Regional variation in cost of neonatal intensive care for extremely preterm infants

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Abstract

Background: Regional variation in cost of neonatal intensive care for extremely preterm infant is not documented. We sought to evaluate regional variation that may lead to benchmarking and cost saving.

Methods: An analysis of a Canadian national costing data from the payor perspective. We included all liveborn 23–28-week preterm infants in 2011–2015. We calculated variation in costs between provinces using non-parametric tests and a generalized linear model to evaluate cost variation after adjustment for gestational age, survival, and length of stay.

Results: We analysed 6932 infant records. The median total cost for all infants was $66,668 (Inter-Quartile Range (IQR): $4920–$125,551). Medians for the regions varied more than two-fold and ranged from $48,144 in Ontario to $122,526 in Saskatchewan. Median cost for infants who survived the first 3 days of life was $91,000 (IQR: $56,500–$188,757). Median daily cost for all infants was $1940 (IQR: $1518–$2619). Regional variation was significant after adjusting for survival more than 3 days, length of stay, gestational age, and year (pseudo-R 2 = 0.9, p < 0.01). Applying the model on the second lowest-cost region to the rest of the regions resulted in a total savings of $71,768,361 (95%CI: $65,527,634–$81,129,451) over the 5-year period ($14,353,672 annually), or over 11% savings for the total program cost of $643,837,303 over the study period.

Conclusion: Costs of neonatal intensive care are high. There is large regional variation that persists after adjustment for length of stay and survival. Our results can be used for benchmarking and as a target for focused cost optimization, savings, and investment in healthcare.

Table of contents summary
A national data analysis evaluated regional differences in cost of neonatal intensive care for preterm infants and the potential cost saving in benchmarking better performers.

What is known on this subject
Neonatal intensive care for extremely premature infants (< 29 weeks) is prolonged and expensive. Regional variation has not been described in this population and can assist in cost reduction by learning from high performers.

What this study adds
There is a wide regional variation in the remarkably high cost of neonatal intensive care that suggests a potential for benchmarking and focused cost savings.

Background
Prematurity affects almost one in ten newborns [1], with 1% of all newborns being extremely preterm (born before 29 weeks, or weighing less than 1500 grams [2, 3]). These fragile infants are often hospitalized for many weeks in a neonatal intensive care unit (NICU), requiring prolonged respiratory support, parenteral nutrition,
and undergo many interventions such as ultrasonograms, surgeries, and blood tests. The complex care for this population involves multiple specialists in a level 3 (high acuity) NICU for several months. The intensive care provided is reflected in its high cost [4–6]. Extremely preterm infants accounted for some of the highest patient expenditures in hospitals [7, 8].

In recent years, support for infants born at 23 and 24 weeks gestational age, previously thought to be unviable, has become common in tertiary NICUs [2, 9, 10]. Indeed, most of these extremely preterm infants are resuscitated, with the majority surviving and being discharged home [2]. This has “pushed the envelope” for neonatal viability. Indeed, in many jurisdictions, it is standard practice to provide life support to newborns born at 23 or more weeks of gestation [9, 10].

Costs for providing care to this most vulnerable group have been uncertain [11–14]. Understanding these costs is important for health policy makers and planners in allocation decisions [15, 16]. As well, it has broad applicability since cost is considered a component of quality within the Institute of Healthcare Improvement’s (IHI) Quadruple Aim of Healthcare Quality [17]. Previous work with cost effectiveness analyses (CEAs) has estimated the cost-effectiveness of NICU care in various situations [18–26]. For example, neonatal resuscitation at 23 weeks had an estimated cost-utility of $15,134 to $22,256 per Quality-Adjusted Life Year (QALY) [19]. Variation in total cost can also affect the cost-effectiveness of the intervention.

As with all high-cost interventions, there is frequently wide variation in overall amounts. In this situation of extreme expense, documenting regional variation can help sites streamline processes and improve performance by learning from high performers. Thus, we sought to evaluate the cost and cost variation of care for these fragile preterm infants.

Methods

Data source
We used data from the Canadian Institute for Health Information (CIHI) database, a Canadian national agency responsible for the collection and analysis of health information. We received information on total cost of the neonatal stay from birth to discharge home or death, subcategorized by gestational age, province, and year. CIHI data is subject to quality checks, with ≥98% correlation with patient charts in multiple studies [27, 28]. Costing components are detailed in CIHI indicator library [29].

We included all newborn deliveries at 23–28 weeks gestational age, between January 1st, 2011 and December 31st, 2015. This represented years when 23-week infants began to be frequently supported in NICUs across Canada. There is usually a long delay in data availability as a result of extensive quality and audit checks precluding more current information.

We did not include Quebec as they do not submit data to CIHI. As well, the Canadian territories (Yukon, Northwest, and Nunavut) and the province of Prince Edward Island were excluded because of small numbers of deliveries and incomplete cost data. We also excluded stillbirths.

We used the province-submitted total cost for each patient for the complete neonatal hospital stay from birth to discharge home or death, including all hospital transfers. This excluded physician compensation. Which is not included in the database. Costing data is collected in the national database, CIHI, from the provinces using a standardized costing method [30]. This reflects the complete cost to the payor—the Ministries of Health—thereby providing a public perspective. Costing followed CIHI’s standardized approach [31–33]. Cost was adjusted to the published Canadian Healthcare Consumer Price Index [34] in 2011 Canadian dollars.

Statistical analysis

Sunnybrook Hospital Research Ethics Board and CIHI approved the study protocol.

We calculated means, 95% confidence intervals [95%CI], medians, interquartile ranges [IQR] and standard deviations (SD) for each patient group. We compared groups using the Mann-Whitney-Wilcoxon test and Kruskal-Wallis test for non-normally distributed data. For variance, we used the Fligner-Killeen test for variance of multiple, non-normally distributed variables. For trends, we calculated the coefficient of determination ($r^2$). We evaluated regional variation by adjusting for gestational age, length of stay, and year, using a multivariate analysis of cost. Length of stay was added to the multivariate analysis to correct for variation in hospitalization practices and discharge criteria variations. We calculated confidence intervals for each coefficient, pseudo-$R^2$ and Akaike Information Criterion (AIC) to assess the model’s robustness. We repeated the model with cost data on infants who survived the first 3 days to accurately capture the cost impact of NICU stay, eliminating those who were too ill to survive or those who may have been withdrawn of life support. We also eliminated extreme outliers by calculating Cook’s D. Analyses were performed in R statistical language v4 and SPSS v21.

Results

We analysed the costs for 6932 extremely preterm infants from 2011 to 2015 (Table 1). There were 5033 infants who survived more than 3 days. The absolute numbers of births for the 23–28-week age group was
### Table 1

Number of extremely premature infants admitted, length of stay, total cost and daily cost by gestational age and province, excludes Canadian provinces of Quebec and Prince Edward Island, and the Canadian territories.

| Province | Gestational Age (Weeks) | n  | %n | Length of Stay (Days) | Cost (CAD) | Daily Cost (CAD) |
|----------|-------------------------|----|----|-----------------------|------------|------------------|
|          |                         |    |    | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR |
| All      | 23                      | 699 | 10.08% | 1 | 1 | 21.4 | 272 | 6 | 950 | 2294 | 743,360 | 23,329 | 633 | 2012 | 2622 | 146,939 | 1101 |
|          | 24                      | 933 | 13.46% | 1 | 21 | 53.7 | 1101 | 103 | 645 | 55,290 | 112,767 | 1,577,166 | 220,515 | 645 | 2379 | 2627.1 | 84,852 | 1083 |
|          | 25                      | 1065 | 15.36% | 1 | 55 | 415 | 94 | 1422 | 97,398 | 123,043 | 816,337 | 201,981 | 722 | 2186 | 2516 | 94,451 | 1116 |
|          | 26                      | 1227 | 17.70% | 1 | 56 | 56.5 | 270 | 74 | 813 | 87,436 | 109,685 | 662,927 | 124,666 | 496 | 1943 | 2191.8 | 62,612 | 1161 |
|          | 27                      | 1366 | 19.71% | 1 | 48 | 49.7 | 395 | 55 | 813 | 72,193 | 90,246 | 813,162 | 112,767.5 | 407 | 1789 | 2196.5 | 71,547 | 1056 |
|          | 28                      | 1642 | 23.69% | 1 | 40 | 41 | 371 | 52 | 804 | 58,778 | 71,611 | 813,162 | 77,111 | 581 | 1653 | 2196.5 | 32,599 | 866 |
|          | < 26                    | 2697 | 38.9% | 1 | 17 | 47.4 | 1011 | 91 | 645 | 44,482 | 99,515.1 | 1,577,166 | 174,862 | 633 | 2179 | 2582 | 146,939 | 1143 |
|          | 23–28                   | 6932 | 1 | 41 | 48 | 1011 | 76 | 645 | 66,668 | 92,879 | 1,577,166 | 120,631 | 407 | 1940 | 2278.8 | 146,939 | 1103 |
| AB       | 23                      | 113 | 8.2% | 1 | 2 | 35.1 | 171 | 72 | 2018 | 9847 | 94,980 | 743,360 | 192,864 | 1769 | 2763 | 4400 | 146,939 | 1513 |
|          | 24                      | 198 | 14.3% | 1 | 35 | 53.5 | 164 | 102 | 2018 | 99,551 | 142,704 | 576,323 | 120,631 | 1125 | 2812 | 3123 | 7446 | 1334 |
|          | 25                      | 235 | 17.0% | 1 | 60 | 57.8 | 234 | 81 | 2018 | 127,449 | 147,628 | 610,540 | 198,446 | 891 | 2618 | 2278.8 | 91,423 | 1107 |
|          | 26                      | 270 | 19.5% | 1 | 48 | 47.1 | 141 | 45 | 2018 | 94,078 | 115,980 | 810,246 | 130,200 | 947 | 2182 | 2223 | 94,451 | 1126 |
|          | 27                      | 349 | 25.2% | 1 | 35 | 37.5 | 122 | 44 | 2018 | 71,281 | 98,460 | 810,246 | 77,111 | 947 | 2182 | 2223 | 71,547 | 1056 |
|          | 28                      | 529 | 38.3% | 1 | 40 | 51.3 | 234 | 97 | 2018 | 102,602 | 134,539 | 743,360 | 129,361 | 891 | 2500 | 2867.8 | 146,939 | 1190 |
|          | < 26                    | 313 | 34.9% | 1 | 29 | 40 | 415 | 100 | 1018 | 63,487 | 108,407 | 816,337 | 198,000 | 947 | 2024 | 2223.2 | 4913 | 953 |
|          | 23–28                   | 896 | 1 | 52 | 55.9 | 415 | 82 | 1018 | 76,735 | 98,118 | 816,337 | 129,361 | 891 | 2500 | 2867.8 | 146,939 | 1165 |
| BC       | 23                      | 76 | 8.5% | 1 | 25 | 182 | 7 | 1018 | 2165 | 52,508 | 582,267 | 29,772 | 1017 | 1780 | 2161 | 4913 | 729 |
|          | 24                      | 113 | 12.6% | 1 | 68 | 386 | 112 | 1537 | 111,392 | 137,693 | 788,913 | 228,354 | 1081 | 2024 | 2223 | 3943 | 936 |
|          | 25                      | 124 | 13.8% | 1 | 48 | 59.2 | 199 | 99 | 1546 | 93,312 | 115,980 | 816,337 | 195,154 | 947 | 2118 | 2224 | 4146 | 868 |
|          | 26                      | 164 | 18.3% | 1 | 70 | 63.2 | 212 | 82 | 1251 | 93,184 | 111,824 | 548,446 | 146,223 | 778 | 1851 | 1910.4 | 3979 | 926 |
|          | 27                      | 182 | 20.3% | 1 | 64 | 61.3 | 395 | 46 | 1527 | 77,792 | 98,460 | 813,162 | 61,571 | 612 | 1546 | 1736.2 | 4025 | 897 |
|          | 28                      | 237 | 26.5% | 1 | 47 | 48.4 | 371 | 49 | 1336 | 64,509 | 74,783 | 599,894 | 55,101 | 582 | 1463 | 1667.5 | 3593 | 747 |
|          | < 26                    | 313 | 34.9% | 1 | 29 | 54.5 | 415 | 100 | 1018 | 63,487 | 112,174 | 565,165 | 239,201 | 893 | 1943 | 2325.9 | 5801 | 1058 |
|          | 23–28                   | 896 | 1 | 52 | 55.9 | 415 | 82 | 1018 | 76,735 | 98,118 | 816,337 | 129,361 | 893 | 1943 | 2325.9 | 5801 | 1058 |
| Province | Gestational Age (Weeks) | n | % | Length of Stay (Days) | Cost (CAD) | Daily Cost (CAD) |
|----------|-------------------------|---|---|----------------------|-----------|-----------------|
|          |                         |   |   | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR |
| NB       | 23–28                   | 352 | 1 | 63 | 61.5 | 114,168.1 | 565,165 | 204,335 | 740 | 1862 | 2244.3 | 50,717 | 1058 |
|          | 23                       | 9  | 6.52% | 1 | 1.8 | 8 | 0 | 1851 | 1608 | 5703 | 35,324 | 1014 | 1515 | 1608 | 2269 | 4415 | 1014 |
|          | 24                       | 16 | 11.59% | 1 | 22.3 | 110 | 16 | 1860 | 29,330 | 49,574 | 237,209 | 34,149 | 1439 | 2348 | 2399 | 3634 | 484 |
|          | 8                        | 5.80% | 2 | 29 | 108 | 72,741 | 202,599 | 104,119 | 1489 | 2289 | 2625 | 4489 | 1472 |
|          | 26                       | 16 | 18.84% | 53 | 101 | 1355 | 223,810 | 54,192 | 1264 | 2264 | 2625 | 4489 | 1472 |
|          | 27                       | 34 | 24.64% | 1 | 57 | 106 | 38 | 1596 | 83,932 | 89,968 | 237,209 | 48,127 | 628 | 1494 | 1914 | 13,178 | 659 |
|          | 28                       | 45 | 32.61% | 57 | 84 | 7203 | 211,229 | 104,119 | 1489 | 2289 | 2625 | 4489 | 1472 |
|          | < 26                     | 33 | 23.9% | 1 | 20.8 | 110 | 16 | 1515 | 12,951 | 43,226 | 237,209 | 42,222 | 1439 | 2257 | 2418 | 4489 | 921 |
| NL       | 23                       | 17 | 14.29% | 1 | 13.5 | 185 | 6 | 1818 | 1693 | 24,678 | 278,211 | 16,828 | 1504 | 1907 | 2382 | 5112 | 843 |
|          | 24                       | 15 | 12.61% | 1 | 138 | 1428 | 236,013 | 278,211 | 16,828 | 1504 | 1907 | 2382 | 5112 | 843 |
|          | 25                       | 19 | 15.97% | 1 | 125 | 109 | 248 | 2758 | 265,420 | 250,195 | 116,870 | 1148 | 2230 | 2272 | 3853 | 810 |
|          | 26                       | 17 | 14.29% | 1 | 88 | 88.8 | 260 | 97 | 1473 | 197,098 | 197,098 | 661,937 | 262,666 | 984 | 2119 | 2125 | 3205 | 1240 |
|          | 27                       | 22 | 18.49% | 81 | 185 | 219,382 | 608,293 | 161,148 | 1131 | 2079 | 2203 | 4072 | 1263 |
|          | 28                       | 29 | 24.37% | 1 | 68 | 121 | 32 | 1669 | 107,445 | 128,643 | 265,420 | 1514 | 2149 | 2272 | 4489 | 921 |
|          | < 26                     | 51 | 42.9% | 1 | 74 | 126 | 110 | 248 | 1473 | 95,475 | 244,145 | 756 | 1494 | 1914 | 13,178 | 659 |
| NS       | 23                       | 17 | 7.5% | 1 | 52.2 | 199 | 95 | 1851 | 1211 | 1778 | 6046 | 70,843 | 464 |
|          | 24                       | 39 | 17.3% | 1 | 106 | 111 | 123 | 1626 | 230,891 | 220,282 | 1,577,166 | 250,440 | 696 | 2384 | 2307 | 4091 | 955 |
|          | 25                       | 27 | 11.9% | 1 | 100 | 95.2 | 66 | 346 | 1503 | 202,290 | 174,881 | 475,022 | 2272 | 4489 | 921 |
|          | 26                       | 35 | 15.5% | 1 | 91.6 | 220 | 33 | 1699 | 107,445 | 128,643 | 265,420 | 1514 | 2149 | 2272 | 4489 | 921 |
|          | 27                       | 49 | 21.7% | 1 | 78 | 78.4 | 193 | 33 | 1599 | 107,445 | 128,643 | 265,420 | 1514 | 2149 | 2272 | 4489 | 921 |
|          | 28                       | 59 | 26.1% | 1 | 66 | 82.5 | 260 | 32 | 1668 | 78,565 | 142,215 | 475,022 | 2272 | 4489 | 921 |
|          | < 26                     | 83 | 36.7% | 1 | 99 | 96.9 | 112 | 66 | 1584 | 175,442 | 182,756 | 249,140 | 696 | 2079 | 2203 | 4072 | 1263 |
| ON       | 23                       | 395 | 11.3% | 1 | 17.9 | 272 | 2 | 950 | 300,504 | 33,727.4 | 523,396 | 7079 | 633 | 1693 | 2120 | 13,449 | 1079 |
|          | 24                       | 464 | 13.3% | 1 | 13 | 44 | 343 | 90 | 645 | 35,399 | 82,091.4 | 636,658 | 144,203 | 645 | 2088 | 2539.8 | 848,525 | 977 |
|          | 25                       | 552 | 15.8% | 1 | 52.5 | 364 | 84 | 1422 | 78,565 | 95,991 | 743,225 | 136,611 | 722 | 1956 | 2277 | 94,451 | 909 |
|          | 26                       | 616 | 17.6% | 1 | 49 | 270 | 70 | 813 | 71,306 | 82,063 | 542,585 | 87,721 | 496 | 1713 | 2007.5 | 626,122 | 922 |
|          | 27                       | 683 | 19.6% | 1 | 38 | 40.8 | 218 | 55 | 813 | 54,472 | 64,745 | 456,931 | 63,708 | 407 | 1582 | 2149.2 | 71,547 | 807 |
|          | 28                       | 781 | 22.4% | 1 | 29 | 33.6 | 165 | 45 | 804 | 40,524 | 50,655.8 | 454,455 | 58,179 | 581 | 1494 | 1737.5 | 325,999 | 632 |
Table 1 Number of extremely premature infants admitted, length of Stay, Total cost and daily cost by gestational age and province, excludes Canadian provinces of Quebec and Prince Edward Island, and the Canadian territories (Continued)

| Province | Gestational Age (Weeks) | n     | %n   | Length of Stay (Days) | Cost (CAD) | Daily Cost (CAD) |
|----------|------------------------|-------|------|-----------------------|------------|-----------------|
|          |                        |       |      | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR | Min. | Median | Mean | Max. | IQR |
| < 26     |                        | 1411  | 40.4%| 1    | 9     | 40.2 | 364 | 75  | 645  | 27,614 | 73,989.9 | 743,222 | 108,605 | 633  | 1957 | 2319 | 94,451 |
| 23–28    |                        | 3491  | 11.0%| 1    | 12    | 12.5 | 118 | 0   | 1876 | 2098   | 31,655    | 302,674 | 1845  | 1876 | 2098 | 2805   |
| SK       | 23                     | 36    | 11.0%| 1    | 1     | 12.5 | 118 | 0   | 1942 | 160,914 | 167,326 | 368,115 | 229,716 | 1004 | 2722 | 2745 | 5434 |
|          | 24                     | 50    | 15.3%| 1    | 12    | 43.1 | 151 | 100 | 2048 | 273,698 | 215,947 | 646,856 | 197,285 | 812  | 2906 | 2902 | 5434   |
|          | 25                     | 57    | 17.4%| 1    | 92    | 78.8 | 214 | 85  | 2048 | 273,698 | 215,947 | 646,856 | 197,285 | 812  | 2906 | 2902 | 5434   |
|          | 26                     | 64    | 19.6%| 1    | 78    | 68.1 | 193 | 88  | 1942 | 160,914 | 167,326 | 368,115 | 229,716 | 1004 | 2722 | 2745 | 5434 |
|          | 27                     | 62    | 19.0%| 1    | 79    | 73   | 136 | 33  | 2699 | 233,511 | 186,384 | 334,666 | 166,386 | 904  | 2736 | 2735 | 5352 |
|          | 28                     | 58    | 17.7%| 1    | 44    | 56.6 | 204 | 102 | 1630 | 116,113 | 161,897 | 331,300 | 162,243 | 1108 | 2673 | 2836 | 13,886 |
| < 26     |                        | 143   | 43.7%| 1    | 18    | 49.6 | 214 | 102 | 1728 | 62,846  | 134,676 | 646,856 | 283,360 | 795  | 2657 | 2893 | 16,285 |
| 23–28    |                        | 327   | 94.7%| 1    | 69    | 59.7 | 214 | 95  | 1630 | 122,526 | 155,698 | 646,856 | 265,411 | 795  | 2695 | 2826 | 16,285 |
relatively constant year to year. The proportion of 23- and 24-week infants related to the total of 28 weeks and under was stable and ranged from 22.3–25.4% during the years of study ($p = 0.5$). Ontario accounted for 50.3% of all infant data, and Alberta, British Columbia, and Ontario together accounted for to 83% of the infants in all ages. For 23-week infants, Ontario accounted for 56% of the cohort. The proportion of 23-week infants was stable during the study years.

**Length of stay**
The median length of stay (LOS) was 41 days (IQR: 1–77). Ontario had the lowest median LOS (29 days, IQR: 1–66) and Nova Scotia had the highest median LOS of 77 days (IQR: 53–106). (Table 1) For infants who survived more than 3 days, the median LOS was 61 days (IQR: 34–90) and ranged from 51 days (IQR: 27–82) in Ontario to 88 days (IQR: 64–126) in Newfoundland.

**Cost**
The median total cost was $66,668 (IQR: $49,200–$125,551). This ranged from $48,144 in Ontario (IQR: $28,07–$90,619) to $122,526 in Saskatchewan (IQR: $82,888–$273,699). The lowest costing for the entire regional cohort was in Ontario, with median cost of $48,144 (IQR: $28,07–$90,619), and the second lowest was in New Brunswick, with median cost of $72,956 (IQR: $33,265–$89,216). Figure 1 demonstrates the regional variation in cost for the entire cohort by gestational age. For infants who survived more than 3 days, the median total cost was $91,137 (IQR: $56,596–$188,757). The median daily cost was $1940 (IQR: $1515–$2619) and ranged from $1661 in New Brunswick (IQR: $1325–$2567) to $2696 in Saskatchewan (IQR: $1958–$3420). The median daily cost for infants who survived more than 3 days was $1805 (IQR: $1392–$2419) and ranged from $1567 in New Brunswick (IQR: $1252–$2325) to $2764 in Saskatchewan (IQR: $1931–$3436). There was a small increase in the median total cost over the years of the study ($r^2 = 0.043, p < 0.001$).

There was wide variation between regions even within similar age groups (Fig. 1). For example, median total costs for 25-week infants in Saskatchewan were as high as $273,698 while in Ontario the median was $78,565,
and in New Brunswick it was $57,356, a 4.8-fold difference. We examined for regional cost variation for infants born at 28-week gestation (Fig. 2), a typically more stable population, with fewer complications of NICU stay. The median costs in Ontario were $40,524, in Manitoba they were $80,829, and in Saskatchewan they were $116,113, a 2.9-fold difference. There was wide regional variation in cost for every gestational age when compared to the entire cohort. The variation in costs of hospitalization between the regions for each age group were significant \( (p < 0.001) \). In a multivariate analysis using a generalized model, fitted to its Gamma distribution, and after elimination of extreme outliers, we demonstrated a persistent regional variation in cost of care after adjustment for length of stay, survival more than 3 days, gestational age, and year of study \( (n = 6890) \). For example, for 28-week infants, the adjusted variation was up to 1.87-fold in cost. This model was robust, demonstrated by a pseudo-\( R^2 = 0.93 \), \( p < 0.001 \).

Using the model to estimate potential cost savings, we applied the lowest cost to the other regions in the cohort. The total cost saving calculated was $87,801,982 (95%CI: $95,783,981–$83,810,983) over the 5 years, representing 13.6% saving of the total budget of $643,837,303 over the same timeframe, or $17,560,396 annually.

For a more achievable benchmark [35], we applied the second-lowest cost region to the other regions in the cohort. This resulted in a total cost savings of $71,768,361 (95%CI: $65,527,634–$81,129,451) over the 5-year period. This represented 11.15% of the total budget of, or $14,353,672 annually.

**Discussion**

We evaluated all extremely premature infants born in Canada from 2011 through 2015. We demonstrated high overall cost for premature infants and their complications. There was up to 8-fold regional variation in cost. The effects persisted even after adjustment for differences in survival, gestational age, length of stay, and year of birth. We found that overall, the median cost of care was $66,668 and for infants who survived more than 3 days median cost was $91,000. This did not change significantly over the study period. We also found that the median length of stay for the entire cohort was 41 days and did not change over time. Moreover, we found that significant savings could be achieved with benchmarking to lower cost regions. In a recent cost evaluation study, Rios et al. [36] reported the cost of tertiary NICU care using a predictive model, estimating the cost of the age group of < 29 week infants at $100,423 (IQR: $56,800–$159,358) and a mean daily cost of $1964. Our study differed in focusing on regional differences and the inclusion of the different age groups and stay at different level of hospital units.

Our study has several strengths. First, we used a reliable, quality-standardized, national-level dataset that includes cost and gestational age. Second, our study
reflects data from time periods when infants born at 23 weeks gestation began to be routinely supported. Third, our findings follow the patient care pathway in the complete hospitalization from birth to discharge home or death. This includes hospital transfers to higher and lower acuity sites, thus providing the cost of care for the infant prolonged stay, at the provincial level, from the payor perspective. Fourth, our cost modelling shows robust, significant variation after adjustment for several variables.

Healthcare spending in Canada is determined regionally, where each province is responsible for most of its own healthcare services [37]. The coverage and costing are influenced by local healthcare policies in the context of local economies, and by differences in clinical practices, as well as medical decisions. Notably, regional differences in healthcare costs were demonstrated previously in other areas of healthcare [18–23] but not in NICU patients.

International reports through the World Health Organization (WHO) and the Organization for Economic Cooperation and Development (OECD) have compared national outcomes and financial performance in healthcare for many years. Regional variation has previously been reported in various healthcare expenditures [38–41] at the national level, both in per capita calculations and in relationship to GDP. National comparisons are fraught with difficulties in comparing like elements. In contrast, regional comparisons can often be more standardized. Indeed, regional cost differences have been demonstrated in cancer care [38], cochlear implants [42], tuberculosis care [43], and long-term care [44]. The latter, for example, demonstrated 5-fold variation in regional cost in the same country [44]. Quantifying this variation within a country is important for the regional policymakers to allocate resources, and for policymakers in other countries to compare and benchmark their results and variation. This variation is sometimes reflective of local policies and costing mechanisms. Our data differ because of the consistency in the costing and outcome methods. We found that the variation persisted regardless of the gestational age. Indeed, the variation in median total costs was striking even after rigorous adjustments. For example, median costs for infants born at 28 weeks gestation, a more stable population in this cohort, varied 2.9-fold between the regions. These differences persisted in the multivariate model, supporting the notion that regional variation contributed significantly to the cost of care. Examining the costs for 28-week infants is highly illustrative because their survival rate is close to 100%, and they would complete their stay to discharge. Indeed, their course is typically less complicated [2, 45] and expected to be less expensive. Therefore, regional practices and their inherent costs are more explanatory of the variation in their cost of care.

There are several potential causes for cost variation. Previously listed [46] drivers of healthcare cost are population complexity, physician billing, inflation, pharmaceuticals, materials, remunerations and administrative costs. Some have noted [35] that acuity and complexity can drive these cost differences. However, less is known about cost differences between jurisdictions when comparing the same condition with similar acuity. While there are demonstrable variations in specific cost components between regions, we currently cannot determine the specific causes, or subcategories, of the differences in our data [47]. This is well demonstrated in the fact that one province (SK) had higher median cost while having another had a relatively shorter length of stay (NFL). The differences may stem from local hospital costs, medication and procedural practices, and expensive interventions such as ventilation and parenteral nutrition. The variation in these practices are reflected in national level reports [2] but have not been translated to costs.

Our study has several limitations. First, we excluded some jurisdictions from the analysis due to availability of or quality of data. Nevertheless, we include over 70% of the national population. Additional data may only add to the observed variation. Second, as in many studies, our findings rely on coding accuracy and consistency of administrative data. However, the standardized approach to cost calculation that has been applied to acute care hospital across Canada in CIHI methodologies [27, 28] was demonstrated to be highly accurate. This enables the calculation of accumulated cost of hospital stay of a preterm infant from birth, through hospital units or transfers, to discharge or demise. Third, our analyses considered only hospital costs from the birth to discharge home or death. It did not include health services in later life that many of these infants, who suffer from complications related to preterm birth, will require. While this may lead to an underestimate of costs, our focus was on the costing of entire hospital stay, thereby better reflecting the local policies. Fourth, the cost of care did not adjust for clinical outcomes or adverse events. These important aspects need to be included within an in-depth comparison of programs, which should be considered in future work. Fifth, we were unable to adjust for clinical practice differences (such as particular procedures, ventilation modes, staffing, or nutrition). This could assist in calculation of cost avoidance due to local systemic contributors to costing. Confidentiality agreements or data limitations prevented us from performing this type of analysis. Sixth, physician compensations are not included in this analysis since this is not reported to CIHI as part of the cost of care calculation. Although this puts an underestimation to the societal cost, this emphasizes even more the high cost in preterm care. Finally, we report cost of hospital stay.
without ethical consideration regarding quality of life, and without performing a formal cost-effectiveness or a cost-utility analysis. Indeed, ethics in the costs of medical care have been considered in other policy relevant work [14, 18–23, 48–50].

Conclusions
We found extensive regional cost variation for extremely preterm infants. The findings persisted after adjusting for several predictive factors. These results demonstrate that there is much room for cost reduction and standardization in support of cost reduction, one of the quadruple aims of healthcare quality improvement [51]. Reducing large cost variation through standardization can lead to cost savings [52, 53]. Our findings may be useful to policymakers for planning and resource allocation decisions. Moreover, small cost differences can be amplified over large patient cohorts. In our study, even a small cost variation of 3% translated to large total differences of $2786 per patient and $19,315,117 in total. These were further magnified when potentially achievable amounts for lower cost regions were applied broadly and over several years [54]. Decreasing such variation can help centres and regions decrease their cost while maintaining excellent care. In this, there will allow for channeling the savings towards further investments and innovations to improve the care of these fragile infants.

Abbreviations
AB: Alberta; BC: British Columbia; MB: Manitoba; NB: New Brunswick; NL: Newfoundland and Labrador; ON: Ontario; SK: Saskatchewan; CAD: Canadian Dollar; GA: Gestational age; NICU: Neonatal intensive care unit

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Authors’ contributions
AR conceptualized and designed the study, collected the data, performed the analyses, drafted, and revised the manuscript. SU critically reviewed the design, reviewed the data analysis, reviewed the draft, and revised the manuscript. DU critically reviewed the design, revised the analysis, reviewed the draft, and revised the manuscript. CB conceptualized the design, collected the data, reviewed the analysis, critically reviewed, and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Availability of data and materials
The datasets generated and/or analysed during the current study are not publicly available due to data sharing agreements but are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
Study was approved by Sunnybrook Health Sciences Centre REB, #485–2016 and Canadian Institute for Health Information approved and released the data.

Consent for publication
Not Applicable.

Competing interests
The authors have no conflicts of interest relevant to this article to disclose.

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