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Trends in incidence of neonatal abstinence syndrome in Canada and associated healthcare resource utilization

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ABSTRACT

Background: Neonatal abstinence syndrome (NAS) is a collection of symptoms that occurs primarily due to antenatal opioid exposure. National data on incidence, hospital resource utilization, and demographic features of NAS have not been previously described for Canada.

Methods: Secondary analysis was performed with data from hospitals in all Canadian provinces and territories, excluding Quebec. Infants with NAS were identified by searching for ICD-10-CA code P96.1 in the Canadian Institute for Health Information's discharge abstract database. We examined incidence, hospital beds occupied per day, length of stay (fiscal 2003–2014), hospital costs, and demographic features (due to data availability, limited to fiscal 2010–2014).

Results: The incidence of NAS in Canada tripled between 2003 and 2014 (1.8–5.4 per 1000 live births), with an average annual increase of 0.33 cases per 1000 live births (95% CI 0.31, 0.34). Provincial incidence in 2014 ranged from 2.7 (Alberta) to 9.7 (New Brunswick) per 1000 live births. Between 2010 and 2014 total and mean per-patient costs rose from $15.7 to $26.9 million CAD and $14,629 to $17,367 CAD, respectively, with substantial inter-provincial variation in expenditure. Mean length of stay was 14.4 days in 2003 and 14.8 days in 2014, and beds occupied per day rose from 19.7 in 2003 to 69.4 in 2014.

Conclusions: The incidence of NAS is increasing in Canada with associated rise in healthcare resource utilization. Inter-provincial variability in incidence and resource utilization underscores the need to further explore best practices for cost-effective prevention and management of NAS.

1. Introduction

Neonatal abstinence syndrome (NAS) is a collection of symptoms that occurs as a result of antenatal exposure to a number of drugs, most commonly opioids (Doberczak et al., 1991; Behnke and Smith, 2013). Other implicated drugs include alcohol, barbiturates, caffeine, benzodiazepines, and selective serotonin reuptake inhibitors (Hudak and Tan, 2012). NAS is characterized by irritability, poor feeding, hypertonia, tremors, diarrhea, respiratory distress, and occasionally seizures (Hudak and Tan, 2012; Kocherlakota, 2014) and develops in up to 80% of newborns exposed prenatally to opioids (Doberczak et al., 1991). Infants with NAS often require pharmacological treatment (Hudak and Tan, 2012), and the condition frequently leads to prolonged hospital stays after birth and admission to neonatal intensive care units. It has potential long-term effects on behaviour and development (Behnke and Smith, 2013; Kocherlakota, 2014).

The incidence of NAS has increased significantly in the United States over the past decade (Tolia et al., 2015), with associated increases in healthcare costs from $61 million in 2003 to $316 million in 2013 (Corr and Hollenbeak, 2017) and a 35% increase in cost per admission between 2000 and 2009 (Patrick et al., 2012). There has also been a documented 15-fold increase in the incidence of NAS in the Canadian province of Ontario from 1992 to 2011 (Turner et al., 2015) and an almost 15-fold increase in total NAS-related costs in that province from 2003 to 2013 (Brogly et al., 2017). However, overall Canadian data on incidence and other epidemiological features of NAS have not been previously described. In the context of a growing opioid crisis in Canada (Philpott and Hoskins, 2016) and rising antenatal opioid use among Canadian women (Public Health Agency of Canada, 2009; Provincial Council for Maternal and Child Health, 2011; Hayes and Brown, 2012), our aim was to quantify and provide inter-provincial comparative data on NAS incidence and NAS-related hospital resource utilization and costs. In doing so, we hope to contribute data that can inform future maternal and child health practices and policies in Canada. Further standardization of practice in prevention and management of NAS can be applied globally to help reduce the burden of this

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illness.

2. Methods

2.1. Setting and data sources

2.1.1. Overview

Canada is made up of ten provinces and three territories, and healthcare generally falls under provincial or territorial rather than federal jurisdiction. Universal coverage of insured health services is provided to residents through a single payer, i.e., provincial or territorial health authority. Accordingly, all hospitalizations are captured in provincial and territorial administrative health databases. Aggregate data at the provincial, territorial, and national level were obtained from three sources for this project, as described below. All data were provided and are reported for fiscal years, but for simplicity we use "year" throughout the text. This study was reviewed for ethical compliance by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board in Kingston, Ontario.

2.1.2. Ontario Provincial Council for Maternal and Child Health (PCMCH)

Ontario's PCMCH receives limited NAS-related data from the Canadian Institute for Health Information (CIHI). Cases of NAS are identified by searching for ICD-10-CA code P96.1 (neonatal withdrawal symptoms from maternal use of drugs of addiction) (Canadian Institute for Health Information, 2009) in any diagnostic field in the Discharge Abstract Database (see next section) before 29 days of age. For this project, the PCMCH provided the following data for 2003–2014: number of total and unique cases of NAS discharged from hospital in each year, mean hospital length of stay, and number of hospital beds occupied per day by infants with NAS (NICU and rooming-in). The latter is a summary measure provided by CIHI to the PCMCH and is derived by multiplying the total number of NAS cases discharged in a particular year by the average length of stay in days and dividing the result by 365.

2.1.3. Canadian Institute for Health Information (CIHI)

CIHI maintains the discharge abstract database, which receives information on hospital stays directly from hospitals/health authorities. Facilities in all provinces and territories are required to report to CIHI except the province of Quebec (Canadian Institute for Health Information, 2012) (as a result, any references to "Canada" or "national" exclude data from Quebec). Because the PCMCH does not collect cost or demographic data, we requested the following information from CIHI through its graduate student data access program for 2010–2014 (note that only five years of data are available through the program): number of unique NAS cases (for consistency, we specified the same case definition that the PCMCH uses), mean per-patient hospital costs for NAS (initial admissions only), total hospital costs (sum of per-initial NAS hospital costs), and number of in-hospital live births. CIHI performed the cost analysis using the provincial cost of a standard hospital stay (Canadian Institute for Health Information, 2017) multiplied by the resource intensity weight (Canadian Institute for Health Information, 2015) and linked maternal and child health records to provide summary data on gestational age, birth weight, maternal age, and the number of late preterm births (34–36 weeks' gestational age) for the NAS population. In accordance with CIHI's privacy policy, all cell counts of 1–4 were suppressed in the data files provided to the research team, and, where necessary to prevent identification of suppressed counts, the final digit for the Canadian counts was also suppressed.

2.1.4. Statistics Canada

In order to calculate incidence rates, we obtained the number of live births by month and year based on the mother's place of residence for 2003–2012 through Statistics Canada's open-access Canadian Socio-Economic Information Management System (CANSIM) database (Statistics Canada, 2016a). These data were not available for 2013 and 2014 at the time of this writing. We also obtained national and provincial mean birth weights for 2010–2013 through CANSIM (Statistics Canada, 2016b). Data for 2014 were not available at the time of this writing.

2.2. Analysis

2.2.1. NAS incidence and analysis of trends

Annual incidence rates per 1000 live births were calculated using the number of unique NAS cases discharged in each year as the numerator and the number of live births by mother's place of residence for 2003–2012 and the number of in-hospital live births for 2013 and 2014 as the denominator (different sources were used because of data availability, as described above). These rates were calculated for Canada overall (excluding Quebec) and, to preserve confidentiality, only for those regions where the number of NAS cases was 0 or greater than 4 for each year of the study period. As a result, incidence figures are not provided for the provinces of Newfoundland and Labrador and Prince Edward Island, or for the three Territories, and those regions were not included in the trend analysis.

Generalized linear models were fit in SPSS version 24 (IBM Corporation) using the logit link. To assess whether there was a non-linear trend over the study period, we first fit models that only included the time variable (mean-centered year) as a linear term. We then fit a second model that included a quadratic transformation of the time variable and then a third model that additionally included a cubic transformation (YRBSS, 2016). The best-fitting model was selected by comparing the deviance statistic for one model to that for the model containing the next higher-order term using the chi-square test.

If a model with a quadratic or cubic term provided the best fit to the data, the Joinpoint Regression Program, version 4.3.1.0 (Calverton, MD: Statistical Research and Applications Branch, National Cancer Institute) was used to ascertain the year(s) in which there was a change in linear trend. Separate models for each segment were then fit in SPSS.

The average annual change in the incidence of NAS over the relevant time period(s), as well as 95% confidence intervals, were then summarized using the exponentiated parameters estimates (e.g., an exponentiated point estimate (i.e., odds ratio) of 1.08 represented an average annual increase of 8%). The average annual change per 1000 live births was also determined by re-fitting the models and specifying the identity rather than the logit link. These were essentially linear regression models, where the β coefficients represented the change in the dependent variable (number of NAS cases/incidence per 1000 live births) for every one-unit change in the independent variable (year).

2.2.2. Hospital resource utilization and costs

As previously noted, information on hospital resource utilization, costs, and demographics were provided as aggregate data and are primarily reported as minimum and maximum values. To compare total hospital costs for NAS among the nine provinces for which CIHI data were available, each province's costs were summed for 2010–2014, divided by the five-year sum of total NAS-related hospital costs for Canada overall, and converted to a percentage. A similar calculation was performed for total in-hospital births. We determined the difference between the provincial mean birth weight and the mean birth weight of NAS cases for each year. We then determined the mean of the reduction over the four-year period (2010–2013).

3. Results

3.1. NAS incidence and analysis of trends

Between 2003 and 2014, the incidence of NAS tripled in Canada from 1.8 to 5.4 cases per 1000 live births. Where a significant quadratic