International Journal of Population Data Science

Journal Website: www.ijpds.org

Preventive Care Uptake and Long-Term Healthcare Use Among Children with Fetal Opioid Exposure in Ontario, Canada: A Population-Based Retrospective Cohort Study

Arum Han[1], Gabrielle Pratt Tremblay[1,2], Michael Pugliese[3], Deshayne B Fell[2], and Daniel J Corsi[1,2,3,*]

Submission History

Submitted:	11/08/2025
Accepted:	09/03/2026
Published:	02/06/2026

[1] School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[2] Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada
[3] ICES uOttawa, Ottawa Hospital Research Institute, Ottawa, ON, Canada

Abstract

Introduction
Data on preventive care visits and long-term healthcare use patterns among children with prenatal opioid exposure remain limited. From a life course perspective, early impacts on health care engagement may shape patterns of health service use across childhood.

Objective
To characterise early and long-term healthcare service visits among children with prenatal opioid exposure using linked population-based health administrative databases from Ontario, Canada.

Methods
We conducted a population-based retrospective cohort study of live-born infants born between April 1, 2007, and March 31, 2018, who were born to mothers aged 15-50 years and who were eligible for provincial health insurance for at least 3 months before conception. Prenatal opioid use identified during routine prenatal care was extracted from clinical and perinatal health records. The primary outcome was the uptake of well-child visits until 24 months of age, an important early life preventive care period. Rates of all-cause inpatient, outpatient, and emergency department visits were examined and compared across the follow-up period and within specific time intervals up to 13 years of age.

Results
The final cohort totalled 1,343,653 live births, of whom 13,290 children (0.99%) had documented prenatal exposure to opioids. Prenatal opioid exposure was associated with reduced incidence of well-child visits (adjusted incidence rate ratio: 0.82 (95% CI: 0.81, 0.83)) from birth to 2 years. Exposed children were less likely to receive an enhanced 18-month well-child visit (adjusted risk ratio: 0.89 (95% CI: 0.88, 0.90)). Prenatal exposure was associated with increased rates of emergency department visits, specialist visits, hospitalisations and same-day surgery visits over the follow-up period. Differences in rates of health care visits were most pronounced in early childhood and attenuated for some services at older ages.

Conclusions
Prenatal opioid exposure was associated with reduced uptake of preventive health services and greater use of ambulatory care. This finding is consistent with a life course model, in which early gaps in preventive care may influence later-life care use patterns, and highlights the need for effective strategies to promote access to and engagement with preventive care services for opioid-exposed children.

Keywords
prenatal opioid exposure, paediatric healthcare utilisation, preventive health services, well-child care, emergency department use, early childhood, health equity

*Corresponding Author:
Email Address: dcorsi@cheo.on.ca (Daniel J Corsi)

https://doi.org/10.23889/ijpds.v11i3.3229
June 2026 © The Authors. Open Access under CC BY 4.0 (https://creativecommons.org/licenses/by/4.0/deed.en)

Introduction

Within the context of the opioid epidemic, opioid use during pregnancy has emerged as a significant public health problem in Canada and internationally [1]. While the prevalence of opioid use in pregnancy increased in earlier decades, a population-based study from Ontario indicated a decline in prenatal opioid exposure in Ontario between 2014 and 2019, from 6% to 4.5%, driven by reductions in prescribed analgesic use [2]. In contrast, an analysis of Ontario's birth registry, which captures maternal self-reported opioid use in pregnancy, suggested a lower overall prevalence and a decline in prevalence from 1.3% to 1.1% between 2012 and 2018 [3]. Prenatal opioid use has been associated with an increased risk of fetal growth restriction, congenital anomalies, preterm birth, low birth weight, stillbirth, and sudden infant death syndrome [3–5]. Newborns exposed to opioids *in utero* often exhibit withdrawal symptoms involving the central and autonomic nervous system and gastrointestinal distress [5].

Although short-term withdrawal symptoms are often resolved relatively quickly, children with a history of prenatal opioid exposure may be at risk of long-term health consequences, including otitis media and other ophthalmologic conditions [6–8], mental health problems, attention-deficit-hyperactivity disorder and autism spectrum disorder [9–11]. While neonatal abstinence syndrome diagnoses have been associated with poorer academic assessments and increased need for classroom therapies or services under disability criteria [12, 13], a diagnosis may not be made in all infants with prenatal opioid exposure, and it may mask differences between mothers on treatment and those with unregulated opioid use. Despite limitations in attributing a causal effect of fetal opioid exposure or neonatal abstinence syndrome on long-term outcomes, exposed children are likely at elevated risk for adverse outcomes extending beyond infancy and into childhood.

Prenatal opioid exposure occurs within a complex environmental and social context and represents a meaningful early life exposure. Life course and developmental origins frameworks emphasise that health trajectories are shaped by social, environmental, and biological influences during key developmental periods and that early exposures can have lasting effects beyond infancy [14–16]. These frameworks also support intergenerational processes, whereby maternal health and social conditions during pregnancy may influence long-term offspring developmental trajectories and thus potentially contribute to intergenerational transmission of health inequalities [17]. Within the life course framework, early childhood is an optimal period for surveillance and intervention, and adequate health care access during this period can influence the developmental and care use trajectories impacted by perinatal exposures [18]. Well-child care visits provide an opportunity to monitor a child's growth and developmental milestones, address any medical or psychosocial concerns, and improve overall health outcomes, such as adherence to immunisation schedules and reductions in hospitalisations and emergency department visits [19, 20]. For children with prenatal opioid exposure, well-child visits are particularly valuable for early identification of health or developmental issues requiring timely specialised care [4]. However, mothers who use opioids during pregnancy often face significant barriers to healthcare access, including environmental factors, the fear of legal consequences, involvement with child welfare services, apprehension, and stigma related to opioid use [21, 22].

Previous studies reported mixed findings in well-child visit use among children exposed to intrauterine opioids. In Ontario, a population-based study reported disparities in well-child visit attendance among children with prenatal opioid exposure by age 2, with patterns varying by type of prenatal opioid exposure [23]. In the United States, children prenatally exposed to opioids were 26% less likely to receive recommended well-child visits, despite receiving timely immunisations [24, 25]. Conversely, Medicaid-enrolled infants with a diagnosis of NAS and prenatal opioid exposure had higher adherence to well-child visits and more vaccination visits in the first one to two years of life than their unexposed counterparts without an NAS diagnosis [26, 27]. Differences in healthcare system organisation, eligibility for and access to publicly funded care, and policy responses may limit the generalizability of the US findings to the Canadian context.

Within the literature on prenatal opioid exposure, important gaps remain. Many prior studies have focused on outcomes in infancy or early childhood, relied mainly on neonatal abstinence syndrome diagnoses to proxy exposure, or have not distinguished between preventive and acute health care use. These limitations restrict our understanding of how prenatal opioid exposure may influence longer-term healthcare use trajectories, particularly in the context of a universal, publicly funded health system.

Here, within a life course perspective, we aimed to characterise healthcare service use among children exposed to opioids during pregnancy using linked, population-wide databases from Ontario, Canada. We assessed the rates and timeliness of well-child visit attendance from birth to two years of age and evaluated patterns of healthcare use, including outpatient visits, emergency department visits, and hospitalisations, from infancy through age 13 years. We use a broad, multi-source definition of prenatal opioid exposure and examine health care use trajectories from infancy to adolescence across both preventive and acute care. Based on previous research, we hypothesised that, independent of other health and social risk factors, prenatal opioid exposure would be associated with lower rates of preventive healthcare service use and increased use of acute care services such as emergency department visits and hospitalisations.

Methods

Study Design, Setting, and Population

This population-based retrospective cohort study included all live births in Ontario hospitals between April 1, 2007, and March 31, 2018, born to mothers aged 15 to 50 years who were continuously eligible for the Ontario Health Insurance Plan (OHIP) from three months prior to conception until delivery. Continuous OHIP eligibility reflects residency in Ontario and meeting provincial requirements for physical presence during the study period. We used linked health administrative databases at ICES (https://www.ices.on.ca/) to identify opioid exposure during pregnancy and evaluate

long-term health outcomes in children, based on maternal-child health service encounters.

The cohort was identified from the Ontario birth registry, the Better Outcomes Registry & Network (BORN). Births occurring between April 1, 2007, and March 31, 2012, were identified from the BORN Niday Perinatal Database, a historical subset of the BORN registry capturing hospital births up to 2012. Births occurring between April 1, 2012, and March 31, 2018, were identified from the BORN Information System (BIS), which is the current perinatal database. For this study, infants were followed up until March 31, 2020 (up to 13 years), or until they lost eligibility for provincial healthcare services, by linking their birth records to healthcare administrative databases [28].

We first excluded stillbirths and maternal and infant records with linkage errors or warnings. Children born to non-Ontario residents, those without a valid health card number, those with missing or implausible gestational age and birth weight, either infants or mothers with an invalid identifier and mismatched birthdates between the Registered Persons Database (RPDB) and BORN and those without healthcare eligibility at birth or within 60 days after birth were excluded. Children with an invalid date of death from the RPDB and those with zero follow-up time were excluded (Figure 1). A timeline of exposure, covariate, and outcome ascertainment is shown (Supplementary Appendix 1). We report this study according to the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) reporting guideline [29].

Data Sources

BORN Ontario (https://www.bornontario.ca/) is the provincial pregnancy, birth, and childhood registry [30]. The Niday and BIS databases in BORN capture maternal-newborn records from hospital births of at least 500g and at least 20 weeks of gestational age in Ontario, with >99% coverage of births in the province. The routine data collection in BORN includes maternal demographics, health behaviours, prenatal screening, pregnancy and obstetric complications, birth outcomes, and newborn outcomes. BORN Ontario applies a comprehensive framework, including both internal and external audits, to maintain quality in all aspects of the database and ensure the reliability, accuracy, validity, and completeness of the data1567424698 [31–34]. We used this database to establish the study cohort and to ascertain prenatal opioid exposure and covariates regarding pregnancy and birth information.

After establishing the cohort, the following databases were linked to identify study outcomes and to supplement exposure and covariate data: the Ontario Health Insurance Program (OHIP) Claims Database, capturing outpatient physician visits through physician billings, the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) to capture inpatient hospital admissions, the CIHI National Ambulatory Care Reporting System (NACRS) to capture emergency department visits, and the Same-Day Surgery (SDS) database to collect data on outpatient surgical procedures. The Ontario Mental Health Reporting System (OMHRS) was used to acquire information on inpatient admissions to mental health facilities during pregnancy. The Registered Persons Database (RPDB) eligibility data set was used to identify participants with active healthcare coverage. Vital status and length of follow-up for infants were also obtained from the RPDB. The full list of administrative databases that were used in this study, including additional ICES-derived databases, is detailed in Supplementary Appendix 2.

Data Linkage, Access, Privacy, and Ethical Considerations

Mother-infant records from the Niday/BIS Perinatal Database were linked to other health services and administrative databases using unique encoded identifiers and analysed at ICES. This independent and non-profit research entity is authorised to collect and store health administrative data for health system evaluation and improvement under Section 45 of the Personal Health Information Protection Act in Ontario. A unique encoded identifier, the ICES Key Number, is assigned to each record based on direct personal identifiers, enabling records to be deterministically linked across datasets while protecting privacy and confidentiality [35].

Exposure

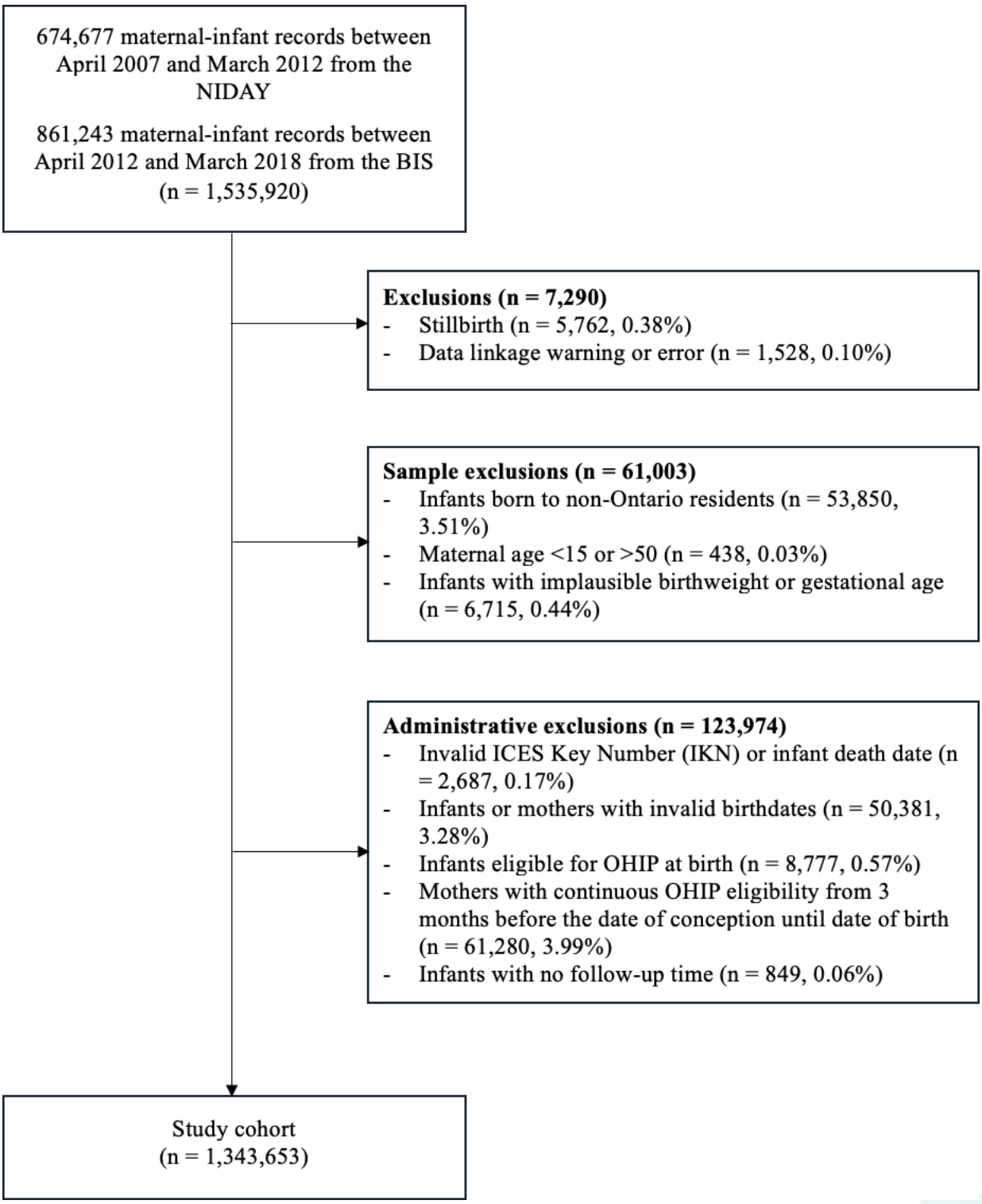
Prenatal opioid exposure was defined as any indication of maternal opioid use from three months before the estimated date of conception through the date of delivery, capturing opioid exposure across the entire pregnancy period. Prenatal opioid exposure was ascertained through provider-documented data collected during routine prenatal care in BORN or through maternal opioid-related health services records identified in DAD, OHIP, NACRS, or OMHRS. This definition includes any illicit, prescribed, or medication for opioid use disorder (methadone or buprenorphine). BORN collects information on substance or medication use, including opioids, at the first prenatal visit using a standardised perinatal record. A previous re-abstraction study found that the opioid use reported in BORN Ontario had a sensitivity of 84% (95% CI: 60–97%) and a specificity of 98% (95% CI: 91%–99%) compared to clinical records [3].

To identify additional maternal opioid exposure, we used supplemental databases to identify opioid-related health service encounters, including diagnoses of opioid use, abuse, or dependence; opioid poisoning; adverse drug reactions; multiple drug dependence involving opioids; and monthly management under an opioid agonist maintenance programme. These encounters were identified using ICD-10, DSM-IV, and OHIP billing codes from the DAD, OHIP, NACRS, or OMHRS databases (Supplementary Appendix 3). The Narcotics Monitoring System (NMS) database, which provides data on prescribed opioids after July 2012, was used for sensitivity analyses (Supplementary Appendix 8).

Outcome

The Canadian Paediatric Society recommends routine child examinations in the first week after discharge from birth, at 2, 4, 6, 9, 12, 18, and 24 months, and then once every year until five years of age [36]. The primary outcome was the uptake of well-child visits from birth until 24 months of age.

Figure 1: Study Flow Diagram



The frequency of well-child visits, including the enhanced 18-month well-child visit, was determined using the diagnostic or billing codes from outpatient physician visits (Supplementary Appendix 3). A well-child visit was defined as any check-up, assessment, or periodic health visit in an outpatient setting. To specifically assess receipt of the enhanced 18-month well-child visit, recommended between 17-24 months and considered a critical period for developmental surveillance, we captured the presence of any preventive visit between 515 and 761 days after birth. For this outcome, the cohort was restricted to children with continuous OHIP eligibility from birth until 761 days (Supplementary Appendix 1).

Secondary outcomes included all-cause use of health services. The rates of all-cause inpatient, outpatient, and emergency department visits were examined to determine the pattern of health services use throughout the entire follow-up period and within specific time intervals: 6 and 12 months of age, 2 years, 3 years, and between 3 years and

13 years of age. The outpatient encounters were examined by comparing primary care and specialty care. Primary care visits were ascertained from the OHIP database. They were defined as any outpatient visits billed by a family physician or a paediatrician with at least one of the OHIP billing codes associated with primary care. Specialist visits were defined as any OHIP encounters billed by specialists, excluding primary care visits billed by a paediatrician. The number of inpatient hospitalisations and emergency room visits was determined from DAD and NACRS encounters, respectively. If an emergency department visit led to hospitalisation, it was counted as one emergency department visit and one hospitalisation to reflect the frequency of service use.

Covariates and Confounding Variables

Potential covariates were identified a priori through a literature search. These included maternal age at delivery, neighbourhood marginalisation index, income, adequacy of prenatal care, maternal psychiatric diagnoses, other substance use during pregnancy, maternal pre-existing health conditions, pregnancy complications, congenital anomalies, preterm birth, small for gestational age, admission to the neonatal intensive care unit (NICU) and infant sex. The hypothesised relationships among exposure, outcome, and covariates, along with the minimal sufficient adjustment set, were determined using a directed acyclic graph (Supplementary Appendix 4). Maternal age at delivery was categorised as less than 20 years, 20-29 years, 30-39 years, and 40 years and older. We measured area-based socioeconomic conditions at the census-tract level using the Ontario Marginalization Index [37], a composite index comprised of four dimensions that estimate marginalisation, households and dwellings, material resources, age and labour force, and racialised and newcomer populations, based on Census data (Supplementary Appendix 2). Each dimension was compiled and divided into quintiles, representing low (quintile 1) to high (quintile 5) marginalisation. Income is the median household income at the dissemination area level and is categorised into quintiles. We used the Revised Graduated Prenatal Care Utilisation Index adapted for Ontario to determine prenatal care adequacy, which was categorised into 6 groups (intensive, adequate, intermediate, inadequate, no care, and missing care). Maternal psychiatric diagnoses, including substance-related disorder, mood affective/anxiety disorder, personality and behaviour disorders, and schizophrenia, delusional and psychotic disorders, were each dichotomised (yes or no). Other substance use during the pregnancy was dichotomised by substance and included use of cannabis, tobacco, alcohol, cocaine, hallucinogens, other prescriptions and other substances. Supplementary Appendix 5 provides a comprehensive list of covariates, including the selected confounding variables used in the study, as well as the databases employed to ascertain them.

Missingness

The proportion of missingness for individual variables included in the analyses varied from $<0.1\%$ (n=11, small for gestational age) and 5.5% (tobacco, cocaine, and hallucinogen use during pregnancy), and 10.4% of records had missing information for at least one covariate. We assumed a missing at random (MAR) mechanism for the missing data and used a fully conditional specification approach to impute missing values. We first compared sociodemographic and clinical variables between individuals with complete and incomplete data. Missingness was associated with several observed characteristics, which supports the use of multiple imputation under the MAR framework, and these factors were included in the imputation model. We used the PROC MI procedure in SAS to generate 10 imputed datasets; the list of variables included in the imputation model is provided in Supplementary Appendix 5. In addition, exposure, mediator (preterm birth), and primary outcome (all well-child visits until 24 months of age) variables were included in the imputation model. For the main analyses, statistical models were repeated on each imputed dataset, and parameter estimates and standard errors were combined to produce pooled estimates of association with a corresponding 95% confidence interval (CI).

Statistical Analyses

Baseline characteristics were compared between the two exposure groups using standardised mean differences (SMD). An absolute SMD above 0.1 was considered an imbalance and a meaningful difference of covariate distribution between the exposure groups [38]. Poisson regression models (or negative binomial models when overdispersion was present) were used to estimate the incidence rate of well-child visits up to 24 months and all-cause health services use, with the natural logarithm of follow-up time for each outcome serving as an offset variable. The incidence rate ratio and corresponding 95% CI were calculated and reported. We used a log-binomial model to estimate risk ratios and 95% CIs for the receipt of an 18-month well-child visit between 17 and 24 months of age. All multivariable models were adjusted for the minimal sufficient adjustment set identified from a directed acyclic graph (DAG), including maternal age, neighbourhood marginalisation (ON-Marg), neighbourhood income, adequacy of prenatal care, maternal psychiatric diagnoses, and substance use during pregnancy.

Subgroup Analyses

Selected main analyses (uptake of well-child visit during the 18-month interval, incidence rates of well-child visits and specialist visits until the age of 2 years) were repeated among subgroups to account for preterm birth and multiple gestations. Newborns with prenatal opioid exposure are often born preterm [39], which increases the risk of health consequences in newborns [40, 41]. We restricted the cohort to infants born at $\geq$37 weeks of gestational age to minimise confounding by preterm birth. To account for multiple births, the cohort was restricted to singletons to control for potential confounding.

Sensitivity Analyses

Several sensitivity analyses were done to assess the robustness of the results. We used coarsened exact matching (CEM) to match opioid-exposed children to unexposed children across covariates to reduce the imbalance in baseline characteristics

between exposure groups. CEM was conducted across 10 multiply imputed datasets to account for missing covariate data, with an average of 10,515 exposed and 693,945 unexposed individuals across these datasets. Further details of the CEM methods are given in Supplementary Appendix 6.

Results

We identified 1,535,920 births in BORN between April 2007 and March 2018. 674,677 births were captured in Niday between April 1, 2007, and March 31, 2012, and 861,243 births were captured in BIS between April 1, 2012, and March 31, 2018 (Figure 1). Due to data linkage warnings or errors, we excluded 5,762 (0.38%) stillbirths and 1,528 (0.10%) infants and maternal records. An additional 61,003 infant records were excluded due to maternal age at delivery ($<$15 or $>$50 years) (473), being born to non-Ontario residents (53,850 [3.51%]) or an implausible birth weight or gestational age (6,715 [0.44%]). Finally, an additional 123,974 records were excluded due to an invalid identifier or birthdate (53,068 [3.47]), infant ineligibility for OHIP at time of birth (8,777 [0.57%]), mother with non-continuous OHIP eligibility from 3 months before the date of conception until the date of birth (61,280 [3.99%]) or no follow-up time or an invalid date of death (849 [0.06%]). In total, 192,267 (12.5%) records were excluded, and the final study cohort consisted of 1,343,653 live births.

Of the children included in the final study cohort, 13,290 (0.99%) were exposed to opioids *in utero* (Table 1). Mothers who used opioids during pregnancy were younger and more socioeconomically disadvantaged in all five measures of marginalisation, as indicated by a SMD $>$ 0.10. Furthermore, a higher proportion of mothers who used opioids during pregnancy had hepatitis B (SMD 0.12) and mental health conditions (substance-related disorder (SMD 1.72), mood affective disorder (SMD 0.34), personality and behaviour disorders (SMD 0.16), and schizophrenia, delusional and psychotic disorders (0.14)). Mothers who used opioids during pregnancy also used other substances (tobacco (SMD 1.32), cocaine (SMD 0.41), hallucinogens (SMD 0.11), cannabis (SMD 0.51) and other substances (SMD 0.48)) during the pregnancy. A higher proportion of mothers who used opioids received inadequate prenatal care (32.6%) than unexposed mothers (13.8%, SMD 0.46). Exposed infants had a lower median birth weight than unexposed infants (SMD 0.37). A higher proportion of exposed infants were small for gestational age (15.3% versus 9.5% in unexposed infants) and born preterm (16.0% versus 7.7% in unexposed infants). 43.8% of exposed infants were admitted to the NICU during the neonatal period compared to 12.6% of unexposed infants (SMD 0.74). The median length of birth hospitalisation in days (SMD 0.92) and NICU stays in hours (SMD 0.76) were longer for exposed infants.

Preventive Health Service Use Until 24 Months of Age

Children exposed to opioids *in utero* had lower incidence rates of well-child visits until the age of 24 months (incidence rate ratio [IRR]: 0.73, 95% CI: 0.72, 0.73), and the association was attenuated slightly but remained statistically significant after adjusting for confounders (adjusted incidence rate ratio [aIRR]: 0.82, 95% CI: 0.81, 0.83) (Table 2). Between 17 to 24 months of age, 67.8% of exposed children received any well-child visits, and they were 0.89 times as likely to receive any well-child visit between 17 to 24 months (adjusted risk ratio [aRR]: 0.89, 95% CI: 0.88, 0.90), adjusted for confounders (Table 3). When the definition of well-child visit was narrowed to the enhanced well-child visit, and using a new fee code implemented in May 2008, the uptake lowered among both exposed and unexposed children (36.1% vs 55.9%), and the risk ratio was also lowered to 0.82 (95% CI: 0.80, 0.84). We used CEM to match and weight the cohort across covariates and to reduce residual confounding. After these adjustments, the association between opioid use and preventive care visits was attenuated towards the null, although it remained statistically significant (Supplementary Appendix 6).

All-Cause Health Services Use

Rates of well-child visits and primary care visits were significantly lower among exposed children than unexposed children throughout the follow-up period (aIRR: 0.92, 95% CI: 0.91, 0.93; Figure 2). The associations remained unchanged until 0-3 years (aIRR: 0.84, 95% CI: 0.83, 0.85) and attenuated between 3 to 13 years (aIRR: 0.90, 95% CI: 0.88, 0.92). Exposed children had a higher incidence rate of specialist visits at the intervals between 0 to 3 years (aIRR: 1.54, 95% CI: 1.48, 1.59), and the associations attenuated progressively with age. Between 3 to 13 years, the specialist visits and prenatal opioid exposure were no longer associated with statistical significance (aIRR 1.05, 95% CI: 1.00, 1.10).

As seen in Figure 2, the exposed children had higher incidence rates of emergency department visits consistently throughout the follow-up period, regardless of the age. Prenatal opioid exposure was associated with increased rates of hospitalisations throughout the follow-up period, but the associations gradually increased with age. Similarly, rate of same-day surgery increased with age and became statistically significant. The mean length of stay for hospitalisations were between 11.7-13 days for exposed children and 4.5-5.2 days for unexposed children, which persisted until 0 to 3 years of age (Supplementary Appendix 7).

Additional Analyses

Associations observed in the subgroup analyses of singleton and full-term births were consistent with the main analyses for preventive care outcomes, suggesting that multiple births or prematurity did not confound the associations (Table 4). Compared to the main analysis, the associations between the number of specialist visits and prenatal opioid exposure remained unchanged in singleton births from birth to 2 years of age. When the cohort was limited to infants born full-term, the association with specialist visits increased slightly between birth and 6 months (aIRR 2.14, 95% CI: 2.07, 2.21) and between 6 months and 12 months (aIRR 1.90, 95% CI: 1.84, 1.97). The association became comparable between birth and two years of age (aIRR 1.64, 95% CI: 1.59, 1.70).

In sensitivity analyses comparing alternative exposure definitions, we found no meaningful differences in well-child visit uptake between exposure groups, suggesting robust

Table 1: Baseline characteristics of the study cohort (n = 1,343,653)

Characteristics (%)	Opioid use during pregnancy[1]		SMD
	Yes n = 13,290 (0.99%)	**No n = 1,330,363 (99.01%)**	
Median maternal age at delivery (in years) (IQR)	28 (24-32)	31 (27-34)	0.48
Maternal age at delivery (in years)			
<20	706 (5.3%)	36,654 (2.8%)	0.13
20–29	7,577 (57.0%)	510,730 (38.4%)	0.38
30–39	4,715 (35.5%)	728,398 (54.8%)	0.40
≥40	292 (2.2%)	54,581 (4.1%)	0.11
Households and dwellings			
1 (lowest)	1,015 (7.6%)	297,808 (22.4%)	0.42
2	1,653 (12.4%)	252,122 (19.0%)	0.18
3	2,076 (15.6%)	237,406 (17.8%)	0.06
4	3,016 (22.7%)	247,026 (18.6%)	0.10
5 (highest)	3,825 (28.8%)	283,050 (21.3%)	0.17
Missing	1,705 (12.8%)	12,951 (1.0%)	0.48
Material resources			
1 (lowest)	1,162 (8.7%)	256,360 (19.3%)	0.31
2	1,459 (11.0%)	254,786 (19.2%)	0.23
3	1,757 (13.2%)	251,605 (18.9%)	0.16
4	2,397 (18.0%)	252,250 (19.0%)	0.02
5 (highest)	4,810 (36.2%)	302,411 (22.7%)	0.30
Missing	1,705 (12.8%)	12,951 (1.0%)	0.48
Age and labour force			
1 (lowest)	2,229 (16.8%)	445,444 (33.5%)	0.39
2	2,261 (17.0%)	282,012 (21.2%)	0.11
3	2,459 (18.5%)	226,229 (17.0%)	0.04
4	2,325 (17.5%)	195,795 (14.7%)	0.08
5 (highest)	2,311 (17.4%)	167,932 (12.6%)	0.13
Missing	1,705 (12.8%)	12,951 (1.0%)	0.48
Racialised and newcomer populations			
1 (lowest)	2,759 (20.8%)	174,949 (13.2%)	0.20
2	2,926 (22.0%)	195,818 (14.7%)	0.19
3	2,400 (18.1%)	224,296 (16.9%)	0.03
4	2,076 (15.6%)	279,445 (21.0%)	0.14
5 (highest)	1,424 (10.7%)	442,904 (33.3%)	0.57
Missing	1,705 (12.8%)	12,951 (1.0%)	0.48
Neighbourhood income quintile			
1 (lowest)	5,673 (42.7%)	283,265 (21.3%)	0.47
2	2,545 (19.1%)	264,097 (19.9%)	0.02
3	1,982 (14.9%)	274,205 (20.6%)	0.15
4	1,679 (12.6%)	282,047 (21.2%)	0.23
5 (highest)	1,193 (9.0%)	222,126 (16.7%)	0.23
Missing	218 (1.6%)	4,623 (0.3%)	0.13
Maternal health conditions			
Pre-existing diabetes	256 (1.9%)	15,200 (1.1%)	0.06
Pre-existing hypertension	187 (1.4%)	13,308 (1.0%)	0.04
Hepatitis B	226 (1.7%)	6,648 (0.5%)	0.12
HIV	34 (0.3%)	651 (0.0%)	0.05
Substance-relate disorder	8,326 (62.6%)	22,360 (1.7%)	1.72
Mood affective disorder	3,895 (29.3%)	202,279 (15.2%)	0.34
Personality and behaviour disorders	565 (4.3%)	21,012 (1.6%)	0.16
Schizophrenia, delusional, and psychotic disorders	185 (1.4%)	2,383 (0.2%)	0.14

Continued

Table 1: Continued

Characteristics (%)	Opioid use during pregnancy[1] Yes n = 13,290 (0.99%)	No n = 1,330,363 (99.01%)	SMD
Maternal substance use during pregnancy			
Tobacco			
Yes	8,303 (62.5%)	126,203 (9.5%)	1.32
Missing	145 (1.1%)	39,740 (3.0%)	0.13
Cocaine			
Yes	1,060 (8.0%)	1,755 (0.1%)	0.41
Missing	360 (2.7%)	73,332 (5.5%)	0.14
Hallucinogen			
Yes	80 (0.6%)	189 (0.0%)	0.11
Missing	360 (2.7%)	73,332 (5.5%)	0.14
Cannabis			
Yes	1,843 (13.9%)	12,194 (0.9%)	0.51
Missing	360 (2.7%)	73,332 (5.5%)	0.14
Other prescriptions			
Yes	2,798 (21.1%)	699,591 (52.6%)	0.69
Missing	318 (2.4%)	93,249 (7.0%)	0.22
Other substances			
Yes	1,768 (13.3%)	16,424 (1.2%)	0.48
Missing	172 (1.3%)	69,478 (5.2%)	0.22
Pregnancy information			
Parity			
0	4,270 (32.1%)	564,678 (42.4%)	0.22
1	3,859 (29.0%)	472,423 (35.5%)	0.14
2+	5,118 (38.5%)	279,252 (21.0%)	0.39
Missing	43 (0.3%)	14,010 (1.1%)	0.09
Prenatal care index			
Intensive	289 (2.2%)	18,543 (1.4%)	0.06
Adequate	2,199 (16.5%)	353,339 (26.6%)	0.25
Intermediate	5,259 (39.6%)	687,319 (51.7%)	0.25
Inadequate	4,333 (32.6%)	183,194 (13.8%)	0.46
No care	1,210 (9.1%)	87,968 (6.6%)	0.09
Hypertension disorder during pregnancy	678 (5.1%)	60,592 (4.6%)	0.03
Premature rupture of membrane	616 (4.6%)	44,629 (3.4%)	0.07
Placental complications	332 (2.5%)	17,932 (1.3%)	0.08
Gestational diabetes	471 (3.5%)	74,874 (5.6%)	0.10
Multiple birth	392 (2.9%)	45,573 (3.4%)	0.03
Birth information			
Infant sex			
Female	6,491 (48.8%)	647,885 (48.7%)	0.00
Male	6,799 (51.2%)	682,478 (51.3%)	0.00
Median birthweight (IQR)	3165 (2775-3538)	3375 (3037-3710)	0.37
Median gestational age at birth in weeks (IQR)	39 (37-40)	39 (38-40)	0.31
Small for gestational age	2,032 (15.3%)	125,978 (9.5%)	0.18
Mode of delivery			
Vaginal	9,450 (71.1%)	949,127 (71.3%)	0.01
C-section	3,840 (28.9%)	381,236 (28.7%)	0.01
Preterm birth	2,133 (16.0%)	102,396 (7.7%)	0.26
Median length of birth hospitalisation in days (IQR)	4 (2-10)	2 (1-2)	0.92
NICU admission during neonatal period	5,818 (43.8%)	167,728 (12.6%)	0.74

Continued

Table 1: Continued

Characteristics (%)	Opioid use during pregnancy[1] Yes n = 13,290 (0.99%)	No n = 1,330,363 (99.01%)	SMD
Median length of neonatal period NICU stays in hours (IQR)	0 (0-181)	0 (0-0)	0.76
Major congenital anomalies	875 (6.6%)	47,445 (3.6%)	0.14
Apgar score 5 minutes after birth			
<4	65 (0.5%)	2,930 (0.2%)	0.02
≥4	13,110 (98.6%)	1,315,891 (98.9%)	0.05
Missing	115 (0.9%)	11,542 (0.9%)	0.00
Child mortality			
Any time during follow-up	103 (0.8%)	3,644 (0.3%)	0.07
0–365 days	65 (0.5%)	2,663 (0.2%)	0.05
0–730 days	82 (0.6%)	2,979 (0.2%)	0.06
366–730 days	17 (0.1%)	316 (0.0%)	0.04
731 days onwards	21 (0.2%)	665 (0.0%)	0.03

[1]Opioid use during pregnancy was defined using a composite measure that included any indication of illicit opioid use, prescribed opioid use, or medication for opioid use disorder (methadone or buprenorphine) identified through prenatal care records in BORN Ontario or maternal opioid-related health service encounters in administrative databases.

Table 2: Association between prenatal opioid exposure and well-child visits until the age of 24 months

Prenatal opioid exposure status	Sample size (N=1,343,653)	Number of events	Follow-up time (person-years)	Crude incidence rate ratio (95% CI)	Adjusted incidence rate ratio (95% CI)	CEM[1] adjusted rate ratio (95% CI)
Unexposed	1,330,363	15,927,545	2,760,839	Ref.	Ref.	Ref.
Exposed	13,290	113,882	27,212	0.73 (0.72, 0.73)	0.82 (0.81, 0.83)	0.84 (0.83, 0.84)

[1]In CEM analysis, n = 704,460. Exposed (n) = 10,515 (1.5%), Unexposed (n) =693,945 (98.5%).
The regression models were adjusted for maternal age, ON-Marg, income, substance-related disorders, affective mood disorders, personality and behaviour disorders, schizophrenia, and delusional psychotic disorders, tobacco use, cocaine use, hallucinogen use, cannabis, and other substance use during pregnancy, and adequacy of prenatal care.

Table 3: Association between prenatal opioid exposure and completion of ≥1 well-child visits between 17-24 months of age

Prenatal opioid exposure status	Sample size (N=1,322,997)[1]	Number of events	Crude risk ratio (95% CI)	Adjusted risk ratio (95% CI)	CEM[2] adjusted risk ratio (95% CI)
Unexposed	1,310,278	1,148,357	Ref.	Ref.	Ref.
Exposed	12,719	8,623	0.77(0.76, 0.78)	0.89(0.88, 0.90)	0.95(0.95, 0.96)

[1]Overall sample was restricted to eligible individuals with ≥ 761 days of follow-up.
[2]In CEM analysis, n = 693,524. Exposed (n) = 10,088 (1.5%), Unexposed (n) =683,436 (98.5%).
The regression models were adjusted for maternal age, ON-Marg, income, substance-related disorders, affective mood disorders, personality and behaviour disorders, schizophrenia, and delusional psychotic disorders, tobacco use, cocaine use, hallucinogen use, cannabis, and other substance use during pregnancy, and adequacy of prenatal care.

associations across exposure-ascertainment approaches. For example, the rates of preventive and well-child visits were lower among children with opioid exposure identified in BORN, (aIRR 0.87, 95% CI: 0.86-0.88) and this was similar to those with opioid exposure identified using the original definition + ORT (aIRR 0.86, 95% CI: 0.85-0.87) and the original definition + ORT + NAS (aIRR 0.87, 95% CI: 0.86-0.88).

Discussion

Between April 2007 and March 2018, 0.99% of Ontario-born infants were identified as having been exposed to prenatal opioids. Prenatal opioid exposure in this cohort was associated with decreased use of well-child visits from birth until 24 months of age, including the recommended

Figure 2: Adjusted associations between prenatal opioid exposure and health service use from birth until 13 years of age. The study sample for this analysis included all eligible children (n = 1,343,653)

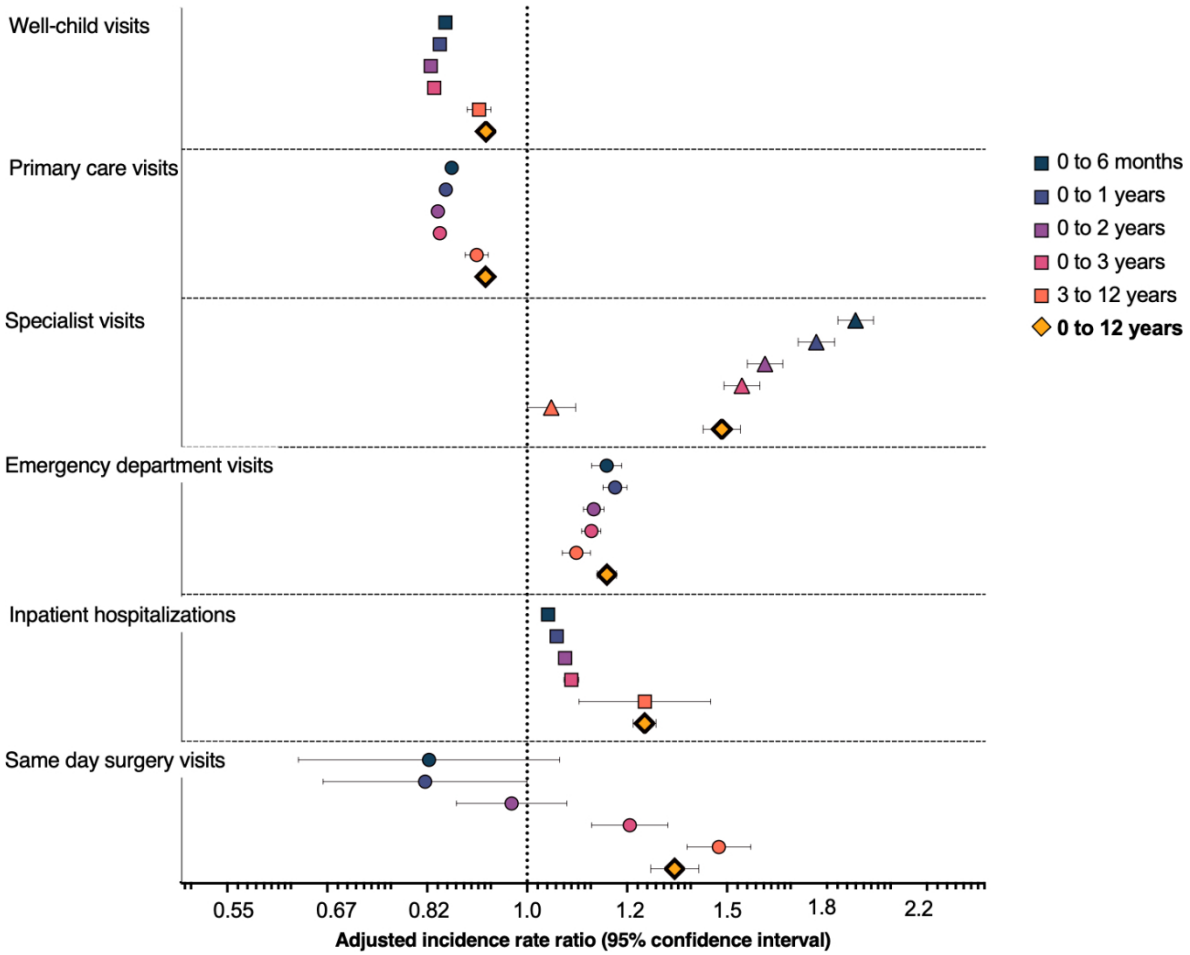


Table 4: Subgroup analyses restricted to term births and singleton births

Outcome	Main analysis	Term births (≥ 37 weeks gestation)	Singleton births
		Adjusted incidence rate ratio (95% CI)	
All well-child visits until 24 months of age	0.82 (0.81, 0.83)	0.81 (0.81, 0.82)	0.82 (0.81, 0.83)
Specialist visits 0-6m	1.93 (1.86, 2.00)	2.14 (2.07, 2.21)	1.95 (1.88, 2.02)
Specialist visits 0-1y	1.78 (1.72, 1.85)	1.90 (1.84, 1.97)	1.79 (1.73, 1.86)
Specialist visits 0-2y	1.61 (1.55, 1.67)	1.64 (1.59, 1.70)	1.61 (1.55, 1.67)
		Adjusted risk ratio (95% CI)	
Completion of 1+ well-child visit between 17-24 months of life[1]	0.89 (0.88, 0.90)	0.90 (0.89, 0.91)	0.90 (0.89, 0.91)

[1]The sample was restricted to all eligible individuals with ≥ 761 days of follow-up.

period for an enhanced visit between 17-24 months. When assessing overall all-cause health services use, exposed infants had lower rates of primary care and well-child visits but higher rates of specialist visits from birth until three years of age, with the disparity diminishing with increasing age. However, prenatal opioid exposure was consistently associated with higher rates of emergency department visits throughout the follow-up period. These findings are consistent with the life course model that would suggest early gaps in care engagement may influence later-life health care trajectories, and this may attenuate for some services over time. Unlike the patterns observed in other health services, the associations with inpatient hospitalisations and same-day surgery visits increased with age. Sensitivity analyses were conducted to account for possible misclassification of exposure and residual confounding, and association estimates remained consistent.

Children with prenatal opioid exposure demonstrated lower rates of well-child visits and were less likely to receive a well-child visit during the recommended 18-month period. Similar findings have been reported in recent studies from the United States [24, 26, 42]. In the Canadian context, a recent study reported that children with prenatal opioid exposure had a

lower attendance of the 18-month enhanced well-child visit (53%) compared to the general Ontario children (61%) [23, 43]. However, our study observed an even lower attendance rate (36.1%), likely due to differences in the definition of prenatal opioid exposure. The exposure definition in this study was designed to capture prenatal opioid use beyond short-term prescribed analgesics, and integrated self-reported opioid use at the first prenatal visit with opioid-related health care encounters during pregnancy. Although this approach may preferentially identify sustained or clinically recognised opioid use, we are not able to reliably classify opioid use severity or differentiate between regulated and unregulated use. Camden et al. [44] employed a broader definition to capture a wider spectrum of prenatal opioid exposure. However, our findings aligned closely with the attendance rates among mothers who used medication for opioid use disorder (34.3%) or had unregulated opioid use during pregnancy (36.6%) [23].

Patterns of health services use varied by the service type across different age intervals up to three years. Exposed infants had higher rates of specialist visits and hospitalisations but lower rates of primary care. Similar trends in inpatient claims and emergency department visits have been observed among privately insured and Medicaid-eligible infants in the US at both 12 [26, 45] and 36 months of age [27]. A systematic review also found that children with a NAS history had lower rates of preventive care utilisation and a higher risk of emergency department visits and hospital readmission [46], aligning with our findings. After the third year, the rates of primary care use and specialist visits declined, while hospitalisations and same-day surgery visits increased with increasing age. Notably, rates of emergency department visits remained consistently high throughout the follow-up period, which did not change with age. A prior study on Medicaid-enrolled children with NAS found that increased healthcare use persisted for the first three years of life but became comparable to non-exposed children afterwards [27]. In contrast, another US study reported that privately insured children with NAS had elevated claims for all types of health services up to eight years of age [45]. While healthcare utilisation declined from birth to three years, overall healthcare use and costs progressively increased from three to eight years among children with NAS. The divergence in findings may be attributable to population characteristics, including insurance type. Insurance coverage has been identified as an important sociodemographic factor influencing healthcare utilisation [46]. In the United States, infants with prenatal opioid exposure or NAS may also have follow-up through child protective services which could influence rates of health care utilisation [46]. Unlike Medicaid-eligible children in previous studies [27], our findings demonstrated an increase in hospitalisation with age, with the largest difference between exposure groups occurring between 3-13 years of age. Although we did not assess the reasons or procedures during the hospitalisations, the persistent disparities suggest that exposed children face ongoing healthcare challenges.

Our findings indicate that children with prenatal opioid exposure experience poorer overall health and face barriers to accessing preventive care services [26, 45]. In addition, some opioid-exposed children in Ontario, and in particular those living on reserve, may receive primary care from nurse-led clinics that do not submit physician billings [47]. This could lead to overestimation of well-child and primary care visits. The lower rates of preventive care use may contribute to greater reliance on ambulatory care services across all age groups. Previous work in Ontario has shown that children with prenatal opioid exposure are less likely to have a primary care provider, which is correlated with well-child visit uptake [23]. Lack of access to a consistent primary care provider may contribute to reduced preventive care uptake and higher emergency department use among opioid-exposed children. These patterns are consistent with those observed in children with chronic health conditions or those from lower-income families [48–51]. Several factors may contribute to low adherence to well-child visits among exposed children. Medical complications during the neonatal period may necessitate immediate medical attention, increasing hospitalisation duration and, subsequently, interfering with attendance at well-child visits [24]. Additionally, mothers with opioid use disorder often encounter barriers when seeking well-child visits, including stigmatisation, concerns about child custody and welfare involvement, limited access to family doctors, and maternal mental health challenges [52]. Furthermore, mothers who use opioids are often reported to experience increased rates of mental health and mood disorders, a history of trauma and abuse, and insufficient social support [53]. These factors are associated with lower satisfaction with healthcare providers, reduced use of primary care, and negative attitudes toward parenting [54], all of which may negatively affect the well-being of their children.

Within the life course theory framework, prenatal opioid exposure can be understood as an adverse exposure that can lead to a chain of events, including an inadequate health care use trajectory or additional adverse exposures. Primary care in early life, particularly well-child visits, may offer opportunities to identify needs, support families, and disrupt adverse trajectories [16]. Within the context of Canada's healthcare system, well-child visits up to 2 years of age could serve as a pragmatic and scalable platform for applying a life course framework in practice to improve developmental and health trajectories for children, including those affected by prenatal opioid exposure. Well-child visits provide critical opportunities for primary care providers to monitor child development, address any parental stress, promote positive parenting strategies, and connect families with early intervention or social support services, and potentially reduce intergenerational transmission of health inequities [22, 55, 56]. Interventions aimed at increasing access to non-traditional preventive care options, such as home visits, group well-child visits, mobile community clinics, or follow-up visits with clinic nurses, may help improve adherence to well-child visits among families affected by prenatal opioid exposure.

Prenatal opioid exposure is entangled with complex environmental and social determinants that may amplify its effects, and residual confounding remains a potential concern. To address this, we applied CEM, which yielded consistent results, albeit with slightly attenuated effect estimates. This suggests that the observed associations largely reflect the independent effect of opioid exposure, with exposed children being more susceptible to residual confounding than their unexposed counterparts.

Additionally, our study examined different exposure definitions and identified variations in maternal characteristics while observing consistent health use outcomes. Exposed mothers identified through opioid-related healthcare encounters had a higher prevalence of substance use disorders, tobacco use, and NICU admissions, whereas those identified through the BIS were more socioeconomically disadvantaged (Supplementary Appendix 8). This distinction may indicate that mothers identified through healthcare encounters represent high-risk individuals who receive medical attention. In contrast, those identified through the BIS may represent high-risk individuals engaged in illicit opioid use. Despite these differences, the associations with uptake of well-child visits and specialist visits remained consistent, highlighting the persistent disparities in health care access among children with prenatal opioid exposure and may be influenced by systemic barriers, social context, and stigma. Notably, self-reported opioid use, despite its potential limitations, proved valuable in identifying maternal opioid use during pregnancy. When the different exposure definitions were compared, 44% were identified using more than one definition (BORN and healthcare encounters), but 40% of the exposure was identified using only the self-reported data from BORN. In addition, we found that the prescription data on opioid replacement therapy did not identify many additional exposed mothers compared to those exposed identified from BORN and maternal opioid use-related healthcare service encounters. Despite differences in case ascertainment across data sources, estimates of well-child visit uptake and health service use were consistent across exposure definitions in sensitivity analyses, suggesting that reliance on prescription or NAS-based definitions alone would primarily alter exposure prevalence rather than meaningfully influence associations with outcomes. Self-reported substance use is typically impacted by social stigma and desirability bias, and the literature reports a moderate correlation between self-reports and urine testing [57–59]. Previous work in BORN has reported a high sensitivity and specificity between the perinatal and clinical records for identifying opioid use, which supports the value of using BORN in identifying maternal opioid use during pregnancy, including unregulated or illicit opioid use [3].

Limitations

This study has several limitations. First, outpatient billing codes were used to ascertain well-child visits and immunisation outcomes, which may have led to an underestimation of preventive care adherence among children who use non-traditional healthcare settings. Families affected by prenatal opioid exposure are less likely to have a primary care provider and may rely on community-based services, which may not directly bill, introducing a potential undercount in billing codes. Further, as discussed above, a proportion of infants exposed to opioids may receive care from non-billing primary care settings, which could potentially exaggerate observed differences in well-child and primary care visit rates. Emergency department, hospitalisation, and acute care outcomes would be less susceptible to incomplete capture. Second, area level socioeconomic data were used in place of individual-level data due to limitations in data quality and completeness. Consequently, important maternal predictors such as health literacy, employment status, social support, and marital status could not be directly assessed. Additionally, the study cohort spanned births from 2007 to 2018, while socioeconomic variables were derived from the 2016 Canadian Census, introducing a temporal gap that may have resulted in misclassification. Third, the cohort may comprise heterogeneous subpopulations affected by opioid exposure in varying ways over time and type of opioid exposure. Although we used multiple data sources to broadly capture varying types of prenatal opioid use, we were not able to fully distinguish medication for opioid use disorder and unregulated use across all individuals. Opioid use during pregnancy is partly ascertained using self-reported data recorded at the first prenatal visit, which likely underestimates true prevalence due to stigma and underreporting. In addition, the available data cannot reliably distinguish the type of opioid, dose, timing, or patterns of use across pregnancy. Given evidence that child health outcomes vary by type and context of prenatal opioid exposure, this exposure heterogeneity may have contributed to non-differential misclassification and attenuation of observed associations. Differences in health care engagement and social context related to opioid type may also contribute to additional heterogeneity in the observed preventive and acute care use patterns. Policy changes, such as the 2011 implementation of Ontario's Narcotics Safety and Awareness Act, may have influenced opioid prescribing patterns and prenatal opioid exposure prevalence. As reported by Corsi et al. [3] and Brogly et al. [1], prenatal opioid exposure decreased since 2012 due to changes in opioid prescribing guidelines to reduce prescribing opioids, analgesics, and cough medicines [2]. However, despite the decreasing trend, the prevalence of presumed illicit opioid use, maternal opioid-related hospital care, and neonatal abstinence syndrome remained largely unchanged [2, 3]. We also attempted to address the impacts of potential temporal changes in the opioid crisis by performing subgroup analyses of children born after July 2012. In this subgroup, the prevalence of prenatal opioid exposure was 1.3% between 2012-2018, compared to 0.99% across the full 2007-2018 period. Finally, our findings may be generalisable only to populations with universal healthcare systems. Insurance coverage has been identified as a key determinant of healthcare utilisation, and US-based studies have indicated that Medicaid eligibility significantly influences service use patterns [45, 46, 60–62]. However, given that over 75% of US children with prenatal opioid exposure are Medicaid-eligible, our findings remain relevant for a substantial proportion of this population [60].

Implications for Public Health and Future Research

Our findings highlight the need to improve preventive healthcare use among children with prenatal opioid exposure. Future research should focus on identifying and implementing targeted interventions to increase adherence to well-child visits, such as expanding access to home visits, mobile clinics, and group well-child visits. Additionally, addressing healthcare provider biases and enhancing parental health literacy may help mitigate barriers to care. These strategies are crucial for ensuring that children affected by prenatal opioid exposure

receive timely preventive care and appropriate healthcare resources.

Conclusion

In summary, prenatal opioid exposure was associated with decreased well-child visit attendance by two years of age and increased emergency department visits throughout early childhood. Furthermore, exposed children had higher rates of specialist visits, hospitalisations, and same-day surgeries, while primary care use remained lower. These findings underscore the need for targeted interventions to improve preventive care access and mitigate adverse health outcomes among children with prenatal opioid exposure.

Acknowledgements

This work was supported by a Canadian Institutes of Health Research (CIHR) Frederick Banting and Charles Best Canada Graduate Scholarship–Master's Award (to AH) and by ICES, which is funded by an annual grant from the Ontario Ministry of Health and the Ministry of Long-Term Care. DJC received an Early Career Investigator Grant in Maternal, Reproductive, Child & Youth Health grant from CIHR. This document used data adapted from the Statistics Canada Postal Code^{OM} Conversion File, which is based on data licensed from Canada Post Corporation, and/or data adapted from the Ontario Ministry of Health Postal Code Conversion File, which contains data copied under licence from ©Canada Post Corporation and Statistics Canada. Parts of this material are based on data and/or information compiled and provided by CIHI, the Ontario Ministry of Health and the Better Outcomes Registry and Network (BORN), part of the Children's Hospital of Eastern Ontario. The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred. We thank IQVIA Solutions Canada Inc. for the use of their Drug Information File.

Statement on Conflicts of Interest

When this project was funded and initiated, DBF was employed by the University of Ottawa and had an academic appointment at the Children's hospital of Eastern Ontario Research Institute; she is now employed by Pfizer and works on an unrelated topic.

Ethics Statement

Research ethics approval for this study was granted by the Research Ethics board of the Children's Hospital of Eastern Ontario, and the privacy impact assessment was approved by the ICES Privacy and Legal Office. The de-identified and linked data were accessed and analysed within a secure environment at ICES, adhering to provincial and institutional privacy policies and procedures.

Data Availability Statement

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organisations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

References

1. Brogly SB, Turner S, Lajkosz K, Davies G, Newman A, Johnson A, et al. Infants born to opioid-dependent women in Ontario, 2002-2014. J Obstet Gynaecol Can. 2017;39(3):157-65. https://doi.org/10.1016/j.jogc.2016.11.009

2. Camden A, Ray JG, To T, Gomes T, Bai L, Guttmann A. Prevalence of prenatal opioid exposure in Ontario, Canada, 2014-2019. JAMA Netw Open. 2021;4(2):e2037388. https://doi.org/10.1001/jamanetworkopen.2020.37388

3. Corsi DJ, Hsu H, Fell DB, Wen SW, Walker M. Association of maternal opioid use in pregnancy with adverse perinatal outcomes in Ontario, Canada, from 2012 to 2018. JAMA Netw Open. 2020;3(7):e208256. https://doi.org/10.1001/jamanetworkopen.2020.8256

4. Kocherlakota P. Neonatal abstinence syndrome. Pediatrics. 2014;134(2):e547-e61. https://doi.org/10.1542/peds.2013-3524

5. Coyle MG, Brogly SB, Ahmed MS, Patrick SW, Jones HE. Neonatal abstinence syndrome. Nat Rev Dis Prim. 2018;4(1):47. https://doi.org/10.1038/s41572-018-0045-0

6. Yoo SH, Jansson LM, Park HJ. Sensorimotor outcomes in children with prenatal exposure to methadone. J AAPOS. 2017;21(4):316-21. https://doi.org/10.1016/j.jaapos.2017.05.025

7. Kelty E, Hulse G. A retrospective cohort study of the health of children prenatally exposed to methadone, buprenorphine or naltrexone compared with non-exposed control children. Am J Addict. 2017;26(8):845-51. https://doi.org/10.1111/ajad.12642

8. Melinder A, Konijnenberg C, Sarfi M. Deviant smooth pursuit in preschool children exposed prenatally to methadone or buprenorphine and tobacco affects integrative visuomotor capabilities. Addiction. 2013;108(12):2175-82. https://doi.org/10.1111/add.12267

9. Ornoy A. The impact of intrauterine exposure versus postnatal environment in neurodevelopmental toxicity: long-term neurobehavioral studies in children at risk for developmental disorders. Toxicol Lett. 2003;140-141:171-81. https://doi.org/10.1016/s0378-4274(02)00505-2

10. Sandtorv LB, Fevang SKE, Nilsen SA, Bøe T, Gjestad R, Haugland S, et al. Symptoms associated with attention deficit/hyperactivity disorder and autism spectrum disorders in school-aged children prenatally exposed to substances. Subst Abuse. 2018;12:1178221818765773. https://doi.org/10.1177/1178221818765773

11. Nygaard E, Slinning K, Moe V, Walhovd KB. Behavior and attention problems in eight-year-old children with prenatal opiate and poly-substance exposure: A longitudinal study. PLoS One. 2016;11(6):e0158054. https://doi.org/10.1371/journal.pone.0158054

12. Fill MA, Miller AM, Wilkinson RH, Warren MD, Dunn JR, Schaffner W, et al. Educational disabilities among children born with neonatal abstinence syndrome. Pediatrics. 2018;142(3):e20180562. https://doi.org/10.1542/peds.2018-0562

13. Oei JL, Melhuish E, Uebel H, Azzam N, Breen C, Burns L, et al. Neonatal abstinence syndrome and high school performance. Pediatrics. 2017;139(2):e20162651. https://doi.org/10.1542/peds.2016-2651

14. Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, et al. Origins of lifetime health around the time of conception: Causes and consequences. Lancet. 2018;391(10132):1842-52. https://doi.org/10.1016/S0140-6736(18)30312-X

15. Pies C, Kotelchuck M. Bringing the MCH Life Course Perspective to life. Matern Child Health J. 2014;18(2):335-8. https://doi.org/10.1007/s10995-013-1408-5

16. World Health Organization. Framework to implement a life course approach in practice [Internet]. 2025. Available from: https://www.who.int/publications/i/item/9789240112575

17. Lynch J, Davey Smith G. A life course approach to chronic disease epidemiology. Annu Rev Public Health. 2005;26:1-35. https://doi.org/10.1146/annurev.publhealth.26.021304.144505

18. Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse health development: Past, present and future. Matern Child Health J. 2014;18(2):344-65. https://doi.org/10.1007/s10995-013-1346-2

19. Pittard WB 3rd, Laditka JN, Laditka SB. Early and periodic screening, diagnosis, and treatment and infant health outcomes in Medicaid-insured infants in South Carolina. J Pediatr. 2007;151(4):414-8. https://doi.org/10.1016/j.jpeds.2007.04.006

20. Tom JO, Mangione-Smith R, Grossman DC, Solomon C, Tseng CW. Well-child care visits and risk of ambulatory care-sensitive hospitalizations. Am J Manag Care. 2013;19(5):354-60. https://www.ajmc.com/view/well-child-care-visits-and-risk-of-ambulatory-caresensitive-hospitalizations

21. Villapiano NL, Winkelman TN, Kozhimannil KB, Davis MM, Patrick SW. Rural and urban differences in neonatal abstinence syndrome and maternal opioid use, 2004 to 2013. JAMA Pediatr. 2017;171(2):194-6. https://doi.org/10.1001/jamapediatrics.2016.3750

22. O'Donnell M, Nassar N, Leonard H, Hagan R, Mathews R, Patterson Y, et al. Increasing prevalence of neonatal withdrawal syndrome: Population study of maternal factors and child protection involvement. Pediatrics. 2009;123(4):e614-21. https://doi.org/10.1542/peds.2008-2888

23. Camden A, To T, Gomes T, Ray J, Bai L, Guttmann A. Prenatal opioid exposure and well-child care in the first 2 years of life: Population-based cohort study. Arch Dis Child. 2023;108(9):754-61. https://doi.org/10.1136/archdischild-2022-325029

24. Goyal NK, Rohde JF, Short V, Patrick SW, Abatemarco D, Chung EK. Well-child care adherence after intrauterine opioid exposure. Pediatrics. 2020;145(2):e20191275. https://doi.org/10.1542/peds.2019-1275

25. Chung E, Short V, Hand D, Gubernick R, Abatemarco D. Poor prenatal care does not predict well child care for children born to mothers with opioid use disorder. J Subst Use. 2020;25:1-7. https://doi.org/10.1080/14659891.2020.1736665

26. Ko JY, Yoon J, Tong VT, Haight SC, Patel R, Rockhill KM, et al. Maternal opioid exposure, neonatal abstinence syndrome, and infant healthcare utilization: A retrospective cohort analysis. Drug Alcohol Depend. 2021;223:108704. https://doi.org/10.1016/j.drugalcdep.2021.108704

27. Corr TE, Xing X, Liu G. Longitudinal health care utilization of Medicaid-insured children with a history of neonatal abstinence syndrome. J Pediatr. 2021;233:82-9.e1. https://doi.org/10.1016/j.jpeds.2021.01.067

28. Stukel TA, Austin PC, Azimaee M, Bronskill SE, Guttmann A, Paterson JM, et al. Envisioning a data science strategy for ICES [Internet]. Toronto, ON, CA: Institute for Clinical Evaluative Sciences; 2017. Available from: https://www.ices.on.ca/publications/research-reports/envisioning-a-data-science-strategy-for-ices/

29. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015;12(10):e1001885. https://doi.org/10.1371/journal.pmed.1001885

30. Better Outcomes Registry & Network (BORN) Ontario [Internet]. Available from: https://www.bornontario.ca/en/index.aspx.

31. Murphy MSQ, Fell DB, Sprague AE, Corsi DJ, Dougan S, Dunn SI, et al. Data resource profile: Better Outcomes Registry & Network (BORN) Ontario. Int J Epidemiol. 2021;50(5):1416-17. https://doi.org/10.1093/ije/dyab033

32. Dunn S, Bottomley J, Ali A, Walker M. 2008 Niday Perinatal Database quality audit: Report of a quality assurance project. Chronic Dis Inj Can. 2011;32(1):32-42. https://doi.org/10.24095/hpcdp.32.1.05

33. Dunn S, Lanes A, Sprague AE, Fell DB, Weiss D, Reszel J, et al. Data accuracy in the Ontario birth registry: A chart re-abstraction study. BMC Health Serv Res. 2019;19(1):1001. https://doi.org/10.1186/s12913-019-4825-3

34. BORN information system: A data quality assessment for public health monitoring [Internet]. Toronto, ON, CA: Public Health Ontario; 2016. Available from: https://coilink.org/20.500.12592/k9pfnb.

35. Working with ICES data [Internet]. Available from: https://www.ices.on.ca/Data-and-Privacy/ICES-data/Working-with-ICES-Data.

36. Canadian Paediatric Society. Schedule of well-child visits [Internet] Ottawa, ON: Canadian Paediatric Society; 2026. Available from: https://www.caringforkids.cps.ca/handouts/schedule_of_well_child_visits.

37. Public Health Ontario. Ontario Marginalization Index (ON-Marg) [Internet]. 2023. Available from: https://www.publichealthontario.ca/en/Data-and-Analysis/Health-Equity/Ontario-Marginalization-Index.

38. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Commun Stat Simul Comput. 2009;38(6):1228-34. https://doi.org/10.1080/03610910902859574

39. Finnegan LP. Effects of maternal opiate abuse on the newborn. Fed Proc. 1985;44(7):2314-7. https://pubmed.ncbi.nlm.nih.gov/3884386/

40. Petrou S, Mehta Z, Hockley C, Cook-Mozaffari P, Henderson J, Goldacre M. The impact of preterm birth on hospital inpatient admissions and costs during the first 5 years of life. Pediatrics. 2003;112(6 Pt 1):1290-7. https://doi.org/10.1542/peds.112.6.1290

41. Rüdiger M, Heinrich L, Arnold K, Druschke D, Reichert J, Schmitt J. Impact of birthweight on health-care utilization during early childhood – A birth cohort study. BMC Pediatr. 2019;19(1):69. https://doi.org/10.1186/s12887-019-1424-8

42. Jarlenski MP, Krans EE, Kim JY, Donohue JM, James AE, 3rd, Kelley D, et al. Five-year outcomes among Medicaid-enrolled children with in utero opioid exposure. Health Aff (Millwood). 2020;39(2):247-55. https://doi.org/10.1377/hlthaff.2019.00740

43. Guttmann A, Saunders NR, Kumar M, Gandhi S, Diong C, MacCon K, et al. Implementation of a physician incentive program for 18-Month developmental screening in Ontario, Canada. J Pediatr. 2020;226:213-20.e1. https://doi.org/10.1016/j.jpeds.2020.03.016

44. Camden A, Ray JG, To T, Gomes T, Bai L, Guttmann A. Identification of prenatal opioid exposure within health administrative databases. Pediatrics. 2021;147(1):e2020018507. https://doi.org/10.1542/peds.2020-018507

45. Liu G, Kong L, Leslie DL, Corr TE. A longitudinal healthcare use profile of children with a history of neonatal abstinence syndrome. J Pediatr. 2019;204:111-7.e1. https://doi.org/10.1016/j.jpeds.2018.08.032

46. Van Horn A, Powell W, Wicker A, Mahairas AD, Creel LM, Bush ML. Outpatient healthcare access and utilization for neonatal abstinence syndrome children: A systematic review. J Clin Transl Sci. 2019;4(5):389-97. https://doi.org/10.1017/cts.2019.407

47. Chiefs of Ontario. Mental health and addictions system performance in Ontario First Nations (2009-2019) [Internet]. 2023. Available from: https://chiefs-of-ontario.org/wp-content/uploads/2023/05/Mental-Health-and-addictions-System-performance-final-report-April-25-2023.pdf.

48. Davidoff A, Kenney G, Dubay L. Effects of the state children's health insurance program expansions on children with chronic health conditions. Pediatrics. 2005;116(1):e34-42. https://doi.org/10.1542/peds.2004-2297

49. Feinberg E, Swartz K, Zaslavsky A, Gardner J, Walker DK. Family income and the impact of a children's health insurance program on reported need for health services and unmet health need. Pediatrics. 2002;109(2):E29. https://doi.org/10.1542/peds.109.2.e29

50. Mayer ML, Skinner AC, Slifkin RT. Unmet need for routine and specialty care: Data from the National Survey of Children With Special Health Care Needs. Pediatrics. 2004;113(2):e109-15. https://doi.org/10.1542/peds.113.2.e109

51. Kaestner R, Joyce T, Racine A. Medicaid eligibility and the incidence of ambulatory care sensitive hospitalizations for children. Soc Sci Med. 2001;52(2):305-13. https://doi.org/10.1016/s0277-9536(00)00133-7

52. Spehr MK, Coddington J, Ahmed AH, Jones E. Parental opioid abuse: Barriers to care, policy, and implications for primary care pediatric providers. J Pediatr Health Care. 2017;31(6):695-702. https://doi.org/10.1016/j.pedhc.2017.05.007

53. Benningfield MM, Arria AM, Kaltenbach K, Heil SH, Stine SM, Coyle MG, et al. Co-occurring psychiatric symptoms are associated with increased psychological, social, and medical impairment in opioid dependent pregnant women. Am J Addict. 2010;19(5):416-21. https://doi.org/10.1111/j.1521-0391.2010.00064.x

54. Rizzo RA, Neumann AM, King SO, Hoey RF, Finnell DS, Blondell RD. Parenting and concerns of pregnant women in buprenorphine treatment. MCN Am J Matern Child Nurs. 2014;39(5):319-24. https://doi.org/10.1097/NMC.0000000000000066

55. McGlade A, Ware R, Crawford M. Child protection outcomes for infants of substance-using mothers: A matched-cohort study. Pediatrics. 2009;124(1):285-93. https://doi.org/10.1542/peds.2008-0576

56. Whiteman VE, Salemi JL, Mogos MF, Cain MA, Aliyu MH, Salihu HM. Maternal opioid drug use during pregnancy and its impact on perinatal morbidity, mortality, and the costs of medical care in the United States. J Pregnancy. 2014:906723. https://doi.org/10.1155/2014/906723

57. Stone R. Pregnant women and substance use: fear, stigma, and barriers to care. Health Justice. 2015;3(1):2. https://doi.org/10.1186/s40352-015-0015-5

58. El Marroun H, Tiemeier H, Jaddoe VW, Hofman A, Verhulst FC, van den Brink W, et al. Agreement between maternal cannabis use during pregnancy according to self-report and urinalysis in a population-based cohort: The Generation R Study. Eur Addict Res. 2011;17(1):37-43. https://doi.org/10.1159/000320550

59. Yonkers KA, Howell HB, Gotman N, Rounsaville BJ. Self-report of illicit substance use versus urine toxicology results from at-risk pregnant women. J Subst Use. 2011;16(5):372-89. https://doi.org/10.3109/14659891003721133

60. Taylor WM, Lu Y, Wang S, Sun LS, Li G, Ing C. Long-term healthcare utilization by Medicaid enrolled children with neonatal abstinence syndrome. J Pediatr. 2020;221:55-63.e6. https://doi.org/10.1016/j.jpeds.2020.02.077

61. Patrick SW, Burke JF, Biel TJ, Auger KA, Goyal NK, Cooper WO. Risk of hospital readmission among infants with neonatal abstinence syndrome. Hosp Pediatr. 2015;5(10):513-9. https://doi.org/10.1542/hpeds.2015-0024

62. Corr TE, Hollenbeak CS. The economic burden of neonatal abstinence syndrome in the United States. Addiction. 2017;112(9):1590-9. https://doi.org/10.1111/add.13842

Abbreviations

aIRR:	Adjusted incidence rate ratio
BIS:	BORN Information System
BORN:	Better Outcomes Registry & Network
CEM:	Coarsened Exact Matching
CI:	Confidence Interval
CIHI:	Canadian Institute for Health Information
DAD:	Discharge Abstract Database
ICES:	Institute for Clinical Evaluative Sciences
IRR:	Incidence rate ratio
NACRS:	National Ambulatory Care Reporting System
NAS:	Neonatal abstinence syndrome
NICU:	Neonatal intensive care unit
NIDAY:	Niday Perinatal database
NMS:	Narcotics Monitoring System
OHIP:	Ontario Health Insurance Plan
OMHRS:	Ontario Mental Health Reporting System
RECORD:	Reporting of studies Conducted using Observational Routinely-collected health Data
RPDB:	Registered Persons Database
SDS:	Same-Day Surgery
SMD:	Standardised mean difference

Supplementary Appendices

Supplementary Appendix 1

Exposure, covariates, and outcome ascertainment timeline

Description: Visual timeline of the ascertainment of maternal covariates, opioid-related health services, self-reported opioid exposure during routine prenatal care, birth outcomes, well-child visits and all-cause health services use, spanning pre-conception to 13 years after the birth of the offspring.

Supplementary Appendix 2

List of health administrative databases used in the study

Description: Includes information on the ICES health administrative databases that were linked BORN/NIDAY to produce the study's dataset, including the variables ascertained from these databases.

Supplementary Appendix 3

Exposure and outcome definitions

Description: Tables including the definitions of each exposure and outcome variable, their data source and identifier codes.

Supplementary Appendix 4

Directed acyclic graph

Description: Directed acyclic graph illustrating associations and causal assumptions between prenatal opioid exposure and offspring health services use.

Supplementary Appendix 5

Complete list of potential covariates and confounding

Description: Table including the definition and/or data source for potential covariates, including maternal demographic variables, maternal health conditions, pregnancy-related information and infant characteristics.

Supplementary Appendix 6

Coarsened Exact Matching

Description: Description of coarsened exact matching and elaboration on the process of applying this analytic method to the study population.

Supplementary Appendix 7

The mean length of stay for hospitalisations

Description: Mean length of stay for hospitalisation by age intervals and exposure status among the entire study population.

Supplementary Appendix 8

Baseline characteristics of children identified as exposed using different exposure definitions among children born between July 2012–March 2018 (n=583,332).

Description: Baseline characteristics of eligible children, born between July 2012 and March 2018, by exposure definition and overall.