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TITLE PAGE

Neighbourhood material deprivation and severe maternal morbidity: A population-based cohort study in Ontario, Canada

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ABSTRACT

Objectives: Rates of age-associated severe maternal morbidity (SMM) have increased in Canada, and an association with neighbourhood income is well established. Our aim was to examine SMM trends according to neighbourhood material deprivation quintile, and to assess whether neighbourhood deprivation effects are moderated by maternal age.

Design, setting, participants: A population-based retrospective cohort study using linked administrative databases in Ontario, Canada. We included primiparous women with a live birth or stillbirth at ≥20 weeks gestational age.

Primary outcome: SMM from pregnancy onset to 42 days postpartum. We calculated SMM rate differences (RD) and rate ratios (RR) by neighbourhood material deprivation quintile for each of four 4-year cohorts from 1 April 2002 to 31 March 2018. Log-binomial multivariable regression adjusted for maternal age, demographic, and pregnancy-related variables.

Results: There were 1,048,845 primiparous births during the study period. The overall rate of SMM was 18.0 per 1,000 births. SMM rates were elevated for women living in areas with high material deprivation. In the final 4-year cohort, the RD between women living in high versus low deprivation neighbourhoods was 3.91 SMM cases per 1,000 births (95% CI: 2.12, 5.70). This was higher than the difference observed during the first 4-year cohort (RD 2.09, 95% CI: 0.62, 3.56). SMM remained associated with neighbourhood material deprivation following multivariable adjustment in the pooled sample (RR 1.16, 95% CI: 1.11, 1,21). There was no evidence of interaction with maternal age.

Conclusion: SMM rate increases were more pronounced for primiparous women living in neighbourhoods with high material deprivation compared to those living in low deprivation

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areas. This raises concerns of a widening social gap in maternal health disparities and highlights an opportunity to focus risk reduction efforts toward disadvantaged women during pregnancy and postpartum.

Keywords: severe maternal morbidity; maternal mortality; maternal health; pregnancy; perinatal epidemiology; social epidemiology; social inequalities; deprivation

Strengths and Limitations of this Study

- Data were from population linked administrative and health registries that capture all hospital births in Ontario, Canada
- Neighbourhood material deprivation was measured using the Ontario Marginalization Index, which was developed using theoretical frameworks on marginalization and deprivation specific to Ontario
- Limiting our study to primiparous women enabled the evaluation of population SMM trends and reduced confounding from previous births
- It was not possible to control for all covariates associated with SMM, including body mass index and the use of assisted reproductive technology

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INTRODUCTION

Each year, approximately 4,000 Canadian women survive a maternal "near-miss"—a life-threatening event associated with pregnancy.[1] To characterize maternal near-misses in a standardized way, the World Health Organization proposed the concept of severe maternal morbidity (SMM), a composite of conditions that represent end-organ dysfunction or states of heightened maternal mortality risk associated with pregnancy, birth, or the postpartum period.[2, 3] Advances in the recognition and management of SMM have resulted in low maternal mortality rates in economically developed nations. Women living in high income countries are now more likely to survive a life-threatening pregnancy condition and, correspondingly, the rates of SMM are 100-fold higher than maternal mortality rates in Canada.[1] However, recent trends in Canada and other high income countries show an increase in SMM rates coinciding with advancing maternal age [4-7]. In a recent Canadian study, women from low-income neighbourhoods had a higher risk of SMM.[4] Women of advanced maternal age tend to come from more advantaged socioeconomic backgrounds and are more likely to have planned pregnancies.[8-10] The effects of maternal age and neighbourhood-level marginalization may therefore interact, with the highest SMM risk among older mothers living in neighbourhoods with higher material deprivation.

Our first objective was to evaluate trends in SMM rates among primiparous women in Ontario by neighbourhood material deprivation quintile between 1 April 2002 and 31 March 2018. Our second objective was to determine if maternal age moderates the effect of neighbourhood material deprivation. We hypothesized that SMM rates would increase disproportionately over time among women living in neighbourhoods with high material

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deprivation. We further hypothesized that the highest risk of SMM would be among women of advanced maternal age living in neighbourhood with the highest material deprivation.

METHODS

This population-based retrospective cohort study used linked administrative datasets for Ontario, held at ICES, which is an independent non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. We followed the RECORD guidelines (REporting of studies Conducted using Observational Routinely-collected Data) for reporting this study.[11]

Patient and public involvement

There was no direct patient or public involvement in this study.

Study population and data sources

The Canadian Institute for Health Information Discharge Abstract Database (DAD) was used to capture all hospital admissions for birth and link to newborn records using the ICES-derived MOMBABY dataset. We included primiparous women aged 10-55 years who had a hospital birth in Ontario and were enrolled in the province's universal health insurance program (OHIP). We identified the first live birth or stillbirth delivery at a gestational age of ≥20 weeks. We used gestational age at birth to calculate pregnancy onset. Women were included if the onset of their first pregnancy was on or after 1 April 2002 and the

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corresponding birth occurred on or before 17 February 2018—allowing 42 days of postpartum follow-up through the study end date of 31 March 2018. Women who had a previous birth within 14 years prior to the index date were excluded. We linked these data with the Registered Persons Database (RPDB), DAD, and OHIP Claims Database to identify exposures and outcomes of interest. To identify women who had recently immigrated to Ontario, we used the Ontario portion of the federal Immigration, Refugees and Citizenship Canada (IRCC) Permanent Resident Database. For neighbourhood material deprivation, we used the 2001 and 2006 Canadian Census, and Ontario Marginalization Index (ON-MARG) database.[12] These datasets were linked using unique encoded identifiers and analyzed at ICES and are shown in **Appendix 1**.

Main outcome

The main outcome was a composite of medical conditions and interventions that comprise SMM. Previously validated indicators for Canada have been used to identify cases of SMM with diagnosis and procedural codes (International Statistical Classification of Diseases and Related Health Problems, 10th revision [ICD-10] and Canadian Classification of Health Interventions, respectively) within administrative databases.[9, 13-15] The composite SMM outcome included: 1) causes of direct obstetric death and conditions related to these (antepartum, intrapartum, and postpartum hemorrhage; hypertensive disorders of pregnancy; eclampsia, and HELLP syndrome; puerperal sepsis; uterine rupture; obstetric embolus); 2) severe organ system dysfunction (cardiac arrest, failure, or arrhythmia; renal or hepatic failure; coagulation defect; thromboembolism; respiratory failure; coma or non-eclamptic seizure; psychosis); 3) procedures or interventions accompanying life-threatening conditions or health states (cesarean or postpartum hysterectomy; pelvic vessel ligation;

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surgical repair of bowel, bladder, or urethra; endotracheal or tracheostomy ventilation; dialysis; blood transfusion in the context of severe blood loss); and 4) deaths that were ill-defined or sudden, as these could not reliably be classified as non-obstetric deaths.

Appendix 1 shows the list of SMM indicators for this study. We specified a binary SMM outcome variable for the presence of one or more indicators occurring from the onset of pregnancy up to and including 42 days after birth.

Exposures and covariates

Our main exposure of interest was neighbourhood material deprivation quintile from the Ontario Marginalization Index (ON-MARG).[12] The index is a neighbourhood-level composite measure of income, educational attainment, single-parent families, and housing quality and is based on Census data from 2001 and 2006. We used the 2001 material deprivation index for births between years 2002-2003, and the 2006 index for years 2004-2018. The change from mandatory Census reporting to the voluntary National Household Survey and resulting data quality concerns meant that the 2011 index was comprised from alternate data sources.[12] We used the 2006 version for all years after 2004 to avoid operationalizing this variable differently between study years. ON-MARG has been used to demonstrate inequalities in various health measures and is stable over time.[16-18] The ON-MARG index is a continuous variable which we modelled in quintiles, with quintile 1 representing neighbourhoods with the lowest material deprivation, and quintile 5 representing neighbourhoods with the highest deprivation.

We included maternal age at birth, categorized in 5-year bands. We adjusted for rural setting using the 2004 and 2008 Rurality Index of Ontario (RIO).[19] We used the 2004 RIO

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index for pregnancies between years 2002 and 2006, and the 2008 index for years 2007 to 2018. We adjusted for number of years since immigration using data from the IRCC. Additional demographic and pregnancy related variables included delivery mode and multiple gestations. For multiple gestation pregnancies, delivery mode was specified based on highest level of intervention: unassisted vaginal birth of all fetuses (lowest), assisted vaginal birth of one or more fetuses, assisted vaginal breech birth of one or more fetuses, and caesarean birth of one or more fetuses (highest). We examined SMM rates by gestational age at birth, induction of labour, and the use of epidural analgesia, however these variables were not adjusted-for in the multivariable models.

Statistical analysis

We summarized baseline characteristics and SMM rates overall for the study population. Due to low birth counts for ages 10-14 years, we collapsed these into an age <20 years group for analysis. We plotted SMM rates by year for the whole study population, and then to evaluate changes over time, we divided the population into four, 4-year cohorts based on pregnancy onset: 1 April 2002 to 31 March 2006 (cohort 1); 1 April 2006 to 31 March 2010 (cohort 2); 1 April 2010 to 31 March 2014 (cohort 3); and 1 April 2014 to 31 March 2018 (cohort 4). To address our first objective, we calculated average annual SMM rates for each 4-year cohort by neighbourhood material deprivation quintile. Within each cohort, we estimated unadjusted absolute rate differences (RD) and rate ratios (RR) with 95% confidence intervals (CI) comparing women in quintile 5 (highest deprivation) with women in quintile 1 (lowest deprivation).

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Our second objective was to evaluate the effect of neighbourhood material deprivation, adjusting for covariates and testing for interaction with maternal age for the overall study population. We constructed multivariable log-binomial regression models. We initially fit a model with neighbourhood material deprivation, adjusting only for year of pregnancy onset (model 1). We then added maternal age (model 2), followed by demographic and pregnancy-related covariates, immigration status, and rurality (model 3). We tested for interaction between material deprivation and maternal age using a cross product term. We did not adjust for stillbirth or gestational age at birth, as these are variables are considered colliders rather than true confounders of outcomes associated with SMM.[20] We did not include induction of labour or epidural analgesia, as these interventions are associated with clinical decisions surrounding birth rather than SMM risk factors. We excluded women with missing information for neighbourhood material deprivation from the multivariable analysis, as these women represented less than 2 percent of the study population (n=17,130).

We performed two additional analyses evaluating SMM rate trends (RD and RR) over the study period, comparing the 4-year average annual rates during cohort 4 to cohort 1 separately by maternal age and by neighbourhood material deprivation quintile. We also examined the 4-year average rates of SMM excluding cases defined by HIV disease. This was done in reference to recently proposed changes to the Canadian SMM composite indicator excluding chronic, asymptomatic HIV disease.[21, 22] Statistical analyses were performed using SAS (version 7.15, SAS Institute Inc., Cary, NC) and STATA (version 13, StataCorp., College Station, TX).

RESULTS

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There were 2,143,045 hospital-based births in Ontario between 1 April 2002 and 17 February 2018, of which 1,048,845 were primiparous births and included in the study (**Figure 1**). The overall SMM rate across the study period was 18.0 per 1,000 births, and increased from 16.7 per 1,000 births in 2002/03 (95% CI: 15.6, 17.9) to 23.0 per 1,000 births in 2017/18 (95% CI: 21.2, 25.0, **Supplementary Figure 1**). Baseline characteristics and SMM rates for each characteristic are presented in **Table 1**. SMM rates were higher at the extremes of maternal age, and among women living in neighbourhoods with the highest material deprivation.

Table 2 presents SMM rates by material deprivation quintile for each of the four 4-year cohorts. The RD was 2.09 cases per 1,000 births (95% CI: 0.62, 3.56), corresponding with a RR of 1.13 (95% CI: 1.04, 1.23) comparing women in quintile 5 with women in quintile 1 during the first 4-year cohort. This increased to a RD of 3.91 cases per 1,000 births (95% CI: 2.12, 5.70) and RR of 1.21 (95% CI: 1.11, 1.32) in the final 4-year cohort of the study period. Average annual SMM rates increased between cohort 1 and cohort 4 for women aged 30-34, and ≥40 years (**Supplementary Table 1**, **Supplementary Figure 2**). For the latter group, the absolute increase was 14.69 cases per 1,000 births (95% CI: 7.96-21.43, **Supplementary Table 2**). SMM rates increased over time for women in each quintile of neighbourhood deprivation, and this increase was most pronounced for women in the highest quintile of neighbourhood deprivation (RD 4.19 cases per 1,000 births 95% CI: 4.13-4.24, **Supplementary Table 2**).

In the multivariable regression analysis for the overall study population, women living in neighbourhoods with the highest material deprivation had higher rates of SMM compared those in neighbourhoods with the lowest after adjusting for pregnancy year (RR: 1.11, 95%

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CI: 1.06, 1.16, **Table 3**). Full adjustment for age, demographic, pregnancy-related variables, and rurality had minimal effect on the association between material deprivation and SMM rates (adjusted RR: 1.16, 95% CI: 1.11, 1.21, **Table 3**). The association between age and SMM persisted in the fully adjusted model, with higher risk for women <20 and ≥30 years of age. We did not find evidence of statistical interaction between maternal age and neighbourhood material deprivation quintile.

DISCUSSION

Main findings

This study demonstrated an association between neighbourhood material deprivation and severe maternal morbidity among primiparous women in Ontario from 2002-2018. Rates of SMM increased across all material deprivation quintiles, and we found some evidence that women in the highest deprivation quintile experienced a higher magnitude SMM rate increase over the 16-year study period compared with women in the lowest deprivation quintile. This finding suggests a possible widening of the gap between the most and least deprived.

Strengths/ limitations

The current study was a population-based analysis of all primiparous hospital births at ≥20 weeks' gestational age in Ontario. Hospital births account for over 98% of births in the province. We used a measure of neighbourhood marginalization that includes income along with other measures of material resources, and that is stable across different health outcomes.[16, 23] Our study nonetheless had some limitations. We were unable to account for births prior to 20 weeks' gestation or births that occurred outside of the province. Our

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measure of SMM was based on validated perinatal health data for Canada.[9, 15] A revision of the Canadian SMM composite was recently proposed which resolves issues surrounding the inclusion of some pre-eclampsia and HELLP syndrome measures, as well as the exclusion of HIV infection—a condition that is unlikely to represent SMM when asymptomatic [21, 22]. We elected to use the former SMM composite for comparison with other world literature, recognizing this may complicate direct comparison with recent Canadian studies [4, 6, 21, 22]. The proportion of women with SMM defined by HIV disease was around 2% for each of the 4-year cohorts, and thus we do not believe these cases substantively altered the results of this study. Several patient-related risk factors, including pre-pregnancy co-morbidities and obesity, contribute to rising SMM rates.[24] Additionally, increased use of assisted reproductive technologies may partially explain SMM trends.[25, 26]. Unfortunately we were unable to control for these factors. Information on immigrants arriving prior to 1985 is not captured in the IRCC Permanent Resident Database. In addition, the IRCC database available at ICES is not able to identify immigrants who landed in other provinces and subsequently moved to Ontario. Although we used a measure of neighbourhood material deprivation developed for Ontario [12], the ON-MARG index does not include individual-level indicators of marginalization or socioeconomic status. Important social determinants may differ among individuals living in areas characterized by similar measures of neighbourhood deprivation.[27]

Interpretation

The present study contributes to our understanding of the association between neighbourhood marginalization and SMM and provides preliminary evidence of a possible widening of this health disparity over time in Ontario. The association between

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neighbourhood-level measures of inequality and risk of SMM has been demonstrated previously in several high-income countries. [6, 26, 28-34] Notably in Canada, Aoyama and colleagues reported a rise in SMM linked to the relative increase in maternal age and found a significant association between SMM and neighbourhood income quintile.[4]. Our study confirms this finding using a measure that encompasses income along with additional measures of neighbourhood material deprivation. Moreover, we extend the current understanding of this association by providing evidence suggesting a possible disproportionate rise in SMM risk experienced by women living in marginalized neighbourhoods over time. We interpret this last finding with caution, however, as our study showed significant rate differences by neighbourhood marginalization only during the first and final 4-year cohorts of the 16-year study period. SMM risks have been demonstrated among other social determinants of health; For example, lower occupational class, Black ethnicity,[35] and non-private health insurance[29] are associated with higher risk of SMM in the US. Interaction between socioeconomic indicators—including ethnicity, education, and poverty—likely contribute to the social gradient of risk such that the protective effects afforded by higher education and income do not fully ameliorate racial disparities in SMM.[30] Our study showed an association between neighbourhood deprivation and SMM suggesting the effects of marginalization persist even in the context of universal healthcare. This is a consistent finding across countries that have similar publicly funded healthcare systems.[33, 36, 37] The factors contributing to social inequality are myriad; ethnicity and country of origin, rurality and access to care, income, material resources, education, and psychosocial supports all have worrisome associations with maternal reproductive health risks.[6, 22, 29, 30, 33, 35-41] How these factors contribute to

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widening health gaps, and what interventions may attenuate their effects will be imperative lines of inquiry going forward as the global challenge to lower SMM continues.

Conclusion

Our study found that women living in areas with higher neighbourhood material deprivation experienced the highest risk of SMM, and this was not fully explained by maternal age. Additionally, women living in high-deprivation neighbourhoods may have experienced a disproportionate increase in the risk of SMM over time. Future work must focus on addressing the widening social gap in maternal health disparities.

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TABLES

Table 1. Baseline characteristics of the study population, 2002/03-2017/18. N=1,048,845 births.

Variable	Number of births	Percent	SMM rate per 1,000 births
Overall study population	1,048,845	100	18.00
Maternal age at birth, years			
10-14	1,330	0.1	26.32
15-19	72,579	6.9	17.79
20-24	178,074	17.0	15.07
25-29	342,003	32.6	15.57
30-34	305,898	29.2	18.48
35-39	123,698	11.8	24.39
≥40	25,263	2.4	34.68
Gestational age at birth, weeks			
20-23	2,751	0.3	53.44
24-27	4,158	0.4	73.59
28-33	17,688	1.7	62.42
34-36	59,040	5.6	33.30
37-41	961,322	91.7	15.89
≥42	3,886	0.4	20.33
Induced labour	275,262	26.2	21.20
Epidural	655,107	62.5	16.35
Delivery mode			
Vaginal unassisted	579,814	55.3	11.01
Vaginal assisted	156,383	14.9	17.42
Vaginal breech	2,328	0.2	40.81
Caesarean	310,320	29.6	31.18
Multiple gestations	20,850	2.0	54.53
Stillbirth	3,645	0.3	54.60
Rurality			
Urban	993,282	94.7	17.93
Rural	55,563	5.3	19.19
Immigration Status			
Non-immigrant / before 1985	739,252	70.5	17.89
Immigrated >10 years	62,381	5.9	18.68
Immigrated 5-10 years	62,090	5.9	20.12
Immigrated <5 years	185,122	17.7	17.52
Neighbourhood material deprivation			

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Quintile 1 (least deprived)	237,877	22.7	17.58
Quintile 2	186,550	17.8	16.68
Quintile 3	189,575	18.1	17.55
Quintile 4	191,376	18.2	17.89
Quintile 5 (most deprived)	226,337	21.6	19.43
Missing	17,130	1.6	25.57

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Table 2. Four-year average SMM rates per 1,000 births for neighbourhood material deprivation quintiles, by study period cohort.

Cohort[a]	*SMM rates by material deprivation quintile* Q1 (least)	Q2	Q3	Q4	Q5 (most)	*Q5 vs Q1* Rate difference (95% CI)	Rate ratio (95% CI)
1	16.05	16.36	17.46	16.49	18.14	2.09 (0.62, 3.56)**	1.13 (1.04, 1.23)**
2	16.58	15.97	15.73	16.37	17.32	0.75 (-0.70, 2.20)	1.05 (0.96, 1.14)
3	19.36	16.17	18.34	19.19	20.78	1.41 (-0.20, 3.02)	1.07 (0.99, 1.16)
4	18.41	18.52	18.99	20.18	22.32	3.91 (2.12, 5.70)***	1.21 (1.11, 1.32)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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Table 3. Neighbourhood material deprivation and risk of SMM: Adjusted multivariable models, RR (95% CI). N=1,031,715 births.

Variable	Model 1[a]	Model 2[b]	Model[c]
Maternal age (years)			
<20		1.05 (0.99, 1.12)	1.20 (1.13, 1.28)
20-24		0.95 (0.90, 0.99)	1.01 (0.96, 1.06)
25-29		1 (ref)	1 (ref)
30-34		1.19 (1.14, 1.23)	1.10 (1.06, 1.15)
35-39		1.56 (1.49, 1.63)	1.34 (1.28, 1.40)
≥40		2.21 (2.06, 2.37)	1.73 (1.61, 1.86)
Material deprivation			
Quintile 1 (least)	1 (ref)	1 (ref)	1 (ref)
Quintile 2	0.95 (0.91, 0.99)	0.97 (0.93, 1.02)	0.97 (0.92, 1.01)
Quintile 3	1.00 (0.96, 1.05)	1.04 (0.99, 1.08)	1.03 (0.98, 1.07)
Quintile 4	1.02 (0.98, 1.07)	1.07 (1.02, 1.12)	1.06 (1.01, 1.11)
Quintile 5 (most)	1.11 (1.06, 1.16)	1.17 (1.12, 1.22)	1.16 (1.11, 1.21)

[a]adjusted for pregnancy year

[b]adjusted for pregnancy year, age

[c]adjusted for pregnancy year, age, delivery mode, multiple gestations, immigration status, rurality

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FIGURE CAPTIONS

Figure 1. Study inclusion / exclusion flow chart, primiparous births.

SUPPLEMENTARY MATERIAL CAPTIONS

Supplementary Appendix 1. Data sources for the project.

Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002/03-2017/18.

Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.

Supplementary Table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

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Declaration of competing interests

The authors declare no conflicts of interest.

Author contributions

JWS, DF, KEM, and LCR contributed to the overall conception of the study. JWS, ML, LR, DF, and LCR contributed to study design and protocol. TW had full access to data used in the study. JWS, TW, and LCR take responsibility for the integrity of the data analysis. JWS wrote the manuscript. All authors made substantial contributions to the data analysis interpretation, and manuscript editing and revising for this project. All authors approve the final submitted version and agree to be accountable for all aspects of the work.

Ethical approval

ICES is a prescribed entity under section 45 of Ontario's Personal Health Information Protection Act. Section 45 authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects conducted under section 45, by definition, do not require review by a Research Ethics Board. This project was conducted under section 45, and approved by ICES' Privacy and Legal Office.

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Patient consent for publication

None required.

Data availability statement

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

Funding

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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.

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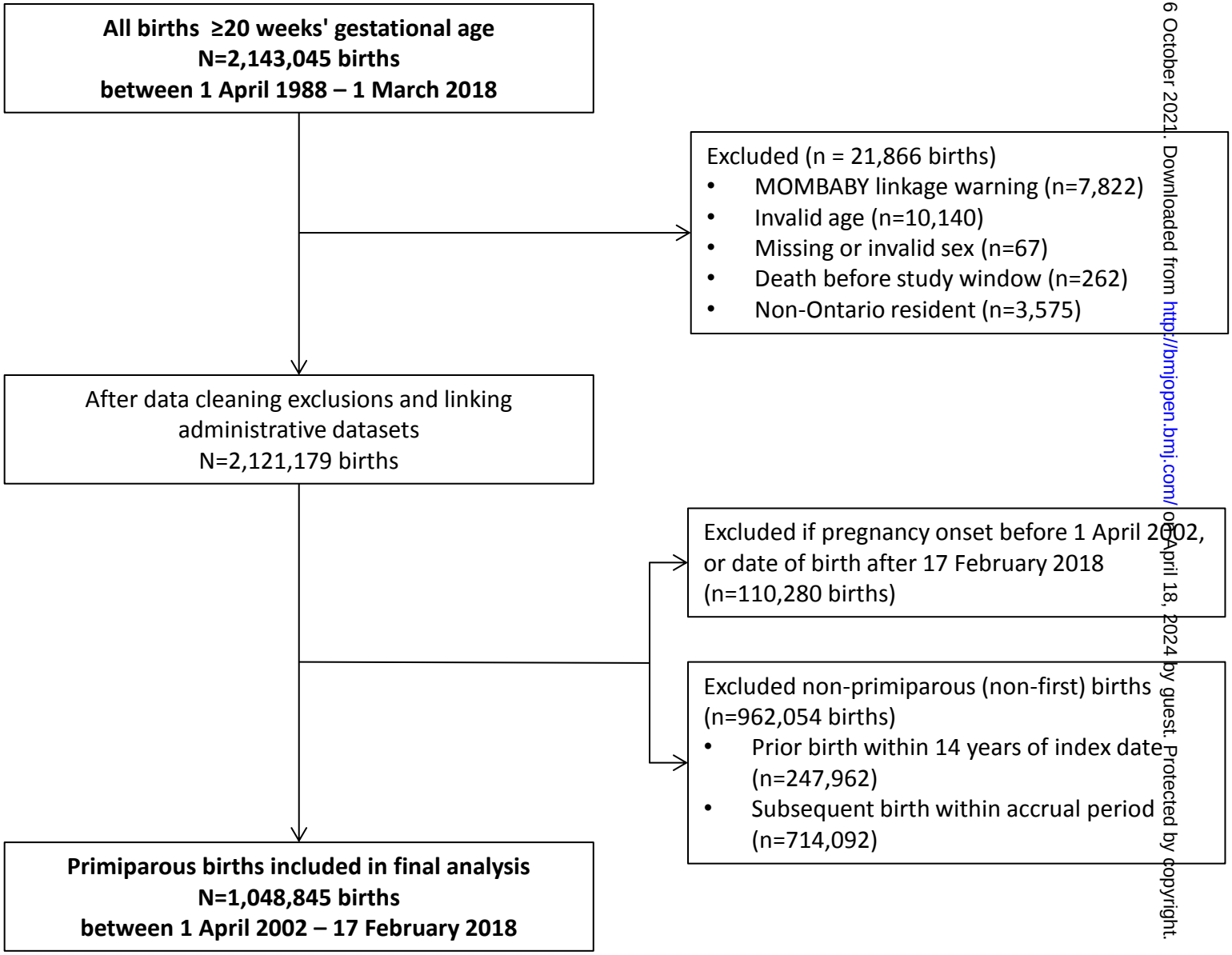
Figure 1. Study inclusion / exclusion flow chart, primiparous births.



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Supplementary Appendix 1. Data sources for project

Discharge Abstract Database (DAD)
The DAD is compiled by the Canadian Institute for Health Information and contains administrative, clinical (diagnoses and procedures/interventions), demographic, and administrative information for all admissions to acute care hospitals, rehab, chronic, and day surgery institutions in Ontario. At ICES, consecutive DAD records are linked together to form 'episodes of care' among the hospitals to which patients have been transferred after their initial admission.

MOMBABY
The ICES MOMBABY Database is an ICES-derived cohort that links the DAD inpatient admission records of delivering mothers and their newborns. From 2002 onward, this linkage is performed deterministically using a maternal-newborn chart matching number. Prior to 2002, mothers were linked to their children by matching on the institutions they were admitted, their postal codes, and their admission/discharge dates.

Registered Persons Database (RPDB)
The RPDB provides basic demographic information (age, sex, location of residence, date of birth, and date of death for deceased individuals) for those issued an Ontario health insurance number. The RPDB also indicates the time periods for which an individual was eligible to receive publicly funded health insurance benefits and the best known

Ontario Health Insurance Plan (OHIP)
The OHIP claims database contains information on inpatient and outpatient services provided to Ontario residents eligible for the province's publicly funded health insurance system by fee-for-service health care practitioners (primarily physicians) and "shadow billings" for those paid through non-fee-for-service payment plans. The main data elements include patient and physician identifiers (encrypted), code for service provided, date of service, associated diagnosis, and fee paid.

Immigration, Refugees, and Citizenship Canada's (IRCC) Permanent Resident Database
The Ontario portion of the IRCC Permanent Resident Database includes immigration application records for people who initially applied to land in Ontario since 1985. The dataset contains permanent residents' demographic information such as country of citizenship, level of education, mother tongue, and landing date. New immigrants who are currently residing in Ontario but originally landed in another province are not captured in this dataset.

Ontario Marginalization Index (ONMARG)
ONMARG is a geographically (census) based index developed to quantify the degree of marginalization occurring across the province of Ontario. It is comprised of four major dimensions thought to underlie the construct of marginalization: residential instability, material deprivation, dependency, and ethnic concentration. The dataset contains census divisions (CD), census tracts (CT), census subdivisions (CSD), consolidated municipal service manager areas (CMSM), public health units (PHU), local health integration networks (LHIN), sub-LHINs, and dissemination areas (DA).

These datasets were linked using unique encoded identifiers and analyzed at ICES.

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

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Inclusion/Exclusion Criteria

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Inclusion Criteria				
Hospital birth (live or stillbirth) at gestational age ≥20 weeks	DAD, MOMBABY	ICD-10 main patient service code for "Obstetrical birth"	Accrual window: 1 April 2002 – 17 Feb 2018	Canadian Institute for Health Information Discharge Abstract Database (DAD, linked to newborn record in MOMBABY dataset) See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=MOMBABY
Exclusion Criteria				
Missing or invalid IKN	RPDB		Index date	Registered Persons Database See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=RPDB
MOMBABY linkage warning	MOMBABY		Index date	
Missing or invalid age (<10 or >55)	RPDB		Index date	
Missing or invalid sex	RPDB		Index date	
Death before the index date	RPDB		Index date	
Non-Ontario residents / invalid OHIP number	RPDB		Index date	
Any births with an index date occurring outside of the accrual period	MOMBABY		Accrual window	Pregnancy onset before 1 April 2002
Any births occurring after accrual end date	MOMBABY		Accrual window	Births after 17 February 2018
Not first birth	MOMBABY		14 years prior to index date	Prior record in MOMBABY within past 14 years of index date
Not first birth in accrual period	MOMBABY		Accrual window	Subsequent records in MOMBABY

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Outcome

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Severe maternal morbidity (SMM)	DAD	ICD 10 CCI	Start of lookback period ("pregnancy onset" = index date – gestational age at birth) to end of observation window (42 days following index date)	Patient considered to have outcome IF ANY code in ANY of the following: 1) Obstetric/ ill-defined or sudden death 2) Hypertensive heart/renal disease 3) Eclampsia 4) Cerebral venous thrombosis 5) Complications of anaesthesia – non-cardiac 6) Complications of anaesthesia – cardiac 7) Cardiac diseases (cardiac arrest, infarction, failure, pulmonary edema) 8) Placental abruption c/ coagulation defect 9) Antepartum hemorrhage c/ coagulation defect 10) Intrapartum hemorrhage c/ coagulation defect 11) Uterine rupture – before labour 12) Uterine rupture – during labour 13) Obstetric shock (including septic shock) 14) Septecemia during labour 15) Puerperal sepsis 16) Pulmonary embolism 17) Obstetric embolism 18) Cardiomyopathy 19) Acute renal failure 20) HIV disease 21) Cerebrovascular disease 22) Acute respiratory distress syndrome 23) Acute abdomen 24) Hepatic failure 25) Acute psychosis 26) Cerebral edema, coma 27) Disseminated intravascular coagulation 28) Sickle cell anemia crisis 29) Status asthmaticus 30) Status epilepticus 31) Assisted ventilation (endotracheal tube or tracheostomy) 32) Caesarean hysterectomy 33) Postpartum hysterectomy 34) Dialysis 35) Evacuation of incisional hematoma 36) Surgical repair of bladder, urethra, intestine 37) Intrapartum hemorrhage with no coagulation defect AND blood transfusion 38) Postpartum hemorrhage AND blood

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				transfusion 39) Placenta previa AND blood transfusion 40) Embolization/ ligation/ suturing AND postpartum hemorrhage See: Joseph KS et al, 2009,[1] Joseph KS et al, 2010,[2] ICD-10CA, 2009,[3] and CCHI, 2012.[4]

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Study exposures, covariates

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Age	RPDB		Index date	
Index year	DAD		Index date	
Material deprivation index	ONMARG		Index date	Ontario Marginalization Index, Material Deprivation, in quintiles. Use version of ONMARG closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=ONMARG
Income quintile	RPDB Census		Index date	Ontario Census area profile: income quintile. Use Census closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CENSUS
Rurality	RPDB		Index date	Rurality Index for Ontario (RIO). Use version of RIO closest to year of index date: RIO2004 for 2002-2006 RIO2008 for 2007-2018
Gestational age at birth	MOMBABY		Index date	
Induction of labour	DAD	CCI code	Within index hospitalization	Canadian Classification of Health Interventions (CCI)
Epidural	DAD OHIP	CCI code OHIP fee code	Within index hospitalization	Canadian Classification of Health Interventions (CCI); Ontario Health Insurance Plan Claims Database (OHIP)
Delivery mode	DAD	CCI code	Within index hospitalization	
Multiple gestations	MOMBABY		Within index hospitalization	
Stillbirth	MOMBABY		Within index hospitalization	
Immigration status	IRCC		Index date	Immigration, Refugees and Citizenship

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				Canada (IRCC)'s Permanent Resident Database Number of years since arrived in Ontario. See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CIC

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4. *Canadian Classification of Health Interventions.* Ottawa: Canadian Institute for Health Information;2012.

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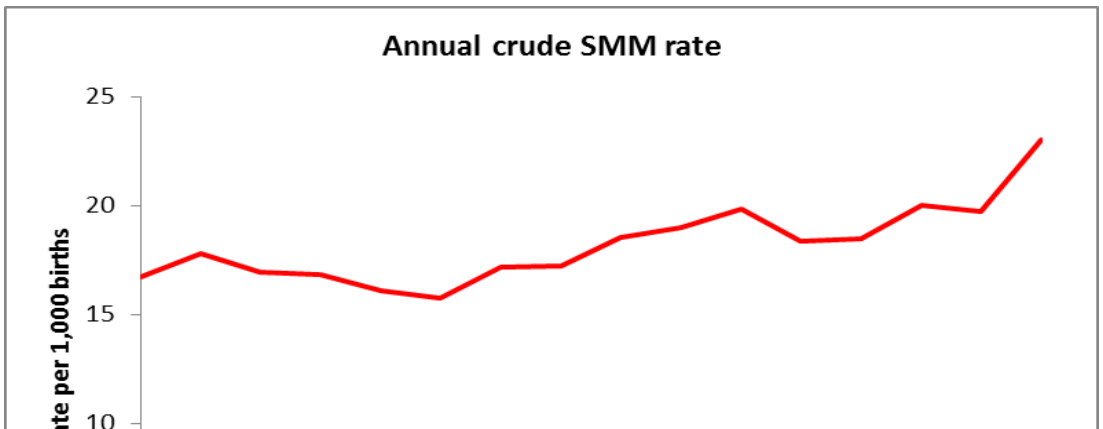
Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002/03-2017/18.



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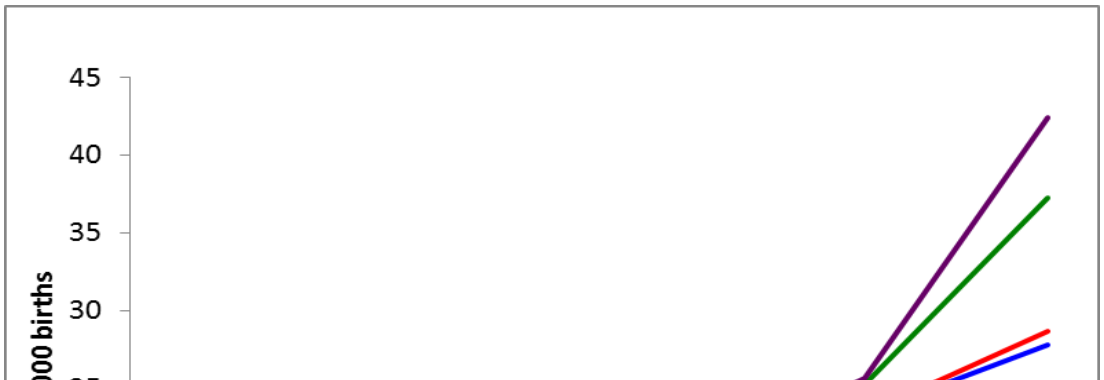
Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.



[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

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Supplementary table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

Variable	*SMM rates by cohort*[a] 1	2	3	4	*SMM rate change, cohort 4 vs 1*[a] Rate difference (95% CI)	Rate ratio (95% CI)
Overall study population	17.10	16.55	18.94	19.82	2.72 (1.96, 3.49)***	1.16 (1.11, 1.21)***
Maternal age (years)						
<20	17.54	17.22	17.97	20.34	2.80 (-0.43, 6.04)	1.15 (0.98, 1.37)
20-24	14.80	13.47	16.32	16.40	1.60 (-0.15, 3.35)	1.11 (0.99, 1.24)
25-29	15.26	14.40	16.37	16.42	1.15 (-0.77, 2.39)	1.08 (0.99, 1.16)
30-34	17.58	17.10	19.21	20.16	2.58 (1.18, 3.97)*	1.15 (1.06, 1.23)***
35-39	23.31	23.35	25.23	25.67	2.36 (-0.16, 4.88)	1.10 (0.99, 1.22)
≥40	27.78	28.68	37.30	42.48	14.69 (7.96, 21.43)*	1.53 (1.24, 1.89)***
Material deprivation						
Quintile 1 (least)	16.05	16.58	19.36	18.41	2.36 (2.31, 2.41)***	1.15 (1.14, 1.15)***
Quintile 2	16.36	15.97	16.17	18.52	2.16 (2.11, 2.22)***	1.13 (1.13, 1.14)***
Quintile 3	17.46	15.73	18.34	18.99	1.54 (1.48, 1.59)***	1.09 (1.08, 1.09)***
Quintile 4	16.49	16.37	19.19	20.18	3.69 (3.63, 3.74)***	1.22 (1.22, 1.23)***
Quintile 5 (most)	18.14	17.32	20.78	22.32	4.19 (4.13, 4.24)***	1.23 (1.22, 1.23)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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The RECORD statement – checklist of items 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	Title page (p.1)	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. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title page, abstract (p. 1-3)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Background p.4-5		
Objectives	3	State specific objectives, including any prespecified hypotheses	Background p.4-5		
Methods					
Study Design	4	Present key elements of study design early in the paper	Methods p.5-9		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods: *Study population and data sources, Main outcome,* p. 5-6		

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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 *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 *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	Cohort study, no matching: Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Appendix 1	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. 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. 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1	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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement).	Methods: *Study population and data sources, Main outcome, Exposures*		

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		Describe comparability of assessment methods if there is more than one group	*and covariates* p. 5-8; Supplementary Appendix 1		
Bias	9	Describe any efforts to address potential sources of bias	Methods: *Exposures and covariates* p. 7-8; Interpretation: *Strengths/ limitations* p.11-12		
Study size	10	Explain how the study size was arrived at	Methods: *Study population and data sources,* p. 5-6; Figure 1		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Methods: *Statistical analysis,* p. 8-9		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of	Methods: *Statistical analysis,* p. 8-9, Results, p.9-11.		

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		sampling strategy (e) Describe any sensitivity analyses			
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. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Methods: *Study population and data sources,* p. 5-6; Supplementary Appendix 1; Author contributions, p. 20
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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1
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) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	Results p.10; Table 1; Figure 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Results p.10; Table 1; Figure 1; Supplementary Appendix 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information	Results p.10; Table 1		

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		on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	Results p.10; Figure 1; Table 1		
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 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results p.10; Table 1-3; Supplementary Figure 1		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Results p.10-11		

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Discussion					
Key results	18	Summarise key results with reference to study objectives	Interpretation, *Main findings* p.11		
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	Interpretation, *Strengths/limitations* p.11-12	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.	Interpretation, *Strengths/limitations* p.11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion, *Main findings* p. 11, *Strengths / Limitations* p. 11-12		
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion, *Interpretation* p.11-12		
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	Funding, p. 21-22		
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.	p. 21; Supplementary Appendix 1

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TITLE PAGE

Neighbourhood material deprivation and severe maternal morbidity: A population-based cohort study in Ontario, Canada

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ABSTRACT

Objectives: Rates of age-associated severe maternal morbidity (SMM) have increased in Canada, and an association with neighbourhood income is well established. Our aim was to examine SMM trends according to neighbourhood material deprivation quintile, and to assess whether neighbourhood deprivation effects are moderated by maternal age.

Design, setting, participants: A population-based retrospective cohort study using linked administrative databases in Ontario, Canada. We included primiparous women with a live birth or stillbirth at ≥20 weeks gestational age.

Primary outcome: SMM from pregnancy onset to 42 days postpartum. We calculated SMM rate differences (RD) and rate ratios (RR) by neighbourhood material deprivation quintile for each of four 4-year cohorts from 1 April 2002 to 31 March 2018. Log-binomial multivariable regression adjusted for maternal age, demographic, and pregnancy-related variables.

Results: There were 1,048,845 primiparous births during the study period. The overall rate of SMM was 18.0 per 1,000 births. SMM rates were elevated for women living in areas with high material deprivation. In the final 4-year cohort, the RD between women living in high versus low deprivation neighbourhoods was 3.91 SMM cases per 1,000 births (95% CI: 2.12, 5.70). This was higher than the difference observed during the first 4-year cohort (RD 2.09, 95% CI: 0.62, 3.56). SMM remained associated with neighbourhood material deprivation following multivariable adjustment in the pooled sample (RR 1.16, 95% CI: 1.11, 1,21). There was no evidence of interaction with maternal age.

Conclusion: SMM rate increases were more pronounced for primiparous women living in neighbourhoods with high material deprivation compared to those living in low deprivation

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areas. This raises concerns of a widening social gap in maternal health disparities and highlights an opportunity to focus risk reduction efforts toward disadvantaged women during pregnancy and postpartum.

Keywords: severe maternal morbidity; maternal mortality; maternal health; pregnancy; perinatal epidemiology; social epidemiology; social inequalities; deprivation

Strengths and Limitations of this Study

- Data were from population linked administrative and health registries that capture all hospital births in Ontario, Canada
- Neighbourhood material deprivation was measured using the Ontario Marginalization Index, a comprehensive area-level measure based on Census data developed using theoretical frameworks on marginalization and deprivation
- Limiting our study to primiparous women enabled the evaluation of population SMM trends and reduced confounding from previous births
- It was not possible to control for all covariates associated with SMM, including body mass index, co-morbidities, and the use of assisted reproductive technology

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INTRODUCTION

Each year, approximately 4,000 Canadian women survive a maternal "near-miss"—a life-threatening event associated with pregnancy.[1] To characterize maternal near-misses in a standardized way, the World Health Organization proposed the concept of severe maternal morbidity (SMM), a composite of conditions that represent end-organ dysfunction or states of heightened maternal mortality risk associated with pregnancy, birth, or the postpartum period.[2, 3] Advances in the recognition and management of SMM have resulted in low maternal mortality rates in economically developed nations. Women living in high income countries are now more likely to survive a life-threatening pregnancy condition and, correspondingly, the rates of SMM are 100-fold higher than the rates of maternal mortality in Canada.[1] However, recent trends in Canada and other high income countries show an increase in SMM rates coinciding with advancing maternal age and corresponding increases in pre-existing co-morbidities and the use of assisted reproductive technology.[4-9]

The literature also shows persistent though complex associations between SMM and the social determinants of health. Low occupational class, Black ethnicity,[10] and non-private health insurance[11] are all associated with higher risk of SMM in the US. Canadian women who experience SMM are more likely to come from a low-income background, and to originate from an African or Caribbean country.[4, 6, 12] A systematic review found evidence for effects of material dimensions of inequality on SMM risk, though it pointed out the need for further work on other dimensions and in elucidating effect mechanisms.[13] Women of advanced maternal age may be more likely to come from more advantaged socioeconomic backgrounds and to have planned pregnancies.[14-16] This suggests the possibility for effect modification, whereby the negative effects of advanced maternal age

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may be attenuated for women who come from more advantaged backgrounds, and exacerbated for women from disadvantaged backgrounds. The effects of maternal age and neighbourhood-level material deprivation may therefore interact, with the highest SMM risk among older women living in neighbourhoods with higher deprivation.

In this study, our first objective was to evaluate trends in SMM rates among primiparous women in Ontario by neighbourhood material deprivation quintile between 1 April 2002 and 31 March 2018. Our second objective was to determine if maternal age moderates the effect of neighbourhood material deprivation. We hypothesized that SMM rates would increase disproportionately over time among women living in neighbourhoods with high material deprivation. We further hypothesized that the highest risk of SMM would be among women of advanced maternal age living in neighbourhoods with the highest material deprivation.

METHODS

This population-based retrospective cohort study used linked administrative datasets for Ontario, held at ICES, which is an independent non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. We followed the RECORD guidelines (REporting of studies Conducted using Observational Routinely-collected Data) for reporting this study.[17]

Patient and public involvement

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There was no direct patient or public involvement in this study.

Study population and data sources

The Canadian Institute for Health Information Discharge Abstract Database (DAD) was used to capture all hospital admissions for birth and link to newborn records using the ICES-derived MOMBABY dataset. We included primiparous women aged 10-55 years who had a hospital birth in Ontario and were enrolled in the province's universal health insurance program (OHIP). We identified the first live birth or stillbirth delivery at a gestational age of ≥20 weeks. We used gestational age at birth to calculate pregnancy onset. Women were included if the onset of their first pregnancy was on or after 1 April 2002 and the corresponding birth occurred on or before 17 February 2018—allowing 42 days of postpartum follow-up through the study end date of 31 March 2018. Women who had a previous birth within 14 years prior to the index date were excluded. We linked these data with the Registered Persons Database (RPDB), DAD, and OHIP Claims Database to identify exposures and outcomes of interest. To identify women who had recently immigrated to Ontario, we used the Ontario portion of the federal Immigration, Refugees and Citizenship Canada (IRCC) Permanent Resident Database. For neighbourhood material deprivation, we used the 2001 and 2006 Canadian Census, and Ontario Marginalization Index (ON-MARG).[18] These datasets were linked using unique encoded identifiers and analyzed at ICES and are shown in **Appendix 1**.

Main outcome

The main outcome was a composite of medical conditions and interventions that comprise SMM. Cases of SMM were identified using diagnosis and procedural codes (International

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Statistical Classification of Diseases and Related Health Problems, 10th revision [ICD-10] and Canadian Classification of Health Interventions, respectively) within the DAD database.[15, 19-21] The DAD data have been validated and shown to accurately reflect the information in medical records.[21, 22] The composite SMM outcome included: 1) causes of direct obstetric death and conditions related to these (antepartum, intrapartum, and postpartum hemorrhage; hypertensive disorders of pregnancy and eclampsia; puerperal sepsis; uterine rupture; obstetric embolus); 2) severe organ system dysfunction (cardiac arrest, failure, or arrhythmia; renal or hepatic failure; coagulation defect; thromboembolism; respiratory failure; coma or non-eclamptic seizure; psychosis); 3) procedures or interventions accompanying life-threatening conditions or health states (cesarean or postpartum hysterectomy; pelvic vessel ligation; surgical repair of bowel, bladder, or urethra; endotracheal or tracheostomy ventilation; dialysis; blood transfusion in the context of severe blood loss); and 4) deaths that were ill-defined or sudden, as these could not reliably be classified as non-obstetric deaths. **Appendix 1** shows the list of SMM indicators for this study. We specified a binary SMM outcome variable for the presence of one or more indicators occurring from the onset of pregnancy up to and including 42 days after birth.

Exposures and covariates

Our main exposure of interest was neighbourhood material deprivation quintile from the Ontario Marginalization Index (ON-MARG). ON-MARG is the Ontario-specific version of the Canadian marginalization index (CAN-MARG).[23] The index was developed based on theoretical frameworks of marginalization and deprivation, and derived empirically using principal component analysis of Canadian Census variables.[18, 23]The material deprivation dimension is comprised of the following Census measures, each expressed as a proportion:

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population aged ≥20 without secondary school graduation, single parent families, households receiving government transfer payments, population aged ≥15 who are unemployed, population living below the low income cut-off (adjusted for community size, household size, and inflation).[18] The geographical unit of aggregation is Dissemination Areas, which average 400-700 people and cover the entirety of Canadian territory.[24] ON-MARG can be operationalized as a standardized interval scale based on factor loadings from the principal component analysis, or as quintiles each representing 20% of Dissemination Areas.[18, 23] We modelled this exposure as quintiles, with quintile 1 representing neighbourhoods with the lowest material deprivation, and quintile 5 representing neighbourhoods with the highest deprivation.[18, 23] ON-MARG has been used to demonstrate inequalities in various health measures and is stable over time.[25-27] We used the 2001 material deprivation index for births between years 2002-2003, and the 2006 index for years 2004-2018. The change from mandatory Census reporting to the voluntary National Household Survey and resulting data quality concerns meant that the 2011 index was comprised from alternate data sources.[28] We used the 2006 version for all years after 2004 to avoid operationalizing this variable differently between study years.

We included maternal age at birth, categorized in 5-year bands. We adjusted for rural setting using the 2004 and 2008 Rurality Index of Ontario (RIO).[29] We used the 2004 RIO index for pregnancies between years 2002 and 2006, and the 2008 index for years 2007 to 2018. We adjusted for number of years since immigration using data from the IRCC.

Additional demographic and pregnancy related variables included delivery mode and multiple gestations. For multiple gestation pregnancies, delivery mode was specified based on highest level of intervention: unassisted vaginal birth of all fetuses (lowest), assisted

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vaginal birth of one or more fetuses, assisted vaginal breech birth of one or more fetuses, and caesarean birth of one or more fetuses (highest). We examined SMM rates by gestational age at birth, induction of labour, and the use of epidural analgesia, however these variables were not adjusted-for in the multivariable models.

Statistical analysis

We summarized baseline characteristics and SMM rates overall for the study population. Due to low birth counts for ages 10-14 years, we collapsed these into an age <20 years group for analysis. We plotted SMM rates by year for the whole study population, and then to evaluate changes over time, we divided the population into four, 4-year cohorts based on pregnancy onset: 1 April 2002 to 31 March 2006 (cohort 1); 1 April 2006 to 31 March 2010 (cohort 2); 1 April 2010 to 31 March 2014 (cohort 3); and 1 April 2014 to 31 March 2018 (cohort 4). To address our first objective, we calculated average annual SMM rates for each 4-year cohort by neighbourhood material deprivation quintile. Within each cohort, we estimated unadjusted absolute rate differences (RD) and rate ratios (RR) with 95% confidence intervals (CI) comparing women in quintile 5 (highest deprivation) with women in quintile 1 (lowest deprivation).

Our second objective was to evaluate the effect of neighbourhood material deprivation, adjusting for covariates and testing for interaction with maternal age for the overall study population. We constructed multivariable log-binomial regression models. We initially fit a model with neighbourhood material deprivation, adjusting only for year of pregnancy onset (model 1). We then added maternal age (model 2), followed by demographic and pregnancy-related covariates, immigration status, and rurality (model 3). We tested for

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interaction between material deprivation and maternal age using a cross product term. We did not adjust for stillbirth or gestational age at birth, as these are variables are considered colliders rather than true confounders of outcomes associated with SMM.[30] We did not include induction of labour or epidural analgesia, as these interventions are associated with clinical decisions surrounding birth rather than SMM risk factors. We excluded women with missing information for neighbourhood material deprivation from the multivariable analysis, as these women represented less than 2 percent of the study population (n=17,130).

We performed two additional analyses evaluating SMM rate trends (RD and RR) over the study period, comparing the 4-year average annual rates during cohort 4 to cohort 1 separately by maternal age and by neighbourhood material deprivation quintile. We also examined the 4-year average rates of SMM excluding cases defined by HIV disease. This was done in reference to recently proposed changes to the Canadian SMM composite indicator excluding chronic, asymptomatic HIV disease.[12, 31] Statistical analyses were performed using SAS (version 7.15, SAS Institute Inc., Cary, NC) and STATA (version 13, StataCorp., College Station, TX).

RESULTS

There were 2,143,045 hospital-based births in Ontario between 1 April 2002 and 17 February 2018, of which 1,048,845 were primiparous births and included in the study (**Figure 1**). The overall SMM rate across the study period was 18.0 per 1,000 births, and increased from 16.7 per 1,000 births in 2002-03 (95% CI: 15.6, 17.9) to 23.0 per 1,000 births in 2017-18 (95% CI: 21.2, 25.0, **Supplementary Figure 1**). Baseline characteristics and SMM case number and rate for each characteristic are presented in **Table 1**. SMM rates were

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higher at the extremes of maternal age, and among women living in neighbourhoods with the highest material deprivation.

Table 2 presents SMM rates by material deprivation quintile for the pooled study sample (2002-2018) and each of the four 4-year cohorts. The RD was 2.09 cases per 1,000 births (95% CI: 0.62, 3.56), corresponding with a RR of 1.13 (95% CI: 1.04, 1.23) comparing women in quintile 5 with women in quintile 1 during the first 4-year cohort. This increased to a RD of 3.91 cases per 1,000 births (95% CI: 2.12, 5.70) and RR of 1.21 (95% CI: 1.11, 1.32) in the final 4-year cohort of the study period. Average annual SMM rates increased between cohort 1 and cohort 4 for women aged 30-34, and ≥40 years (**Supplementary Table 1**, **Supplementary Figure 2**). For the latter group, the absolute increase was 14.69 cases per 1,000 births (95% CI: 7.96-21.43, **Supplementary Table 1**). SMM rates increased over time for women in each quintile of neighbourhood deprivation, and this increase was most pronounced for women in the highest quintile of neighbourhood deprivation (RD 4.19 cases per 1,000 births 95% CI: 4.13-4.24, **Supplementary Table 1**).

In the multivariable regression analysis for the overall study population, women living in neighbourhoods with the highest material deprivation had higher rates of SMM compared to those in neighbourhoods with the lowest after adjusting for pregnancy year (RR: 1.11, 95% CI: 1.06, 1.16, **Table 3**). Full adjustment for age, demographics, pregnancy-related variables, and rurality had minimal effect on the association between material deprivation and SMM rates (adjusted RR: 1.16, 95% CI: 1.11, 1.21, **Table 3**). The association between age and SMM persisted in the fully adjusted model, with higher risk for women <20 and ≥30 years of age. We did not find evidence of statistical interaction between maternal age and neighbourhood material deprivation quintile.

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DISCUSSION

Main findings

This study demonstrated an association between neighbourhood material deprivation and severe maternal morbidity among primiparous women in Ontario from 2002-2018. Rates of SMM increased across all material deprivation quintiles, and we found some evidence that women in the highest deprivation quintile experienced a higher magnitude SMM rate increase over the 16-year study period compared with women in the lowest deprivation quintile. This finding suggests a possible widening of the gap between women living in the most and least deprived neighbourhoods.

Strengths/ limitations

The current study was a population-based analysis of all primiparous hospital births at ≥20 weeks' gestational age in Ontario. Hospital births account for over 98% of births in the province. We used a measure of neighbourhood marginalization that includes income along with other measures of material resources, and that is stable across time and different health outcomes.[23, 25] Our study nonetheless had some limitations. We were unable to account for births prior to 20 weeks' gestation or births that occurred outside of the province. Our measure of SMM was based on validated perinatal health data for Canada.[15, 21] A revision of the Canadian SMM composite was recently developed which resolves issues surrounding the inclusion of some pre-eclampsia and HELLP syndrome measures, as well as the exclusion of HIV infection—a condition that is unlikely to represent SMM when asymptomatic [12, 31]. We elected to use the former SMM composite for comparison with previous literature, recognizing this may complicate direct comparison

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with recent Canadian studies [4, 6, 12, 31]. The proportion of women with SMM defined by HIV disease was around 2 percent for each of the 4-year cohorts, and thus we do not believe these cases substantively altered the results of this study. Information on immigrants arriving prior to 1985 is not captured in the IRCC Permanent Resident Database, and the database does not identify immigrants who landed in other provinces and subsequently moved to Ontario. Although we used a measure of neighbourhood material deprivation developed for Ontario using Canadian Census elements,[28] the ON-MARG index does not include individual-level indicators of marginalization or socioeconomic status. Important social determinants may differ among individuals living in areas characterized by similar measures of neighbourhood deprivation, and it is not possible to elucidate the causal pathways that link social disadvantage to poor health outcomes without incorporating such factors.[32, 33] Finally, pre-pregnancy co-morbidities, obesity, and the use of assisted reproductive technology, contribute to higher SMM rates and may partially explain SMM trends.[8, 9, 34] We were unable to account for these factors. Obstetric comorbidity indices have been developed for risk prediction and adjustment in clinical research. [35, 36] We did not use an obstetric comorbidity index in our adjusted analysis as some index indicators represent SMM outcomes themselves, or are mediators of SMM outcomes. In addition, our aim was to examine population SMM trends rather than individual clinical risk factors.

Interpretation

The present study contributes to our understanding of the association between neighbourhood marginalization and SMM and provides preliminary evidence of a possible widening of this health disparity over time in Ontario. The association between neighbourhood-level measures of inequality and risk of SMM has been demonstrated

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previously in several high-income countries.[6, 9, 11, 13, 37-41] Notably in Canada, Aoyama and colleagues reported a rise in SMM linked to the relative increase in maternal age and found a significant association between SMM and neighbourhood income quintile.[4]. Our study confirms this finding using a measure that encompasses income along with additional measures of neighbourhood material deprivation. Moreover, we extend the current understanding of this association by providing evidence for a possible disproportionate rise in SMM risk experienced by women living in marginalized neighbourhoods over time. We interpret this last finding with caution, as our study showed significant rate differences by neighbourhood marginalization only during the first and final 4-year cohorts of the 16-year study period. SMM risks have been demonstrated among other social determinants of health; for example, lower occupational class, Black ethnicity,[10] and non-private health insurance[11] are associated with higher risk of SMM in the US. Interaction between socioeconomic indicators—including ethnicity, education, and poverty—likely contribute to the social gradient of risk such that the protective effects afforded by higher education and income do not fully ameliorate racial disparities in SMM.[38] Our study showed an association between neighbourhood deprivation and SMM suggesting the effects of marginalization persist even in the context of universal healthcare. This is a consistent finding across countries that have similar publicly funded healthcare systems.[41-43] The factors contributing to social inequality are myriad; ethnicity and country of origin, rurality and access to care, income, material resources, education, and psychosocial supports all have worrisome associations with maternal reproductive health risks.[6, 10-12, 38, 41-47] How these factors contribute to widening health gaps, and what interventions may

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attenuate their effects will be imperative lines of inquiry going forward as the global challenge to lower SMM continues.

Conclusion

Ontario women living in areas with higher neighbourhood material deprivation experienced the highest risk of SMM, and this association was not fully explained by maternal age. Additionally, women living in high-deprivation neighbourhoods may have experienced a disproportionate increase in the risk of SMM over time. Future work must focus on addressing the widening social gap in maternal health disparities.

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TABLES

Table 1. Baseline characteristics of the study population, 2002-2018. N=1,048,845 births.

Variable	Number of births	Percent	Number of SMM cases	SMM rate per 1,000 births
Overall study population	1,048,845	100	18,880	18.00
Maternal age at birth, years				
10-14	1,330	0.1	35	26.32
15-19	72,579	6.9	1,291	17.79
20-24	178,074	17.0	2,684	15.07
25-29	342,003	32.6	5,324	15.57
30-34	305,898	29.2	5,653	18.48
35-39	123,698	11.8	3,017	24.39
≥40	25,263	2.4	876	34.68
Gestational age at birth, weeks				
20-23	2,751	0.3	147	53.44
24-27	4,158	0.4	306	73.59
28-33	17,688	1.7	1,104	62.42
34-36	59,040	5.6	1,966	33.30
37-41	961,322	91.7	15,278	15.89
≥42	3,886	0.4	79	20.33
Induced labour	275,262	26.2	5,836	21.20
Epidural	655,107	62.5	10,713	16.35
Delivery mode				
Vaginal unassisted	579,814	55.3	6,386	11.01
Vaginal assisted	156,383	14.9	2,724	17.42
Vaginal breech	2,328	0.2	95	40.81
Caesarean	310,320	29.6	9,675	31.18
Multiple gestations	20,850	2.0	1,137	54.53
Stillbirth	3,645	0.3	199	54.60
Rurality				
Urban	993,282	94.7	17,814	17.93
Rural	55,563	5.3	1,066	19.19
Immigration Status				
Non-immigrant / before 1985	739,252	70.5	13,222	17.89
Immigrated >10 years	62,381	5.9	1,165	18.68
Immigrated 5-10 years	62,090	5.9	1,249	20.12
Immigrated <5 years	185,122	17.7	3,244	17.52
Neighbourhood marginalization				
Material deprivation				
Quintile 1 (least deprived)	237,877	22.7	4,183	17.58
Quintile 2	186,550	17.8	3,112	16.68
Quintile 3	189,575	18.1	3,327	17.55

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Quintile 4	191,376	18.2	3,423	17.89
Quintile 5 (most deprived)	226,337	21.6	4,397	19.43
Missing	17,130	1.6	438	25.57

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Table 2. Four-year average SMM rates per 1,000 births for neighbourhood material deprivation quintiles, by pooled sample (2002-2018) and by study period cohort.

	SMM rates by material deprivation quintile					*Q5 vs Q1*	
Cohort[a]	**Q1 (least)**	**Q2**	**Q3**	**Q4**	**Q5 (most)**	**Rate difference (95% CI)**	**Rate ratio (95% CI)**
Pooled	17.58	16.68	17.55	17.89	19.43	1.84 (1.82,1.87)***	1.10 (1.10-1.11)***
1	16.05	16.36	17.46	16.49	18.14	2.09 (0.62, 3.56)**	1.13 (1.04, 1.23)**
2	16.58	15.97	15.73	16.37	17.32	0.75 (-0.70, 2.20)	1.05 (0.96, 1.14)
3	19.36	16.17	18.34	19.19	20.78	1.41 (-0.20, 3.02)	1.07 (0.99, 1.16)
4	18.41	18.52	18.99	20.18	22.32	3.91 (2.12, 5.70)***	1.21 (1.11, 1.32)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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Table 3. Neighbourhood material deprivation and risk of SMM: Adjusted multivariable models, RR (95% CI). N=1,031,715 births.

Variable	Model 1[a]	Model 2[b]	Model[c]
Maternal age (years)			
<20		1.05 (0.99, 1.12)	1.20 (1.13, 1.28)
20-24		0.95 (0.90, 0.99)	1.01 (0.96, 1.06)
25-29		1 (ref)	1 (ref)
30-34		1.19 (1.14, 1.23)	1.10 (1.06, 1.15)
35-39		1.56 (1.49, 1.63)	1.34 (1.28, 1.40)
≥40		2.21 (2.06, 2.37)	1.73 (1.61, 1.86)
Material deprivation			
Quintile 1 (least)	1 (ref)	1 (ref)	1 (ref)
Quintile 2	0.95 (0.91, 0.99)	0.97 (0.93, 1.02)	0.97 (0.92, 1.01)
Quintile 3	1.00 (0.96, 1.05)	1.04 (0.99, 1.08)	1.03 (0.98, 1.07)
Quintile 4	1.02 (0.98, 1.07)	1.07 (1.02, 1.12)	1.06 (1.01, 1.11)
Quintile 5 (most)	1.11 (1.06, 1.16)	1.17 (1.12, 1.22)	1.16 (1.11, 1.21)

[a]adjusted for pregnancy year

[b]adjusted for pregnancy year, age

[c]adjusted for pregnancy year, age, delivery mode, multiple gestations, immigration status, rurality

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FIGURE CAPTIONS

Figure 1. Study inclusion / exclusion flow chart, primiparous births.

SUPPLEMENTARY MATERIAL CAPTIONS

Supplementary Appendix 1. Data sources for the project.

Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002-2018.

Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.

Supplementary Table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

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Declaration of competing interests

The authors declare no conflicts of interest.

Author contributions

JWS, DF, KEM, and LCR contributed to the overall conception of the study. JWS, ML, LR, DF, and LCR contributed to study design and protocol. TW had full access to data used in the study. JWS, TW, and LCR take responsibility for the integrity of the data analysis. JWS wrote the manuscript. All authors made substantial contributions to the data analysis interpretation, and manuscript editing and revising for this project. All authors approve the final submitted version and agree to be accountable for all aspects of the work.

Ethical approval

ICES is a prescribed entity under section 45 of Ontario's Personal Health Information Protection Act. Section 45 authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects conducted under section 45, by definition, do not require review by a Research Ethics Board. This project was conducted under section 45, and approved by ICES' Privacy and Legal Office.

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Patient consent for publication

None required.

Data availability statement

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

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those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

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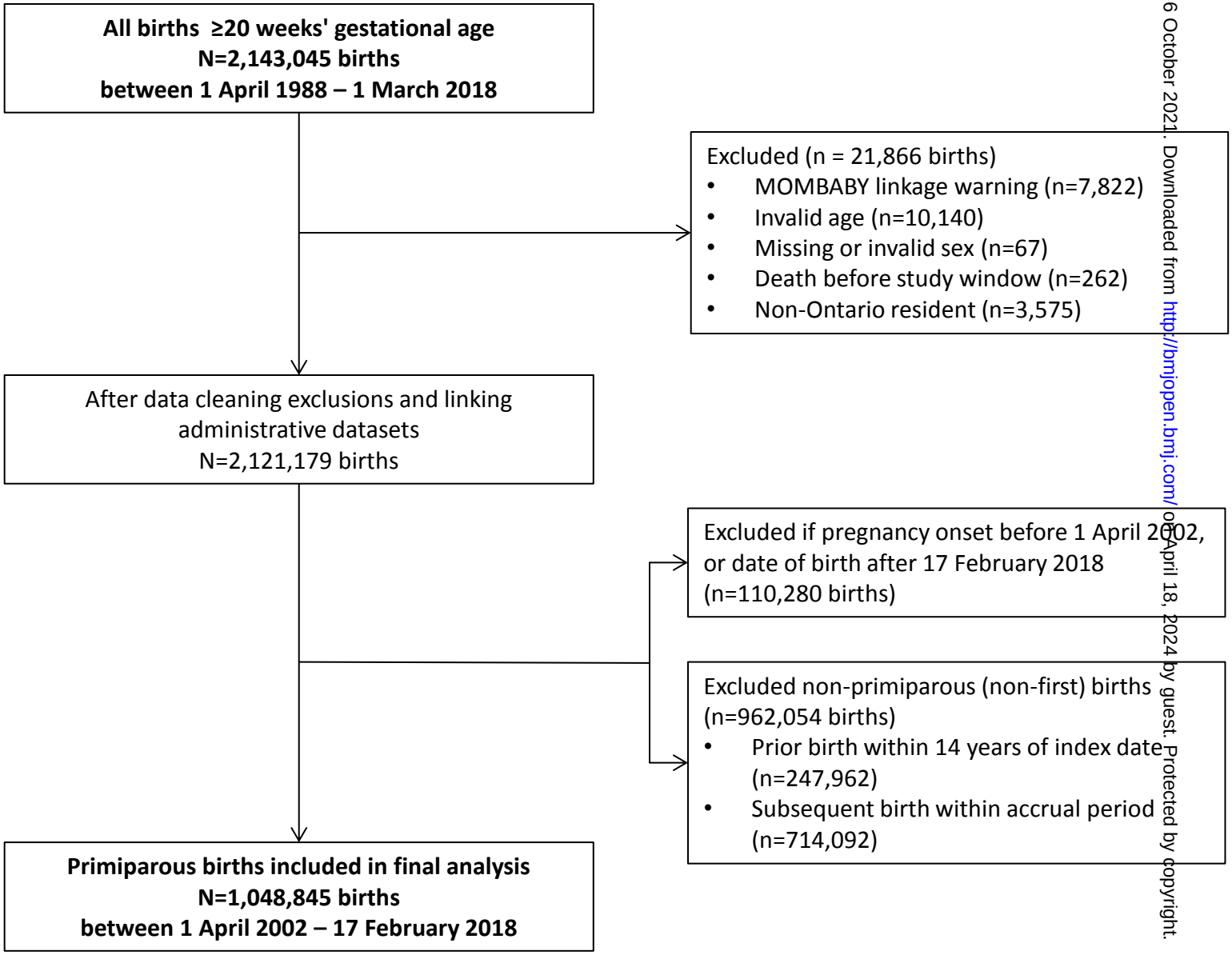
Figure 1. Study inclusion / exclusion flow chart, primiparous births.



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Supplementary Appendix 1. Data sources for project

Discharge Abstract Database (DAD)
The DAD is compiled by the Canadian Institute for Health Information and contains administrative, clinical (diagnoses and procedures/interventions), demographic, and administrative information for all admissions to acute care hospitals, rehab, chronic, and day surgery institutions in Ontario. At ICES, consecutive DAD records are linked together to form 'episodes of care' among the hospitals to which patients have been transferred after their initial admission.

MOMBABY
The ICES MOMBABY Database is an ICES-derived cohort that links the DAD inpatient admission records of delivering mothers and their newborns. From 2002 onward, this linkage is performed deterministically using a maternal-newborn chart matching number. Prior to 2002, mothers were linked to their children by matching on the institutions they were admitted, their postal codes, and their admission/discharge dates.

Registered Persons Database (RPDB)
The RPDB provides basic demographic information (age, sex, location of residence, date of birth, and date of death for deceased individuals) for those issued an Ontario health insurance number. The RPDB also indicates the time periods for which an individual was eligible to receive publicly funded health insurance benefits and the best known

Ontario Health Insurance Plan (OHIP)
The OHIP claims database contains information on inpatient and outpatient services provided to Ontario residents eligible for the province's publicly funded health insurance system by fee-for-service health care practitioners (primarily physicians) and "shadow billings" for those paid through non-fee-for-service payment plans. The main data elements include patient and physician identifiers (encrypted), code for service provided, date of service, associated diagnosis, and fee paid.

Immigration, Refugees, and Citizenship Canada's (IRCC) Permanent Resident Database
The Ontario portion of the IRCC Permanent Resident Database includes immigration application records for people who initially applied to land in Ontario since 1985. The dataset contains permanent residents' demographic information such as country of citizenship, level of education, mother tongue, and landing date. New immigrants who are currently residing in Ontario but originally landed in another province are not captured in this dataset.

Ontario Marginalization Index (ONMARG)
ONMARG is a geographically (census) based index developed to quantify the degree of marginalization occurring across the province of Ontario. It is comprised of four major dimensions thought to underlie the construct of marginalization: residential instability, material deprivation, dependency, and ethnic concentration. The dataset contains census divisions (CD), census tracts (CT), census subdivisions (CSD), consolidated municipal service manager areas (CMSM), public health units (PHU), local health integration networks (LHIN), sub-LHINs, and dissemination areas (DA).

These datasets were linked using unique encoded identifiers and analyzed at ICES.

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

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Inclusion/Exclusion Criteria

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Inclusion Criteria				
Hospital birth (live or stillbirth) at gestational age ≥20 weeks	DAD, MOMBABY	ICD-10 main patient service code for "Obstetrical birth"	Accrual window: 1 April 2002 – 17 Feb 2018	Canadian Institute for Health Information Discharge Abstract Database (DAD, linked to newborn record in MOMBABY dataset) See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=MOMBABY
Exclusion Criteria				
Missing or invalid IKN	RPDB		Index date	Registered Persons Database See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=RPDB
MOMBABY linkage warning	MOMBABY		Index date	
Missing or invalid age (<10 or >55)	RPDB		Index date	
Missing or invalid sex	RPDB		Index date	
Death before the index date	RPDB		Index date	
Non-Ontario residents / invalid OHIP number	RPDB		Index date	
Any births with an index date occurring outside of the accrual period	MOMBABY		Accrual window	Pregnancy onset before 1 April 2002
Any births occurring after accrual end date	MOMBABY		Accrual window	Births after 17 February 2018
Not first birth	MOMBABY		14 years prior to index date	Prior record in MOMBABY within past 14 years of index date
Not first birth in accrual period	MOMBABY		Accrual window	Subsequent records in MOMBABY

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Outcome

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Severe maternal morbidity (SMM)	DAD	ICD 10 CCI	Start of lookback period ("pregnancy onset" = index date – gestational age at birth) to end of observation window (42 days following index date)	Patient considered to have outcome IF ANY code in ANY of the following: 1) Obstetric/ ill-defined or sudden death 2) Hypertensive heart/renal disease 3) Eclampsia 4) Cerebral venous thrombosis 5) Complications of anaesthesia – non-cardiac 6) Complications of anaesthesia – cardiac 7) Cardiac diseases (cardiac arrest, infarction, failure, pulmonary edema) 8) Placental abruption c/ coagulation defect 9) Antepartum hemorrhage c/ coagulation defect 10) Intrapartum hemorrhage c/ coagulation defect 11) Uterine rupture – before labour 12) Uterine rupture – during labour 13) Obstetric shock (including septic shock) 14) Septecemia during labour 15) Puerperal sepsis 16) Pulmonary embolism 17) Obstetric embolism 18) Cardiomyopathy 19) Acute renal failure 20) HIV disease 21) Cerebrovascular disease 22) Acute respiratory distress syndrome 23) Acute abdomen 24) Hepatic failure 25) Acute psychosis 26) Cerebral edema, coma 27) Disseminated intravascular coagulation 28) Sickle cell anemia crisis 29) Status asthmaticus 30) Status epilepticus 31) Assisted ventilation (endotracheal tube or tracheostomy) 32) Caesarean hysterectomy 33) Postpartum hysterectomy 34) Dialysis 35) Evacuation of incisional hematoma 36) Surgical repair of bladder, urethra, intestine 37) Intrapartum hemorrhage with no coagulation defect AND blood transfusion 38) Postpartum hemorrhage AND blood

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				transfusion 39) Placenta previa AND blood transfusion 40) Embolization/ ligation/ suturing AND postpartum hemorrhage See: Joseph KS et al, 2009,[1] Joseph KS et al, 2010,[2] ICD-10CA, 2009,[3] and CCHI, 2012.[4]

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Study exposures, covariates

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Age	RPDB		Index date	
Index year	DAD		Index date	
Material deprivation index	ONMARG		Index date	Ontario Marginalization Index, Material Deprivation, in quintiles. Use version of ONMARG closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=ONMARG
Income quintile	RPDB Census		Index date	Ontario Census area profile: income quintile. Use Census closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CENSUS
Rurality	RPDB		Index date	Rurality Index for Ontario (RIO). Use version of RIO closest to year of index date: RIO2004 for 2002-2006 RIO2008 for 2007-2018
Gestational age at birth	MOMBABY		Index date	
Induction of labour	DAD	CCI code	Within index hospitalization	Canadian Classification of Health Interventions (CCI)
Epidural	DAD OHIP	CCI code OHIP fee code	Within index hospitalization	Canadian Classification of Health Interventions (CCI); Ontario Health Insurance Plan Claims Database (OHIP)
Delivery mode	DAD	CCI code	Within index hospitalization	
Multiple gestations	MOMBABY		Within index hospitalization	
Stillbirth	MOMBABY		Within index hospitalization	
Immigration status	IRCC		Index date	Immigration, Refugees and Citizenship

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				Canada (IRCC)'s Permanent Resident Database Number of years since arrived in Ontario. See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CIC

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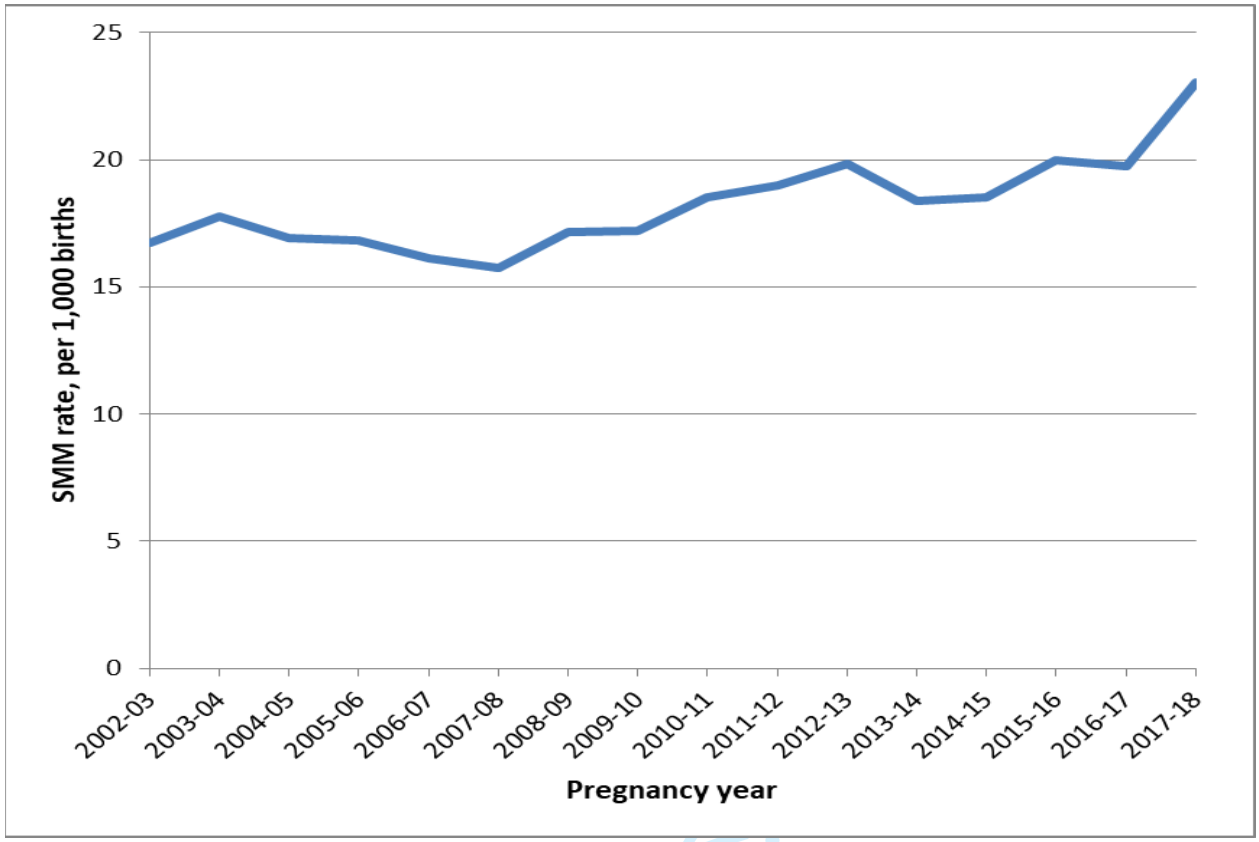
Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002-2018.



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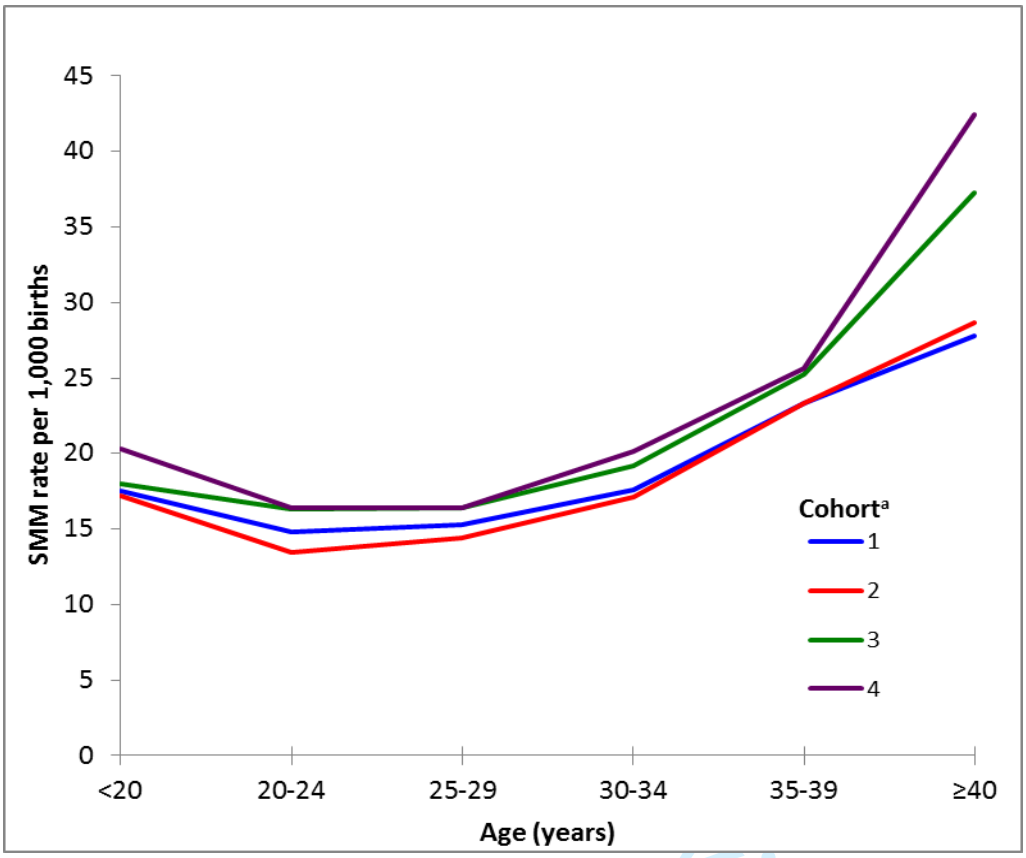
Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.



[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

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Supplementary table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

	SMM rates by cohort[a]				*SMM rate change, cohort 4 vs 1*[a]	
Variable	**1**	**2**	**3**	**4**	**Rate difference (95% CI)**	**Rate ratio (95% CI)**
Overall study population	17.10	16.55	18.94	19.82	2.72 (1.96, 3.49)***	1.16 (1.11, 1.21)***
Maternal age (years)						
<20	17.54	17.22	17.97	20.34	2.80 (-0.43, 6.04)	1.15 (0.98, 1.37)
20-24	14.80	13.47	16.32	16.40	1.60 (-0.15, 3.35)	1.11 (0.99, 1.24)
25-29	15.26	14.40	16.37	16.42	1.15 (-0.77, 2.39)	1.08 (0.99, 1.16)
30-34	17.58	17.10	19.21	20.16	2.58 (1.18, 3.97)*	1.15 (1.06, 1.23)*
35-39	23.31	23.35	25.23	25.67	2.36 (-0.16, 4.88)	1.10 (0.99, 1.22)
≥40	27.78	28.68	37.30	42.48	14.69 (7.96, 21.43)*	1.53 (1.24, 1.89)*
Material deprivation						
Quintile 1 (least)	16.05	16.58	19.36	18.41	2.36 (2.31, 2.41)***	1.15 (1.14, 1.15)***
Quintile 2	16.36	15.97	16.17	18.52	2.16 (2.11, 2.22)***	1.13 (1.13, 1.14)***
Quintile 3	17.46	15.73	18.34	18.99	1.54 (1.48, 1.59)***	1.09 (1.08, 1.09)***
Quintile 4	16.49	16.37	19.19	20.18	3.69 (3.63, 3.74)***	1.22 (1.22, 1.23)***
Quintile 5 (most)	18.14	17.32	20.78	22.32	4.19 (4.13, 4.24)***	1.23 (1.22, 1.23)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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The RECORD statement – checklist of items 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	Title page (p.1)	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. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title page, abstract (p. 1-3)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Background p.4-5		
Objectives	3	State specific objectives, including any prespecified hypotheses	Background p.4-5		
Methods					
Study Design	4	Present key elements of study design early in the paper	Methods p.5-9		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods: *Study population and data sources, Main outcome,* p. 5-6		

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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 *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 *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	Cohort study, no matching: Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Appendix 1	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. 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. 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1	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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement).	Methods: *Study population and data sources, Main outcome, Exposures*		

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		Describe comparability of assessment methods if there is more than one group	*and covariates* p. 5-8; Supplementary Appendix 1		
Bias	9	Describe any efforts to address potential sources of bias	Methods: *Exposures and covariates* p. 7-8; Interpretation: *Strengths/ limitations* p.11-12		
Study size	10	Explain how the study size was arrived at	Methods: *Study population and data sources,* p. 5-6; Figure 1		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Methods: *Statistical analysis,* p. 8-9		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of	Methods: *Statistical analysis,* p. 8-9, Results, p.9-11.		

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		sampling strategy (e) Describe any sensitivity analyses			
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. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Methods: *Study population and data sources,* p. 6; Supplementar Appendix 1; Author contributions, p. 20
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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
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) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	Results p.10; Table 1; Figure 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Results p.10; Table 1; Figure Supplementary Appendix 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information	Results p.10; Table 1		

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		on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	Results p.10; Figure 1; Table 1		
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 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results p.10; Table 1-3; Supplementary Figure 1		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Results p.10-11		

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Discussion					
Key results	18	Summarise key results with reference to study objectives	Interpretation, *Main findings* p.11		
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	Interpretation, *Strengths/limitations* p.11-12	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.	Interpretation, *Strengths/limitations* p.11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion, *Main findings* p. 11, *Strengths / Limitations* p. 11-12		
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion, *Interpretation* p.11-12		
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	Funding, p. 21-22		
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.	p. 21; Supplementary Appendix 1

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*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* 201 in press.

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TITLE PAGE

Neighbourhood material deprivation and severe maternal morbidity: A population-based cohort study in Ontario, Canada

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ABSTRACT

Objectives: Rates of age-associated severe maternal morbidity (SMM) have increased in Canada, and an association with neighbourhood income is well established. Our aim was to examine SMM trends according to neighbourhood material deprivation quintile, and to assess whether neighbourhood deprivation effects are moderated by maternal age.

Design, setting, participants: A population-based retrospective cohort study using linked administrative databases in Ontario, Canada. We included primiparous women with a live birth or stillbirth at ≥20 weeks gestational age.

Primary outcome: SMM from pregnancy onset to 42 days postpartum. We calculated SMM rate differences (RD) and rate ratios (RR) by neighbourhood material deprivation quintile for each of four 4-year cohorts from 1 April 2002 to 31 March 2018. Log-binomial multivariable regression adjusted for maternal age, demographic, and pregnancy-related variables.

Results: There were 1,048,845 primiparous births during the study period. The overall rate of SMM was 18.0 per 1,000 births. SMM rates were elevated for women living in areas with high material deprivation. In the final 4-year cohort, the RD between women living in high versus low deprivation neighbourhoods was 3.91 SMM cases per 1,000 births (95% CI: 2.12, 5.70). This was higher than the difference observed during the first 4-year cohort (RD 2.09, 95% CI: 0.62, 3.56). SMM remained associated with neighbourhood material deprivation following multivariable adjustment in the pooled sample (RR 1.16, 95% CI: 1.11, 1,21). There was no evidence of interaction with maternal age.

Conclusion: SMM rate increases were more pronounced for primiparous women living in neighbourhoods with high material deprivation compared to those living in low deprivation

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areas. This raises concerns of a widening social gap in maternal health disparities and highlights an opportunity to focus risk reduction efforts toward disadvantaged women during pregnancy and postpartum.

Keywords: severe maternal morbidity; maternal mortality; maternal health; pregnancy; perinatal epidemiology; social epidemiology; social inequalities; deprivation

Strengths and Limitations of this Study

- Data were from population linked administrative and health registries that capture all hospital births in Ontario, Canada
- Neighbourhood material deprivation was measured using the Ontario Marginalization Index, a comprehensive area-level measure based on Census data developed using theoretical frameworks on marginalization and deprivation
- Limiting our study to primiparous women enabled the evaluation of population SMM trends and reduced confounding from previous births
- It was not possible to control for all covariates associated with SMM, including body mass index, co-morbidities, and the use of assisted reproductive technology

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INTRODUCTION

Each year, approximately 4,000 Canadian women survive a maternal "near-miss"—a life-threatening event associated with pregnancy.[1] To characterize maternal near-misses in a standardized way, the World Health Organization proposed the concept of severe maternal morbidity (SMM), a composite of conditions that represent end-organ dysfunction or states of heightened maternal mortality risk associated with pregnancy, birth, or the postpartum period.[2, 3] Advances in the recognition and management of SMM have resulted in low maternal mortality rates in economically developed nations. Women living in high income countries are now more likely to survive a life-threatening pregnancy condition and, correspondingly, the rates of SMM are 100-fold higher than the rates of maternal mortality in Canada.[1] However, recent trends in Canada and other high income countries show an increase in SMM rates coinciding with advancing maternal age and corresponding increases in pre-existing co-morbidities and the use of assisted reproductive technology.[4-9]

The literature also shows persistent though complex associations between SMM and the social determinants of health. Low occupational class, Black ethnicity,[10] and non-private health insurance[11] are all associated with higher risk of SMM in the US. Canadian women who experience SMM are more likely to come from a low-income background, and to originate from an African or Caribbean country.[4, 6, 12] A systematic review found evidence for effects of material dimensions of inequality on SMM risk, though it pointed out the need for further work on other dimensions and in elucidating effect mechanisms.[13] Women of advanced maternal age may be more likely to come from more advantaged socioeconomic backgrounds and to have planned pregnancies.[14-16] This suggests the possibility for effect modification, whereby the negative effects of advanced maternal age

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may be attenuated for women who come from more advantaged backgrounds, and exacerbated for women from disadvantaged backgrounds. The effects of maternal age and neighbourhood-level material deprivation may therefore interact, with the highest SMM risk among older women living in neighbourhoods with higher deprivation.

In this study, our first objective was to evaluate trends in SMM rates among primiparous women in Ontario by neighbourhood material deprivation quintile between 1 April 2002 and 31 March 2018. Our second objective was to determine if maternal age moderates the effect of neighbourhood material deprivation. We hypothesized that SMM rates would increase disproportionately over time among women living in neighbourhoods with high material deprivation. We further hypothesized that the highest risk of SMM would be among women of advanced maternal age living in neighbourhoods with the highest material deprivation.

METHODS

This population-based retrospective cohort study used linked administrative datasets for Ontario, held at ICES (formerly, the Institute for Clinical Evaluative Sciences). ICES is an independent, non-profit research institute funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). As a prescribed entity under Ontario's privacy legislation, ICES is authorized to collect and use health care data for the purposes of health system analysis, evaluation and decision support. Secure access to these data is governed by policies and procedures that are approved by the Information and Privacy Commissioner of Ontario. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require

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review by a Research Ethics Board. We followed the RECORD guidelines (REporting of studies Conducted using Observational Routinely-collected Data) for reporting this study.[17]

Patient and public involvement

There was no direct patient or public involvement in this study.

Study population and data sources

The Canadian Institute for Health Information Discharge Abstract Database (DAD) was used to capture all hospital admissions for birth and link to newborn records using the ICES-derived MOMBABY dataset. We included primiparous women aged 10-55 years who had a hospital birth in Ontario and were enrolled in the province's universal health insurance program (OHIP). We identified the first live birth or stillbirth delivery at a gestational age of ≥20 weeks. We used gestational age at birth to calculate pregnancy onset. Women were included if the onset of their first pregnancy was on or after 1 April 2002 and the corresponding birth occurred on or before 17 February 2018—allowing 42 days of postpartum follow-up through the study end date of 31 March 2018. Women who had a previous birth within 14 years prior to the index date were excluded. We linked these data with the Registered Persons Database (RPDB), DAD, and OHIP Claims Database to identify exposures and outcomes of interest. To identify women who had recently immigrated to Ontario, we used the Ontario portion of the federal Immigration, Refugees and Citizenship Canada (IRCC) Permanent Resident Database. For neighbourhood material deprivation, we used the 2001 and 2006 Canadian Census, and Ontario Marginalization Index (ON-

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MARG).[18] These datasets were linked using unique encoded identifiers and analyzed at ICES and are shown in **Appendix 1**.

Main outcome

The main outcome was a composite of medical conditions and interventions that comprise SMM. Cases of SMM were identified using diagnosis and procedural codes (International Statistical Classification of Diseases and Related Health Problems, 10th revision [ICD-10] and Canadian Classification of Health Interventions, respectively) within the DAD database.[15, 19-21] The DAD data have been validated and shown to accurately reflect the information in medical records.[21, 22] The composite SMM outcome included: 1) causes of direct obstetric death and conditions related to these (antepartum, intrapartum, and postpartum hemorrhage; hypertensive disorders of pregnancy and eclampsia; puerperal sepsis; uterine rupture; obstetric embolus); 2) severe organ system dysfunction (cardiac arrest, failure, or arrhythmia; renal or hepatic failure; coagulation defect; thromboembolism; respiratory failure; coma or non-eclamptic seizure; psychosis); 3) procedures or interventions accompanying life-threatening conditions or health states (cesarean or postpartum hysterectomy; pelvic vessel ligation; surgical repair of bowel, bladder, or urethra; endotracheal or tracheostomy ventilation; dialysis; blood transfusion in the context of severe blood loss); and 4) deaths that were ill-defined or sudden, as these could not reliably be classified as non-obstetric deaths. **Appendix 1** shows the list of SMM indicators for this study. We specified a binary SMM outcome variable for the presence of one or more indicators occurring from the onset of pregnancy up to and including 42 days after birth.

Exposures and covariates

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Our main exposure of interest was neighbourhood material deprivation quintile from the Ontario Marginalization Index (ON-MARG). ON-MARG is the Ontario-specific version of the Canadian marginalization index (CAN-MARG).[23] The index was developed based on theoretical frameworks of marginalization and deprivation, and derived empirically using principal component analysis of Canadian Census variables.[18, 23]The material deprivation dimension is comprised of the following Census measures, each expressed as a proportion: population aged ≥20 without secondary school graduation, single parent families, households receiving government transfer payments, population aged ≥15 who are unemployed, population living below the low income cut-off (adjusted for community size, household size, and inflation).[18] The geographical unit of aggregation is Dissemination Areas, which average 400-700 people and cover the entirety of Canadian territory.[24] ON-MARG can be operationalized as a standardized interval scale based on factor loadings from the principal component analysis, or as quintiles each representing 20% of Dissemination Areas.[18, 23] We modelled this exposure as quintiles, with quintile 1 representing neighbourhoods with the lowest material deprivation, and quintile 5 representing neighbourhoods with the highest deprivation.[18, 23] ON-MARG has been used to demonstrate inequalities in various health measures and is stable over time.[25-27] We used the 2001 material deprivation index for births between years 2002-2003, and the 2006 index for years 2004-2018. The change from mandatory Census reporting to the voluntary National Household Survey and resulting data quality concerns meant that the 2011 index was comprised from alternate data sources.[28] We used the 2006 version for all years after 2004 to avoid operationalizing this variable differently between study years.

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We included maternal age at birth, categorized in 5-year bands. We adjusted for rural setting using the 2004 and 2008 Rurality Index of Ontario (RIO).[29] We used the 2004 RIO index for pregnancies between years 2002 and 2006, and the 2008 index for years 2007 to 2018. We adjusted for number of years since immigration using data from the IRCC. Additional demographic and pregnancy related variables included delivery mode and multiple gestations. For multiple gestation pregnancies, delivery mode was specified based on highest level of intervention: unassisted vaginal birth of all fetuses (lowest), forceps or vacuum assisted vaginal birth of one or more fetuses, vaginal breech birth of one or more fetuses, and caesarean birth of one or more fetuses (highest). We examined SMM rates by gestational age at birth, induction of labour, and the use of epidural analgesia, however these variables were not adjusted-for in the multivariable models.

Statistical analysis

We summarized baseline characteristics and SMM rates overall for the study population. Due to low birth counts for ages 10-14 years, we collapsed these into an age <20 years group for analysis. We plotted SMM rates by year for the whole study population, and then to evaluate changes over time, we divided the population into four, 4-year cohorts based on pregnancy onset: 1 April 2002 to 31 March 2006 (cohort 1); 1 April 2006 to 31 March 2010 (cohort 2); 1 April 2010 to 31 March 2014 (cohort 3); and 1 April 2014 to 31 March 2018 (cohort 4). To address our first objective, we calculated average annual SMM rates for each 4-year cohort by neighbourhood material deprivation quintile. Within each cohort, we estimated unadjusted absolute rate differences (RD) and rate ratios (RR) with 95% confidence intervals (CI) comparing women in quintile 5 (highest deprivation) with women in quintile 1 (lowest deprivation).

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Our second objective was to evaluate the effect of neighbourhood material deprivation, adjusting for covariates and testing for interaction with maternal age for the overall study population. We constructed multivariable log-binomial regression models. We initially fit a model with neighbourhood material deprivation, adjusting only for year of pregnancy onset (model 1). We then added maternal age (model 2), followed by demographic and pregnancy-related covariates, immigration status, and rurality (model 3). We tested for interaction between material deprivation and maternal age using a cross product term. We did not adjust for stillbirth or gestational age at birth, as these are variables are considered colliders rather than true confounders of outcomes associated with SMM.[30] We did not include induction of labour or epidural analgesia, as these interventions are associated with clinical decisions surrounding birth rather than SMM risk factors. We excluded women with missing information for neighbourhood material deprivation from the multivariable analysis, as these women represented less than 2 percent of the study population (n=17,130).

We performed two additional analyses evaluating SMM rate trends (RD and RR) over the study period, comparing the 4-year average annual rates during cohort 4 to cohort 1 separately by maternal age and by neighbourhood material deprivation quintile. We also examined the 4-year average rates of SMM excluding cases defined by HIV disease. This was done in reference to recently proposed changes to the Canadian SMM composite indicator excluding chronic, asymptomatic HIV disease.[12, 31] Statistical analyses were performed using SAS (version 7.15, SAS Institute Inc., Cary, NC) and STATA (version 13, StataCorp., College Station, TX).

RESULTS

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There were 2,143,045 hospital-based births in Ontario between 1 April 2002 and 17 February 2018, of which 1,048,845 were primiparous births and included in the study (**Figure 1**). The overall SMM rate across the study period was 18.0 per 1,000 births, and increased from 16.7 per 1,000 births in 2002-03 (95% CI: 15.6, 17.9) to 23.0 per 1,000 births in 2017-18 (95% CI: 21.2, 25.0, **Supplementary Figure 1**). Baseline characteristics and SMM case number and rate for each characteristic are presented in **Table 1**. SMM rates were higher at the extremes of maternal age, and among women living in neighbourhoods with the highest material deprivation.

Table 2 presents SMM rates by material deprivation quintile for the pooled study sample (2002-2018) and each of the four 4-year cohorts. The RD was 2.09 cases per 1,000 births (95% CI: 0.62, 3.56), corresponding with a RR of 1.13 (95% CI: 1.04, 1.23) comparing women in quintile 5 with women in quintile 1 during the first 4-year cohort. This increased to a RD of 3.91 cases per 1,000 births (95% CI: 2.12, 5.70) and RR of 1.21 (95% CI: 1.11, 1.32) in the final 4-year cohort of the study period. Average annual SMM rates increased between cohort 1 and cohort 4 for women aged 30-34, and ≥40 years (**Supplementary Table 1**, **Supplementary Figure 2**). For the latter group, the absolute increase was 14.69 cases per 1,000 births (95% CI: 7.96-21.43, **Supplementary Table 1**). SMM rates increased over time for women in each quintile of neighbourhood deprivation, and this increase was most pronounced for women in the highest quintile of neighbourhood deprivation (RD 4.19 cases per 1,000 births 95% CI: 4.13-4.24, **Supplementary Table 1**).

In the multivariable regression analysis for the overall study population, women living in neighbourhoods with the highest material deprivation had higher rates of SMM compared to those in neighbourhoods with the lowest after adjusting for pregnancy year (RR: 1.11,

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95% CI: 1.06, 1.16, **Table 3**). Full adjustment for age, demographics, pregnancy-related variables, and rurality had minimal effect on the association between material deprivation and SMM rates (adjusted RR: 1.16, 95% CI: 1.11, 1.21, **Table 3**). The association between age and SMM persisted in the fully adjusted model, with higher risk for women <20 and ≥30 years of age. We did not find evidence of statistical interaction between maternal age and neighbourhood material deprivation quintile.

DISCUSSION

Main findings

This study demonstrated an association between neighbourhood material deprivation and severe maternal morbidity among primiparous women in Ontario from 2002-2018. Rates of SMM increased across all material deprivation quintiles, and we found some evidence that women in the highest deprivation quintile experienced a higher magnitude SMM rate increase over the 16-year study period compared with women in the lowest deprivation quintile. This finding suggests a possible widening of the gap between women living in the most and least deprived neighbourhoods.

Strengths/ limitations

The current study was a population-based analysis of all primiparous hospital births at ≥20 weeks' gestational age in Ontario. Hospital births account for over 98% of births in the province. We used a measure of neighbourhood marginalization that includes income along with other measures of material resources, and that is stable across time and different health outcomes.[23, 25] Our study nonetheless had some limitations. We were unable to account for births prior to 20 weeks' gestation or births that occurred outside of the

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province. Our measure of SMM was based on validated perinatal health data for Canada.[15, 21] A revision of the Canadian SMM composite was recently developed which resolves issues surrounding the inclusion of some pre-eclampsia and HELLP syndrome measures, as well as the exclusion of HIV infection—a condition that is unlikely to represent SMM when asymptomatic [12, 31]. We elected to use the former SMM composite for comparison with previous literature, recognizing this may complicate direct comparison with recent Canadian studies [4, 6, 12, 31]. The proportion of women with SMM defined by HIV disease was around 2 percent for each of the 4-year cohorts, and thus we do not believe these cases substantively altered the results of this study. Information on immigrants arriving prior to 1985 is not captured in the IRCC Permanent Resident Database, and the database does not identify immigrants who landed in other provinces and subsequently moved to Ontario. Although we used a measure of neighbourhood material deprivation developed for Ontario using Canadian Census elements,[28] the ON-MARG index does not include individual-level indicators of marginalization or socioeconomic status. Important social determinants may differ among individuals living in areas characterized by similar measures of neighbourhood deprivation, and it is not possible to elucidate the causal pathways that link social disadvantage to poor health outcomes without incorporating such factors.[32, 33] Finally, pre-pregnancy co-morbidities, obesity, and the use of assisted reproductive technology, contribute to higher SMM rates and may partially explain SMM trends.[8, 9, 34] We were unable to account for these factors. Obstetric comorbidity indices have been developed for risk prediction and adjustment in clinical research. [35, 36] We did not use an obstetric comorbidity index in our adjusted analysis as some index indicators

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represent SMM outcomes themselves, or are mediators of SMM outcomes. In addition, our aim was to examine population SMM trends rather than individual clinical risk factors.

Interpretation

The present study contributes to our understanding of the association between neighbourhood marginalization and SMM and provides preliminary evidence of a possible widening of this health disparity over time in Ontario. The association between neighbourhood-level measures of inequality and risk of SMM has been demonstrated previously in several high-income countries.[6, 9, 11, 13, 37-41] Notably in Canada, Aoyama and colleagues reported a rise in SMM linked to the relative increase in maternal age and found a significant association between SMM and neighbourhood income quintile.[4]. Our study confirms this finding using a measure that encompasses income along with additional measures of neighbourhood material deprivation. Moreover, we extend the current understanding of this association by providing evidence for a possible disproportionate rise in SMM risk experienced by women living in marginalized neighbourhoods over time. We interpret this last finding with caution, as our study showed significant rate differences by neighbourhood marginalization only during the first and final 4-year cohorts of the 16-year study period. SMM risks have been demonstrated among other social determinants of health; for example, lower occupational class, Black ethnicity,[10] and non-private health insurance[11] are associated with higher risk of SMM in the US. Interaction between socioeconomic indicators—including ethnicity, education, and poverty—likely contribute to the social gradient of risk such that the protective effects afforded by higher education and income do not fully ameliorate racial disparities in SMM.[38] Our study showed an association between neighbourhood deprivation and SMM suggesting the effects of

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marginalization persist even in the context of universal healthcare. This is a consistent finding across countries that have similar publicly funded healthcare systems.[41-43] The factors contributing to social inequality are myriad; ethnicity and country of origin, rurality and access to care, income, material resources, education, and psychosocial supports all have worrisome associations with maternal reproductive health risks.[6, 10-12, 38, 41-47] How these factors contribute to widening health gaps, and what interventions may attenuate their effects will be imperative lines of inquiry going forward as the global challenge to lower SMM continues.

Conclusion

Ontario women living in areas with higher neighbourhood material deprivation experienced the highest risk of SMM, and this association was not fully explained by maternal age. Additionally, women living in high-deprivation neighbourhoods may have experienced a disproportionate increase in the risk of SMM over time. Future work must focus on addressing the widening social gap in maternal health disparities.

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TABLES

Table 1. Baseline characteristics of the study population, 2002-2018. N=1,048,845 births.

Variable	Number of births	Percent	Number of SMM cases	SMM rate per 1,000 births
Overall study population	1,048,845	100	18,880	18.00
Maternal age at birth, years				
10-14	1,330	0.1	35	26.32
15-19	72,579	6.9	1,291	17.79
20-24	178,074	17.0	2,684	15.07
25-29	342,003	32.6	5,324	15.57
30-34	305,898	29.2	5,653	18.48
35-39	123,698	11.8	3,017	24.39
≥40	25,263	2.4	876	34.68
Gestational age at birth, weeks				
20-23	2,751	0.3	147	53.44
24-27	4,158	0.4	306	73.59
28-33	17,688	1.7	1,104	62.42
34-36	59,040	5.6	1,966	33.30
37-41	961,322	91.7	15,278	15.89
≥42	3,886	0.4	79	20.33
Induced labour	275,262	26.2	5,836	21.20
Epidural	655,107	62.5	10,713	16.35
Delivery mode				
Vaginal unassisted	579,814	55.3	6,386	11.01
Vaginal assisted	156,383	14.9	2,724	17.42
Vaginal breech	2,328	0.2	95	40.81
Caesarean	310,320	29.6	9,675	31.18
Multiple gestations	20,850	2.0	1,137	54.53
Stillbirth	3,645	0.3	199	54.60
Rurality				
Urban	993,282	94.7	17,814	17.93
Rural	55,563	5.3	1,066	19.19
Immigration Status				
Non-immigrant / before 1985	739,252	70.5	13,222	17.89
Immigrated >10 years	62,381	5.9	1,165	18.68
Immigrated 5-10 years	62,090	5.9	1,249	20.12
Immigrated <5 years	185,122	17.7	3,244	17.52
Neighbourhood marginalization				
Material deprivation				
Quintile 1 (least deprived)	237,877	22.7	4,183	17.58
Quintile 2	186,550	17.8	3,112	16.68
Quintile 3	189,575	18.1	3,327	17.55

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Quintile 4	191,376	18.2	3,423	17.89
Quintile 5 (most deprived)	226,337	21.6	4,397	19.43
Missing	17,130	1.6	438	25.57

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Table 2. Four-year average SMM rates per 1,000 births for neighbourhood material deprivation quintiles, by pooled sample (2002-2018) and by study period cohort.

	SMM rates by material deprivation quintile					*Q5 vs Q1*	
Cohort[a]	**Q1 (least)**	**Q2**	**Q3**	**Q4**	**Q5 (most)**	**Rate difference (95% CI)**	**Rate ratio (95% CI)**
Pooled	17.58	16.68	17.55	17.89	19.43	1.84 (1.82,1.87)***	1.10 (1.10-1.11)***
1	16.05	16.36	17.46	16.49	18.14	2.09 (0.62, 3.56)**	1.13 (1.04, 1.23)**
2	16.58	15.97	15.73	16.37	17.32	0.75 (-0.70, 2.20)	1.05 (0.96, 1.14)
3	19.36	16.17	18.34	19.19	20.78	1.41 (-0.20, 3.02)	1.07 (0.99, 1.16)
4	18.41	18.52	18.99	20.18	22.32	3.91 (2.12, 5.70)***	1.21 (1.11, 1.32)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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Table 3. Neighbourhood material deprivation and risk of SMM: Adjusted multivariable models, RR (95% CI). N=1,031,715 births.

Variable	Model 1[a]	Model 2[b]	Model[c]
Maternal age (years)			
<20		1.05 (0.99, 1.12)	1.20 (1.13, 1.28)
20-24		0.95 (0.90, 0.99)	1.01 (0.96, 1.06)
25-29		1 (ref)	1 (ref)
30-34		1.19 (1.14, 1.23)	1.10 (1.06, 1.15)
35-39		1.56 (1.49, 1.63)	1.34 (1.28, 1.40)
≥40		2.21 (2.06, 2.37)	1.73 (1.61, 1.86)
Material deprivation			
Quintile 1 (least)	1 (ref)	1 (ref)	1 (ref)
Quintile 2	0.95 (0.91, 0.99)	0.97 (0.93, 1.02)	0.97 (0.92, 1.01)
Quintile 3	1.00 (0.96, 1.05)	1.04 (0.99, 1.08)	1.03 (0.98, 1.07)
Quintile 4	1.02 (0.98, 1.07)	1.07 (1.02, 1.12)	1.06 (1.01, 1.11)
Quintile 5 (most)	1.11 (1.06, 1.16)	1.17 (1.12, 1.22)	1.16 (1.11, 1.21)

[a]adjusted for pregnancy year

[b]adjusted for pregnancy year, age

[c]adjusted for pregnancy year, age, delivery mode, multiple gestations, immigration status, rurality

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FIGURE CAPTIONS

Figure 1. Study inclusion / exclusion flow chart, primiparous births.

SUPPLEMENTARY MATERIAL CAPTIONS

Supplementary Appendix 1. Data sources for the project.

Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002-2018.

Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.

Supplementary Table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

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Declaration of competing interests

The authors declare no conflicts of interest.

Author contributions

JWS, DF, KEM, and LCR contributed to the overall conception of the study. JWS, ML, LR, DF, and LCR contributed to study design and protocol. TW had full access to data used in the study. JWS, TW, and LCR take responsibility for the integrity of the data analysis. JWS wrote the manuscript. All authors made substantial contributions to the data analysis interpretation, and manuscript editing and revising for this project. All authors approve the final submitted version and agree to be accountable for all aspects of the work.

Ethical approval

ICES is a prescribed entity under section 45 of Ontario's Personal Health Information Protection Act. Section 45 authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects conducted under section 45, by definition, do not require review by a Research Ethics Board. This project was conducted under section 45, and approved by ICES' Privacy and Legal Office.

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Patient consent for publication

None required.

Data availability statement

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

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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.

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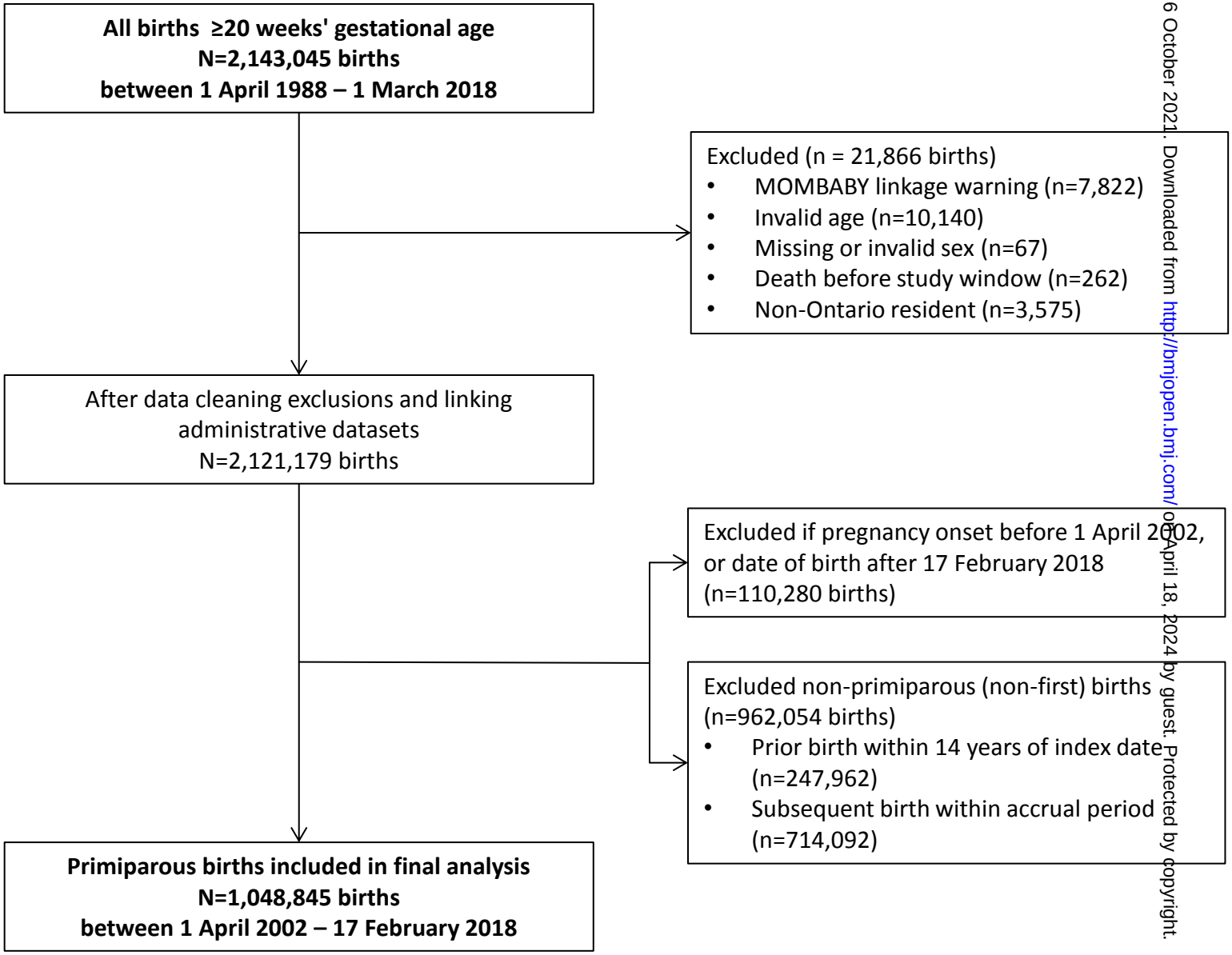
Figure 1. Study inclusion / exclusion flow chart, primiparous births.



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Supplementary Appendix 1. Data sources for project

Discharge Abstract Database (DAD)
The DAD is compiled by the Canadian Institute for Health Information and contains administrative, clinical (diagnoses and procedures/interventions), demographic, and administrative information for all admissions to acute care hospitals, rehab, chronic, and day surgery institutions in Ontario. At ICES, consecutive DAD records are linked together to form 'episodes of care' among the hospitals to which patients have been transferred after their initial admission.

MOMBABY
The ICES MOMBABY Database is an ICES-derived cohort that links the DAD inpatient admission records of delivering mothers and their newborns. From 2002 onward, this linkage is performed deterministically using a maternal-newborn chart matching number. Prior to 2002, mothers were linked to their children by matching on the institutions they were admitted, their postal codes, and their admission/discharge dates.

Registered Persons Database (RPDB)
The RPDB provides basic demographic information (age, sex, location of residence, date of birth, and date of death for deceased individuals) for those issued an Ontario health insurance number. The RPDB also indicates the time periods for which an individual was eligible to receive publicly funded health insurance benefits and the best known

Ontario Health Insurance Plan (OHIP)
The OHIP claims database contains information on inpatient and outpatient services provided to Ontario residents eligible for the province's publicly funded health insurance system by fee-for-service health care practitioners (primarily physicians) and "shadow billings" for those paid through non-fee-for-service payment plans. The main data elements include patient and physician identifiers (encrypted), code for service provided, date of service, associated diagnosis, and fee paid.

Immigration, Refugees, and Citizenship Canada's (IRCC) Permanent Resident Database
The Ontario portion of the IRCC Permanent Resident Database includes immigration application records for people who initially applied to land in Ontario since 1985. The dataset contains permanent residents' demographic information such as country of citizenship, level of education, mother tongue, and landing date. New immigrants who are currently residing in Ontario but originally landed in another province are not captured in this dataset.

Ontario Marginalization Index (ONMARG)
ONMARG is a geographically (census) based index developed to quantify the degree of marginalization occurring across the province of Ontario. It is comprised of four major dimensions thought to underlie the construct of marginalization: residential instability, material deprivation, dependency, and ethnic concentration. The dataset contains census divisions (CD), census tracts (CT), census subdivisions (CSD), consolidated municipal service manager areas (CMSM), public health units (PHU), local health integration networks (LHIN), sub-LHINs, and dissemination areas (DA).

These datasets were linked using unique encoded identifiers and analyzed at ICES.

The dataset from this study is held securely in coded form at ICES. While data sharing agreements 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. 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.

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Inclusion/Exclusion Criteria

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Inclusion Criteria				
Hospital birth (live or stillbirth) at gestational age ≥20 weeks	DAD, MOMBABY	ICD-10 main patient service code for "Obstetrical birth"	Accrual window: 1 April 2002 – 17 Feb 2018	Canadian Institute for Health Information Discharge Abstract Database (DAD, linked to newborn record in MOMBABY dataset) See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=MOMBABY
Exclusion Criteria				
Missing or invalid IKN	RPDB		Index date	Registered Persons Database See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=RPDB
MOMBABY linkage warning	MOMBABY		Index date	
Missing or invalid age (<10 or >55)	RPDB		Index date	
Missing or invalid sex	RPDB		Index date	
Death before the index date	RPDB		Index date	
Non-Ontario residents / invalid OHIP number	RPDB		Index date	
Any births with an index date occurring outside of the accrual period	MOMBABY		Accrual window	Pregnancy onset before 1 April 2002
Any births occurring after accrual end date	MOMBABY		Accrual window	Births after 17 February 2018
Not first birth	MOMBABY		14 years prior to index date	Prior record in MOMBABY within past 14 years of index date
Not first birth in accrual period	MOMBABY		Accrual window	Subsequent records in MOMBABY

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Outcome

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Severe maternal morbidity (SMM)	DAD	ICD 10 CCI	Start of lookback period ("pregnancy onset" = index date – gestational age at birth) to end of observation window (42 days following index date)	Patient considered to have outcome IF ANY code in ANY of the following: 1) Obstetric/ ill-defined or sudden death 2) Hypertensive heart/renal disease 3) Eclampsia 4) Cerebral venous thrombosis 5) Complications of anaesthesia – non-cardiac 6) Complications of anaesthesia – cardiac 7) Cardiac diseases (cardiac arrest, infarction, failure, pulmonary edema) 8) Placental abruption c/ coagulation defect 9) Antepartum hemorrhage c/ coagulation defect 10) Intrapartum hemorrhage c/ coagulation defect 11) Uterine rupture – before labour 12) Uterine rupture – during labour 13) Obstetric shock (including septic shock) 14) Septecemia during labour 15) Puerperal sepsis 16) Pulmonary embolism 17) Obstetric embolism 18) Cardiomyopathy 19) Acute renal failure 20) HIV disease 21) Cerebrovascular disease 22) Acute respiratory distress syndrome 23) Acute abdomen 24) Hepatic failure 25) Acute psychosis 26) Cerebral edema, coma 27) Disseminated intravascular coagulation 28) Sickle cell anemia crisis 29) Status asthmaticus 30) Status epilepticus 31) Assisted ventilation (endotracheal tube or tracheostomy) 32) Caesarean hysterectomy 33) Postpartum hysterectomy 34) Dialysis 35) Evacuation of incisional hematoma 36) Surgical repair of bladder, urethra, intestine 37) Intrapartum hemorrhage with no coagulation defect AND blood transfusion 38) Postpartum hemorrhage AND blood

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				transfusion 39) Placenta previa AND blood transfusion 40) Embolization/ ligation/ suturing AND postpartum hemorrhage See: Joseph KS et al, 2009,[1] Joseph KS et al, 2010,[2] ICD-10CA, 2009,[3] and CCHI, 2012.[4]

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Study exposures, covariates

Concept	Data Sources	Code Type	Window	Notes (including Dataset references)
Age	RPDB		Index date	
Index year	DAD		Index date	
Material deprivation index	ONMARG		Index date	Ontario Marginalization Index, Material Deprivation, in quintiles. Use version of ONMARG closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=ONMARG
Income quintile	RPDB Census		Index date	Ontario Census area profile: income quintile. Use Census closest to year of index date: 2001 for 2002-2003 2006 for 2004-2018 See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CENSUS
Rurality	RPDB		Index date	Rurality Index for Ontario (RIO). Use version of RIO closest to year of index date: RIO2004 for 2002-2006 RIO2008 for 2007-2018
Gestational age at birth	MOMBABY		Index date	
Induction of labour	DAD	CCI code	Within index hospitalization	Canadian Classification of Health Interventions (CCI)
Epidural	DAD OHIP	CCI code OHIP fee code	Within index hospitalization	Canadian Classification of Health Interventions (CCI); Ontario Health Insurance Plan Claims Database (OHIP)
Delivery mode	DAD	CCI code	Within index hospitalization	
Multiple gestations	MOMBABY		Within index hospitalization	
Stillbirth	MOMBABY		Within index hospitalization	
Immigration status	IRCC		Index date	Immigration, Refugees and Citizenship

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				Canada (IRCC)'s Permanent Resident Database Number of years since arrived in Ontario. See: https://datadictionary.ices.on.ca/Applications/DataDictionary/Library.aspx?Library=CIC

References

1. Joseph KS, Fahey J, Canadian Perinatal Surveillance S. Validation of perinatal data in the Discharge Abstract Database of the Canadian Institute for Health Information. *Chronic Diseases in Canada.* 2009;29:96-100.
2. Joseph KS, Liu S, Rouleau J, et al. Severe maternal morbidity in Canada, 2003 to 2007: surveillance using routine hospitalization data and ICD-10CA codes. *Journal of Obstetrics & Gynaecology Canada: JOGC.* 2010;32:837-46.
3. *International Statistical Classification of Diseases and Related Health Problems. 10th Revision. ICD-10CA*: Canadian Institute for Health Information;2009.
4. *Canadian Classification of Health Interventions.* Ottawa: Canadian Institute for Health Information;2012.

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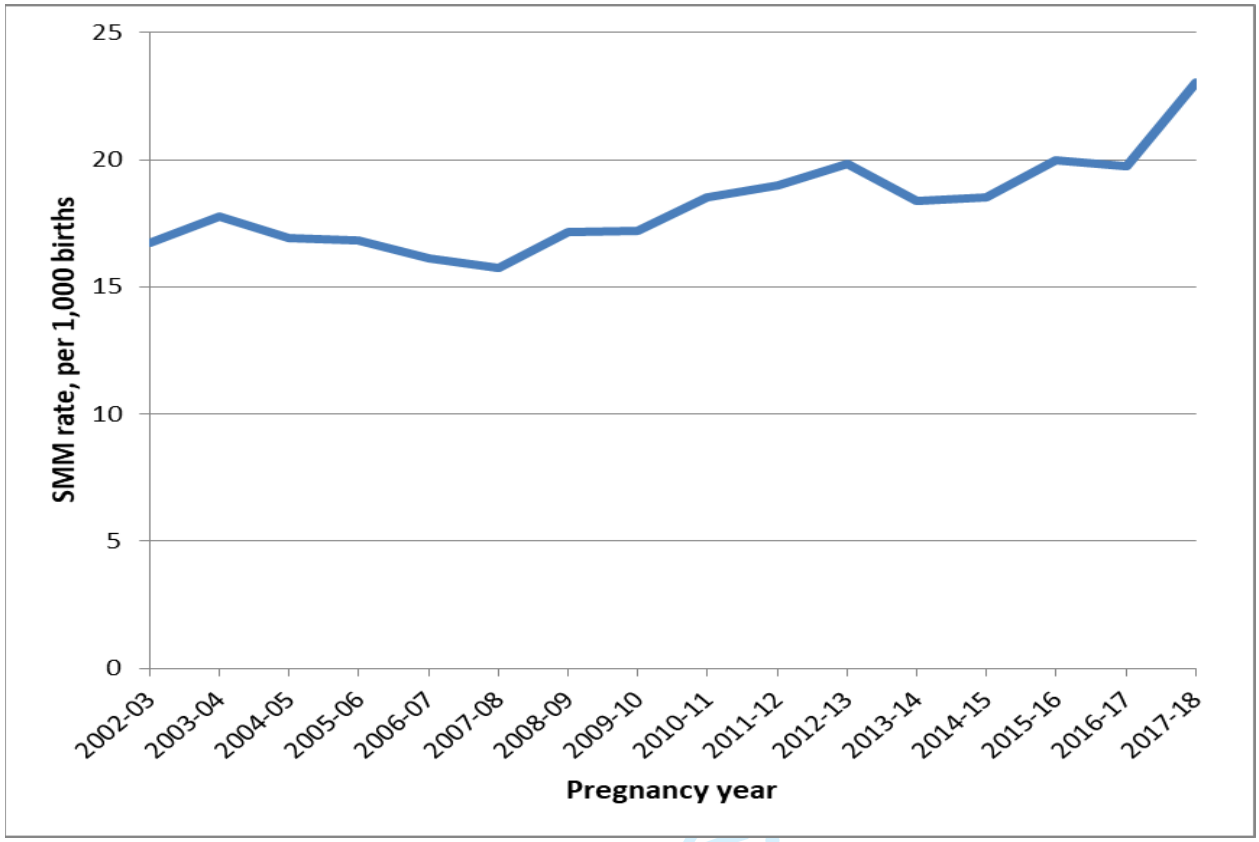
Supplementary Figure 1. Annual crude SMM rate per 1,000 births, 2002-2018.



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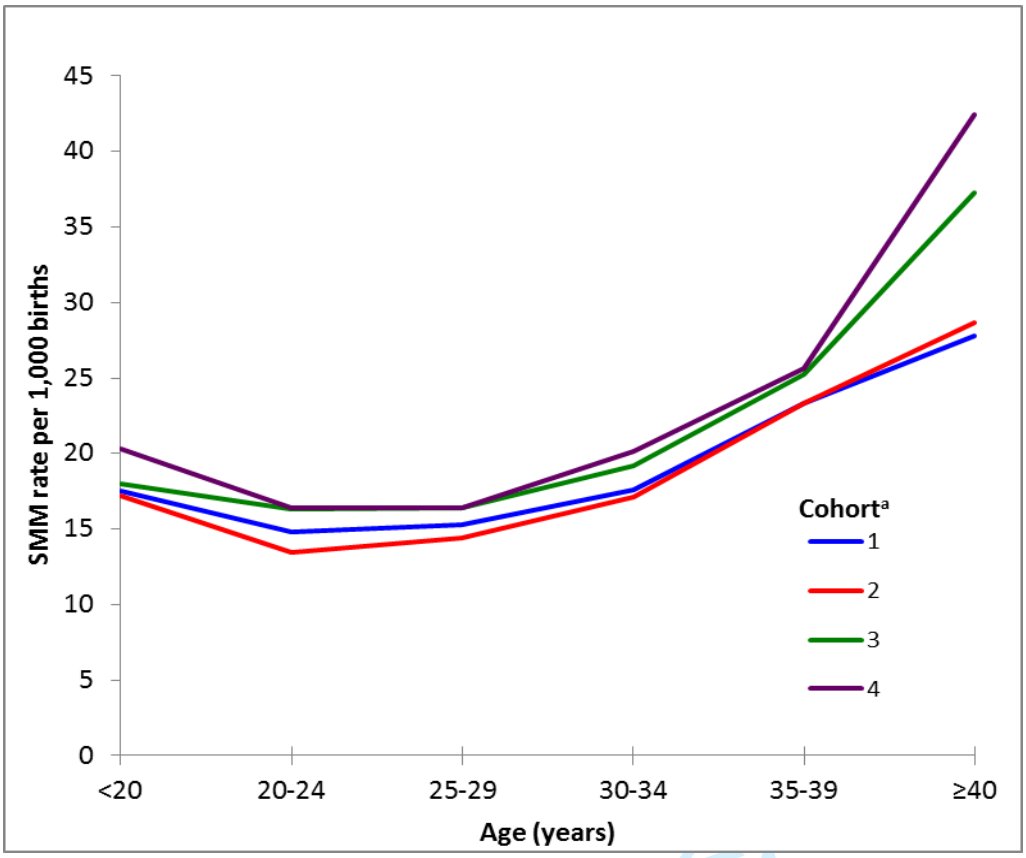
Supplementary Figure 2. Average annual SMM rates per 1,000 births by maternal age.



[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

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Supplementary table 1. Four-year average SMM rates per 1,000 births by age and by material deprivation, and rate change over study period.

	SMM rates by cohort[a]				*SMM rate change, cohort 4 vs 1*[a]	
Variable	**1**	**2**	**3**	**4**	**Rate difference (95% CI)**	**Rate ratio (95% CI)**
Overall study population	17.10	16.55	18.94	19.82	2.72 (1.96, 3.49)***	1.16 (1.11, 1.21)***
Maternal age (years)						
<20	17.54	17.22	17.97	20.34	2.80 (-0.43, 6.04)	1.15 (0.98, 1.37)
20-24	14.80	13.47	16.32	16.40	1.60 (-0.15, 3.35)	1.11 (0.99, 1.24)
25-29	15.26	14.40	16.37	16.42	1.15 (-0.77, 2.39)	1.08 (0.99, 1.16)
30-34	17.58	17.10	19.21	20.16	2.58 (1.18, 3.97)*	1.15 (1.06, 1.23)*
35-39	23.31	23.35	25.23	25.67	2.36 (-0.16, 4.88)	1.10 (0.99, 1.22)
≥40	27.78	28.68	37.30	42.48	14.69 (7.96, 21.43)*	1.53 (1.24, 1.89)*
Material deprivation						
Quintile 1 (least)	16.05	16.58	19.36	18.41	2.36 (2.31, 2.41)***	1.15 (1.14, 1.15)***
Quintile 2	16.36	15.97	16.17	18.52	2.16 (2.11, 2.22)***	1.13 (1.13, 1.14)***
Quintile 3	17.46	15.73	18.34	18.99	1.54 (1.48, 1.59)***	1.09 (1.08, 1.09)***
Quintile 4	16.49	16.37	19.19	20.18	3.69 (3.63, 3.74)***	1.22 (1.22, 1.23)***
Quintile 5 (most)	18.14	17.32	20.78	22.32	4.19 (4.13, 4.24)***	1.23 (1.22, 1.23)***

[a]cohort 1: 1 April 2002 to 31 March 2006; cohort 2: 1 April 2006 to 31 March 2010; cohort 3: 1 April 2010 to 31 March 2014; cohort 4: 1 April 2014 to 31 March 2018

*p<0.05, **p<0.01, ***p<0.001

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The RECORD statement – checklist of items 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	Title page (p.1)	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. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title page, abstract (p. 1-3)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Background p.4-5		
Objectives	3	State specific objectives, including any prespecified hypotheses	Background p.4-5		
Methods					
Study Design	4	Present key elements of study design early in the paper	Methods p.5-9		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods: *Study population and data sources, Main outcome,* p. 5-6		

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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 *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 *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	Cohort study, no matching: Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Appendix 1	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. 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. 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8; Supplementary Appendix 1	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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement).	Methods: *Study population and data sources, Main outcome, Exposures*		

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		Describe comparability of assessment methods if there is more than one group	*and covariates* p. 5-8; Supplementary Appendix 1		
Bias	9	Describe any efforts to address potential sources of bias	Methods: *Exposures and covariates* p. 7-8; Interpretation: *Strengths/ limitations* p.11-12		
Study size	10	Explain how the study size was arrived at	Methods: *Study population and data sources,* p. 5-6; Figure 1		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Methods: *Statistical analysis,* p. 8-9		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of	Methods: *Statistical analysis,* p. 8-9, Results, p.9-11.		

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		sampling strategy (e) Describe any sensitivity analyses			
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. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Methods: *Study population and data sources,* p. 6; Supplementar Appendix 1; Author contributions, p. 20
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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Supplementary Appendix 1
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) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	Results p.10; Table 1; Figure 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.	Methods: *Study population and data sources, Main outcome, Exposures and covariates* p. 5-8 Results p.10; Table 1; Figure Supplementary Appendix 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information	Results p.10; Table 1		

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		on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	Results p.10; Figure 1; Table 1		
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 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results p.10; Table 1-3; Supplementary Figure 1		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Results p.10-11		

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Discussion					
Key results	18	Summarise key results with reference to study objectives	Interpretation, *Main findings* p.11		
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	Interpretation, *Strengths/limitations* p.11-12	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.	Interpretation, *Strengths/limitations* p.11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion, *Main findings* p. 11, *Strengths / Limitations* p. 11-12		
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion, *Interpretation* p.11-12		
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	Funding, p. 21-22		
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.	p. 21; Supplementary Appendix 1

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*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* 201 in press.

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