Vol. 12(3), pp. 238-245, July-September 2020
DOI: 10.5897/JPHE2020.1251
Article Number: 12DF44964762
ISSN 2141-2316

http://www.academicjournals.org/JPHE

ACADEMIC JOURNALS
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Journal of Public Health and Epidemiology

Full Length Research Paper

Birth defects among immigrants: Impact of exposure to a new environment, a 20 year population-based study

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Received 20 July, 2020; Accepted 25 August, 2020

Birth defects remain a global health issue. With increasing rates of migration, it is important to explore the role of immigration and the impact of new environments, especially food fortification, on birth defect prevalence. The prevalence of birth defects in the first year of life was compared between children born to immigrant and non-immigrant mothers in Ontario, Canada. Data on country of origin and arrival date were identified for immigrant mothers. The rate of birth defects among mothers coming from some countries was higher than Canadian mothers including 12 to 27% higher rates among mothers arriving from Sudan, Jamaica, Bangladesh and Afghanistan. The rate of birth defects among immigrant mothers who arrived before food fortification in 2000 was higher than the rate in non-immigrants, but after 2000 it was lower among immigrant mothers. Comparing the birth defect rate among two cohorts at one point in time could be misleading. Higher rates of birth anomalies among immigrant mothers who arrived before food fortification could be due to lack of access to folic acid in their country of origin. After food fortification, immigrant mothers likely had similar exposure to folic acid as non-immigrant mothers and their rate of was the same or lower.

Key words: Birth defects, immigration, food fortification.

INTRODUCTION

While considerable advancements have been made in early recognition, treatment, and surgical techniques for birth defects, there has been little change in the prevalence of birth defects. Findings of some studies indicate that the overall prevalence of major birth defects did not change significantly since the 1980s (CDC, 2008). In fact, in some developed countries, there has been a slight increase in recent years in their overall prevalence (EUROCAT, 1999; Loane et al., 2013; Dolk, 2005). The current pattern in occurrence of birth defects could

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indicate that there have been no major changes in the risk factors that affect prevalence of these conditions. While risk factors for nearly 70% of birth defects are said to be unknown (Brent, 2008); researchers are exploring the wide spectrum of risk factors, from genetic factors to environmental factors. Many believe that environmental factors may be involved in the causal mechanism and, indeed, may provide the basis for therapeutic or preventive intervention (Dolk, 2004; Brent, 2008). Factors such as tobacco smoke, outdoor air pollution, pesticides and polychlorinated biphenyls and organic solvents and chlorophenoxy herbicides (mostly occupational) have been considered as risk factors for low birth weight, preterm delivery, decreased fetal growth and certain birth defects (Stillerman, 2008).

On the other hand, differences in the prevalence of birth defects may be due to variations in genetic predisposition. For example, consanguineous marriages are more frequent in some ethnic groups.

Studies among immigrant populations, with different ethnic backgrounds and moving from one environment to other, has been considered as one of the ways to explore the role of both genetic background and changes in the environmental factors in occurrence of birth defects.

Several studies have reported ethnic differences in perinatal mortality and morbidity, at least partly ascribed to ethnic differences in the prevalence of birth defects (Canfield et al., 2014; Anthony, 2005; Khodr et a., 2013; Emad, 2005; Buczyńska and Tarkowsk, 2005). In 1997, a study in Norway showed that when both parents are born in Pakistan, they have higher odds of having a chid born with a birth defect as compared to Norwegian parents (Stoltenberg, 1997). A recent Dutch study showed that Mediterranean women (Turkish and Moroccan) have a 20% higher risk of giving birth to a child with a birth defect than Dutch women (Anthony, 2005).

In the US, several studies examined the risk of birth defects among foreign- versus U.S.–born mothers. Comparing Hispanic U.S. born mothers with Hispanic foreign mothers, authors found Hispanic mothers born outside U.S., were more likely to have children with spina bifida (Ramadhani et al., 2009). Another U.S. study (Zhu et al., 2006) comparing Hispanic women in New York, found mothers born outside U.S. were less likely to have children with birth defects in general and specifically for cardiovascular defects and central nervous system defects. Another study in the U.S. (Velie et al., 2006) indicated that Mexican-born women had a twofold increased risk of delivering a baby with neural tube defects.

A recent study in the U.S. (Canfield, 2014) explored the association between race/ethnicity and birth defects from 1999 to 2007. Based on the reported results, compared to non-Hispanic Whites, American Indians/Alaska Natives had a significantly higher rates for at least seven major birth defects (such as heart defects, cleft lip, trisomy 18, encephalocele and limb deficiency), while Cubans and especially Chinese and Asian Indians, had lower or similar prevalence of these defects. According to this study, some Asian mothers had significantly higher rates for specific defects such as anotia and tetralogy of Fallot.

In Canada, a recent report indicates that immigrant women may be at higher risk of delivering babies with birth defects (SMH, 2009). The authors believe that differences in using folic acid supplements could be the main reason. According to this report "*about six in 10 Canadian-born mothers take folic-acid supplements in the three-month period before conception, mothers from non-western countries, China, Northern African, Middle Eastern, Caribbean, Latin American or South Pacific countries are less likely to use the supplements* "

Studies of birth defects among immigrant mothers can not be restricted to only country of birth. Other factors such as length of stay in the host country, maternal age at the time of birth, birth order of the child, and risk level for birth defect in the country of birth must be considered in order to have a clearer picture of the birth defects among immigrant population.

One of the possible changes in the environment due to immigration is exposure to folic acid through either higher use or food fortification in the host country. Several studies indicate that use of folic acid by pregnant mothers is a major preventive factor for neural tube defects (NTDs) (MRC, 1991; Czeizel, 1992; Berry et al., 1999; De Wals, 2007). Recent reports (Rosano et al., 1999; Honein et al., 2001; Williams et al., 2002, 2005; Canfield et al., 2005; Besser et al., 2007; De Wals, 2008) have associated folic acid food fortification with the observed decline in the prevalence of NTDs. In several countries, including the United States and Canada, recommendations to consume folic acid supplements are integrated with a public intervention of widespread fortification of flour in the United States and flour, cornmeal, and pasta in Canada, to ensure that the entire population receives at least a small amount of folic acid regardless of access to supplements.

Recent studies in Canada (Agha, 2013, 2016) showed the effect of food fortification in reducing the prevalence of birth defects both in the general public and among mothers diagnosed with pre-gestational diabetes.

The current study is one of the most comprehensive studies to measure birth prevalence of congenital abnormalities among immigrant and non-immigrant women in Canada. In this retrospective cohort study, the birth prevalence of congenital abnormalities among children born to two cohorts of mothers, that is immigrant mothers and non-immigrant mothers were compared. In this cohort study, the effect of several factors including time since arrival as immigrant, birth order of the child, maternal age, risk level of birth defect in the country of birth and food fortification on the risk of birth defect among immigrant mothers arrived in Ontario, Canada

since 1985 were looked into.

Methods

This study is a retrospective cohort study based on the follow-up of all children born to immigrant and non-immigrant mothers in hospital in Ontario, Canada during 1995 and 2014. We accessed administrative health care data through a research agreement with the Ontario Ministry of Health and Long-Term Care. Using a unique and scrambled personal identifier, we linked all data sets. All data analyses conducted at the Institute for Clinical Evaluative Sciences. Research Ethics Board of Sunnybrook Health Sciences Centre in Toronto approved this study.

Data sources

The following data sets were used to create the cohort of mothers and children for this study. Abstract Database of the Canadian Institute for Health Information (CIHI), is a discharge database that captures all hospitalizations occurred in Ontario. CIHI contains information on admission dates, gender of the patient, birth date, diagnosis and all procedures performed on patients. Several studies documented reliability and validity of CIHI (Goel et al., 1996; Juurlink et al., 2006).

Immigration, Refugees and Citizenship Canada's Database (IRCC), includes immigration application records for people initially applied to land in Ontario, Canada. The data contains permanent residents' demographic information such as country of citizenship, level of education, mother tongue, and landing date.

The Registered Persons Database (RPDB) is a registry managed by Ministry of Health in Ontario. This population-based registry contains basic demographic information for all individuals eligible for health care in Ontario. Information such as date of birth, gender, date of death, current address and any address changes are available in this database. MOM-BABY dataset links the CIHI inpatient admission records of delivering mothers and their newborns. Using several indicators such as the institutions mothers were admitted, their postal codes, and their admission/discharge dates, newborns were linked to their mothers.

Study population

All children born in Ontario between 1995 and 2015 were identified from Canadian Institute for Health Information database. We used scrambled encoded health identifier for children and linked them to their mothers through MOM-BABY data set. All children born to same mother are included in this study.

Exposure, outcome and confounding variable

The scrambled encoded identifier for each child was linked back to Canadian Institute for Health Information database. Based on this linkage, we collected all hospitalizations records during their first year of life for newborn. All newborns that had at least one diagnosis in their first-year hospitalization records from the congenital abnormalities chapter of the International Classification of Diseases (ICD) were considered to have birth defects. We used multiple versions of ICD since ICD versions changed over time in Ontario. We used both ICDD-9 and ICD-10 for the corresponding time periods.

Mothers' health card numbers were linked to IRCC data in order to identify mother's immigration status and their date of landing, country of birth and age at the time of landing. Mothers with no record in the IRCC data set were considered non-immigrant. Given the cohort nature of this study, children born to immigrant mothers were considered as those born to the exposed group and those born to Canadian non-immigrant mothers as births among the non-exposed or comparison group. The role of several confounding covariates including time since arrival for immigrant mothers, birth order of the child, maternal age, risk level of birth defect in the country of birth for immigrant mothers and the time period of food fortification in Canada was examined on the birth prevalence of congenital abnormalities among the two cohorts.

Statistical methods

We calculated birth prevalence of birth defects for immigrant and non-immigrant mothers and for the immigrant mothers, by country of birth and world region, based on the World Bank schema (Word Bank, 2017). The top 15 countries of origin that presented the highest rate of birth defects were also identified. We also grouped countries based on the prevalence of birth defects based on data reported by March of Dimes (Christianson et al., 2006). Countries with prevalence rates less than 50 per 1000 births were considered low risk. Other countries were grouped into level 2 (50-60 per 1000), level 3 (60-70 per 1000) and level 4 (70+ per 1000).

Prevalence rates of birth defects were also reported among immigrant mothers with multiple births (first, second, and third+) in order to evaluate the joint effect of time since arrival, mother's age and birth order.

We used logistic regression to estimate the association of possible risk factors with prevalence of birth defects among babies born to immigrant and non-immigrant mothers. The following factors were included in the model: Maternal age, birth weight, history of abnormalities in previous births, prevalence of birth defects in the country of origin, world region of birth, and time since arrival in Canada. Based on the cohort nature of this study, we compared the rate of birth defects among immigrant mothers (exposed group) to the rate among births among Canadian non-immigrant mothers, that is, non-exposed group. In these analytic comparisons we used rates among non-immigrant Canadian mothers as the base for all statistical analyses. The Generalized Estimation Equation (GEE) method was used to account for clustering of children within mothers.

RESULTS

A total of 2,644,905 live births were identified from hospital records during 1995 to 2014. We were able to link 98.2% of them (2,597,661births) to their mothers using MOMBABY data set. Among 2,597,661 children born during this period, 77% were born to Canadian non-immigrant mothers and 594,309 (23%) to immigrant mothers. These newborns were followed for one year and all their hospital records used for diagnoses of diagnosis of congenital abnormalities. In spite of the cohort nature of this study, given lack of data on birth defects among aborted pregnancies and still births, the measure of choice used by every surveillance system is the birth prevalence of birth defects since the true incidence of birth defects is not possible to measure.

Table 1. Prevalence (/1000) and RR for birth defects among immigrant and non-immigrant mothers, 1995-2014, Ontario, Canada.

Year	Non-immigrant mothers			Immigrant mothers				
	Total Births	Births with abnormalities	Rate	Total Births	Births with abnormalities	Rate	RR	95% CI
1995	110381	6627	60.0	19478	1312	67.4	1.12	1.06-1.19
1996	105526	6741	63.9	20081	1290	64.2	1.00	0.95-1.07
1997	103321	6761	65.4	21151	1502	71.0	1.09	1.03-1.15
1998	100864	6937	68.8	21606	1633	75.6	1.10	1.04-1.16
1999	98334	6887	70.0	22608	1812	80.1	1.14	1.09-1.21
2000	95275	6634	69.6	24256	1902	78.4	1.13	1.07-1.19
2001	97747	6838	70.0	26133	1922	73.5	1.05	1.0-1.11
2002	97682	6270	64.2	27948	1688	60.4	0.94	0.89-0.99
2003	100202	6145	61.3	29589	1716	58.0	0.95	0.90-1.0
2004	99042	5901	59.6	31914	1763	55.2	0.93	0.88-0.98
2005	98596	5840	59.2	33559	1770	52.7	0.89	0.84-0.94
2006	99159	5556	56.0	35136	1742	49.6	0.89	0.84-0.93
2007	100634	5804	57.7	36659	1823	49.7	0.86	0.82-0.91
2008	99831	5838	58.5	36280	1884	51.9	0.89	0.84-0.94
2009	99533	6149	61.8	36915	2002	54.2	0.88	0.83-0.92
2010	96882	6248	64.5	37161	2002	53.9	0.84	0.79-0.88
2011	97756	6373	65.2	37272	2132	57.2	0.88	0.84-0.92
2012	96855	6393	66.0	37529	2044	54.5	0.83	0.79-0.87
2013	97641	6697	68.6	34574	2043	59.1	0.86	0.82-0.91
2014	76941	5385	70.0	24460	1532	62.6	0.89	0.85-0.95
Total	1972202	126024	63.9	594309	35514	59.8	0.94	0.92-0.95

Source: Data collected from births to immigrant and non-immigrant mothers in Ontario 1995-2014.

Table 2. Prevalence (/1000) and RR for birth defects based on mother's area of origin, 1995-2014, Ontario.

World area	Total births	Births with abnormalities	Rate/1000	RR (95% CI)	
Canada	**2001251**	**126505**	**63.2**	**Reference group**	
Caribbean	38905	2788	71.7	1.13	(1.09-1.18)
Sub-Saharan Africa	49620	3312	66.7	1.06	(1.02-1.09)
East Asia and Pacific	137579	8195	59.6	0.94	(0.92-0.96)
Middle East and North Africa	54637	3211	58.8	0.93	(0.90-0.96)
South Asia	172901	10160	58.8	0.93	(0.91-0.95)
Hispanic America	46760	2581	55.2	0.87	(0.84-0.91)
Western Nations and Europe	96008	5170	53.8	0.85	(0.83-0.88)

Source: Data collected from births to immigrant and non-immigrant mothers in Ontario 1995-2014.

A total of 161,538 diagnoses of birth defects were identified among these children with 78% of them among non-immigrant and 22% of them among immigrant mothers. Table 1 shows the birth prevalence of birth defects among both groups of mothers through 1995 to 2014. Before 2000, the rates were higher among immigrant mothers, but their rates start to decline after 2000.

Graph 1 shows the trend over time in abnormalities prevalence among two groups and the shifting change among immigrant mothers in early 2000.

Immigration data on mother's country of birth is available since 1985 in Ontario. During this period (1985-2014) women arrived in Ontario from more than 140 different countries. These countries often differ for many socioeconomic factors that could affect the risk of mothers having children with birth defects. We grouped these countries into five major regions. Table 2 shows the birth prevalence of birth defects among mothers who migrated to Ontario from each region as compared to

Table 3. Prevalence (/1000) and RR for birth defects based on mother's country of origin, 1995-2014, Ontario.

Country	All births	Births with abnormalities	abnormalities rate/1000	Relative risk	95% CI
Sudan, Democratic Republic of	1515	126	83.2	1.27	1.07-1.51
Jamaica	13241	1041	78.6	1.20	1.13-1.28
Nigeria	2843	218	76.7	1.17	1.02-1.34
Bangladesh	5436	411	75.6	1.15	1.05-1.27
Afghanistan	5483	404	73.7	1.12	1.02-1.24
Somalia, Democratic Republic	5206	364	69.9	1.07	0.96-1.18
Ghana	3452	241	69.8	1.07	0.94-1.21
Trinidad & Tobago, Republic of	4881	336	68.8	1.05	0.94-1.17
Sri Lanka	19087	1296	67.9	1.04	0.98-1.09
Guyana	8067	543	67.3	1.03	0.94-1.12
Portugal	3752	250	66.6	1.02	0.90-1.15
United Kingdom and Colonies	6170	405	65.6	1.00	0.91-1.10
Canada	1164294	76285	65.5	Reference	
El Salvador	2946	186	63.1	0.96	0.83-1.11
China, People's Republic of	37245	2344	62.9	0.96	0.92-1.00
Lebanon	4672	293	62.7	0.96	0.85-1.07
Iran	6814	427	62.7	0.96	0.87-1.05
Iraq	5121	317	61.9	0.94	0.85-1.05
Philippines	27195	1674	61.6	0.94	0.90-0.99
Hong Kong	6646	408	61.4	0.94	0.85-1.03
Brazil	1762	108	61.3	0.94	0.77-1.13
Pakistan	22363	1369	61.2	0.93	0.89-0.99
Romania	4997	302	60.4	0.92	0.82-1.03
Ethiopia	3809	229	60.1	0.92	0.81-1.04
Vietnam, Socialist Republic of	9937	592	59.6	0.91	0.84-0.99
India	48434	2861	59.1	0.90	0.87-0.94
United States of America	6469	376	58.1	0.89	0.80-0.98
Korea, Republic of	3611	200	55.4	0.85	0.74-0.97
Turkey	2055	111	54.0	0.82	0.68-0.99
Egypt	2753	148	53.8	0.82	0.70-0.96
Ukraine	3456	183	53.0	0.81	0.7-0.93
Mexico	3127	158	50.5	0.77	0.66-0.90
Poland	10513	526	50.0	0.76	0.70-0.83
Yugoslavia	4431	218	49.2	0.75	0.66-0.86

Source: Data collected from births to immigrant and non-immigrant mothers in Ontario 1995-2014.

non-immigrant mothers.

Mothers that arrived from Caribbean and Sub-Saharan Africa had significantly higher rates of birth defects compared to Canadian mothers, while mothers who emigrated from Europe and Hispanic America had significantly lower rates. For other countries, the rate of abnormalities among immigrant mothers was lower than Canadian mothers.

Table 3 shows the rate and relative risk of having a child with birth defects based on mother's country of birth. For this table we selected countries that had a large number of immigrants to Canada.

Table 3 confirms that mothers coming from some countries located in the Caribbean, Africa and some South East Asian countries had higher rates of birth defects as compared to Canadian mothers.

Regardless of country of origin, mothers that arrived in Canada after the year 2000 (the year of food fortification in Canada) had a lower rate of defects in their births as compared to mothers that landed before 2000. Graph 2 shows the prevalence of birth defects among immigrant

Table 4. Results of logistic regression for risk of birth defects among immigrant and non-immigrant mothers.

Variable	level	Canadian			Immigrant		
		OR	95% CI		OR	95% CI	
Food fortification	No	1.05	1.02	1.08	1.12	1.05	1.19
	Yes	Reference					
Maternal age (year)	≥40+	Reference					
	15-19	1.06	0.97	1.16	1.23	1.01	1.50
	20-29	0.99	0.92	1.08	1.10	0.97	1.25
	30-39	0.92	0.86	0.99	0.94	0.83	1.05
Birth weight (grams)	>3500	Reference					
	<1500	12.75	11.73	13.85	12.72	10.91	14.83
	1500-2500	2.80	2.68	2.93	2.69	2.46	2.94
	2500-3500	1.16	1.14	1.19	1.08	1.03	1.13

Source: Data collected from births to immigrant and non-immigrant mothers in Ontario 1995-2014.

mothers based on the year they arrived in Canada. We used logistic regression to evaluate the joint effect of food fortification, maternal and immigration factors for having a child with birth defects. Mothers with multiple births were used as their own control to evaluate the effect of food fortification while controlling for other potential confounders such as mothers age and birth weight. Table 4 shows the estimated odds ratios for having a child with birth defects for Canadian and immigrant mothers giving birth in Ontario.

The timing of introducing food fortification remains a significant factor in reducing the risk of birth defects among both non-immigrant and immigrant mothers in spite of controlling for maternal age and birth weight. While giving birth before food fortification was associated with higher risk of birth defects in both groups, the risk was greater amongst immigrant mothers.

DISCUSSION

Birth defects remain a significant problem in both developing and developed countries. While risk factors for many anomalies are said to be unknown, both environmental factors and genetic factors are the two major suspects in the epidemiology of abnormalities.

The high mobility of population during the 20th and 21st century and surge in immigration from developing countries to developed countries give us the opportunity to explore the possible role of change in the environment and background genetic predisposition on the risk of having a child with birth defects.

In this retrospective cohort study, we estimated birth prevalence of congenital abnormalities among children born to all immigrant women who landed in Canada between 1995 and 2014 and compared them to the rate of diagnosis of abnormalities among those born to Canadian non-immigrant mothers who gave birth during the same period.

Some studies in Europe (Anthony, 2005; Stoltenberg, 1997) and in the US (Canfield et al., 2014; Khodr, 2013; Emad, 2005) reported higher rates of abnormalities among immigrant mothers. A recent report in Canada also indicates that immigrant mothers may be at higher risk for giving birth to a child with abnormalities. None of these studies looked at trends over time and had a snapshot for this association.

Our results indicate that among immigrant mothers that arrived before food fortification around 2000, the rate of abnormalities was higher than Canadian mothers, but the reverse was true for immigrant mothers that arrived after food fortification. Rate of abnormalities among immigrant mothers that arrived after 2000 was lower than for Canadian mothers.

We do not know of any specific policy change in screening of immigrants in the years around 2000, but what we know about the implementation of food fortification around 2000 in Canada. Immigrant mothers arriving after 2000 had access to folic acid through food fortification and this could have reduced their risk of having a birth with abnormalities. Exposure to folic acid during pregnancy has been shown to be a major preventive factor for birth defects and especially for neural tube defects (MRC, 1991; Czeizel, 1992; Berry et al., 1999; De Wals, 2007).

Our study showed that immigrants coming from specific areas of the world have a higher chance of giving birth to a child with abnormalities as compared to non-immigrant mothers. Mothers that migrated from the Caribbean and

Sub-Saharan Africa had higher rates and immigrants from other areas of the world had lower rates of abnormalities compared to Canadian mothers.

Mothers arriving from Sudan, Jamaica, Nigeria, Bangladesh and Afghanistan had a 12 to 27% higher chance of giving birth to a child with abnormalities. Studies among Norwegian and Dutch mothers (Anthony, 2005; Anthony, 2005) showed that mothers coming from Pakistan or Morocco had 20% higher risk of having a birth with abnormalities as compared to non-immigrant mothers. Our study indicates that the rate of abnormalities in births among immigrant mothers was lower than Canadian mothers, as long as the birth was after food fortification.

This finding of this retrospective cohort study shows that comparing children born to immigrant and non-immigrant mothers at one point in time for specific health outcomes may not be a valid approach. For example, while rate of abnormalities was higher amongst births that occurred in immigrant mothers before food fortification in Canada, the rates were lower among immigrant mothers after food fortification.

Mothers that came to Canada and gave birth before food fortification may have had less access to folic acid in their own country and even in Canada. This may have caused them to have higher rates of abnormalities amongst their children. But, after food fortification, immigrant mothers had similar exposure to folic acid as Canadian mothers and interestingly the rate of abnormalities was lower among births in immigrant population.

Other risk factors such as older maternal age and low birth weight played the same role in both immigrant and non-immigrant populations.

This study is the first study to explore the time trend of occurrence of birth defects among immigrant populations. While this study gave us the opportunity to explore the role of many important risk factors such length of stay, risk level in mother's country of birth, birth order and also impact of food fortification, it also has some limitations such as lack of access to data on abortions in this population.

One of main limitations in our study is lack of data on pregnancy termination and prenatal screening for birth defects among immigrant and non-immigrant mothers. Therefore we are not able control for possible effect of these factors. While the abortion rate, especially for birth diagnosed with any defect could be high, we do not have any reason to believe that the abortion rate would be higher among immigrant mothers.

One other factor worth mentioning is the possible healthy-immigrant effect among the immigrant population. People applying for immigration go through a medical check and healthy people have a better chance for being accepted. It is not clear if immigrant mothers are healthier than Canadian mothers and if this has any impact on their risk of having a birth with abnormalities.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

ACKNOWLEDGEMENTS

This study was supported by the ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by the ICES or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred.Immigration data was obtained from the Immigration, Refugees and Citizenship Canada database held at the ICES. We thank Immigration, Refugees and Citizenship Canada (IRCC)'s Permanent Resident Database for use of their database. All datasets were linked using unique encoded identifiers and analyzed at ICES.Richard Glazier is supported as a clinician scientist by the Department of Family and Community Medicine at St. Michael's Hospital and at the University of Toronto.
The researchers would like to thank Anne-Marie Tynan for editing the final manuscript.

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