ORIGINAL ARTICLES

Costs of Neonatal Intensive Care for Canadian Infants with Preterm Birth

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Objective To develop and validate an itemized costing algorithm for in-patient neonatal intensive care unit (NICU) costs for infants born prematurely that can be used for quality improvement and health economic analyses.

Study design We sourced patient resource use data from the Canadian Neonatal Network database, with records from infants admitted to 30 tertiary NICUs in Canada. We sourced unit cost inputs from Ontario hospitals, schedules of benefits, and administrative sources. Costing estimates were generated by matching patient resource use data to the appropriate unit costs. All cost estimates were in 2017 Canadian dollars and assigned from the perspective of a provincial public payer. Results were validated using previous estimates of inpatient NICU costs and hospital case-cost estimates.

Results We assigned costs to 27 742 infants born prematurely admitted from 2015 to 2017. Mean (SD) gestational age and birth weight of the cohort were 31.8 (3.5) weeks and 1843 (739) g, respectively. The median (IQR) cost of hospitalization before NICU discharge was estimated as \$20 184 (\$9739-51 314) for all infants; \$11 810 (\$6410-19 800) for infants born at gestational age of 33-36 weeks; \$30 572 (\$16 597-\$51 857) at gestational age of 29-32 weeks; and \$100 440 (\$56 858-\$159 3867) at gestational age of <29 weeks. Cost estimates correlated with length of stay ($r = 0.97$) and gestational age ($r = -0.65$). The estimates were consistent with provincial resource estimates and previous estimates from Canada.

Conclusions NICU costs for infants with preterm birth increase as gestation decreases and length of stay increases. Our cost estimates are easily accessible, transparent, and congruent with previous cost estimates. *(J Pediatr 2021;229:161-7)*.

Preterm birth, defined as birth at <37 weeks of gestation, is the leading cause of infant death and disability in Canada.[1-3] Preterm birth also has a substantial economic impact on healthcare systems, largely due to the cost of initial hospitalization.[4] There is marked variability in reported estimates of cost per preterm birth across countries due to differences in perspectives, jurisdictions, and methods used to assign cost.[4-6]

Currently, the methods used to estimate the cost of preterm birth are limited with regards to their accessibility, comprehensiveness, or the specificity of their cost estimates.[1] Per diem methods multiply an infant's length of stay (LOS) by the average cost of caring for an infant born prematurely but do not allow for a meaningful comparison of costs between infants with similar LOS unless portions of costs are assigned based on resource use.[7] Cost-to-charge methods, which convert billing data into estimated expenditures using a ratio of cost-to-charge, have been used to estimate the cost of inpatient care for infants born prematurely.[5] These methods are limited by data availability and assumptions on the relationship between billing and resource use.[8]

Detailed case-specific costs estimates, generated by hospital finance departments using financial and clinical data, have been used to evaluate the cost-effectiveness of interventions for infants with preterm birth and their mothers.[9,10] Unfortunately, differences in how hospitals assign costs, variations in costs inputs, and inaccessibility of these estimates for researchers and clinicians are drawbacks of this method.[11] For example, nursing costs can be assigned using

CIHI	Canadian Institute of Health Information
CMG	Case-mix groups
CNN	Canadian Neonatal Network
IHDA	Alberta Interactive Health Data Application
LOS	Length of stay
NICU	Neonatal intensive care unit
OCCI	the Ontario Case Costing Initiative

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a variety of metrics, allowing infants at different sites with similar resource use to have different cost estimates.[12,13] The use of hospital financial data to generate cost estimates creates uncertainty about whether cost differences across sites are explained by variation in input prices, specifically wages, or resource use.[14]

The objective of this study was to develop and validate a costing algorithm for inpatient costs associated with preterm birth for infants admitted to a level 3 Canadian neonatal intensive care unit (NICU) using the Canadian Neonatal Network (CNN) dataset and to compare our estimates with those obtained from hospital case-cost estimates and previous economic evaluations. Costing algorithm estimates were created by matching resource use to unit costs and provide patient-level estimates that are consistent, transparent and easily accessible. These cost-estimates will facilitate the identification of cost drivers, potential cost reductions, and will be used to evaluate the potential economic benefits of emerging interventions.

Methods

The CNN is a consortium of 30 tertiary NICUs in Canada that collect data on baseline characteristics, processes of care, and outcomes from admitted infants. Data are collected using a clinical practice-based, purpose-built, and validated database and transmitted from individual centers to a central coordinating center in Toronto, Canada, for analysis. Data collection at the individual centers is approved by either the local research ethics board or quality improvement committee. Specific approval for this project was obtained from the Mount Sinai Hospital Research Ethics Board. The majority (25/30) of units collect data for all infants; 5 units collect data only for infants with gestational age <33 weeks. A recent internal audit confirmed the internal consistency of the CNN database.[15] We included data for all infants with preterm birth who were admitted from January 1, 2015, to December 31, 2017. This does not represent all preterm births in the country during that period, as several infants born at or after 32 weeks of gestational age are cared for in level 2 NICUs and many infants admitted to level 3 NICUs are retro-transferred to level 2 NICUs for convalescence care after the acute phase.

We created a costing algorithm to generate patient-specific cost estimates for infants admitted to participating NICUs in the CNN. Costs were assigned from the perspective of a provincial public payer. We assigned costs from NICU admission until discharge or death. We sourced patient resource use data from the CNN database. Unit cost inputs were sourced to reflect the NICU at a teaching hospital in the province of Ontario, which is the largest province and cares for 40% of total admissions in the country. We used a single set of unit cost inputs to ensure that variation in cost estimates across centers was due only to differences in resource use (**Table I**; available at www.jpeds.com).[9,18,24,25] Several variables in the CNN database collected information on whether an infant received an intervention but not the frequency. In these cases, expert opinion from study team members was used to inform the frequency an infant would typically receive a particular intervention or testing (eg, head ultrasound scan).

The costing algorithm contained 8 sections, which included the costs of services provided by physicians, nursing, respiratory, transfusions, procedures, imaging, and medications; and other costs. Within the other costs section, we included NICU overhead costs as well as costs associated with social workers, dieticians, and lactation consultants. For each infant, we summated the costs incurred in each of the 8 sections to generate a patient-specific cost estimate. We created a center-adjusted cost estimate that accounts for center-specific differences in cost inputs using the Canadian Institute of Health Information (CIHI) Cost of Standard Hospital Stay indicator.[11] The Cost of Standard Hospital Stay captures the relative cost-efficiency of a center's ability to provide acute inpatient care.[16] Cost of Standard Hospital Stay values were sourced for CNN sites from CIHI's Your Health System interactive tool.[17] The center-adjusted cost estimate was generated by multiplying the patient-specific cost estimate by the relative difference between the admitting center's Cost of Standard Hospital Stay and the average Cost of Standard Hospital Stay at an Ontario teaching hospital. Center-adjusted cost estimates can be used to facilitate the estimation of health system impact of preterm birth. **Figure 1** provides a brief overview of the 8 costing sections and output generated. **Table II** (available at www.jpeds.com)[9,23-25] presents in-depth descriptions of how costs were assigned in each section of the algorithm.

To validate our algorithm, we compared our center-adjusted cost estimates to summaries of hospital finance case cost estimates sourced from Alberta and Ontario. The Ontario Case Costing Initiative (OCCI) and the Alberta Interactive Health Data Application (IHDA) provide summaries of hospital financial cost estimates based on case-mix groups (CMG), which classify patients based on clinical characteristics.[18-20] We compared our algorithm's cost estimates for CMG associated with preterm birth to those sourced from the OCCI and IHDA during the 2016/2017 fiscal year. Both IHDA and OCCI do not capture physician costs. To make our estimates comparable with those from IHDA or OCCI, we excluded the physician cost estimates from our cost algorithm for the purposes of comparison. We also compared our costing algorithm's estimates to previous estimates of Canadian inpatient costs for infants with preterm birth. All costs throughout the study were inflated to 2017 Canadian dollars by adjusting for inflation using the Consumer Price Index for health services.[21]

Statistical Analyses

All data are reported using descriptive statistics such as mean, SD, median, range, skewness, correlation using Spearman rank coefficient, and IQR. Data are presented in individual gestational age in weeks; in gestational age groups (33-36 weeks of gestational age, 29-32 weeks of gestational age, <29 weeks of gestational age); and by survivor status. To

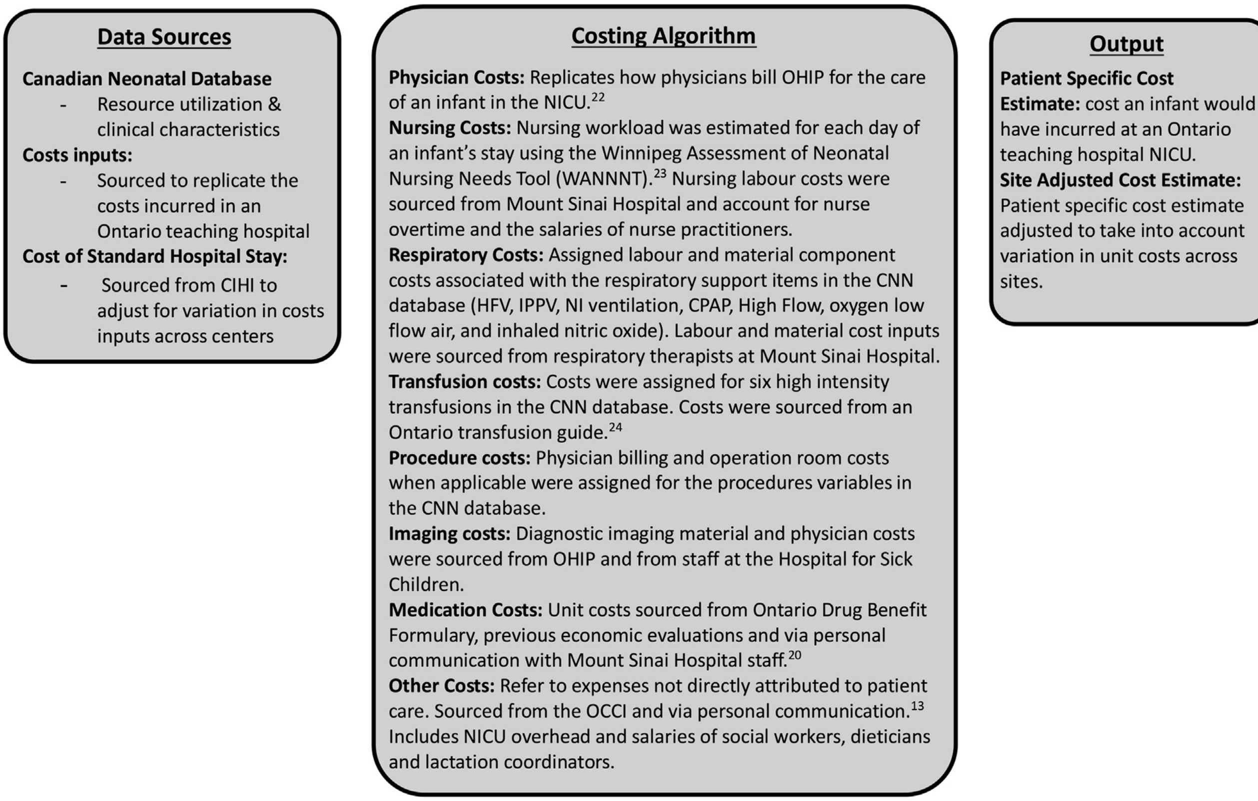

Figure 1. Costing algorithm description. *CPAP*, continuous positive airway pressure; *HFV*, high-frequency ventilation; *IPPV*, intermittent positive-pressure ventilation; *NI*, noninvasive; *OHIP*, Ontario Health Insurance Plan.

assess the effect of retro-transfers on cost estimates, we present results for a subset of infants that were not retro-transferred. CIs were generated using bootstrapping methods. We compared the costing-algorithm's estimates to hospital case costing estimates using mean absolute percentage error.[26] No formal comparison to previous inpatient estimates, sourced from the literature, was conducted. All analyses were conducted using R statistical software.[27]

Results

A total of 47 503 infants were admitted to 30 participating NICUs between 2015 and 2017. Of these, 19 761 infants were excluded because they were born at a gestational age ≥37 weeks; the remaining 27 742 infants were included in this study. The baseline characteristics of the included infants are reported in **Table III**. The median inpatient cost for infants with preterm birth admitted to a tertiary NICU was estimated at $20 184 (95% CI $19 902-20 516), with an IQR of $9739-51 314. **Table IV** provides summary statistics for cost estimates by individual gestational age. Estimates by gestational age groups as well as for infants that were not retro-transferred are provided in **Table V** (available at www.jpeds.com).

Figure 2 (available at www.jpeds.com) represents the distribution of costs by infant LOS in the gestational age groups, suggesting that cost estimates correlate with LOS. Cost estimates were correlated with LOS ($r = 0.97$) and gestational age ($r = -0.65$). Our cost estimates were right-skewed, as 71.3% of patients had lower cost estimates than the mean cost estimate. Estimates of costs for survivors were less skewed compared with those who did not survive (skewness of 2.82 vs 4.83 for nonsurvivors).

The median total cost estimate decreased as gestational age increased for those infants who survived (**Figure 3**; available at www.jpeds.com). This is due to longer LOS and greater cost per day at lower gestational ages. For infants who did not survive, the total cost estimates were relatively similar across different gestational ages. Infants who did not survive had a greater mean cost per day ($3562) compared with infants who survived ($1474). Overall, total costs increased as gestational age decreased, except for infants born at gestational age <24 due to mortality related reductions in LOS. The average cost per day by gestational age grouping and survivor status is provided in **Figure 4** (available at www.jpeds.com).

Table VI (available at www.jpeds.com) provides a summary of the costs for each of the 8 sections of the algorithm by gestational age. All infants incurred some costs in the nursing-, physician-, and imaging-related cost and other cost sections of the algorithm because costs for items in these categories are assigned daily. Nursing and

Table III. Clinical characteristics of the study cohort

Characteristics	Values (N = 27 742)
Gestational age, wk, mean (SD)	31.8 (3.5)
Gestational age <29 wk, n (%)	5509 (20)
Gestational age 29-32 wk, n (%)	8143 (29)
Gestational age 33-36 wk, n (%)	14 094 (51)
Birth weight, g, mean (SD)	1843 (739)
Male, n (%)	15 324 (55)
Cesarean birth, n (%)	15 860 (57)
Inborn, n (%)	22 187 (80)
Multiples, n (%)	7679 (28)
2015 first admission, n (%)	9149 (32)
2016 first admission, n (%)	9246 (34)
2017 first admission, n (%)	9347 (34)
Inborn, n (%)	
Gestational age <37 wk	22 183 (80)
Gestational age <29 wk	4172 (76)
Gestational age 29-32 wk	6636 (81)
Gestational age 33-36 wk	11 375 (81)
Retro-transfer, n (%)	
Gestational age <37 wk	14 307 (52)
Gestational age <29 wk	2878 (52)
Gestational age 29-32 wk	4885 (60)
Gestational age 33-36 wk	6544 (46)
Province, n (%)	
British Columbia	3678 (14)
Alberta	3721 (14)
Saskatchewan	1717 (6)
Manitoba	2033 (8)
Ontario	9427 (34)
Quebec	4452 (16)
New Brunswick	969 (4)
Nova Scotia	1181 (4)
Newfoundland	564 (2)

indirect other costs made up the plurality of total cost estimates. The average cost estimate for each section except the procedure-related costs section decreased as gestational age increased.

Validation

We compared the algorithm's center-adjusted cost estimates for various CMG to estimates sourced from the Alberta IHDA (Figure 5, A) and the OCCI (Figure 5, B). Our algorithm provided similar estimates to those sourced from the Alberta IHDA and also showed the same pattern of lower average cost estimates for less severely ill infants (those with greater CMG). The mean absolute percentage error between cost estimates from our algorithm and the IHDA was 18.4%, with a tendency for the algorithm to provide lower estimates relative to the IHDA, especially for lower gestational age and birthweight groupings. The average absolute difference between cost estimates from our algorithm and the OCCI was 26.5%, with the algorithm providing lower estimates than the OCCI on average. Our costing algorithm provides estimates of costs incurred during an infant's NICU stay which is a subset of the total initial hospitalization estimates provided by the OCCI and IHDA.

We compared the algorithm's cost estimates with those from previous studies of preterm birth (Table VII; available at www.jpeds.com). Johnston et al used per day costing methods and a single estimate of inpatient intensive NICU care.[4] The cost estimates in CIHI's "Too early, too small: A profile of small babies across Canada" were generated using CIHI's relative resource allocation methodology.[28]

Discussion

We developed a comprehensive algorithm to provide easily accessible, gestation-specific cost estimates of inpatient NICU expenditures piggybacked onto a clinical practice-research database. Similar to previous studies, we observed a negative correlation between gestational age and cost estimates.[29] This was due in part to increases in LOS and greater average costs per day. Our cost estimates also show that preterm costs are right-skewed and their distributions vary substantially between survivors and non-survivors.

The cost estimates we generated were comparable with previous studies estimating the inpatient cost of preterm

Table IV. Gestational age–specific estimates of inpatient costs

Gestational ages, n	Median cost (IQR)*	Min*	Max*	Mean cost (SD)*	Mean (SD) LOS, d	Median (IQR) LOS, d	Median cost per day (IQR)*	Mean cost per day (SD)*
22 (46)	87 937 (14 339-249 180)	1563	443 302	139 426 (138 061)	64 (66)	33 (4-128)	2713 (1952-3219)	2742 (904)
23 (363)	121 037 (21 302-219 079)	2518	681 026	135 403 (118 377)	66 (61)	46 (7-118)	2397 (1857-3115)	2723 (1245)
24 (731)	161 385 (37 865-220 126)	2326	751 690	146 473 (106 197)	77 (57)	90 (14-122)	1939 (1721-2559)	2295 (1007)
25 (895)	142 461 (78 230-191 286)	1517	977 179	140 916 (93 514)	77 (48)	82 (38-111)	1805 (1637-2147)	2063 (854)
26 (984)	114 267 (73 157-157 563)	2326	1 084 596	120 026 (79 905)	69 (40)	71 (42-97)	1714 (1539-1931)	1935 (862)
27 (1116)	96 235 (61 370-131 808)	2326	529 595	101 757 (61 788)	62 (36)	63 (36-84)	1635 (1473-1821)	1759 (650)
28 (1373)	76 358 (47 452-103 967)	1260	471 241	82 719 (55 321)	52 (32)	50 (28-70)	1596 (1404-1783)	1685 (577)
29 (1490)	53 633 (26 192-80 179)	1260	452 767	59 428 (44 395)	39 (28)	37 (16-56)	1546 (1342-1779)	1618 (467)
30 (1783)	39 175 (20 147-59 702)	1306	416 307	45 229 (35 330)	32 (24)	29 (12-45)	1430 (1240-1735)	1543 (506)
31 (2237)	29 584 (15 480-46 622)	1630	496 063	35 699 (30 822)	26 (20)	22 (9-37)	1374 (1196-1698)	1501 (501)
32 (2633)	22 933 (12 510-35 477)	1396	428 139	28 613 (28 355)	21 (19)	18 (8-29)	1313 (1157-1621)	1464 (558)
33 (2756)	18 434 (10 654-27 451)	1260	294 015	23 450 (24 265)	18 (16)	15 (7-23)	1254 (1121-1551)	1401 (488)
34 (3801)	13 466 (7592-19 795)	1260	34 628	17 328 (21 291)	13 (13)	11 (5-17)	1207 (1092-1496)	1364 (476)
35 (3770)	10 422 (5524-17 076)	1260	444 329	15 512 (23 041)	11 (14)	8 (4-13)	1220 (1092-1509)	1388 (541)
36 (3768)	8735 (4584-15 393)	1260	315 720	14 423 (21 212)	10 (12)	6 (3-11)	1296 (1116-1602)	1447 (553)

*All costs are shown in 2017 Canadian dollars.

birth and followed a similar ordinal ranking as costs sourced from hospital finance departments. The difference between our cost estimates and those generated by hospital finance departments is due to the algorithm assigning a subset of high-cost inpatient services. The differences in estimates for lower gestational age groupings may have been because infants who were born at younger gestational ages require longer periods of step-down care in inpatient facilities not included in the CNN database.

The greater cost estimates from our algorithm relative to those from Johnston et al may be due to variations in methodology, such as their use of a single per day NICU cost regardless of an infant's gestational age.[4] Our algorithm's cost estimates are very similar to those from CIHI's "Too early, too small: A profile of small babies across Canada," but are easily accessible and allow the identification of patient specific drivers in costs. Previous estimates, may have had fewer cases of retro-transfer relative to those in the CNN database. Infants who were not retro-transferred provide estimates of LOS that are comparable with previous estimates such as those described by Phibbs et al.[5] We were unable to make direct cost comparisons, as the non-retro transfer subgroup may suffer from selection bias compared with infants who were retro-transferred. Differences in costs with previous international studies are likely due in part to differences in cost inputs across jurisdictions.

The mean cost for all preterm births in our study was greater than previous estimates because our estimates only include costs at tertiary sites, which care for a more severe case mix relative to all preterm inpatient admissions. We also estimated costs for a more recent population and included infants born at lower gestational ages than those assessed in previous studies.

The primary strength of our costing algorithm is the ability to generate cost estimates based on detailed resource use for infants. This allows us to conduct a meaningful comparison of costs for infants with similar LOS and clinical characteristics. Our costing estimates are easily accessible to researchers, especially for the transdisciplinary team of researchers currently using the pre-existing CNN infrastructure. In addition, we included all infants admitted to NICU, not only those randomized to intervention as conventionally done along when running clinical trials, providing a pragmatic real-life scenario. The consistent manner in which costs are assigned provides confidence that cost estimates are reflective of the precise resources used by the infant. It also facilitates

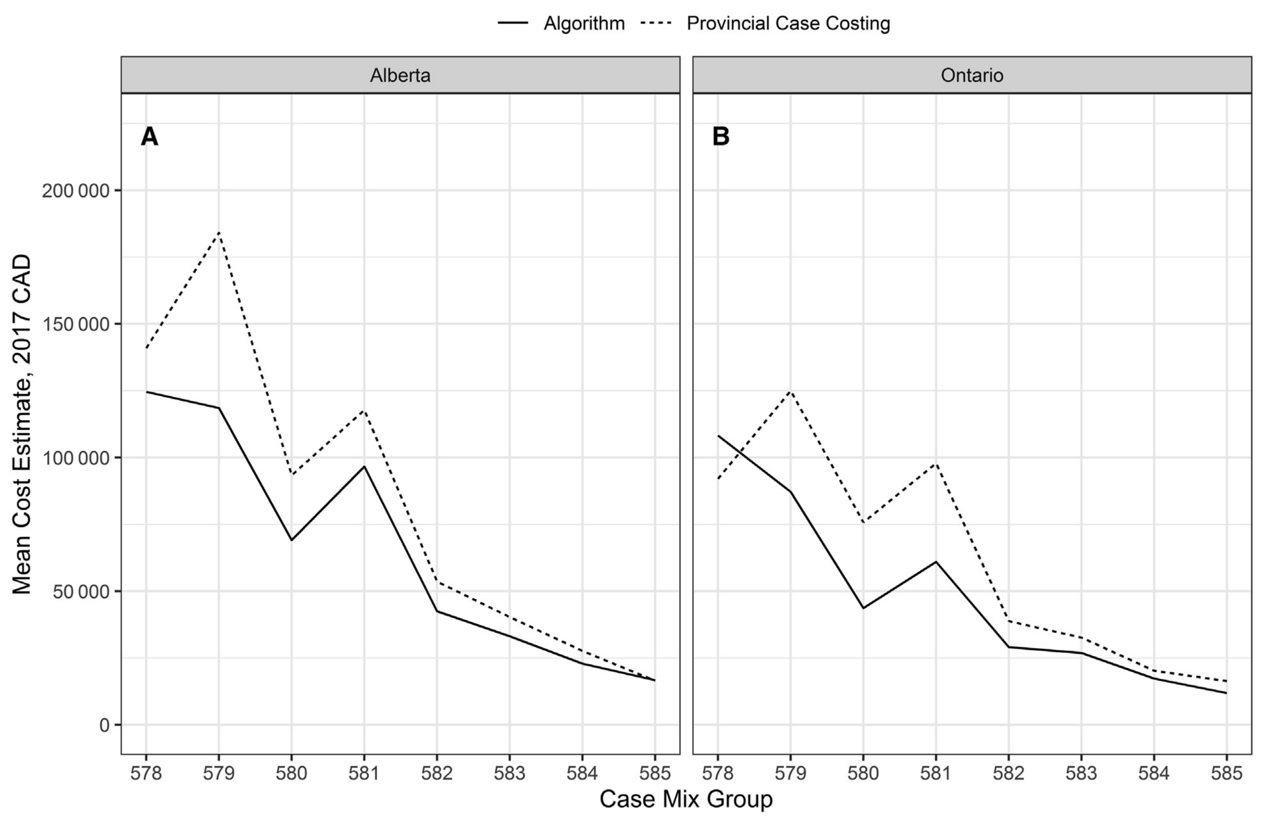

Figure 5. Cost estimates by case-mix group from algorithm compared with Alberta IHDA and Ontario OCCI. CMG = 578: birth weight <750 g; 579: birth weight 750-999 and gestational age <29 weeks; 580: birth weight 750-999 g and gestational age 29+ weeks; 581: birth weight 1000-1499 g and gestational age <29 weeks; 582: birth weight 1000-1499 g and gestational age 29+ weeks; 583: birth weight 1500-1999 g, gestational age <32 weeks; 584: birth weight 1500-1999 g and gestational age 32-34 weeks; and 585: birth weight 1500-1999 g and gestational age 35+ weeks are associated with preterm birth . *CAD*, Canadian dollars.

the comparison of resource use across sites and time by controlling for variation in unit costs. Our algorithm is also able to estimate physician professional fees, which currently are not included in the case costs generated by either OCCI or IHDA. The output from cost-effectiveness analyses and quality improvement projects facilitated by our costing algorithm will provide international decision-makers insight into the effectiveness of various NICU interventions. The descriptions of resource use outlined in this study will provide useful benchmarks for international comparisons of NICU costs.

However, our algorithm has several limitations. First, although the CNN database contains a rich set of clinical information, it does not capture all resource use a patient may incur, eg, for minor surgery. Second, we did not include costs incurred in level II NICU sites that are not participating in the CNN database. Third, when expert opinion was used to determine the frequency of certain items in the CNN database, it was not done at an individual site level. Similarly, we rely on the CSHS to account for variation in input prices across sites, which may not capture the actual site variation in NICU input prices. The costing algorithm is highly customizable and would be able to incorporate site-specific inputs. Fourth, the costing algorithm is not intended to compare total cost across hospitals and comparisons of interventions across hospitals may be hindered by variation in practices being affected by input prices and wages. Lastly, we acknowledge that cost estimates may vary between provinces and even when compared across various countries.

Table II and the CNN algorithm users guide provide detailed descriptions of the assumptions made when assigning costs in each section of the algorithm. An important assumption is that our modifications to the Winnipeg Assessment of Neonatal Nursing Needs Tool resemble actual nursing allocation in the NICU. Nursing staffing decisions are based on a variety of factors, some of which may not be captured by the modified Winnipeg Assessment of Neonatal Nursing Needs Tool.[23]

Future research in this area should focus on extending estimates to cover the costs of preterm birth on infants and their families after discharge from the NICU. We will be using this costing algorithm to identify drivers of costs and resource use across sites and relevant subgroups. Our algorithm can also facilitate analyses of the cost-effectiveness of various novel NICU interventions. We will also focus on sourcing site and province specific inputs to the costing algorithm. The costing algorithm will allow us to compare the costs of similar patients admitted to different NICUs in different provinces to understand variations and optimization opportunities.

We developed a costing algorithm to provide estimates of inpatient costs incurred for infants born prematurely and admitted to Canadian NICUs. We used clinical and resource use data from a clinical practice-based database to generate cost estimates that are easily accessible, comparable across centers, and congruent with estimates of administrative databases. These values can be integrated in other databases and estimates can be generated in real-time. This capability could facilitate assessments of cost-effectiveness for NICU interventions and estimates of the population-level economic impact. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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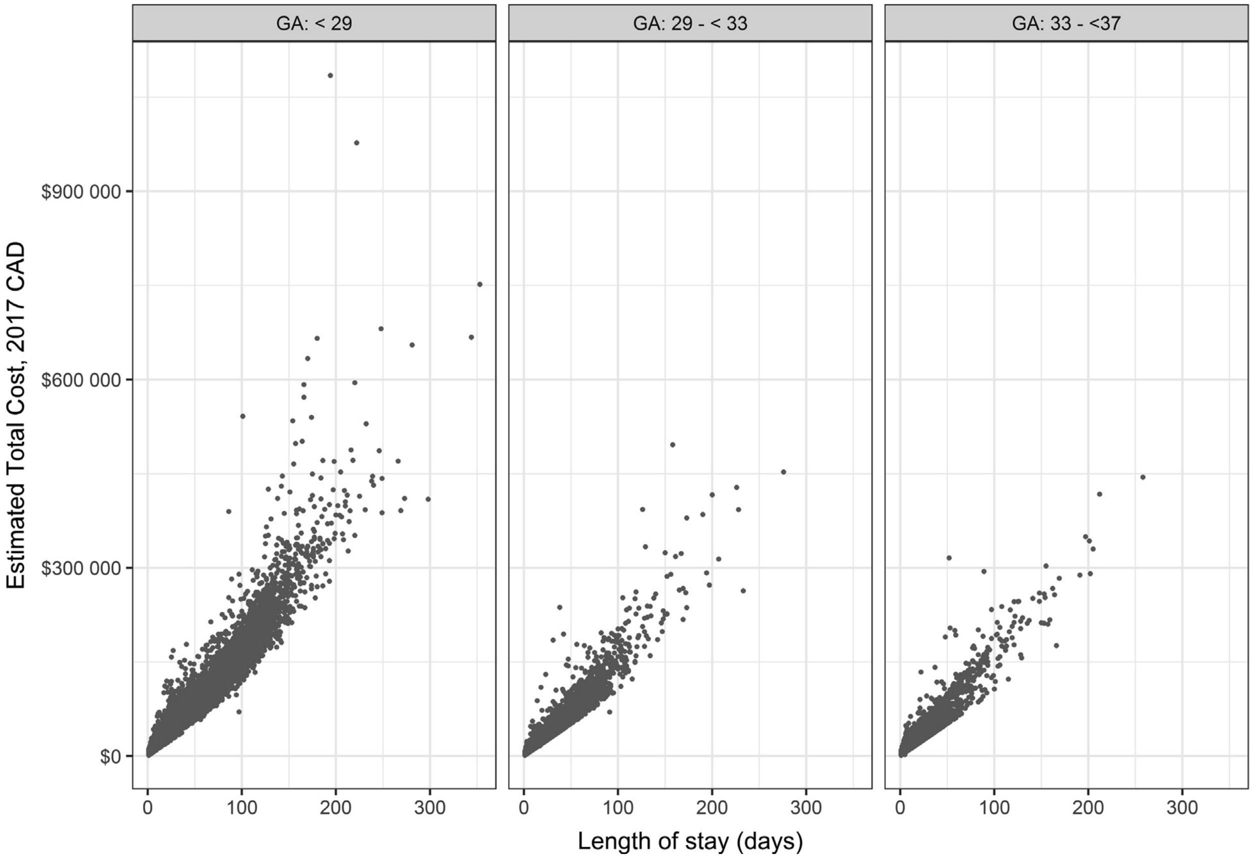

Figure 2. Cost estimates by length of stay and gestational age. *CAD*, Canadian dollars; *GA*, gestational age.

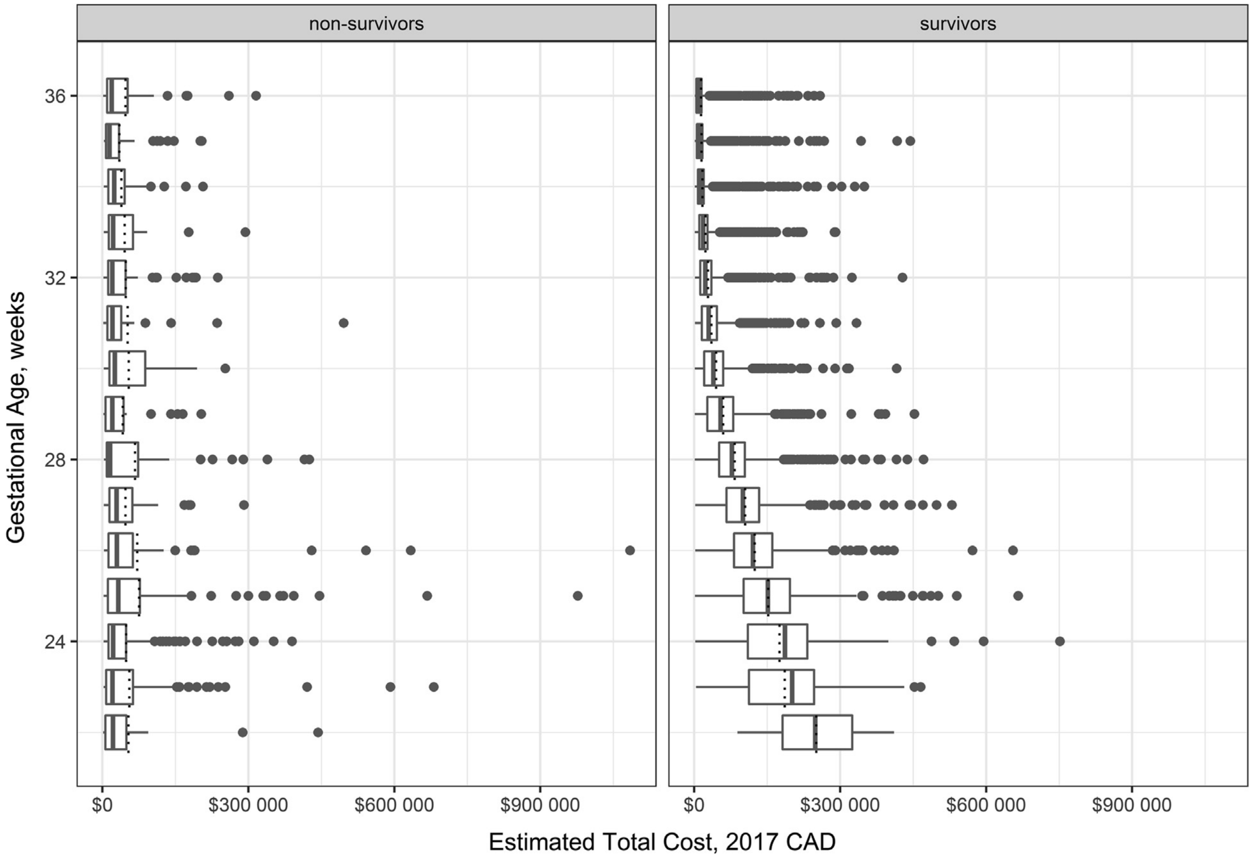

Figure 3. Box plot of cost estimates by gestational age and survivor status. Survivor status indicates whether patients survived to NICU discharge. *Dotted horizontal lines* indicate mean for each gestational age and survival grouping. *Gray horizontal marks* indicate median. *Dots* indicate outliers for each gestational age and survival grouping.

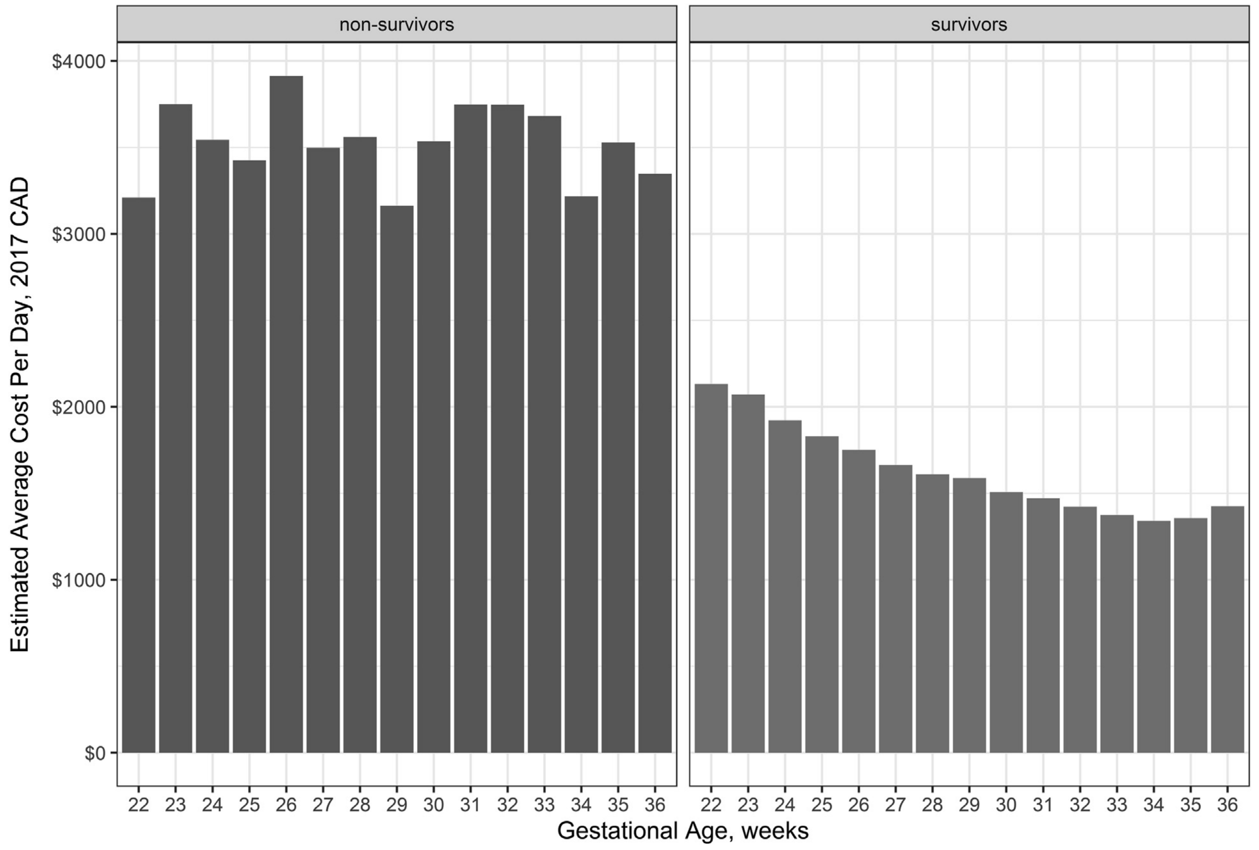

Figure 4. Average cost per day by gestational age and survivor status. Survivor status indicates whether patients survived to NICU discharge.

Table I. Unit costs and sources for costing algorithm

Algorithm section: Costs related to	Unit cost description	Sourced from reference	Value in CAD
Physicians	OHIP Billing Code G600: 1st Day for level A care	22	$358.00
	OHIP Billing Code G604: 1st Day for newborns less than 750 grams or 26 weeks gestational age for level A care	22	$536.95
	OHIP Billing Code G601: Day 2-30 for level A care	22	$198.95
	OHIP Billing Code G602 Day 31 onwards for level A care	22	$89.40
	OHIP Billing Code G610: 1st Day for level B care	22	$245.65
	OHIP Billing Code G611: 2nd Day onwards for level B care	22	$122.80
	OHIP Billing Code G620 1st Day for level C care	22	$155.20
	OHIP Billing Code G621: 2nd Day onwards for level C care	22	$77.60
	OHIP Billing Code: G556: ICU/NICU admission assessment fee (00:00-07:00 admission time)	22	$136.40
Nursing	Adjusted nursing cost per patient hour (includes nurse and nurse practitioner wages and benefits including overtime). Calculated by dividing total NICU nursing labor costs by the total number of hours of patient care. Adjusted so that WANNNT estimates match total number of hours of patient care.	Mount Sinai Hospital: manager, case costing and performance reporting	Not shareable
Respiratory support	Material component costs for HFV schedule of assignment	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Material component costs for IPPV schedule of assignment	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Material component costs for NIVent schedule of assignment	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Material component costs for CPAP schedule of assignment	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Material component costs for high-flow OR oxygen schedule of assignment	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Material component costs for low flow air schedule	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	1 respiratory therapist hourly costs including salary and benefits	Mount Sinai hospital: manager, respiratory therapy	Not shareable
	1 hour inhaled nitric oxide	30	$137.93
Transfusions	IVIG per gram	24	$54.00
	1 unit packed red blood cells	24	$423.00
	Single donor (apheresis) platelets	24	$484.00
	Albumin 5% 500 mL	24	$47.00
	4 units frozen plasma	24	$380.00
	10 units cryoprecipitate	24	$880.00
Procedures	OHIP Billing Code: Z788 Associated with ECMO	22	$366.50
	OHIP Billing Code: S167 Associated with Laparotomy	22	$799.55
	OHIP Billing Code: S166 Associated with Laparotomy	22	$799.55
	OHIP Billing Code: S169 Associated with Laparotomy	22	$1242.90
	OHIP Billing Code: S172 Associated with Laparotomy	22	$2247.70
	OHIP Billing Code: S188 Associated with Laparotomy	22	$2247.70
	OHIP Billing Code: R757 Associated with Thoracotomy	22	$785.90
	OHIP Billing Code: R715 Associated with Thoracotomy	22	$755.80
	OHIP Billing Code: R716 Associated with Thoracotomy	22	$,124.70
	OHIP Billing Code: R717 Associated with Thoracotomy	22	$948.75
	OHIP Billing Code: R718 Associated with Thoracotomy	22	$948.75
	OHIP Billing Code: R768 Associated with Thoracotomy	22	$628.95
	OHIP Billing Code: R771 Associated with Thoracotomy	22	$755.80
	OHIP Billing Code: R907 Associated with Thoracotomy	22	$408.65
	OHIP Billing Code: S346 Associated with Thoracotomy	22	$576.90
	OHIP Billing Code: S347 Associated with Thoracotomy	22	$576.90
	OHIP Billing Code: S103 Associated with Thoracotomy	22	$1153.85
	OHIP Billing Code: N230 Associated with VP shunt	22	$737.00
	OHIP Billing Code: S149 Associated with Ostomy	22	$406.85
	OHIP Billing Code: S157 Associated with Ostomy	22	$406.85
	OHIP Billing Code: S158 Associated with Ostomy	22	$387.40
	OHIP Billing Code: S160 Associated with Ostomy	22	$406.85
	OHIP Billing Code: G275 Associated with Ostomy	22	$205.45
	OHIP Billing Code: Z341 Associated with Chest Tube	22	$69.80
	OHIP Billing Code: R757 Associated with ligation PDA	22	$525.75
	OHIP Billing Code: Z809 Associated with Reservoir drain	22	$370.50
	OHIP Billing Code: R625 Associated with ‘other surgeries’	22	$305.25
	OHIP Billing Code: G297 Associated with ‘other surgeries’	22	$118.70
	OHIP Billing Code: S257 Associated with ‘other surgeries’	22	$275.05
	OHIP Billing Code: R763 Associated with ‘other surgeries’	22	$317.85
	OHIP Billing Code: Z408 Associated with ‘other surgeries’	22	$63.35

(*continued*)

Table I. Continued

Algorithm section: Costs related to	Unit cost description	Sourced from reference	Value in CAD
	OHIP Billing Code: Z360 Associated with 'other surgeries'	22	$474.65
	OHIP Billing Code: M020 Associated with 'other surgeries'	22	$360.45
	OHIP Billing Code: S577 Associated with 'other surgeries'	22	$90.05
	OHIP Billing Code: E908 Associated with 'other surgeries'	22	$304.30
	OHIP Billing Code: E154 Associated with 'other surgeries'	22	$182.75
	OHIP Billing Code: Z515 Associated with 'other surgeries'	22	$68.25
	OHIP Billing Code: J040 Associated with 'other surgeries'	22	$105.30
	OHIP Billing Code: Z527 Associated with 'other surgeries'	22	$82.90
	OHIP Billing Code: E130 Associated with 'other surgeries'	22	$308.30
	OHIP Billing Code: M090 Associated with 'other surgeries'	22	$642.45
	OHIP Billing Code: Z912 Associated with 'other surgeries'	22	$42.15
	OHIP Billing Code: Z629 Associated with 'other surgeries'	22	$153.35
	OHIP Billing Code: R757 Associated with 'other surgeries'	22	$525.75
	OHIP Billing Code: S535 Associated with 'other surgeries'	22	$381.60
	OHIP Billing Code: E940 Associated with 'other surgeries'	22	$105.00
	OHIP Billing Code: Z741 Associated with 'other surgeries'	22	$273.15
	Retrieved procedure cost (average direct cost associated with OR general surgical functional center for cases assigned a CMG associated with preterm birth)	18	$2735.00
Diagnostic imaging	OHIP Billing Code G414 Associated with technical component for full-channel EEG	22	$24.40
	OHIP Billing Code G418 Associated with professional component for full-channel EEG	22	$50.00
	OHIP Billing Code G540 Associated with technical component for CFM or amplitude integrated EEG	22	$9.05
	OHIP Billing Code G545 Associated with professional component for CFM or amplitude integrated EEG	22	$14.70
	OHIP Billing Code X451 Associated with professional component for an MRI	22	$73.35
	MRI - material costs	The Hospital for Sick Children: associate scientist. Neurosciences & Mental Health	Not shareable
	OHIP Billing Code J122 Associated with technical component for an ultrasound	22	$47.20
	OHIP Billing Code J122 Associated with professional component for an ultrasound	22	$23.70
Medications	Beclomethasone - ['QVAR 50 μg/Metered Dose Aero Inh-200 Dose Pk']	25	$33.97
	Betamethasone - [12 mg (1 dose antenatal)]	Mount Sinai Hospital: pharmacist	Not shareable
	Budesonide - ['Pulmicort Nebuamp 0.125 mg/mL Inh Susp']	25	$0.23
	Cosyntropin - [Synacthen Depot 1 mg/mL Inj Susp-1 mL Pk]	25	$680.00
	Dexamethasone - [Apo-Dexamethasone 0.5 mg Tab]	25	$0.08
	Fludrocortisone - [Florinef 0.1 mg Tab]	25	$0.31
	Fluticasone - [Flovent HFA 50 μg/Metered Dose Inh-120 Dose Pk]	25	$24.83
	Hydrocortisone - [injectable form – 100 mg vial]	Mount Sinai Hospital: Pharmacist	Not shareable
	Methylprednisolone - [injectable 40 mg vial]	Mount Sinai Hospital: Pharmacist	Not shareable
	Prednisolone - [Pediapred Oral Liquid 6.7 mg/5 mL O/L]	25	$0.14
	Prednisone - [Apo-Prednisone 5 mg Tab]	25	$0.02
	Midazolam (sedatives) - [midazolam injection 5 mg/mL Inj Sol (with Preservative)]	25	$4.10
	Epinephrine (inotropes) - [adrenalin 30 mg/30 mL Inj Sol-30 mL Pk]	25	$22.23
	Fentanyl (narcotic infusion) - [100 μg/2 mL vial (50 μg/mL)]	25	$1.00
	Caffeine - [Caffeine citrate 20 mg/mL oral suspension (Base 10 mg/mL) – compounded in-house]	Mount Sinai Hospital: pharmacist	Not shareable
	Tobramycin (systemic antibiotics) - [tobramycin 80 mg/2 mL Inj Sol-2 mL Pack or vial]	25	$4.50
	Total parenteral nutrition - [1 bag] labor and drug costs	The Hospital for Sick Children: Pharmacists	Not shareable
	Surfactant - [5 cc vial]	Mount Sinai Hospital: manager, respiratory therapy	Not shareable
	Breast milk - Per ounce	9	$0.14
Other costs	NICU indirect costs per day - (average indirect cost associated with NICU level III care for cases assigned a CMG associated with preterm birth)	18	$404.00
	OR indirect costs (average indirect cost associated with OR general surgery care for cases assigned a CMG associated with preterm birth)	18	$1221.00

(*continued*)

Table I. Continued

Algorithm section: Costs related to	Unit cost description	Sourced from reference	Value in CAD
	Respiratory support indirect costs per day - (average indirect cost associated with respiratory support care for cases assigned a CMG associated with preterm birth)	[18]	$77.20
	Includes salaries of social workers, dieticians, and lactation coordinators	Mount Sinai Hospital	Not shareable

CAD, Canadian dollars; *CMG*, case mix groups; *CPAP*, continuous positive airway pressure; *ECMO*, extracorporeal membrane oxygenation; *EEG*, electroencephalogram; *HFV*, high-frequency ventilation; *ICU*, intensive care unit; *IPPV*, intermittent positive-pressure ventilation; *IVIG*, intravenous immunoglobulin; *MRI*, magnetic resonance imaging; *NIVent*, noninvasive ventilation; *OHIP*, Ontario Health Insurance Plan; *OR*, operating room; *PDA*, patent ductus arteriosus; *VP*, ventriculoperitoneal; *WANNNT*, Winnipeg Assessment of Neonatal Nursing Needs Tool.

Table II. Methods for assigning unit costs

Physician costs for caring for an infant in the NICU
Assigned by replicating how a physician would bill the OHIP. The amount billable for caring for an infant on a given day depends on the type of care required by an infant, their gestational age, and birth weight.[22] We were able to assign the appropriate billing code based on an infant's clinical characteristics and resource use data from the CNN database.
Nursing costs
Each day of a patient's stay was categorized into 1 of 4 nursing ratio categories using a modified version of the WANNNT. The WANNNT was designed to assist in NICU staffing and assigns nurse-to-patient ratios depending on an infant's clinical characteristics and interventions received.[23] We modified the WANNNT to be compatible with the data available in the CNN database. For each day of an infant's stay, the assigned nurse-to-patient ratio was multiplied by a daily nursing labor cost to generate an estimate of nursing labor costs incurred on that day. The daily nursing labor cost was sourced from the Mount Sinai Hospital decision support department and accounted for nurse overtime and the salaries of nurse practitioners. The nursing daily labor costs were calibrated to ensure the algorithm's estimates matched observed nursing workload.
Respiratory costs
HFV, IPPV, NIvent, CPAP, high flow, oxygen, low flow air, and inhaled nitric oxide.
Assigned labor and material component costs for the 7 respiratory support items in the CNN database
With guidance from NICU staff, matched items to their appropriate component costs which included ventilator circuits, transfer sets, prongs, masks and drivers. In addition, each day of respiratory support received by an infant was respiratory therapist labor costs. Respiratory therapist labor costs included salary and benefits and were adjusted to replicate the costs incurred in a NICU with 4 respiratory therapists, each caring for one-fourth of all infants receiving respiratory support in the unit. We also include inhaled nitric oxide costs assigned on per day basis.
Transfusion costs
Packed red blood cells, platelet transfusions, fresh frozen plasma, cryoprecipitate, immunoglobulin, and albumin
Unit costs of administration were sourced from an Ontario transfusion guide while dosing was sourced from clinical experts and NICU medication manuals.[24,31]
Procedure costs
Physician billing and OR costs, when applicable, were assigned to the following procedure variables in the CNN database: extracorporeal membrane oxygenation, laparotomy, thoracotomy, ventriculoperitoneal shunt, ostomy, reservoir drain, other neurosurgery, exchange transfusion, chest tube insertion, and ductal ligation. We matched procedures to their associated OHIP billing codes. An operation room cost was sourced from the OCCI and assigned once if an infant received any procedure in the operating theater.
Imaging costs
MRI, full-channel EEG, amplitude-integrated EEG, cerebral function monitoring, and ultrasonography
Material and physician costs
Sourced from the OHIP Schedule of Benefits and via personal communication with staff from the Department of Diagnostic Imaging at Hospital for Sick Children.[22]
Medication costs
Postnatal steroids, surfactant, total parenteral nutrition, narcotic infusion, breast milk, sedatives, inotropes, caffeine, and antibiotics
We included labor costs associated with preparing total parenteral nutrition. Unit costs were sourced from the Ontario Drug Benefit Formulary, previous economic evaluations and via personal communication with staff from the Department of Pharmacy at Mount Sinai Hospital.[9,25]
Other costs
Expenses associated with the care received by an infant which are not direct patient costs described previously.
WE included indirect costs associated with the NICU, OR, and respiratory therapy. These costs were sourced from the OCCI for CMG associated with preterm birth for the 2016/2017 fiscal year and were assigned based on the type of care received.[18] Also includes salaries of social workers, dieticians, and lactation coordinators sourced from Mount Sinai hospital.

Table V. Gestational age group and retro-transfer subgroup estimates of inpatient expenditures

		Gestational age		
Variables	All infants born preterm <37 weeks	33-36$^{6/7}$ weeks	29-32$^{6/7}$ weeks	<29 weeks
Infants born preterm admitted into a CNN NICU				
Median cost*	20 183	11 871	30 572	100 423
IQR*	9739-51 311	6410-19 800	16 597-51 857	56 800-159 358
Minimum*	1260	1260	1260	1260
Maximum*	1 084 596	444 329	496 063	1 084 596
Mean*	43 310	17 263	39 836	115 085
SD*	58 669	22 583	35 728	85 090
Mean (SD) LOS, d	28 (33)	13 (14)	28 (23)	66 (45)
Median (IQR) LOS, d	15 (7-36)	9 (5-16)	23 (10-40)	63 (30-97)
Median cost per day*	1397	1239	1404	1731
Mean cost per day*	1547	1400	1520	1964
Infants born preterm who were not retro-transferred				
Median cost*	24 763	15 667	46 033	121 254
IQR*	13 289-58 911	9768-22 889	32 864-65 803	70 819-178 883
Minimum*	1563	1732	1994	1563
Maximum*	1 084 596	417 276	496 063	1 084 596
Mean*	49 778	20 130	53 950	129 822
SD*	62 586	21 284	34 284	91 224
Mean (SD) LOS, d	34 (35)	16 (14)	42 (22)	76 (48)
Median (IQR) LOS in days	20 (10-45)	13 (8-19)	38 (28-52)	81 (43-108)
Median cost per day*	1227	1150	1213	1641
Mean cost per day*	1449	1280	1338	2071

*All cost estimates are in 2017 CAD dollars.

Table VI. Costs by algorithm section and gestational age group

Gestational ages	Measure*	Types of cost, $							
		Nursing	Physician	Respiratory	Imaging	Medications	Procedure	Transfusions	Other
22	Median (IQR)	48 546 (6708-128 952)	5950 (1108-15 035)	11 049 (909-22 592)	273 (71-790)	4080 (934-6015)	2388 (846-4432)	0 (0-52)	17 065 (2069-65 969)
	Mean (SD)	69 284 (66 994)	7920 (6913)	19 575 (29 067)	422 (356)	4906 (5107)	3402 (3913)	874 (1860)	33 044 (34 051)
	No. (%) Incurring	46 (100%)	46 (100%)	46 (100%)	46 (100%)	45 (98%)	38 (83%)	12 (26%)	46 (100%)
23	Median (IQR)	61 206 (10 061-114 447)	6936 (1611-13 789)	11 438 (1898-19 318)	339 (142-712)	3864 (1426-6959)	2115 (846-3807)	0 (0-0)	24 822 (3620-60 504)
	Mean (SD)	68 607 (59 691)	8265 (6595)	15 675 (25 007)	437 (335)	5061 (4796)	2798 (3070)	628 (1584)	33 933 (31 262)
	No. (%) Incurring	363 (100%)	363 (100%)	361 (99%)	363 (100%)	361 (99%)	316 (87%)	88 (24%)	363 (100%)
24	Median (IQR)	81 999 (18 446-113 022)	11 227 (2724-14 111)	13 063 (3867-18 784)	577 (142-734)	3855 (1901-6829)	1692 (846-3384)	0 (0-0)	46 464 (7240-62 182)
	Mean (SD)	73 942 (54 129)	9429 (6046)	14 970 (18 945)	500 (311)	5100 (4611)	2501 (3039)	602 (1541)	39 429 (29 100)
	No. (%) Incurring	731 (100%)	731 (100%)	722 (99%)	731 (100%)	726 (99%)	631 (86%)	170 (23%)	731 (100%)
25	Median (IQR)	69 926 (38 946-96 421)	10 289 (6400-12 992)	11 825 (6660-16 293)	532 (314-682)	3772 (2230-6003)	1269 (423-2519)	0 (0-0)	41 887 (19 956-55 990)
	Mean (SD)	70 493 (45 885)	9599 (5023)	14 160 (22 738)	503 (259)	4722 (4081)	1872 (2618)	521 (1463)	39 200 (24 188)
	No. (%) incurring	894 (100%)	894 (100%)	886 (99%)	894 (100%)	884 (99%)	748 (84%)	177 (20%)	894 (100%)
26	Median (IQR)	55 505 (35 550-76 969)	9194 (6594-11 532)	9116 (6010-12 981)	471 (319-603)	2999 (1943-4830)	423 (0-1692)	0 (0-0)	35 726 (21 430-48 780)
	Mean (SD)	58 389 (36 958)	8746 (4121)	12 246 (26 627)	459 (216)	3838 (3181)	1216 (1986)	385 (1267)	34 903 (20 136)
	No. (%) incurring	982 (100%)	982 (100%)	972 (99%)	982 (100%)	969 (99%)	658 (67%)	135 (14%)	982 (100%)
27	Median (IQR)	46 701 (30 016-63 386)	8065 (5723-10 136)	7070 (4409-10 680)	430 (289-537)	2444 (1649-4080)	95 (0-846)	0 (0-0)	30 923 (17 967-41 887)
	Mean (SD)	49 118 (30 092)	7904 (3772)	8793 (10 716)	424 (197)	3326 (2921)	804 (1832)	247 (994)	31 141 (18 268)
	No. (%) incurring	1116 (100%)	1116 (100%)	1101 (99%)	1116 (100%)	1105 (99%)	560 (50%)	105 (9%)	1116 (100%)
28	Median (IQR)	36 556 (22 470-49 971)	6743 (4456-8739)	5512 (2461-7867)	365 (253-466)	2101 (1437-3264)	0 (0-423)	0 (0-0)	24 690 (13 962-34 086)
	Mean (SD)	39 617 (27 048)	6745 (3447)	6665 (9102)	371 (178)	2794 (2544)	498 (1497)	157 (837)	25 871 (16 225)
	No. (%) Incurring	1373 (100%)	1373 (100%)	1350 (98%)	1373 (100%)	1363 (99%)	465 (34%)	101 (7%)	1373 (100%)
29	Median (IQR)	25 153 (12 744-37 730)	4818 (2482-7060)	2452 (1008-5388)	299 (142-395)	1775 (1240-2610)	0 (0-0)	0 (0-0)	17 604 (7606-26 841)
	Mean (SD)	28 276 (21 154)	5091 (3083)	4056 (6263)	299 (162)	2285 (2232)	268 (1316)	152 (789)	19 001 (13 754)
	No. (%) incurring	1490 (100%)	1490 (100%)	1423 (96%)	1490 (100%)	1477 (99%)	296 (20%)	89 (6%)	1490 (100%)
30	Median (IQR)	18 613 (9726-28 507)	3526 (1969-5297)	1103 (551-2287)	258 (142-339)	1414 (902-2076)	0 (0-0)	0 (0-0)	13 720 (5688-21 147)
	Mean (SD)	21 545 (16 931)	3973 (2618)	2332 (4492)	260 (146)	1768 (1921)	152 (674)	131 (753)	15 068 (11 592)
	No. (%) incurring	1783 (100%)	1783 (100%)	1587 (89%)	1783 (100%)	1752 (98%)	231 (13%)	95 (5%)	1783 (100%)
31	Median (IQR)	14 086 (7378-22 470)	2714 (1608-4153)	703 (399-1391)	218 (142-299)	1077 (714-1743)	0 (0-0)	0 (0-0)	10 122 (4423-16 911)
	Mean (SD)	16 983 (14 527)	3185 (2204)	1608 (4993)	226 (127)	1422 (1652)	124 (594)	122 (755)	12 028 (9678)
	No. (%) incurring	2237 (100%)	2237 (100%)	1861 (83%)	2237 (100%)	2178 (97%)	243 (11%)	93 (4%)	2237 (100%)
32	Median (IQR)	11 067 (5869-17 104)	2148 (1333-3210)	428 (0-951)	142 (142-258)	875 (45-1386)	0 (0-0)	0 (0-0)	8076 (3620-13 203)
	Mean (SD)	13 667 (13 890)	2584 (1992)	1125 (4238)	200 (131)	1079 (1640)	89 (584)	113 (678)	9756 (8972)
	No. (%) incurring	2633 (100%)	2633 (100%)	1962 (75%)	2633 (100%)	2432 (92%)	221 (8%)	112 (4%)	2633 (100%)
33	Median (IQR)	8720 (5031-13 247)	1749 (1173-2546)	276 (0-667)	142 (142-223)	538 (9-1064)	0 (0-0)	0 (0-0)	6602 (3521-10 122)
	Mean (SD)	11 221 (11 971)	2159 (1776)	751 (2612)	174 (114)	838 (1474)	74 (588)	138 (763)	8094 (7685)
	No. (%) incurring	2756 (100%)	2756 (100%)	1625 (59%)	2756 (100%)	2241 (81%)	209 (8%)	123 (4%)	2756 (100%)
34	Median (IQR)	6372 (3521-9558)	1326 (871-1880)	0 (0-428)	142 (71-142)	14 (0-755)	0 (0-0)	0 (0-0)	4841 (2509-7482)
	Mean (SD)	8336 (10 687)	1631 (1518)	512 (1949)	145 (99)	581 (1556)	55 (366)	106 (672)	5960 (6346)
	No. (%) incurring	3800 (100%)	3800 (100%)	1687 (44%)	3800 (100%)	2407 (63%)	214 (6%)	148 (4%)	3800 (100%)
35	Median (IQR)	4863 (2515-8049)	1080 (680-1632)	0 (0-428)	142 (71-142)	9 (0-599)	0 (0-0)	0 (0-0)	3598 (1837-6161)
	Mean (SD)	7437 (11 617)	1464 (1588)	591 (2768)	142 (129)	542 (1691)	76 (513)	149 (800)	5112 (6502)
	No. (%) incurring	3769 (100%)	3769 (100%)	1691 (45%)	3769 (100%)	2041 (54%)	253 (7%)	189 (5%)	3769 (100%)
36	Median (IQR)	4025 (2180-7378)	938 (602-1486)	0 (0-428)	142 (71-142)	9 (0-525)	0 (0-0)	0 (0-0)	3081 (1551-5149)
	Mean (SD)	6906 (10 179)	1363 (1491)	659 (4327)	140 (143)	532 (1406)	80 (474)	202 (903)	4542 (5762)
	No. (%) incurring	3768 (100%)	3768 (100%)	1703 (45%)	3768 (100%)	2008 (53%)	313 (8%)	236 (6%)	3768 (100%)

*All costs in CAD.

Table VII. (Comparison of) cost estimates from algorithm and previous reports

Studies	Gestational age group, weeks	Costing algorithm estimate, 2017 CAD*	Validation estimate, 2017 CAD†
Johnston et al. The Economic Burden of Prematurity in Canada[4]	33-36	$18 299	$4331
	28-32	$46 024	$48 755
	<28	$125 899	$61 690
"Too early, too small: A profile of small babies across Canada"[28]	34-36	$15 759	$7435
	32-33	$28 826	$27 865
	28-31	$60 862	$62 368
	<28	$125 899	$119 823

*Estimated cost of inpatient neonatal intensive care unit costs for neonates born preterm.
†Previous estimate of inpatient cost for preterm neonates adjusted for inflation.