NICU database. In 2010, this database included data from 29 of the 30 tertiary-level NICUs in Canada, comprising 95% of tertiary-level NICU admissions in Canada. Data are abstracted from infant medical records according to standardized definitions[21] and electronically transmitted to the CNN coordinating center as previously described.[22] This retrospective observational study included data from preterm infants born at fewer than 33 weeks' gestation and admitted to CNN NICUs between January 1, 2010, and December 31, 2012. Infants who were outborn, had a major congenital anomaly defined according to CNN standard definitions,[21] were moribund on admission (palliative care planned at birth), or missing data on admission temperature were excluded. Waiver of need for consent and ethics approval for data collection and analysis was granted by the research ethics board of Mount Sinai Hospital, Toronto, Ontario, Canada.

Outcomes and Variables

The primary outcome was a composite outcome defined as mortality or any of the following major neonatal morbidities: severe neurological injury, defined as grade 3 or 4 intraventricular hemorrhage according to the criteria of Papile et al[23] or periventricular leukomalacia; severe retinopathy of prematurity, defined as stage 3 or higher according to the International Classification;[24] stage 2 or higher NEC according to the criteria of Bell et al[25]; bronchopulmonary dysplasia, defined as oxygen dependency at 36 weeks' corrected gestational age or the time of transfer to a level 2 center[26]; and nosocomial infection, defined as culture-positive sepsis or meningitis at older than 48 hours.[27] Secondary outcomes included the individual components of the primary outcome and duration of ventilation.

The following variables were investigated for association with admission temperature: maternal variables including maternal antibiotics (systemic antibiotics given to mother <24 hours before birth), antenatal steroid use, single/multiple birth, rupture of membranes for more than 24 hours, mode of delivery, and maternal hypertension; infant variables including

sex, birth weight, and gestational age; and delivery room variables including Apgar scores and resuscitation (use of any of the following: continuous positive airway pressure, positive pressure ventilation via bag and mask or via endotracheal tube, chest compressions for 30 seconds or longer, or epinephrine).

Axillary or rectal body temperature was recorded at admission to a participating NICU from the delivery room of the same hospital. Admission temperature was defined as the temperature taken with the first vital signs after admission to NICU during the first hour of admission. Gestational age was determined as the best estimate according to the hierarchy of first-trimester ultrasound, last menstrual period, obstetric estimate, and pediatric estimate. Infants were classified as small for gestational age if their birth weight was lower than the 10th percentile for gestational age according to Canadian population-based growth charts.[28]

Statistical Analysis

Characteristics of the study population were summarized using descriptive statistical methods. Infants were categorized according to their admission temperature in 9 groups with 0.5°C increments from lower than 34.5°C to 38.0°C or higher. To examine the association between infant characteristics and admission temperature, infant characteristics were compared in temperature groups using the χ^2 test for categorical variables and analysis of variance (F test) for continuous variables. Multiple linear regression analysis was also conducted to determine the independent relationships between maternal and infant characteristics and admission temperature, adjusted for the characteristics associated with temperature identified in the univariate analyses using stepwise variable selection procedures. Owing to high collinearity with birth weight, gestational age was not included in the models. To assess the association between admission temperature and neonatal outcomes and NICU resource use, the rates of adverse neonatal outcomes were compared in the temperature groups using the χ^2 test for categorical variables and the F test or Wilcoxon rank sum test (as appropriate) for continuous variables.

To determine if there was a U-shaped association between neonatal outcomes and admission temperature, nonlinear regression analyses using the quadratic model $y = ax^2 + bx + c$ were conducted to fit the outcome rates. When the coefficient of the quadratic term was significantly more than zero, this implied a significant U-shaped relationship between the rate of outcome and admission temperature. Multiple logistic regression with quadratic models using a generalized estimating equation approach was also conducted to further examine the U-shaped association between binary outcomes and admission temperature. The symmetric covariance structure was used in the models to account for the correlation owing to the clustering of participants in the hospital. In fitting the models, a birth weight z score instead of birth weight was used to reduce the collinearity between birth weight and admission temperature. Owing to a highly positive skew in the length of ventilation data, the U-shaped association between length of ventilation and admission temperature was examined using zero-inflated negative binomial regression models adjusted for the covariates mentioned earlier. Data management and statistical analyses were performed using R version 2.15 (R Project for Statistical Computing; http://www.r-project.org) and SAS version 9.3 (SAS Institute Inc). A 2-sided P value of .05 was used to determine statistical significance.

Table 1. Characteristics of 9833 Infants

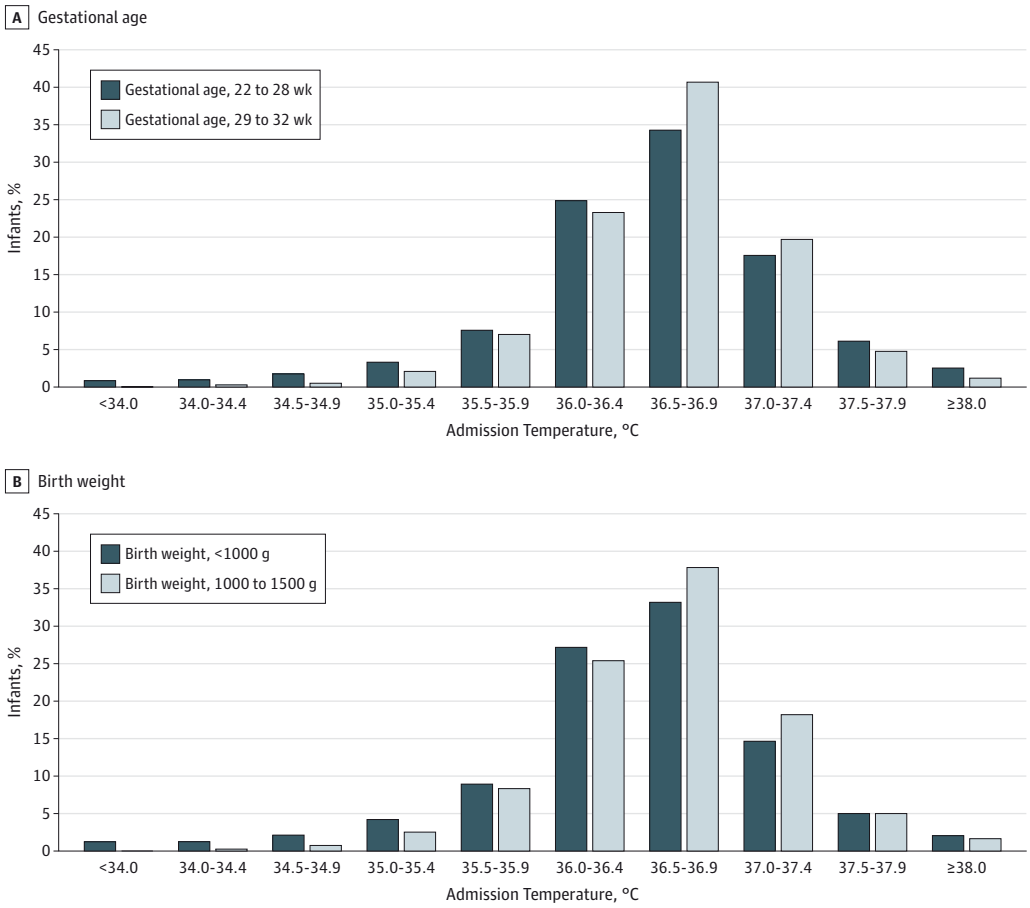
Characteristic	No. (%)
Maternal	
Antenatal steroid use	8913 (91.6)
Antibiotics	6717 (70.0)
Hypertension	1970 (20.3)
Cesarean birth	5928 (60.4)
Rupture of membranes, >24 h	2016 (22.7)
Infant	
Admission temperature, °C	
<34.5	96 (1.0)
34.5-34.9	101 (1.0)
35.0-35.4	256 (2.6)
35.5-35.9	716 (7.3)
36.0-36.4	2347 (23.9)
36.5-36.9	3767 (38.3)
37.0-37.4	1856 (18.9)
37.5-37.9	526 (5.3)
≥38.0	168 (1.7)
Male sex	5315 (54.1)
Birth weight, mean (SD), g	1323 (455)
Birth weight group, g	
<1000	2732 (27.8)
1000-1499	3591 (36.5)
1500-1999	2843 (28.9)
≥2000	667 (6.8)
Gestational age, mean (SD)	29 (2.5)
Gestational age group, wk	
22-25	1185 (12.1)
26-29	2499 (25.4)
30-32	6149 (62.5)
Singleton	6517 (66.3)
Small for gestational age	1019 (10.4)
Resuscitation needed	8932 (90.9)
Apgar score <7 at 5 min	2404 (24.5)
SNAP II score >20	1591 (16.4)

Abbreviation: SNAP II, Score for Neonatal Acute Physiology II.

Results

A total of 10 560 inborn infants born at fewer than 33 weeks' gestation were admitted on their day of birth to CNN NICUs during 2010 to 2012, of which 538 infants (5.1%) were excluded owing to the presence of major congenital anomalies (n = 480) or being moribund on admission (n = 58). Additionally, 189 infants (1.9%) with missing temperature data were excluded. The remaining 9833 infants were included in this analysis and their characteristics are described in **Table 1**. The mean (SD) admission temperature of all included infants was 36.6°C

Figure 1. Temperature Distribution According to Gestational Age and Birth Weight



(0.7°C), with a range of 32.0°C to 41.0°C. A total of 57.3% of the study population had an admission temperature in the World Health Organization recommended range of 36.5°C to 37.4°C, with the largest group (38.3%) being infants with an admission temperature between 36.5°C and 36.9°C. A total of 35.8% of infants had an admission temperature lower than 36.5°C and 7.1% had an admission temperature higher than 37.5°C. The distributions of infants across the range of admission temperatures recorded according to gestational age and birth weight are reported in **Figure 1**.

Examination of the association between admission temperature and neonatal adverse outcomes in univariate analyses indicated that all the adverse outcomes were significantly associated with admission temperature ($P < .04$) and that the rate of each outcome reached a minimum in a specific admission temperature category. For example, the rate of the composite outcome in univariate analyses was the lowest in those infants with an admission temperature between 37.0°C and 37.4°C (**Table 2**). A U-shaped association between all neonatal outcomes assessed and admission temperature was identified ($P < .05$; **Figure 2**; eFigure 1 in the Supplement). Duration of ventilation also had a U-shaped relationship with admission temperature.

The univariate analysis indicated that birth weight, gestational age, small for gestational age, an Apgar score less than 7 at 5 minutes, singleton birth, cesarean birth, rupture of membranes for more than 24 hours, need for resuscitation, maternal hypertension, antenatal steroid use, and maternal antibiotic use were associated with admission temperature. After adjustment in multivariable analyses, birth weight was significantly associated with admission temperature so that admission temperature was 0.025°C higher with each 100-g increase in birth weight. Rupture of membranes for more than 24 hours, resuscitation, antenatal steroid use, and maternal antibiotic use were also significantly associated with higher admission temperature while singleton births, cesarean birth, and maternal hypertension were significantly associated with lower admission temperature (eTable in the Supplement).

The U-shaped relationships between admission temperature and the composite outcome, severe neurological injury, severe retinopathy of prematurity, NEC, bronchopulmonary dysplasia, nosocomial infection, and duration of ventilation were confirmed ($\alpha > 0$ [$P < .05$]) in multivariable analyses that used admission temperature as a continuous variable and adjusted for confounding variables. Analyses indicated that for each outcome, an admission temperature could be estimated where the rate of the outcome was at its minimum (**Table 3**). For example, in the multivariable analyses, the rate of the composite outcome was lowest at an admission temperature of 36.8°C while the rates of the secondary outcomes, with the ex-

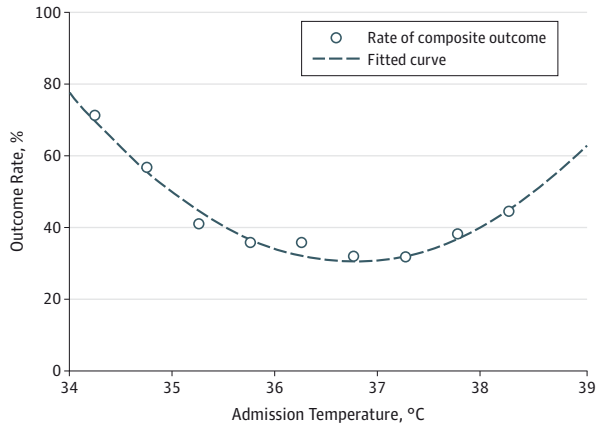
Table 2. Univariate Analysis of Association Between Outcomes and Temperature at Admission

Outcome	Admission Temperature, No. (%)										P Value[a]
	Overall	<34.5°C (n = 96)	34.5°C-34.9°C (n = 101)	35.0°C-35.4°C (n = 256)	35.5°C-35.9°C (n = 716)	36.0°C-36.4°C (n = 2347)	36.5°C-36.9°C (n = 3767)	37.0°C-37.4°C (n = 1856)	37.5°C-37.9°C (n = 526)	≥38.0°C (n = 168)	
Composite outcome	3356 (34.1)	68 (70.8)	57 (56.4)	104 (40.6)	253 (35.3)	829 (35.3)	1190 (31.6)	582 (31.4)	199 (37.8)	74 (44.1)	<.001
Mortality	619 (6.3)	25 (26.0)	21 (20.8)	28 (10.9)	53 (7.4)	163 (7.0)	200 (5.3)	90 (4.9)	28 (5.3)	11 (6.6)	<.001
Severe neurological injury	861 (10.7)	23 (27.1)	12 (14.0)	24 (10.6)	54 (8.8)	201 (10.1)	305 (10.2)	166 (11.4)	58 (13.6)	18 (12.8)	<.001
Severe ROP	401 (4.1)	13 (13.8)	7 (7.0)	16 (6.3)	22 (3.1)	113 (4.8)	141 (3.8)	57 (3.1)	17 (3.3)	15 (9.0)	<.001
NEC	424 (4.3)	10 (10.4)	6 (5.9)	17 (6.6)	30 (4.2)	98 (4.2)	142 (3.8)	88 (4.7)	24 (4.6)	9 (5.4)	.03
BPD	1640 (17.7)	21 (29.6)	26 (31.0)	45 (19.6)	107 (16.1)	407 (18.5)	593 (16.6)	296 (16.7)	108 (21.6)	37 (23.3)	<.001
Nosocomial infection	1342 (13.7)	29 (30.2)	23 (22.8)	46 (18.0)	120 (16.8)	320 (13.6)	479 (12.7)	226 (12.2)	73 (13.9)	26 (15.5)	<.001
Ventilation, median (range), d	0 (0-4)	6 (2-31.5)	5 (0-30.0)	2 (0-11.0)	1 (0-8.0)	1 (0-5.0)	0 (0-3.0)	0 (0-3.0)	1 (0-5.0)	2 (0-12.0)	<.001

Abbreviations: BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity.

[a] Based on χ^2 test for categorical variables and *F* test and Wilcoxon rank sum test as appropriate for continuous variables.

Figure 2. Association of Admission Temperature With a Composite Mortality/Morbidity Outcome



Unadjusted data for rate of a composite mortality/morbidity outcome plotted against admission temperature and fitted with a curve indicating the U-shaped relationship between admission temperature and the composite outcome.

ception of mortality, were at a minimum at admission temperatures ranging from 36.5°C to 37.2°C. Mortality was linearly and negatively associated with admission temperature after adjustment for confounding variables. Post hoc subgroup analyses of neonates born at fewer than 29 weeks' gestation also revealed a similar pattern, with the lowest rates of the adverse outcomes estimated to occur between 36.5°C and 37.2°C (eFigure 2 in the Supplement).

Discussion

To our knowledge, this is the first study to describe a U-shaped relationship between admission temperature and rates of major adverse neonatal outcomes. Using these data, we were able to identify an overall admission temperature range of 36.5°C to 37.2°C in which the rates of a composite mortality/morbidity outcome and the individual morbidities of severe neurological injury, severe retinopathy of prematurity, NEC, bronchopulmonary dysplasia, and nosocomial infection as well as duration of ventilation were lowest in our population. This information will be useful in the application of evidence-based quality improvement initiatives aimed at reducing adverse outcomes by targeting practices to maintain admission temperatures in the range identified.

With changes to the Neonatal Resuscitation Program guidelines[29] on temperature control across the years, the proportion of infants with a low temperature at birth has decreased. For example, studies of US cohorts have reported a drop in the rate of very low-birth-weight infants with an admission temperature lower than 36.0°C from 46.9% in 2002 to 2003[11] to 25.7% in 2006 to 2007.[12] Pinheiro et al[30] also reported that fewer than 10% of inborn very low-birth-weight neonates had admission temperatures lower than 36.0°C after implementation of a thermoregulation bundle. The Brazilian Neonatal Network reported the mean rate of hypothermia (<36.0°C) to be 51%, with rates varying from 13% to 62% between centers when measured at 5 minutes of age and 25% to 75% at the time of NICU admission.[31] In our study, only 11.9% of infants had an admission temperature of lower than 36.0°C. Similarly, in the early 1980s, the incidence of axillary admission temperatures lower than 35.0°C in very low-birth-weight inborn infants in Canada was reported to be 11.5%.[7] In this study, only 2.0% of infants had an admission temperature lower than 35.0°C. However, 25.9% of infants in our study had an admission temperature of 37.0°C or higher and 1.7% had an admission temperature of 38.0°C or higher, which is higher than previously reported in the US studies (10.8% at ≥37.0°C[11] and 0.8% at ≥38.0°C[12]). This change reinforces the concept that continued vigilance for hyperthermia is also necessary because most thermoregulatory efforts in preterm neonates are currently directed toward the prevention of hypothermia. Our

Table 3. Multivariable Analysis of Association Between Outcomes and Temperature at Admission

Outcome	Model With Adjustment (95% CI)[a]		
	Temperature β	Temperature × Temperature α	Minimum Point, °C
Composite outcome[b]	−11.418 (−15.88 to −6.96)[c]	0.155 (0.082 to 0.228)[c]	36.8 (36.7 to 37.0)
Mortality[b]	−0.427 (−0.584 to −0.270)[c]	NA	NA
Severe neurological injury[b]	−5.636 (−10.85 to −0.422)[d]	0.077 (0.0045 to 0.1495)[d]	36.6 (36.5 to 36.7)
Severe ROP[b]	−11.045 (−19.46 to −2.63)[d]	0.150 (0.034 to 0.266)[d]	36.8 (36.6 to 37.0)
NEC[b]	−10.445 (−17.25 to −3.638)[e]	0.143 (0.049 to 0.237)[e]	36.5 (36.3 to 36.7)
BPD[b]	−8.264 (−13.39 to −3.14)[e]	0.113 (0.042 to 0.184)[e]	36.6 (36.4 to 36.7)
Nosocomial infection[b]	−5.329 (−10.48 to −0.174)[d]	0.0717 (0.0011 to 0.142)[d]	37.2 (36.9 to 37.3)
Length of ventilation[f]	−8.26 (−12.43 to −4.085)[c]	0.111 (0.105 to 0.117)[c]	37.2 (37.0 to 37.4)

Abbreviations: BPD, bronchopulmonary dysplasia; NA, not available; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity.

[a] Temperature indicates temperature at admission; temperature × temperature indicates the quadratic term of the temperature; β and α indicate estimated coefficients of temperature and temperature × temperature in the model, respectively; minimum point indicates the estimated minimum point (−β/[2α]) at which the fitted curve reached the minimum.

[b] Multiple logistic regression models adjusted for sex, birth weight *z* score, Apgar score at 5 minutes, singleton birth, cesarean birth, rupture of membranes for more than 24 hours, resuscitation, maternal hypertension, antenatal steroid use, and maternal antibiotic use with a generalized estimating equation approach to account for correlated data owing to the clustering of patients by site.

[c] $P < .001$.

[d] $P < .05$.

[e] $P < .01$.

[f] Zero-inflated negative binomial model was used and adjusted for sex, birth weight *z* score, Apgar score at 5 minutes, singleton birth, cesarean birth, rupture of membranes for more than 24 hours, resuscitation, maternal hypertension, antenatal steroid use, and maternal antibiotic use.

data also revealed that only 57.2% of infants were identified as having the best outcomes, included in admission temperature groups of 36.5°C to 36.9°C and 37.0°C to 37.4°C, indicating a high-priority need for quality improvement initiatives to address this problem. Although data on delivery room practices to keep infants euthermic were not collected, we assume that standard practices based on the Neonatal Resuscitation Program guidelines were followed by all CNN NICUs during the study, including the use of radiant warmers, plastic wraps, and/or chemical mattresses. Further study of the implementation of these and other potentially best practices is needed.

Our finding that rates of adverse neonatal outcomes in preterm infants born at fewer than 33 weeks' gestation were lowest between 36.5°C and 37.2°C is consistent not only with the World Health Organization's thermal protection recommendations[18] but also with several other studies on optimal neonatal temperature according to physiological outcomes, such as heart rate in the first 12 hours of life[32] and oxygen consumption.[33] When examining the association between admission temperature and adverse neonatal outcomes, previous studies have used varying approaches, including categorizing admission temperature using cutoff points to classify infants as nonhypothermic, moderately hypothermic, or severely hypothermic[12] and using temperature as a continuous variable, assuming that the association between admission temperature and adverse outcomes is linear.[11] This latter approach does not take into consideration the effect of hyperthermia on clinical outcomes. In contrast, we identified a nonlinear relationship between admission temperature and neonatal outcomes and used quadratic regression to test that relationship. Thus, we were able to evaluate the association of both hypothermia and hyperthermia with clinical adverse outcomes and identify the temperature range at which the rates of those outcomes were lowest. Although the relationship of mortality to admission temperature also initially exhibited a U-shaped curve, we found that after adjustment for confounding variables, mortality was inversely related to admission temperature, which may have been related to the low number of deaths in the extreme high-temperature group or the possibility that deaths are often a result of other adverse outcomes and confounding variables.

The associations between admission temperature and various maternal, intrapartum, and infant characteristics observed in this study are mostly consistent with previous studies.[11,12] The association between cesarean delivery and lower admission temperature may be related to the fact that operating rooms are often kept at a lower temperature and to the use of neuraxial anesthesia, where lower body sympathectomy produces core-to-peripheral redistribution of heat.[6] Horn et al[34] reported that active warming during cesarean delivery can decrease maternal shivering and produce a higher neonatal core temperature. We also identified that resuscitation in the first 30 minutes after birth was associated with increased admission temperature. This is inconsistent with Miller et al,[12] who reported a decreased odds of hypothermia following no resuscitative efforts during the delivery and proposed that this may have been because infants who do not require resuscitation are usually healthier and better able to maintain their core body temperature. In addition, in the midst of resuscitation, measures to keep infants warm may be difficult to maintain or neglected altogether. We speculate that an infant requiring resuscitation is likely to be more sick and require more care, which should result in the care team ensuring that all practices are followed, including attending to body temperature. For an infant who seems healthy enough not to require resuscitation, body temperature regulation may still be required and should be attended to carefully.

Strengths of our study included the use of data from a large NICU-based cohort, which provided temperature measure-

ments on admission and information on potential confounders and mediating factors to help us better understand the association between body temperature and adverse outcomes. The large data set also enabled us to evaluate the association across a full temperature range, which aided in assessing the U-shaped association that exists between admission temperature and neonatal outcome. Our finding that the optimal admission temperature range in preterm infants born at fewer than 33 weeks' gestation was 36.5°C to 37.2°C is consistent not only with the World Health Organization's thermal protection recommendations,[18] but also with several other studies. Knobel et al[32] reported that optimal abdominal temperature was between 36.8°C and 36.9°C based on heart rate in extremely low-birth-weight infants (born at <29 weeks' gestation) during the first 12 hours of life. Malin et al[33] reported that abdominal temperatures of 36.5°C to 37.5°C kept oxygen consumption to a minimum for premature neonates. These findings provide some evidence to support the recommendation and suggest this work is generalizable. However, for effective use of our analytical approach in quality improvement activities, temperature outcome curves and the temperature range for minimum outcome rates need to be generated using data from target populations. The existence of the U-shaped relationship should allow the definition of a target temperature range according to a desired or achievable target outcome rate.

Limitations of the study included that it was a retrospective observational study and admission body temperatures were not collected using uniform methods. Admission temperatures were recorded at different times in the first hour of admission using varying instruments from different body areas. We used a mixture of rectal and axillary temperature measurements because our data collection system did not allow us to separate these 2 categories. In such a large sample, this may not have led to a biased estimate. In a systemic review, Craig et al[35] reported that the pooled mean temperature difference between rectal and axillary temperature for neonates was 0.17°C (limits of agreement, −0.15°C to 0.50°C). This was also reported in several other studies.[36,37] We acknowledge that most of our neonates were born at more than 30 weeks' gestation whereas most immediate postnatal interventions occur in neonates born at fewer than 29 weeks' gestation, which renders them at risk for hypothermia. This should be kept in mind when interpreting our results. Given the limitations of using retrospective observational data, we need to further evaluate the influence of admission temperature on neonatal outcomes using a prospective study where body temperatures at admission are collected using uniform methods and timing.

Conclusions

In this nationwide population of inborn preterm infants born at fewer than 33 weeks' gestation from Canadian NICUs, we identified U-shaped relationships between admission temperature and a composite adverse outcome, including severe neurological injury, severe retinopathy of prematurity, bronchopulmonary dysplasia, NEC, nosocomial infection, and duration of mechanical ventilation. The admission temperature range at which the rates of these outcomes were lowest was 36.5°C to 37.2°C. More than 40% of the infants in our study had admission temperatures outside the identified range, indicating a need to more closely monitor the admission temperatures of preterm infants.

ARTICLE INFORMATION

Accepted for Publication: February 1, 2015.

Published Online: April 6, 2015. doi:10.1001/jamapediatrics.2015.0277.

Author Contributions: Dr Shah had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Lyu, Ye.
Acquisition, analysis, or interpretation of data: All authors.
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Statistical analysis: Shah, Ye.
Obtained funding: Lyu, Lee.
Administrative, technical, or material support: Lee.
Study supervision: Shah, Lee.

Conflict of Interest Disclosures: None reported.

Funding/Support: Organizational support was provided by the Canadian Neonatal Network Coordinating Centre, which is based at the Maternal-Infant Care Research Centre (MiCare) at Mount Sinai Hospital in Toronto, Ontario, Canada. MiCare is supported by grant funding from the Canadian Institutes of Health Research and in-kind support from Mount Sinai Hospital, Toronto, Ontario. Dr Lyu was supported by grant 2012A0030340000017 from the Beijing Outstanding Talents Oversea Training Project. Dr Shah holds an applied research chair in Reproductive and Child Health Services and Policy Research awarded by the Canadian Institutes of Health Research.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Additional Contributions: We thank the data abstractors of the Canadian Neonatal Network and staff of the Canadian Neonatal Network Coordinating Centre for providing organizational support to the Canadian Neonatal Network. As employees of MiCare; Mount Sinai Hospital, Toronto, Ontario; or their respective hospitals, all these individuals received salaried compensation for their assistance.

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