# Infants, children, youth and young adults with a serious illness in British Columbia: a population-based analysis using linked administrative data

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| Keywords: | Pediatrics, Palliative medicine, Health services research |
| More Detailed Keywords: | Life-threatening conditions, Life-limiting conditions, Serious illnesses |
| Abstract: | Background<br>Infants, children, youth and young adults (ICYA) with serious illnesses follow unpredictable trajectories living with complex healthcare needs. Pediatric palliative care (PPC) encompasses more than the final days of life, attempting to improve quality of life among ICYA with serious illnesses, sometimes over many years. We describe the population aged 0-25 with serious illnesses in British Columbia (BC) and identify factors associated with clinical instability, to inform PPC program planning.<br><br>Methods<br>Population-based analysis using linked administrative health data for years 2012-13 – 2016-17. We apply a validated coding framework to estimate the number of BC residents aged 0-25 years with serious illnesses and identify 5 clinical stages. We describe demographic characteristics, estimate prevalence and model risk of instability, defined as experiencing urgent hospitalizations, ICU visits or death.<br><br>Results<br>Approximately 2,500 ICYA were diagnosed with serious illnesses during a hospitalization each year; ~50% were infants, and ~60% presented perinatal or congenital diagnoses. The most severely ill patients constitute 28% of this population. Infants had the highest risk of instability (OR 5.25, 95% CI 4.63 to 5.95). Compared to oncology patients, perinatal and congenital patients had lower risk; ICYA with other conditions had higher risk, except for metabolic patients whose risk was similar to the reference group.<br><br>Interpretation |

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| | The size of the population of ICYA with serious illnesses in BC is substantially larger than that currently receiving PPC. Future planning of these services needs to consider expanding its reach, focusing particularly on infants and other subpopulations with high risk of instability. |
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**The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.**

| | Item No. | STROBE items | Location in manuscript where items are reported | RECORD items | Location in manuscript where items are reported |
|---|---|---|---|---|---|
| **Title and abstract** | | | | | |
| | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found | (a) page 1<br><br>(b) page 2 | RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.<br><br>RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.<br><br>RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract. | 1.1: page 2 (name of databases on page 4 under *Data Sources*)<br><br>1.2: page 2<br><br>1.3: page 2 |
| **Introduction** | | | | | |
| Background rationale | 2 | Explain the scientific background and rationale for the investigation being reported | page 3 | | |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | page 3 | | |
| **Methods** | | | | | |
| Study Design | 4 | Present key elements of study design early in the paper | page 3 | | |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | page 3 | | |

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| Participants | 6 | *(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants<br><br>*(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study* - For matched studies, give matching criteria and the number of controls per case | (a) page 4 | RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.<br><br>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided.<br><br>RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage. | 6.1: page 4<br><br>6.2: citation 16<br><br>6.3: citation 26 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | pages 4, 5 and 6 | RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided. | Appendix 1 |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement).<br>Describe comparability of assessment methods if there is more than one group | pages 4, 5 and 6 | | |

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| Bias | 9 | Describe any efforts to address potential sources of bias | page 5 | | |
| Study size | 10 | Explain how the study size was arrived at | page 4 | | |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | pages 4, 5 and 6 | | |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) *Cohort study* - If applicable, explain how loss to follow-up was addressed<br>*Case-control study* - If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy<br>(e) Describe any sensitivity analyses | (a) pages 5 and 6<br>(c) page 6 | | |
| Data access and cleaning methods | | .. | | RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. | page 3 and 4 |

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| | | | | RECORD 12.2: Authors should provide information on the data cleaning methods used in the study. | N/A |
| Linkage | | .. | | RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided. | page 3 |
| **Results** | | | | | |
| Participants | 13 | (a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)<br>(b) Give reasons for non-participation at each stage.<br>(c) Consider use of a flow diagram | (a) page 9 (table 1) | RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.*, study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram. | page 4 |
| Descriptive data | 14 | (a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate the number of participants with missing data for each variable of interest<br>(c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount) | (a) page 9 (table 1)<br>(b) page 6 | | |
| Outcome data | 15 | *Cohort study* - Report numbers of outcome events or summary measures over time<br>*Case-control study* - Report numbers in each exposure | page 7 and page 10 (table 4) | | |

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| | | category, or summary measures of exposure<br>*Cross-sectional study* - Report numbers of outcome events or summary measures | | | |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | (a) page 10 (table 4)<br>(b) page 10 (table 4) | | |
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | N/A | | |
| **Discussion** | | | | | |
| Key results | 18 | Summarise key results with reference to study objectives | page 7 | | |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | page 8 | RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported. | page 8 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, | page 7 | | |

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| | | limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | | | |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | page 7 | | |
| **Other Information** | | | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | page 11 | | |
| Accessibility of protocol, raw data, and programming code | | .. | | RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code. | page 11 |

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

# Infants, children, youth and young adults with a serious illness in British Columbia: a population-based analysis using linked administrative data

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**Competing interests:** The authors report no competing interests.

**Abstract** (249 words)

***Background:*** Infants, children, youth and young adults (ICYA) with serious illnesses follow unpredictable trajectories living with complex healthcare needs. Pediatric palliative care (PPC) encompasses more than the final days of life, attempting to improve quality of life among ICYA with serious illnesses, sometimes over many years. We describe the population aged 0-25 with serious illnesses in British Columbia (BC) and identify factors associated with clinical instability, to inform PPC program planning.

***Methods:*** Population-based analysis using linked administrative health data for years 2012-13 – 2016-17. We apply a validated coding framework to estimate the number of BC residents aged 0-25 years with serious illnesses and identify 5 clinical stages. We describe demographic characteristics, estimate prevalence and model risk of instability, defined as experiencing urgent hospitalizations, ICU visits or death.

***Results:*** Approximately 2,500 ICYA were diagnosed with serious illnesses during a hospitalization each year; ~50% were infants, and ~60% presented perinatal or congenital diagnoses. The most severely ill patients constitute 28% of this population. Infants had the highest risk of instability (OR 5.25, 95% CI 4.63 to 5.95). Compared to oncology patients, perinatal and congenital patients had lower risk; ICYA with other conditions had higher risk, except for metabolic patients whose risk was similar to the reference group.

***Interpretation:*** The size of the population of ICYA with serious illnesses in BC is substantially larger than that currently receiving PPC. Future planning of these services needs to consider expanding its reach, focusing particularly on infants and other subpopulations with high risk of instability.

## Introduction

Pediatric Palliative Care (PPC) works to improve quality of life among Infants, Children, Youth and Young Adults (ICYA) with serious illnesses through the prevention and relief of suffering. PPC identifies and treats physical and psychosocial symptoms and supports families, including provision of bereavement support.[1] PPC encompasses more than the final days of life, providing complex care for ICYA and their families for as long as necessary, in many cases over years.[2–8] Identifying all ICYA who would benefit from PPC input earlier in their journey is beneficial to both them and their families, and is needed to inform health and social services planning.[9,10]

There is an ongoing discussion about the ideal term to describe the health conditions relevant to PPC including life-limiting conditions,[11] life-threatening conditions,[12] and serious illnesses. We will use the term *serious illnesses* for health conditions acquired before birth or during childhood, that put ICYA at risk of dying before adulthood, and should therefore be assessed for PPC services.

While there have been attempts to estimate the size of the service population,[13] the number of ICYA with serious illnesses in Canada is unknown. Previous international research has provided estimates of the prevalence of children eligible for PPC ranging from 3.75 to 95.7 per 10,000.[14,15] We utilize an innovative framework developed and applied in the United Kingdom (UK),[14,16] with the objective of providing an accurate estimate of the number of ICYA living with serious illnesses in British Columbia (BC). Our goals are to describe the population demographics, their clinical stages using measures of healthcare use, and their risk of instability, defined as experiencing urgent hospitalizations, Intensive Care Unit (ICU) stays or death.

## Methods

### Study Design

We used population-based individual-level linked administrative health data to describe the population of ICYA living with serious illnesses in BC over repeated annual cross-sections (2012-13 to 2016-17), and a panel model to explore factors associated with risk of instability over this period.

### Setting

BC and Yukon are served by Canuck Place Children's Hospice, a PPC program with provincial scope. Canuck Place provides respite, specialist symptom management, end-of-life care and bereavement in two hospice locations, in-hospital consultation and in families' homes.[17] Pediatric patients with serious illnesses in BC can also access Canuck Place care through BC Children's Hospital inpatient and outpatient services,[18] and through regional hospitals.[19]

### Data Sources

Population Data BC provided linked, de-identified, administrative data for this study. We accessed and analyzed the data through Population Data BC's Secure Research Environment, using SAS Statistical Software v9.4 (SAS Institute).

We obtained data from the Discharge Abstracts Database (DAD),[20] the National Ambulatory Care Reporting System (NACRS) dataset,[21] the MSP payment file,[22] the Vital Statistics Deaths dataset,[23] the PharmaNet data set,[24] and Population Data BC's Consolidation File.[25] Information on data preparation and linkage is described elsewhere.[26]

Study Population

We used a validated coding framework developed by Fraser et al[14,16] to identify individuals with serious illnesses of interest in a pediatric population. The framework is based on codes from the International Classification of Diseases, 10th Revision (ICD-10) applied to ICYA using hospice-palliative care in the UK.[16]

The study population is defined as ICYA aged 0-25 years, living in BC and with a serious illness diagnosis (by the coding framework) during an inpatient hospital visit between April 1, 2012 and March 31, 2017. For a given year, we consider as living in BC individuals registered for public health insurance, with prescriptions (PharmaNet records) or receiving services provided by fee-for-service practitioners (MSP payment file records) in BC.

For reporting the size and characteristics of this population over time, we analyzed individuals diagnosed with a serious illness during an inpatient hospital visit in a given year. For calculating prevalence and modeling the risk of instability we considered all ICYA diagnosed with a serious illness during an inpatient hospital visit in a 5-year timeframe, between April 1, 2012 and March 31, 2017.

Variables

*Demographics*

We obtained patients' date of birth, sex and socioeconomic status (neighborhood income quintile) from Population Data BC's Consolidation File. Sex is the documented sex; it is not possible to distinguish between assigned sex, legal sex and gender based on this information. For each year, we calculated individuals' age on the last day of the fiscal year, or the date of death when applicable. We grouped age according to clinically relevant stages for pediatric populations.

We obtained individuals' date of death from the Vital Statistics Deaths dataset, and from the DAD and the NACRS datasets as supplementary sources.

*Serious Illnesses*

We extracted diagnoses from the DAD. The coding framework clusters conditions into 11 coding groups. Every year we assigned patients to a primary diagnostic group; the most frequent. We assigned patients to "*multiple*" when they had more than one modal diagnostic group during a given year. Additionally, we found that many pediatric diagnoses of relevance are assigned to the ICD-10 *congenital* group rather than to an organ system. For example, most pediatric heart defects are assigned to *congenital* (Q00-99) rather than *circulatory* (I00-99). Therefore, we combined several coding groups that either were somewhat misleading as to the underlying

condition or had small numbers. Seven coding groups (haematology, genitourinary, respiratory, gastrointestinal, circulatory, other, and multiple) were thus merged into a new taxonomic unit called *otherwise specified* (Appendix 1). For the model, if a person did not have a primary diagnostic category in a given year, we assigned the taxonomic unit from the closest preceding year if applicable, or the closest subsequent year otherwise.

Initially, we captured a large group of neonates using the described methodology, more than we report here. Additional exploration found that many were assigned ICD-10 code P28.5, *Respiratory failure of newborn*; however, in most cases where this was the only code assigned, or when it was combined with six other specific ICD-10 codes (Appendix 2), there were no further Emergency Department (ED) visits or urgent hospitalizations, suggesting that their health improved. We decided to remove these patients from the study. This process helped to increase the accuracy of the selecting approach.

*Clinical Stages*

In 2017, Jarvis et al[14], using UK data, defined four clinical stages (stable, unstable, deteriorating and dying) based on healthcare utilization. We adapted this approach, distinguishing between ED visits and urgent/unplanned admissions, thereby identifying five clinical stages for this study:

- Stable – When a patient was not in any of the other stages at any point during a given year.
- Unstable-ED – When a patient had ED visits during a given year, not leading to hospitalization.
- Unstable-Hosp – When a patient had urgent/unplanned inpatient admissions during a given year, not including ICU.
- Deteriorating – When a patient had unplanned ICU admissions during a given year.
- Died – When a death date was recorded.

We obtained data on hospitalizations and ICU admissions from the DAD, and ED visits from the NACRS table as the primary source, and from the MSP payment file and the DAD as supplementary sources. For each patient, the most severe clinical stage was recorded every year.

Statistical analysis

*Descriptive statistics*

We generated a frequency table characterizing the population of ICYA with serious illnesses, reporting the number and percentage for each demographic variable by study year.

*Prevalence and Rate of Hospitalizations*

We calculated the one-year period prevalence of ICYA with serious illnesses per 10,000 people for the fiscal year 2016-17. Additionally, we calculated the yearly rate of hospitalizations. Population at risk was determined from census-derived mid-year estimates.[27,28]

*Modelling*

We modeled the risk of instability for this population with a multiple logistic regression with random intercept. For the model, we created a new variable collapsing Stable and Unstable-ED in one group, and Unstable-Hosp, Deteriorating and Died in another group. We use this new variable as the dependent variable. Sex, age group, socioeconomic status and taxonomic unit were included as predictors.

Adolescents transition from the Canuck Place program after their 19th birthday. We therefore chose the 20 to 25 age group as the reference category for the model in order to evaluate how eligible children for the Canuck Place program compare to them. We chose Oncology as the reference category for taxonomic unit because the epidemiology is well known and the diagnoses are certain. Other serious illnesses for this population can be more difficult to define and diagnose, and might overlap with other conditions.

For each year, patients were excluded from the models if they had missing data for any variable.

Ethics Approval

This study was approved by the UBC Research Ethics Board. UBC number H18-00645.

**Results**

Demographics

The number of ICYA with a serious illness diagnosis during an inpatient hospital visit remained stable over time at around 2,500 patients each year. Neonates and infants accounted for over half of this population. The number of newly-diagnosed patients greatly decreased after one year of age, and continued to decline gradually until adolescence, when it increased. For people aged 20 years and older, the rise might be partly due to new onset adulthood conditions rather than exacerbation of childhood conditions that led to a hospitalization. A lower percentage of individuals in the study live in highest income quintile neighbourhoods (between 13.9% and 17.6%), than in the general population (20%). Around 60% of the patients had perinatal or congenital diagnoses each year (Table 1).

We did not find missing data for age, sex or taxonomic unit. Less than 1.8% of ICYA had missing data for socioeconomic status in any year.

Clinical Stages

We consider individuals in stages Unstable-Hosp, Deteriorating and Died as the most severely ill patients. They constituted 28% of this population on average, and are those in greater need for palliative care (Table 2).

Prevalence and Rate of Hospitalizations

In 2016-17, there were 9,940 ICYA living with a serious illness in BC based on a hospital diagnosis made between April 1, 2012 and March 31, 2017. This results in a prevalence in 2016-

17 of 73.1 per 10,000 population. Reflecting the different acuity levels and service needs, 2,457 of these ICYA had at least one hospital visit during that year. Thus, while 25% of this population requires hospitalizations each year, the rest might still benefit from PPC in the community.

The rate of hospitalizations is higher in infants than in children and young adults (Table 3). As an exercise, we recalculated this rate without the infant group, many of whom may be cared for entirely within the Neonatal Intensive Care environment. Excluding the infants, the rate of hospitalizations for ages 1-25 was 9.1 per 10,000 on average.

Modelling

Compared to people aged 20-25, we find an increased risk of instability in infants, a lower risk among those aged 1-14, and no significantly different risk in those aged 15-19.

For taxonomic unit, perinatal and congenital diagnoses had lower risk, neurology and the otherwise specified category indicated a higher risk of instability, and metabolic diagnoses did not show a significantly different risk to that of the reference group, oncology.

Sex and socio-economic status were not significant predictors of instability.

**Interpretation**

This study presents the number of ICYA in BC living with serious illness as described by a previously validated, innovative coding system. This coding system is distinct based on its focus on PPC rather than the broader group of children with medical complexity, and by the fact that the clinician-derived ICD codes were validated against a PPC program population[16]. This is the first application of this system outside the UK.

Roughly 2,500 ICYA living with serious illness in BC have inpatient hospital visits every year. On average, the most severely ill patients account for 28% of this population, and the yearly prevalence of ICYA with serious illnesses was around 73 per 10,000 people. Infants and patients with a neurological or otherwise specified diagnosis were at the highest risk of instability. Infants were the largest group, and also the more complex to analyze. Understanding the clinical trajectory of infants with serious illnesses presents challenges as they may be very ill in the neonatal period but then go on to have good outcomes. Results likely apply to other Canadian provinces which share similar population and health system characteristics.

A Canuck Place report showed that 579 ICYA were on program at some point between FY 2016-17 and 2019-20,[29] indicating that while many of these at-risk individuals are being cared for, there are others still in need of these services. These results will be useful in guiding the future provision of PPC in BC, for instance, by helping to define the target group who will receive services, based on clinical stages.

The work presented here focused on ICYA whose medical condition needed hospital inpatient care during a given year. Outpatient data that might describe ICYA who are less fragile, including Medical Services Plan (MSP) reporting, is not considered to be uniform or reliable

enough for our project. For future research it is important to expand the scope of this work to follow ICYA with serious illnesses over time to have a wider perspective of their health trajectories, and also to improve the ability to track the population through outpatient services when there is no hospitalization, thus developing a better understanding of the Stable component of the cohort.

Limitations

Limited capture of secondary diagnoses ("Type 3" diagnoses in CIHI guidelines) may mean that findings represent an underestimation of the number of ICYA with serious illnesses in this analysis, but this does not impact the conclusion that current palliative care capacity is not adequate to meet total potential need. Additionally, there might be ICYA living with health conditions of interest who were not captured in this study because they did not have an inpatient admission related to their serious illness in any of the study years. The coding framework developed by Fraser and colleagues has been shown to capture more than 700 diagnoses of relevance.[14,16] There may be additional conditions not identified, although it is likely a small number. Furthermore, our work focuses on the population *at risk* of dying young from a medical condition; it does not describe the total mortality risk profile for ICYA that includes mental health conditions leading to suicide, risky behaviour related deaths, or accidents. Individuals with these specified conditions may receive care from palliative care programs either right at end of life, for example in the ICU, or their families may access bereavement through a PPC program. This study intended to be strictly aligned with one previously undertaken by Jarvis, Fraser and colleagues in Scotland.[14] However, we uncovered differences in the underlying data structures and in the local context that made exact duplication impossible. In the end, both studies are congruent as they share methods and examine the same issue but use slightly different approaches

Conclusion

The present provision of palliative care for ICYA in BC needs to expand to cover all individuals living with serious illnesses and not yet receiving PPC, with a special focus on infants and other subpopulations with high risk of instability. A follow-up analysis involving a cohort structure over a longer period would be suitable to explore the larger population of ICYA who might be living with serious illnesses, but without frequent hospitalizations.

*(2,496 words)*

Tables

Table 1. Demographic characteristics of ICYA with serious illnesses diagnosed at hospital in BC

| Characteristic | Fiscal year | | | | |
|---|---|---|---|---|---|
| | 2012/13 | 2013/14 | 2014/15 | 2015/16 | 2016/17 |
| Number of ICYA | 2455 | 2508 | 2509 | 2448 | 2457 |
| Age group, n (%) | | | | | |
| Under 1 year | 1252 (51.0) | 1334 (53.2) | 1375 (54.8) | 1276 (52.1) | 1242 (50.5) |
| 1 to 4 years | 340 (13.8) | 315 (12.6) | 278 (11.1) | 285 (11.6) | 294 (12.0) |
| 5 to 9 years | 147 (6.0) | 155 (6.2) | 171 (6.8) | 164 (6.7) | 176 (7.2) |
| 10 to 14 years | 150 (6.1) | 142 (5.7) | 135 (5.4) | 138 (5.6) | 131 (5.3) |
| 15 to 19 years | 217 (8.8) | 210 (8.4) | 200 (8.0) | 221 (9.0) | 245 (10.0) |
| 20 to 25 years | 349 (14.2) | 352 (14.0) | 350 (13.9) | 364 (14.9) | 369 (15.0) |
| Sex, n (%) | | | | | |
| Male | 1378 (56.1) | 1423 (56.7) | 1368 (54.5) | 1364 (55.7) | 1368 (55.7) |
| Female | 1077 (43.9) | 1085 (43.3) | 1141 (45.5) | 1084 (44.3) | 1089 (44.3) |
| SES, n (%) | | | | | |
| 1 (lowest quintile) | 554 (22.6) | 536 (21.4) | 527 (21.0) | 565 (23.1) | 512 (20.8) |
| 2 | 517 (21.1) | 514 (20.5) | 562 (22.4) | 518 (21.2) | 479 (19.5) |
| 3 | 474 (19.3) | 478 (19.1) | 487 (19.4) | 459 (18.8) | 492 (20.0) |
| 4 | 492 (20.0) | 526 (21.0) | 496 (19.8) | 524 (21.4) | 499 (20.3) |
| 5 (highest quintile) | 389 (15.8) | 430 (17.1) | 404 (16.1) | 341 (13.9) | 432 (17.6) |
| Missing/unknown | 29 (1.2) | 24 (1.0) | 33 (1.3) | 41 (1.7) | 43 (1.8) |
| Taxonomic unit, n (%) | | | | | |
| Perinatal | 1003 (40.9) | 1052 (41.9) | 1121 (44.7) | 1032 (42.2) | 980 (39.9) |
| Congenital | 444 (18.1) | 458 (18.3) | 436 (17.4) | 434 (17.7) | 456 (18.6) |
| Oncology | 390 (15.9) | 401 (16.0) | 380 (15.1) | 393 (16.1) | 413 (16.8) |
| Neurology | 134 (5.5) | 128 (5.1) | 112 (4.5) | 122 (5.0) | 125 (5.1) |
| Metabolic | 32 (1.3) | 26 (1.0) | 31 (1.2) | 29 (1.2) | 30 (1.2) |
| Otherwise Specified | 452 (18.4) | 443 (17.7) | 429 (17.1) | 438 (17.9) | 453 (18.4) |

Note: SES = socioeconomic status (neighbourhood income quintile)

Table 2. ICYA with serious illnesses diagnosed at hospital in BC by clinical stage

| Clinical Stage | Fiscal year | | | | |
|---|---|---|---|---|---|
| | 2012/13 | 2013/14 | 2014/15 | 2015/16 | 2016/17 |
| Number of ICYA | 2455 | 2508 | 2509 | 2448 | 2457 |
| Stage, n (%) | | | | | |
| Stable | 809 (33.0) | 866 (34.5) | 880 (35.1) | 761 (31.1) | 741 (30.2) |
| Unstable-ED | 956 (38.9) | 960 (38.3) | 948 (37.8) | 994 (40.6) | 1037 (42.2) |
| Unstable-Hosp | 192 (7.8) | 197 (7.9) | 176 (7.0) | 148 (6.0) | 138 (5.6) |
| Deteriorating | 417 (17.0) | 380 (15.2) | 425 (16.9) | 449 (18.3) | 432 (17.6) |
| Died | 81 (3.3) | 105 (4.2) | 80 (3.2) | 96 (3.9) | 109 (4.4) |

Table 3. Rate of hospitalizations (per 10,000 population) of ICYA with serious illnesses diagnosed at hospital in BC by age

| Age group | Fiscal year | | | | |
|---|---|---|---|---|---|
| | 2012/13 | 2013/14 | 2014/15 | 2015/16 | 2016/17 |
| Under 1 year | 286.7 | 302.0 | 312.6 | 284.7 | 276.4 |
| 1 to 4 years | 18.9 | 17.6 | 15.4 | 15.7 | 15.9 |
| 5 to 9 years | 6.6 | 6.9 | 7.5 | 7.0 | 7.4 |
| 10 to 14 years | 6.4 | 6.1 | 5.8 | 5.9 | 5.6 |
| 15 to 19 years | 7.7 | 7.6 | 7.3 | 8.1 | 9.0 |
| 20 to 25 years | 9.4 | 9.3 | 9.1 | 9.4 | 9.6 |
| Total (0 to 25 years) | 18.4 | 18.7 | 18.6 | 18.1 | 18.1 |

Table 4. Odds ratio for risk of instability

| Variable | Univariable models | | | Multivariable model | | |
|---|---|---|---|---|---|---|
| | OR | (95% CI) | p-value | OR | (95% CI) | p-value |
| Sex | | | | | | |
| Female | Ref | | | Ref | | |
| Male | 1.01 | (0.94 to 1.09) | 0.79 | 1.02 | (0.95 to 1.1) | 0.59 |
| Age range | | | | | | |
| Under 1 year | 1.75 | (1.59 to 1.94) | <0.01 | 5.25 | (4.63 to 5.95) | <0.01 |
| 1 to 4 years | 0.35 | (0.31 to 0.39) | <0.01 | 0.80 | (0.70 to 0.90) | <0.01 |
| 5 to 9 years | 0.70 | (0.60 to 0.82) | <0.01 | 0.77 | (0.66 to 0.90) | <0.01 |
| 10 to 14 years | 0.73 | (0.63 to 0.86) | <0.01 | 0.78 | (0.67 to 0.92) | <0.01 |
| 15 to 19 years | 0.90 | (0.79 to 1.03) | 0.12 | 0.94 | (0.83 to 1.07) | 0.38 |
| 20 to 25 years | Ref | | | Ref | | |
| SES | | | | | | |
| 1 - lowest quintile | Ref | | | Ref | | |
| 2 | 0.88 | (0.79 to 0.98) | 0.02 | 0.91 | (0.81 to 1.01) | 0.08 |
| 3 | 0.85 | (0.76 to 0.94) | <0.01 | 0.89 | (0.79 to 0.99) | 0.04 |
| 4 | 0.93 | (0.84 to 1.04) | 0.20 | 0.99 | (0.89 to 1.10) | 0.81 |
| 5 - highest quintile | 0.88 | (0.79 to 0.98) | 0.02 | 0.91 | (0.81 to 1.02) | 0.09 |
| Taxonomic unit | | | | | | |
| Oncology | Ref | | | Ref | | |
| Perinatal | 0.61 | (0.55 to 0.67) | <0.01 | 0.26 | (0.23 to 0.30) | <0.01 |
| Congenital | 1.16 | (1.04 to 1.30) | <0.01 | 0.78 | (0.68 to 0.88) | <0.01 |
| Neurology | 1.44 | (1.22 to 1.71) | <0.01 | 1.43 | (1.20 to 1.70) | <0.01 |
| Metabolic | 1.22 | (0.88 to 1.68) | 0.23 | 0.99 | (0.71 to 1.39) | 0.96 |
| Otherwise Specified | 1.72 | (1.55 to 1.91) | <0.01 | 1.55 | (1.39 to 1.73) | <0.01 |

*Data used: 38,715 observations (4,129 events) from 11,196 individuals*

Note: Otherwise Specified: Haematology, Genitourinary, Respiratory, Gastrointestinal, Circulatory, Other, Multiple

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Disclaimer

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Data sharing

The data that support the findings of this study are approved for use by data stewards and accessed through a process managed by Population Data BC. The data sets used for this study will be archived, and requests for access to them in the context of verification of study findings can be made to PopData (https://www.popdata.bc.ca/data_access). We are not permitted to share the research extract used in this analysis with other researchers, but the same datasets are accessible via Population Data BC.

Contributors

Harold Siden conceptualized the study. Harold Siden and Elisa Castro Noriega designed the study and drafted the manuscript. Elisa Castro Noriega performed all analyses with methodologic support from Ruth Lavergne. All authors edited the manuscript, revised it critically for important intellectual content, approved the final manuscript and agreed to be accountable for all aspects of the work.

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**Appendix 1 – Coding framework (ICD-10 codes used to identify serious illnesses)**

| Taxonomic unit | ICD-10 Code | Description |
|---|---|---|
| Oncology | C00-C97 | All malignancies |
| | D33.0 | Benign neoplasm of brain, supratentorial |
| | D43.0 | Neoplasm of uncertain behavior of brain, supratentorial |
| | D44.4 | Neoplasm of uncertain behavior of craniopharyngeal duct |
| | D48.0 | Neoplasm of uncertain behavior of bone and articular cartilage |
| Perinatal | P10.1 | Cerebral hemorrhage due to birth injury |
| | P11.2 | Unspecified brain damage due to birth injury |
| | P21 | Birth asphyxia |
| | P28.5 | Respiratory failure of the newborn |
| | P29.0 | Neonatal cardiac failure |
| | P29.3 | Persistent fetal circulation |
| | P35.0 | Congenital rubella syndrome |
| | P35.1 | Congenital cytomegalovirus infection |
| | P35.8 | Other congenital viral diseases |
| | P37.1 | Congenital toxoplasmosis |
| | P52.4 | Intracerebral (nontraumatic) hemorrhage of the newborn |
| | P52.5 | Subarachnoid (nontraumatic) hemorrhage of the newborn |
| | P52.9 | Intracranial (nontraumatic) hemorrhage of the newborn, unspecified |
| | P83.2 | Hydrops fetalis not due to hemolytic disease |
| | P91.2 | Neonatal cerebral leukomalacia |
| | P91.6 | Hypoxic ischemic encephalopathy (HIE) |
| | P96.0 | Congenital renal failure |
| Congenital | Q00 | Anencephaly |
| | Q01 | Frontal encephalocele |
| | Q03.1 | Atresia of foramina of Magendie and Luschka |
| | Q03.9 | Congenital hydrocephalus, unspecified |
| | Q04.0 | Congenital malformations of corpus callosum |
| | Q04.2 | Holoprosencephaly |
| | Q04.3 | Other reduction deformities of the brain |
| | Q04.4 | Septo-optic dysplasia of the brain |
| | Q04.6 | Congenital cerebral cysts |
| | Q04.9 | Congenital malformation of the brain, unspecified |
| | Q07.0 | Arnold-Chiari syndrome |
| | Q20.0 | Common arterial trunk |
| | Q20.3 | Discordant ventriculoarterial connection |
| | Q20.4 | Double inlet ventricle |
| | Q20.6 | Isomerism of the atrial appendages |
| | Q20.8 | Other congenital malformations cardiac chambers and connections |

| | | |
|---|---|---|
| **Congenital** | Q21.3 | Tetralogy of Fallot |
| | Q21.8 | Other congenital malformations of cardiac septa |
| | Q22.0 | Pulmonary valve atresia |
| | Q22.1 | Congenital pulmonary valve stenosis |
| | Q22.4 | Congenital tricuspid valve stenosis |
| | Q22.5 | Ebstein's anomaly |
| | Q22.6 | Hypoplastic right heart syndrome |
| | Q23.0 | Congenital stenosis of the aortic valve |
| | Q23.2 | Congenital mitral stenosis |
| | Q23.4 | Hypoplastic left heart syndrome |
| | Q23.9 | Congenital malformation of aortic and mitral valves, unspecified |
| | Q25.4 | Other congenital malformations of the aorta |
| | Q25.6 | Stenosis of the pulmonary artery |
| | Q26.2 | Total anomalous pulmonary venous connection |
| | Q26.4 | Anomalous pulmonary venous connection, unspecified |
| | Q26.8 | Other congenital malformations of the great veins |
| | Q28.2 | Arteriovenous malformation of the cerebral vessels |
| | Q32.1 | Other congenital malformations of the trachea |
| | Q33.6 | Congenital hypoplasia and dysplasia of the lung |
| | Q39.6 | Congenital diverticulum of the esophagus |
| | Q41.0 | Congenital absence, atresia and stenosis of the duodenum |
| | Q41.9 | Congenital absence, atresia and stenosis of the small intestine, part unspecified |
| | Q43.7 | Persistent cloaca |
| | Q44.2 | Atresia of the bile ducts |
| | Q44.7 | Other congenital malformation of the liver |
| | Q60.1 | Renal agenesis, bilateral |
| | Q60.6 | Potter's syndrome |
| | Q61.4 | Renal dysplasia |
| | Q61.9 | Cystic kidney disease, unspecified |
| | Q64.2 | Congenital posterior urethral valves |
| | Q74.3 | Arthrogryposis multiplex congenital |
| | Q75.0 | Craniosynostosis |
| | Q77.2 | Short rib syndrome |
| | Q77.3 | Chondrodysplasia pun |
| | Q77.4 | Achondroplasia |
| | Q78.0 | Osteogenesis imperfecta |
| | Q78.5 | Metaphyseal dysplasia |
| | Q79.2 | Exomphalos |
| | Q79.3 | Gastroschisis |
| | Q80.4 | Harlequin fetus |
| | Q81.0 | Epidermolysis bullosa simplex |
| | Q82.1 | Xeroderma pigmentosum |

| | | |
|---|---|---|
| **Congenital** | Q82.4 | Ectodermal dysplasia (anhidrotic) |
| | Q85.8 | Other phakomatoses, not elsewhere classified |
| | Q86.0 | Fetal alcohol syndrome (dysmorphic) |
| | Q87.0 | Congenital malformation syndromes predominantly affecting facial appearance |
| | Q87.1 | Congenital malformation syndromes predominantly associated with short stature |
| | Q87.2 | Congenital malformation syndromes predominantly involving limbs |
| | Q87.8 | Other specified congenital malformation syndromes, not elsewhere classified |
| | Q91.0 | Trisomy 18, nonmosaicism (meiotic nondisjunction) |
| | Q92.0 | Whole chromosome trisomy, nonmosaicism (meotic nondisjunction) |
| | Q92.1 | Whole chromosome trisomy, mosaicism (mitotic nondisjunction) |
| | Q92.4 | Duplications seen only at prometaphase |
| | Q92.7 | Triploidy and polyploidy |
| | Q92.8 | Other specified trisomies and partial trisomies of autosomes |
| | Q93.2 | Chromosome replaced with ring, dicentric or isochromosome |
| | Q93.3 | Deletion of short arm of chromosome 4 |
| | Q93.4 | Deletion of short arm of chromosome 5 |
| | Q93.5 | Other deletions of part of a chromosome |
| | Q93.8 | Other deletions from the autosomes |
| | Q95.2 | Balanced autosomal rearrangement in abnormal individual |
| **Neurology** | A17.0 | Tuberculous meningitis |
| | A81.0 | Creutzfeldt-Jakob disease |
| | A81.1 | Subacute sclerosing panencephalitis |
| | F84.2 | Rett's syndrome |
| | G10 | Huntington's disease |
| | G11.1 | Early-onset cerebellar ataxia |
| | G11.3 | Cerebellar ataxia with defective DNA repair |
| | G12.0 | Infantile spinal muscular atrophy, type I (Werdnig-Hoffman) |
| | G20 | Parkinson disease |
| | G23.0 | Hallervorden-Spatz disease |
| | G23.8 | Other specified degenerative diseases of the basal ganglia |
| | G31.8 | Other specified degenerative diseases of the nervous system |
| | G31.9 | Degenerative disease of the nervous system, unspecified |
| | G35 | Multiple sclerosis |
| | G40.4 | Other generalized epilepsy and epileptic syndromes, not intractable |
| | G40.5 | Epileptic seizures related to external causes, not intractable |
| | G60.0 | Hereditary motor and sensory neuropathy |
| | G60.1 | Refsum's disease |
| | G70.2 | Congenital and developmental myasthenia |

| | | | |
|---|---|---|---|
| **Neurology** | | G70.9 | Myoneural disorder, unspecified |
| | | G71.0 | Muscular dystrophy |
| | | G71.1 | Myotonic disorders |
| | | G71.2 | Congenital myopathies |
| | | G71.3 | Mitochondrial myopathy, not elsewhere classified |
| | | G80.0 | Spastic quadriplegic cerebral palsy |
| | | G80.8 | Other cerebral palsy |
| | | G82.3 | Flaccid tetraplegia |
| | | G82.4 | Spastic tetraplegia |
| | | G82.5 | Quadriplegia |
| | | G93.4 | Other and unspecified encephalopathy |
| | | G93.6 | Cerebral edema |
| | | G93.7 | Reye's syndrome |
| **Metabolic** | | E31.0 | Autoimmune polyglandular failure |
| | | E34.8 | Other specified endocrine disorders |
| | | E70.2 | Disorder of tyrosine metabolism, unspecified |
| | | E71.0 | Maple-syrup-urine disease |
| | | E72.0 | Diseases of amino acide transport |
| | | E74.0 | Glycogen storage disease |
| | | E75.0 | GM2 gangliosidosis |
| | | E76.0 | Mucopolysaccharidosis, type I |
| | | E77.0 | Defects in post-translational modification of lysosomal enzymes |
| | | E79.1 | Lesch-Nyhan syndrome |
| | | E83.0 | Disorders of copper metabolism |
| | | E88.0 | Disorders of plasma-protein metabolism, not elsewhere classified |
| | | E88.1 | Lipodystrophy, not elsewhere classified |
| **Otherwise Specified** | **Haematology** | B20 | HIV resulting in infectious and parasitic diseases |
| | | B21 | HIV resulting in malignant neoplasms |
| | | B22 | HIV resulting in other specified diseases |
| | | B23 | HIV resulting in other conditions |
| | | B24 | Unspecified HIV disease |
| | | D56.1 | Beta thalassemia |
| | | D61.0 | Constitutional aplastic anemia |
| | | D61.9 | Aplastic anemia, unspecified |
| | | D70.0 | Congenital agranulocytosis |
| | | D76.1 | Hemophagocytic lymphohistiocytosis |
| | | D81.0 | Severe combined immunodeficiency (SCID) with reticular dysgenesis |
| | | D82.1 | Di George's syndrome |
| | | D83.0 | Common variable immunodeficiency with predominant abnormalities of B-cells |
| | | D89.1 | Cryoglobulinemia |

| | | | |
|---|---|---|---|
| **Otherwise Specified** | **Respiratory** | E84.0 | Cystic fibrosis with pulmonary manifestations |
| | | J84.1 | Other interstitial pulmonary diseases with fibrosis |
| | | J96.0 | Acute respiratory failure |
| | | J98.4 | Other disorders of lung |
| | **Circulatory** | I21.0 | ST elevation (STEMI) myocardial infarction of anterior wall |
| | | I27.0 | Primary pulmonary hypertension |
| | | I42.0 | Dilated cardiomyopathy |
| | | I61.3 | Nontraumatic intracerebral hemorrhage in the brain stem |
| | | I81 | Portal vein thrombosis |
| | **Gastrointestinal** | K55.0 | Acute vascular disorders of the intestine |
| | | K55.9 | Vascular disorder of the intestine, unspecified |
| | | K72.0 | Acute and subacute hepatic failure |
| | | K74.0 | Hepatic fibrosis |
| | | K76.5 | Hepatic veno-occlusive disease |
| | | K86.8 | Other specified diseases of the pancreas |
| | **Genitourinary** | N17.0 | Acute kidney failure with tubular necrosis |
| | | N18 | Chronic kidney disease |
| | | N19 | Unspecified kidney failure |
| | | N25.8 | Other disorders resulting from impaired renal tubular function |
| | **Other** | H11.1 | Conjunctival degenerations and deposits |
| | | H49.8 | Other paralytic strabismus |
| | | H35.5 | Hereditary retinal dystrophy |
| | | M31.3 | Wegener's granulomatosis |
| | | M32.1 | Systemic lupus erythematosus with organ or system involvement |
| | | M89.5 | Osteolysis |
| | | T86.0 | Complications of bone marrow transplant |
| | | T86.2 | Complications of heart transplant |
| | | Z51.5 | Encounter for palliative care |

**Appendix 2 – ICD-10 codes used to refine the selection of neonates**

| ICD-10 Code | Description |
|---|---|
| P59.9 | Neonatal jaundice, unspecified |
| Z29.2 | Other prophylactic chemotherapy |
| P04.0 | Fetus and newborn affected by maternal anaesthesia and analgesia in pregnancy, labour and delivery |
| P07.3 | Other preterm infants |
| P22.1 | Transient tachypnoea of newborn |
| P70.4 | Other neonatal hypoglycaemia |