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Preterm birth and severe small-for-gestational age birthweight among infants of mothers from the Philippines

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Abstract

Objectives: Women from the Philippines form one of the largest immigrant groups to North America. Their newborns experience higher rates of preterm birth (PTB), and separately, small-for-gestational age (SGA) birthweight, compared to other East Asians. It is not known if Filipina women are at elevated risk of concomitant PTB and severe SGA (PTB-SGA), a pathological state likely reflective of placental dysfunction and neonatal morbidity.

Methods: We conducted a population-based study of all singleton or twin livebirths in Ontario, from 2002 to 2011, among immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) and China (N = 42,517). We used modified Poisson regression to generate relative risks (RR) of PTB-SGA, defined as a birth < 37 weeks' gestation and a birthweight < 5th percentile. RRs were adjusted for maternal age, parity, marital status, income quintile, infant sex and twin births.

Results: Relative to mothers from China (2.3 per 1000), the rate of PTB-SGA was significantly higher among infants of mothers from the Philippines (6.5 per 1000; RR 2.91, 95% CI 2.27-3.73), and those from Vietnam (3.7 per 1000; RR 1.68, 95% CI 1.21-2.34). The RR of PTB-SGA was not higher for infants of mothers from Hong Kong or South Korea.

Interpretation: Among infants born to immigrant women from five East Asian countries, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.

Keywords: Preterm birth; small for gestational age birthweight; ethnicity; race; immigrant; East Asia; Philippines; Filipina; Viet Nam.

Article summary: Strengths and limitations of this study

- We conducted a population-based study of all livebirths in Ontario, comparing immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) to those from China (N = 42,517).
- The rate of PTB-SGA was highest among infants of mothers from the Philippines (6.5 per 1000), which was 2.91 (95% confidence interval [CI] 2.27-3.73) times higher than women from China.
- Among infants born to immigrant women from five East Asian countries, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.
- We excluded stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA.
- We lacked data on skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight.

Background

A pregnancy resulting in a preterm birth (PTB) and concomitant small for gestational age birthweight (SGA) – "PTB-SGA" – is thought to be most pathological, in terms of both being due to placental dysfunction(1, 2) and their adverse sequelae for the newborn infant(3, 4). Relative to infants born either PTB alone or SGA alone, those affected by PTB-SGA are 15 times more likely to die in the first month of life(3).

PTB(5) and SGA(6) are each more frequent in women from the Philippines. Chronic hypertension(7) and preterm onset of preeclampsia(8) are each risk factors for provider-initiated ("iatrogenic") PTB and SGA, and they are significantly more likely to present in Filipina women than Caucasian or other East Asian women. What remains unknown is whether the risk of PTB-SGA is higher among Filipina women than their counterparts from other East Asian countries.

Herein, we performed a study in Ontario, Canada, where foreign-born individuals comprise 20% of the population and nearly 35% of all births, the highest proportion of G8 countries.(9) We compared the risk of PTB-SGA among five East Asian groups, using a < 5^{th} percentile cut-point to define severe SGA, which is more predictive of adverse perinatal outcomes than a < 10^{th} percentile cut-point(10).

Methods

Study sample

This population-based study comprised all live singletons and twin births in Ontario between 2002 and 2011. Data were retrieved from livebirth records provided by Vital Statistics. We excluded stillbirths, as information on parental country of origin is missing for 12% of records(11). As all records were de-identified, a given woman may have contributed more than one birth during the study period, but we adjusted for parity, as described below. All pregnancy and newborn care is universally covered under Ontario's Health Insurance Plan. Approximately 95% of Ontarian women undergo prenatal ultrasonography before 20 weeks gestation, enhancing accuracy of gestational age determined at birth.(12)

Exposures and outcomes

The main exposure was maternal country of birth, which was self-reported on the infant's birth record. Each newborn was then assigned to one of five maternal East Asian countries of origin: (1) China (the referent), (2) Hong Kong, (3) South Korea, (4) Vietnam, and (5) the Philippines. Women from China were chosen as the reference group as they are the largest East Asian immigrant group in Ontario(9), and are have relatively lower rates of PTB and SGA(5, 6). The main study outcome was PTB-SGA, defined as PTB < 37 weeks and severe SGA < 5th percentile(10). The birthweight percentile curves used herein were those for all livebirths in Ontario, and were not otherwise customized by maternal ethnicity or other factors (6,11). Reasons for the latter were that we restricted our cohort solely to births of East Asian mothers, and that defining severe SGA at < 5th percentile is a cut-point that reflects pathological intrauterine growth restriction (10). Secondary outcomes were PTB without severe SGA, and severe SGA without PTB.

Data analysis

We used modified Poisson regression models to estimate relative risks (RR) and 95% confidence intervals (CI) for each study outcome in association with maternal country of origin. RR were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown)(13), infant sex, and twin births.

For the main outcome of PTB-SGA, we additionally performed stratified analyses to examine potential effect measure modification by parity (nulliparous vs. parous) and by maternal age (< 35 years vs. ≥ 35 years).

As the study focus was to compare immigrants from different East Asian countries, Canadian-born mothers were not included in regression models. However, for comparative purposes, we describe herein the characteristics of Canadian-born mothers and their infants.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary NC). Ethics approval was provided by the Research Ethics Board of St. Michael's Hospital, Toronto, Ontario.

Results

Between 2002 and 2011, there were 956,994 liveborn singleton or twin births in Ontario to mothers born in Canada, China, Hong Kong, South Korea, Vietnam or the Philippines. We excluded 893 infants (0.09%) whose gestational age was < 24 or > 42 weeks, and 487 infants (0.05%) whose gestational age at birth was unknown. We further excluded infants whose birthweight was unknown (n = 31) or < 500 g (n = 55), whose sex was unknown (n = 1), or in which maternal age (n = 108) or parity (n = 239) were unknown.

The final cohort comprised 42,517 births to mothers from China, 5,618 from Hong Kong, 5,148 from South Korea, 15,297 from Vietnam, and 27,946 from the Philippines. The remainder were newborns of mothers from Canada (Table 1). In general, mothers from East Asian countries tended to be older than Canadian-born women, but of similar parity. Filipina-born mothers were similar in age, marital status and income to Chinese-born mothers (Table 1).

Compared to mothers from China, the outcomes of PTB without severe SGA, and severe SGA without PTB, were significantly more prevalent among newborns of mothers from Hong Kong, Vietnam and the Philippines, but not South Korea (Figure 1). The more severe outcome of PTB-SGA was significantly more common among newborns of mothers from Vietnam (3.7 per 1000; aRR 1.68 95% CI 1.21 to 2.34), compared to those of mothers from China (2.3 per 1000). For newborns of Filipina women, the rate (6.5 per 1000) and aRR (2.91, 95% CI 2.27 to 3.73) were even higher.

In our stratified analyses, the risk of PTB-SGA was somewhat more pronounced among Filipina women aged ≥ 35 years or older (Figure 2, upper) and those who were nulliparous (Figure 2, lower).

Finally, limiting the dataset to singleton births did not appreciably change the RR of PTB-SGA, even heightening the RR among Filipina women (Supplementary file 1).

Interpretation

Newborns of mothers from the Philippines were most vulnerable to PTB-SGA, especially among women ≥ 35 years, who comprised 37% of all Filipina mothers, and in whom the rate of PTB-SGA was nearly 1%.

Strengths and limitations

We evaluated nearly 100,000 livebirths among women born in five East Asian countries, which are major sources of immigrants to Ontario, in a setting of universal healthcare. Infants of Chinese-born women provided an ideal reference group, as China is the largest source of immigrants from East Asia to Ontario, and they have a low incidence of adverse neonatal and maternal outcomes(5, 14). The < 5th percentile cut-off used to define severe SGA reflects a degree of smallness that is more likely to be pathological, rather than constitutional(10). Still, the outcome of PTB-SGA was not rare – occurring in 6.5 per 1000 infants of Filipina mothers. We were able to account for some previously noted risk factors for PTB or SGA, such as maternal age, infant sex, parity, income level and marital status.

A limitation of this study was the exclusion of stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA(15, 16). We lacked data on factors associated with the so-called "healthy immigrant effect"(17), such as skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight – which may influence newborn weight – or conditions such as maternal chronic hypertension and diabetes mellitus, or maternal behavioural risk factors (e.g. smoking, drug/substance abuse).

Implications

In 2011, 13.1% of all newcomers to Canada were from the Philippines(9). Women from the Philippines were at exceptionally high risk of PTB-SGA, peaking at nearly 1% among those aged 35 years and older, and who represent one-third of all Filipina women giving birth in Ontario. From a public health perspective, there is value in reducing the incidence of PTB-SGA, and such a strategy might start with Filipina women. For healthcare providers – including family doctors, obstetricians, or midwives – the priority would be to address risk factors in these women. This can be done at several time points – before becoming pregnant, during pregnancy, and at the time of delivery. Before pregnancy, providers can counsel Filipina women, especially those women older than 35 years of age, on the possibility of adverse perinatal outcomes. During the pregnancy, risk factors can be identified and managed. Chronic hypertension is one important

risk factor for both PTB(18) and SGA(19, 20), and also for preeclampsia(21), which can give rise to PTB-SGA(22). Chronic hypertension is highly prevalent among Filipina women in Ontario(7); therefore, efforts to regulate blood pressure and prevent preeclampsia may help reduce the risk of SGA-PTB among Filipina women, and also those from Vietnam. Such interventions include aspirin(23-25) and early pregnancy blood pressure assessments(26). By the third trimester of pregnancy, periodic sonographic assessment of fetal growth and well-being should be considered, as there is evidence that this helps the clinician balance the risks of prematurity against a worsening intrauterine environment(27).

Conclusions

What differentiates a Filipina woman from another East Asian woman is her heightened risk of having a liveborn affected by PTB-SGA, a severe pathological state. For Filipina immigrant women, appropriate cautionary measures should be taken to ensure that mother and baby remain healthy throughout the pregnancy and delivery. Future research should aim to identify specific, and ideally modifiable, traits of Filipina women that increase the risk of PTB-SGA during pregnancy.

Authors contributions: Bartsch contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision and approval of final version. Ray contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Park contributed to the analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Jairam contributed to the interpretation of the data and approval of final version.

Data sharing statement: No additional data available.

Details of ethics approval: Ethics approval was granted by the Research Ethics Board of St. Michael's Hospital in Toronto, Ontario, Canada.

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Competing interests: None.

FIGURE LEGENDS

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Table 1. Characteristics of live singleton and twin births and their mothers, who delivered at 24 to 42 weeks' gestation in Ontario, 2002 to 2011. All data are presented as a number (%) unless otherwise indicated.

	East Asian maternal country of birth					
Characteristic	**China (n = 42,517)**	**Hong Kong (n = 5618)**	**South Korea (n = 5148)**	**Vietnam (n = 15,297)**	**Philippines (n = 27,946)**	**Canadian maternal country of birth (n = 858,654)**
Of the mother						
Mean (*SD*) age, years	32.3 (4.7)	33.5 (4.3)	32.1 (3.9)	31.4 (4.8)	32.6 (5.4)	29.5 (5.5)
Age category, years						
< 20	81 (0.2)	17 (0.3)	7 (0.1)	68 (0.4)	353 (1.3)	38920 (4.5)
20-34	28163 (66.2)	3346 (59.6)	3801 (73.8)	11178 (73.1)	17042 (61.0)	662500 (77.2)
≥ 35	14273 (33.6)	2255 (40.1)	1340 (26.0)	4051 (26.5)	10551 (37.8)	157234 (18.3)
Unknown						
Parity	1 (0-1)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
0	21160 (49.8)	3104 (55.3)	2552 (49.6)	6809 (44.5)	12698 (45.4)	389635 (45.4)
1	17836 (42.0)	2023 (36.0)	1990 (38.7)	5984 (39.1)	9905 (35.4)	304847 (35.5)
2	3012 (7.1)	413 (7.4)	505 (9.8)	1896 (12.4)	3921 (14.0)	111814 (13.0)
3	410 (1.0)	59 (1.1)	78 (1.5)	470 (3.1)	1047 (3.7)	33591 (3.9)
≥ 4	99 (0.2)	19 (0.3)	23 (0.4)	138 (0.9)	375 (1.3)	18767 (2.2)
Marital status						
Married/common-law	36668 (86.2)	5205 (92.6)	4829 (93.8)	10899 (71.2)	22304 (79.8)	578402 (67.4)
Unmarried	3764 (8.9)	236 (4.2)	107 (2.1)	2388 (15.6)	3125 (11.2)	132698 (15.5)
Unknown	2085 (4.9)	177 (3.2)	212 (4.1)	2010 (13.1)	2517 (9.0)	147554 (17.2)
Residential income quintile (*Q*)						
Q1 (lowest)	12391 (29.1)	512 (9.1)	1183 (23.0)	4091 (26.7)	8992 (32.2)	150194 (17.5)
Q2	11092 (26.1)	1119 (19.9)	976 (19.0)	3454 (22.6)	6770 (24.2)	159370 (18.6)
Q3	7328 (17.2)	1193 (21.2)	1021 (19.8)	3336 (21.8)	5445 (19.5)	177349 (20.7)
Q4	6236 (14.7)	1487 (26.5)	1021 (19.8)	2526 (16.5)	4183 (15.0)	192726 (22.4)
Q5 (highest)	3971 (9.3)	1148 (20.4)	852 (16.6)	1387 (9.1)	2342 (8.4)	166173 (19.4)
Unknown	1499 (3.5)	159 (2.8)	95 (1.8)	503 (3.3)	214 (0.8)	12842 (1.5)
Of the newborn infant						
Female sex	20519 (48.3)	2703 (48.1)	2444 (47.5)	7381 (48.3)	13491 (48.3)	418726 (48.8)
Twin births	901 (2.1)	156 (2.8)	105 (2.0)	286 (1.9)	554 (2.0)	29075 (3.4)

SD Standard deviation

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

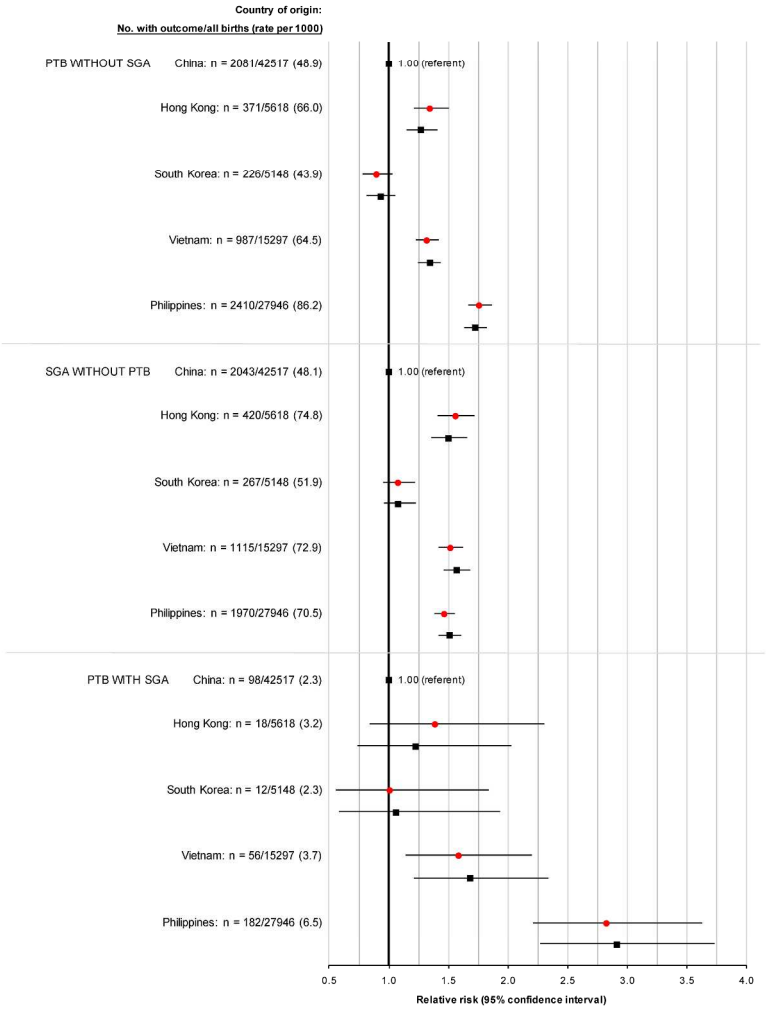

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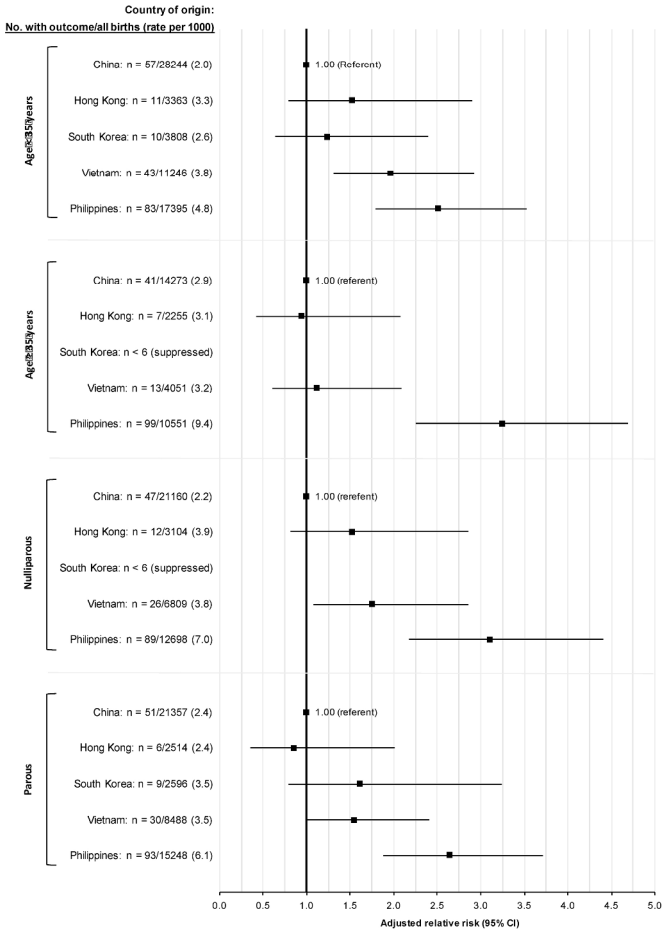
Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.



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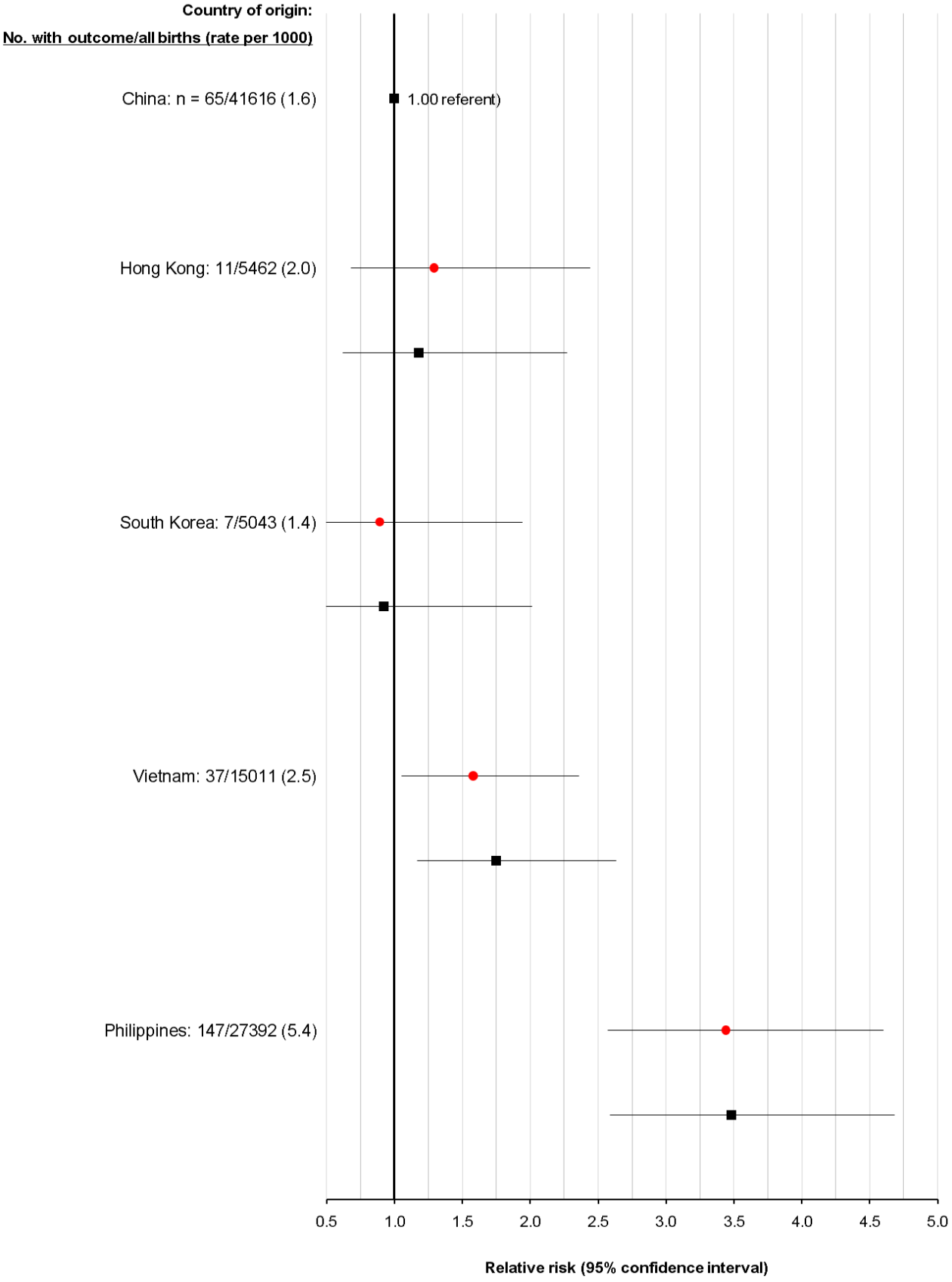
Supplementary file 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn singleton infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown) and infant sex.



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Concomitant preterm birth and severe small-for-gestational age birthweight among infants of immigrant mothers in Ontario originating from the Philippines and East Asia

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Abstract

Objectives: Women from the Philippines form one of the largest immigrant groups to North America. Their newborns experience higher rates of preterm birth (PTB), and separately, small-for-gestational age (SGA) birthweight, compared to other East Asians. It is not known if Filipina women are at elevated risk of concomitant PTB and severe SGA (PTB-SGA), a pathological state likely reflective of placental dysfunction and neonatal morbidity.

Methods: We conducted a population-based study of all singleton or twin livebirths in Ontario, from 2002 to 2011, among immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) and China (N = 42,517). We used modified Poisson regression to generate relative risks (RR) of PTB-SGA, defined as a birth < 37 weeks' gestation and a birthweight < 5th percentile. RRs were adjusted for maternal age, parity, marital status, income quintile, infant sex and twin births.

Results: Relative to mothers from China (2.3 per 1000), the rate of PTB-SGA was significantly higher among infants of mothers from the Philippines (6.5 per 1000; RR 2.91, 95% CI 2.27-3.73), and those from Vietnam (3.7 per 1000; RR 1.68, 95% CI 1.21-2.34). The RR of PTB-SGA was not higher for infants of mothers from Hong Kong or South Korea.

Interpretation: Among infants born to immigrant women from five East Asian birthplaces, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.

Keywords: Preterm birth; small for gestational age birthweight; ethnicity; race; immigrant; East Asia; Philippines; Filipina; Viet Nam.

Article summary: Strengths and limitations of this study

- We conducted a population-based study of all livebirths in Ontario, comparing immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) to those from China (N = 42,517).
- The rate of PTB-SGA was highest among infants of mothers from the Philippines (6.5 per 1000), which was 2.91 (95% confidence interval [CI] 2.27-3.73) times higher than women from China.
- Among infants born to immigrant women from five East Asian birthplaces, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.
- We excluded stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA.
- We lacked data on skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight.

Background

A pregnancy resulting in a preterm birth (PTB) and concomitant small for gestational age birthweight (SGA) – "PTB-SGA" – is thought to be most pathological, in terms of both being due to placental dysfunction[1 2] and their adverse sequelae for the newborn infant[3 4]. Relative to infants born either PTB alone or SGA alone, those affected by PTB-SGA are 15 times more likely to die in the first month of life[3].

PTB[5] and SGA[6] are each more frequent in women from the Philippines. Chronic hypertension[7] and preterm onset of preeclampsia[8] are each risk factors for provider-initiated ("iatrogenic") PTB and SGA, and they are significantly more likely to present in Filipina women than Caucasian or other East Asian women. What remains unknown is whether the risk of PTB-SGA is higher among Filipina women than their counterparts from other East Asian regions.

Herein, we performed a study in Ontario, Canada, where foreign-born individuals comprise 20% of the population and nearly 35% of all births, the highest proportion of G8 countries.[9] We compared the risk of PTB-SGA among five East Asian groups, using a < 5th percentile cut-off to define severe SGA, which is more predictive of adverse perinatal outcomes than a < 10th percentile cut-off[10].

Methods

Study sample

This population-based study comprised all live singletons and twin births in Ontario between 2002 and 2011. Data were retrieved from livebirth records provided by Vital Statistics. We excluded stillbirths, as information on parental place of birth is missing for 12% of records[11]. As all records were de-identified, a given woman may have contributed more than one birth during the study period, but we adjusted for parity, as described below. All pregnancy and newborn care is universally covered under Ontario's Health Insurance Plan. Approximately 95% of Ontarian women undergo prenatal ultrasonography before 20 weeks gestation, enhancing accuracy of gestational age determined at birth.[12]

Exposures and outcomes

The main exposure was maternal place of birth, which was self-reported on the infant's birth record. Each newborn was then assigned to one of five maternal East Asian birthplaces: (1) China (the referent), (2) Hong Kong, (3) South Korea, (4) Vietnam, and (5) the Philippines. Women from China were chosen as the reference group as they are the largest East Asian immigrant group in Ontario[9], and are have relatively lower rates of PTB and SGA[5 6]. The main study outcome was PTB-SGA, defined as PTB < 37 weeks and severe SGA < 5th percentile[10]. The birthweight percentile curves used herein were those for all livebirths in Ontario, and were not otherwise customized by maternal ethnicity or other factors (6,11). Reasons for the latter were that we restricted our cohort solely to births of East Asian mothers, and that defining severe SGA at < 5th percentile is a cut-off that reflects pathological intrauterine growth restriction (10). Secondary outcomes were PTB without severe SGA, and severe SGA without PTB.

Data analysis

We used modified Poisson regression models to estimate relative risks (RR) and 95% confidence intervals (CI) for each study outcome in association with maternal place of birth. RR were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown)[13], infant sex, and twin births. The "unknown" categories of marital status and residential income quintile were included in the multivariable models. However, for maternal age and parity, we excluded those pregnancies with "unknown" status, given the rarity of this situation and the need to allow model convergence, accordingly.

For the main outcome of PTB-SGA, we additionally performed stratified analyses to examine potential effect measure modification by parity (nulliparous vs. parous) and by maternal age (< 35 years vs. ≥ 35 years).

As the study focus was to compare immigrants from different East Asian birthplaces, Canadian-born mothers were not included in main regression models. However, for comparative purposes, we described the characteristics of Canadian-born mothers and their

infants, and ran an additional analysis of the main model of PTB-SGA with Canadian-born mothers as the referent.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary NC). Ethics approval was provided by the Research Ethics Board of St. Michael's Hospital, Toronto, Ontario.

Results

Between 2002 and 2011, there were 956,994 liveborn singleton or twin births in Ontario to mothers born in Canada, China, Hong Kong, South Korea, Vietnam or the Philippines. We excluded 893 infants (0.09%) whose gestational age was < 24 or > 42 weeks, and 487 infants (0.05%) whose gestational age at birth was unknown. We further excluded infants whose birthweight was unknown (n = 31) or < 500 g (n = 55), whose sex was unknown (n = 1), or in which maternal age (n = 108) or parity (n = 239) were unknown.

The final cohort comprised 42,517 births to mothers from China, 5,618 from Hong Kong, 5,148 from South Korea, 15,297 from Vietnam, and 27,946 from the Philippines. The remainder were newborns of mothers from Canada (Table 1). In general, mothers from East Asia tended to be older than Canadian-born women, but of similar parity. Filipina-born mothers were similar in age, marital status and income to Chinese-born mothers (Table 1).

Compared to mothers from China, the outcomes of PTB without severe SGA, and severe SGA without PTB, were significantly more prevalent among newborns of mothers from Hong Kong, Vietnam and the Philippines, but not South Korea (Figure 1). The more severe outcome of PTB-SGA was significantly more common among newborns of mothers from Vietnam (3.7 per 1000; aRR 1.68 95% CI 1.21 to 2.34), compared to those of mothers from China (2.3 per 1000) (Figure 1). For newborns of Filipina women, the rate (6.5 per 1000) and aRR (2.91, 95% CI 2.27 to 3.73) were even higher (Figure 1).

In our stratified analyses, the risk of PTB-SGA was somewhat more pronounced among Filipina women aged ≥ 35 years or older (Figure 2, upper) and those who were nulliparous (Figure 2, lower).

Limiting the dataset to singleton births did not appreciably change the RR of PTB-SGA, even heightening the RR among Filipina women (Supplementary file 1).

Re-running the main model of PTB-SGA, with Canadian-born mothers as the referent, showed that only the offspring of Filipina mothers were at higher risk of PTB-SGA (Supplementary file 2).

Interpretation

Newborns of mothers from the Philippines were most vulnerable to PTB-SGA, especially among women ≥ 35 years, who comprised 37% of all Filipina mothers, and in whom the rate of PTB-SGA was nearly 1%.

Strengths and limitations

We evaluated nearly 100,000 livebirths among women born in five East Asian regions, which are major sources of immigrants to Ontario, in a setting of universal healthcare. Infants of Chinese-born women provided an ideal reference group, as China is the largest source of immigrants from East Asia to Ontario, and they have a low incidence of adverse neonatal and maternal outcomes[5, 14]. The < 5th percentile cut-off used to define severe SGA reflects a degree of smallness that is more likely to be pathological, rather than constitutional[10]. Still, the outcome of PTB-SGA was not rare – occurring in 6.5 per 1000 infants of Filipina mothers. Through our analysis, we were able to account for some previously noted risk factors for PTB or SGA, such as maternal age, infant sex, parity, income level and marital status.

A limitation of this study was the exclusion of stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA[15, 16]. We lacked data on factors associated with the so-called "healthy immigrant effect"[17], such as skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight – which may influence newborn weight – or conditions such as maternal chronic hypertension and diabetes mellitus, or maternal behavioural risk factors (e.g. smoking, drug or substance use). However, Filipina women of reproductive age living in Canada have a rate of smoking under 6.0%, comparable to that of their East Asian counterparts[7], and the corresponding rate in pregnancy would be expected to be even lower. The body mass index (BMI) of Filipina women of reproductive age tends to be higher than that of other East Asians[7]. It is unlikely that access to prenatal care

explains the current findings, as 88% of Filipina women and 85% of other East Asian women in Canada have a regular medical doctor[7]. Finally, we could not identify the specific causes of PTB-SGA from the dataset used herein, which is certainly worthy of a focused study focused on differentiating spontaneous vs. provider-initiated PTB.

Implications

In 2011, 13.1% of all newcomers to Canada were from the Philippines[9]. Women from the Philippines were at exceptionally high risk of PTB-SGA, peaking at nearly 1% among those aged 35 years and older, and who represent one-third of all Filipina women giving birth in Ontario. From a public health perspective, there is value in reducing the incidence of PTB-SGA, and such a strategy might start with Filipina women. For healthcare providers – including family doctors, obstetricians, or midwives – the priority would be to address risk factors in these women. This can be done at several time points – before becoming pregnant, during pregnancy, and at the time of delivery. Before pregnancy, providers can counsel Filipina women, especially those women older than 35 years of age, on the possibility of adverse perinatal outcomes. During the pregnancy, risk factors can be identified and managed. Chronic hypertension is one important risk factor for both PTB[18] and SGA[19 20], and also for preeclampsia[21], which can give rise to PTB-SGA[22]. Chronic hypertension is highly prevalent among Filipina women in Ontario[7]; therefore, efforts to regulate blood pressure and prevent preeclampsia may help reduce the risk of SGA-PTB among Filipina women, and also those from Vietnam. Such interventions include aspirin[23-25] and early pregnancy blood pressure assessments[26]. By the third trimester of pregnancy, periodic sonographic assessment of fetal growth and well-being should be considered, as there is evidence that this helps the clinician identify SGA infants and balance the risks of prematurity against a worsening intrauterine environment[27 28].

Conclusions

What differentiates a Filipina woman from another East Asian woman is her heightened risk of having a liveborn affected by PTB-SGA, a severe pathological state. For Filipina immigrant women, appropriate cautionary measures should be taken to ensure that mother and baby

remain healthy throughout the pregnancy and delivery. Future research should aim to identify specific, and ideally modifiable, traits of Filipina women that increase the risk of PTB-SGA during pregnancy. Specifically, it would be worthwhile to evaluate whether the rates of smoking, high BMI, or other socioeconomic indicators differ between pregnant Filipina women and those women from other East Asian birthplaces.

Authors contributions: Bartsch contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision and approval of final version. Ray contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Park contributed to the analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Jairam contributed to the interpretation of the data and approval of final version.

Data sharing statement: No additional data available.

Details of ethics approval: Ethics approval was granted by the Research Ethics Board of St. Michael's Hospital in Toronto, Ontario, Canada.

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Competing interests: None.

FIGURE LEGENDS

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Table 1. Characteristics of live singleton and twin births and their mothers, who delivered at 24 to 42 weeks' gestation in Ontario, 2002 to 2011. All data are presented as a number (%) unless otherwise indicated.

	East Asian maternal place of birth					
Characteristic	**China (n = 42,517)**	**Hong Kong (n = 5618)**	**South Korea (n = 5148)**	**Vietnam (n = 15,297)**	**Philippines (n = 27,946)**	**Canadian maternal country of birth (n = 858,654)**
Of the mother						
Mean (*SD*) age, years	32.3 (4.7)	33.5 (4.3)	32.1 (3.9)	31.4 (4.8)	32.6 (5.4)	29.5 (5.5)
Age category, years						
< 20	81 (0.2)	17 (0.3)	7 (0.1)	68 (0.4)	353 (1.3)	38920 (4.5)
20-34	28163 (66.2)	3346 (59.6)	3801 (73.8)	11178 (73.1)	17042 (61.0)	662500 (77.2)
≥ 35	14273 (33.6)	2255 (40.1)	1340 (26.0)	4051 (26.5)	10551 (37.8)	157234 (18.3)
Parity	1 (0-1)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
0	21160 (49.8)	3104 (55.3)	2552 (49.6)	6809 (44.5)	12698 (45.4)	389635 (45.4)
1	17836 (42.0)	2023 (36.0)	1990 (38.7)	5984 (39.1)	9905 (35.4)	304847 (35.5)
2	3012 (7.1)	413 (7.4)	505 (9.8)	1896 (12.4)	3921 (14.0)	111814 (13.0)
3	410 (1.0)	59 (1.1)	78 (1.5)	470 (3.1)	1047 (3.7)	33591 (3.9)
≥ 4	99 (0.2)	19 (0.3)	23 (0.4)	138 (0.9)	375 (1.3)	18767 (2.2)
Marital status						
Married/common-law	36668 (86.2)	5205 (92.6)	4829 (93.8)	10899 (71.2)	22304 (79.8)	578402 (67.4)
Unmarried	3764 (8.9)	236 (4.2)	107 (2.1)	2388 (15.6)	3125 (11.2)	132698 (15.5)
Unknown	2085 (4.9)	177 (3.2)	212 (4.1)	2010 (13.1)	2517 (9.0)	147554 (17.2)
Residential income quintile (*Q*)						
Q1 (lowest)	12391 (29.1)	512 (9.1)	1183 (23.0)	4091 (26.7)	8992 (32.2)	150194 (17.5)
Q2	11092 (26.1)	1119 (19.9)	976 (19.0)	3454 (22.6)	6770 (24.2)	159370 (18.6)
Q3	7328 (17.2)	1193 (21.2)	1021 (19.8)	3336 (21.8)	5445 (19.5)	177349 (20.7)
Q4	6236 (14.7)	1487 (26.5)	1021 (19.8)	2526 (16.5)	4183 (15.0)	192726 (22.4)
Q5 (highest)	3971 (9.3)	1148 (20.4)	852 (16.6)	1387 (9.1)	2342 (8.4)	166173 (19.4)
Unknown	1499 (3.5)	159 (2.8)	95 (1.8)	503 (3.3)	214 (0.8)	12842 (1.5)
Of the newborn infant						
Female sex	20519 (48.3)	2703 (48.1)	2444 (47.5)	7381 (48.3)	13491 (48.3)	418726 (48.8)
Twin births	901 (2.1)	156 (2.8)	105 (2.0)	286 (1.9)	554 (2.0)	29075 (3.4)

SD Standard deviation

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

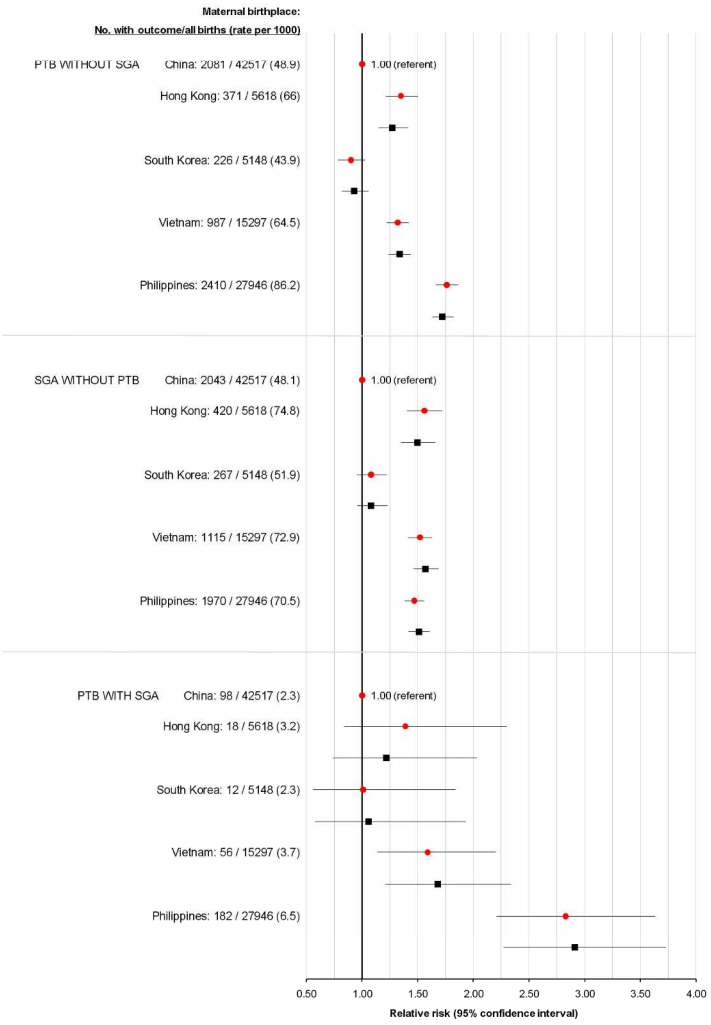

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots).
Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

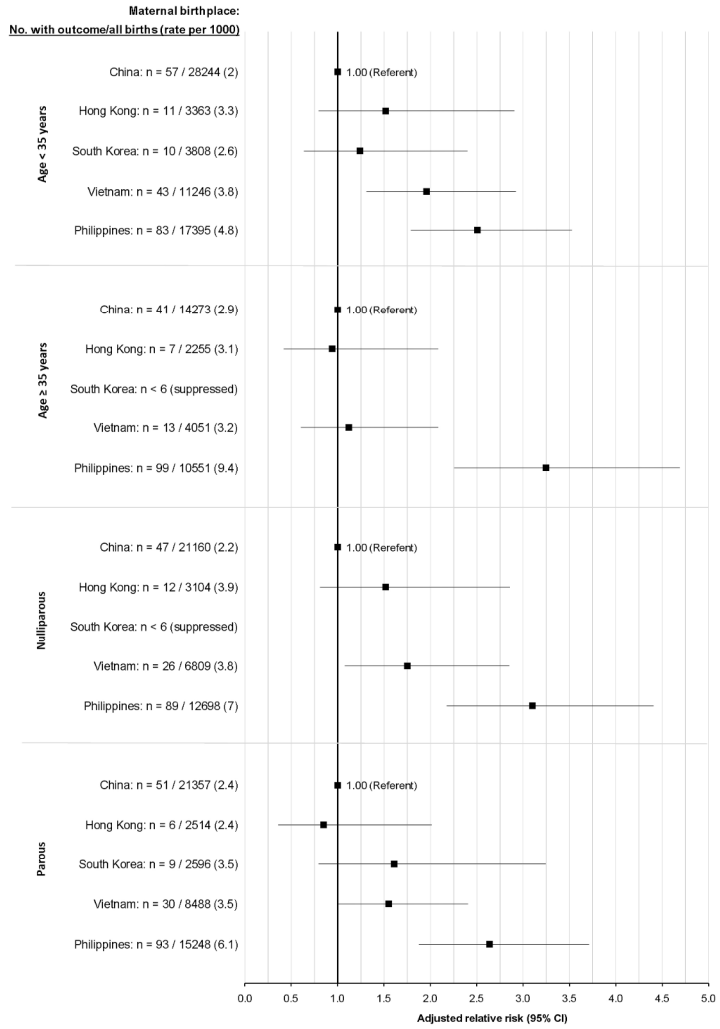

Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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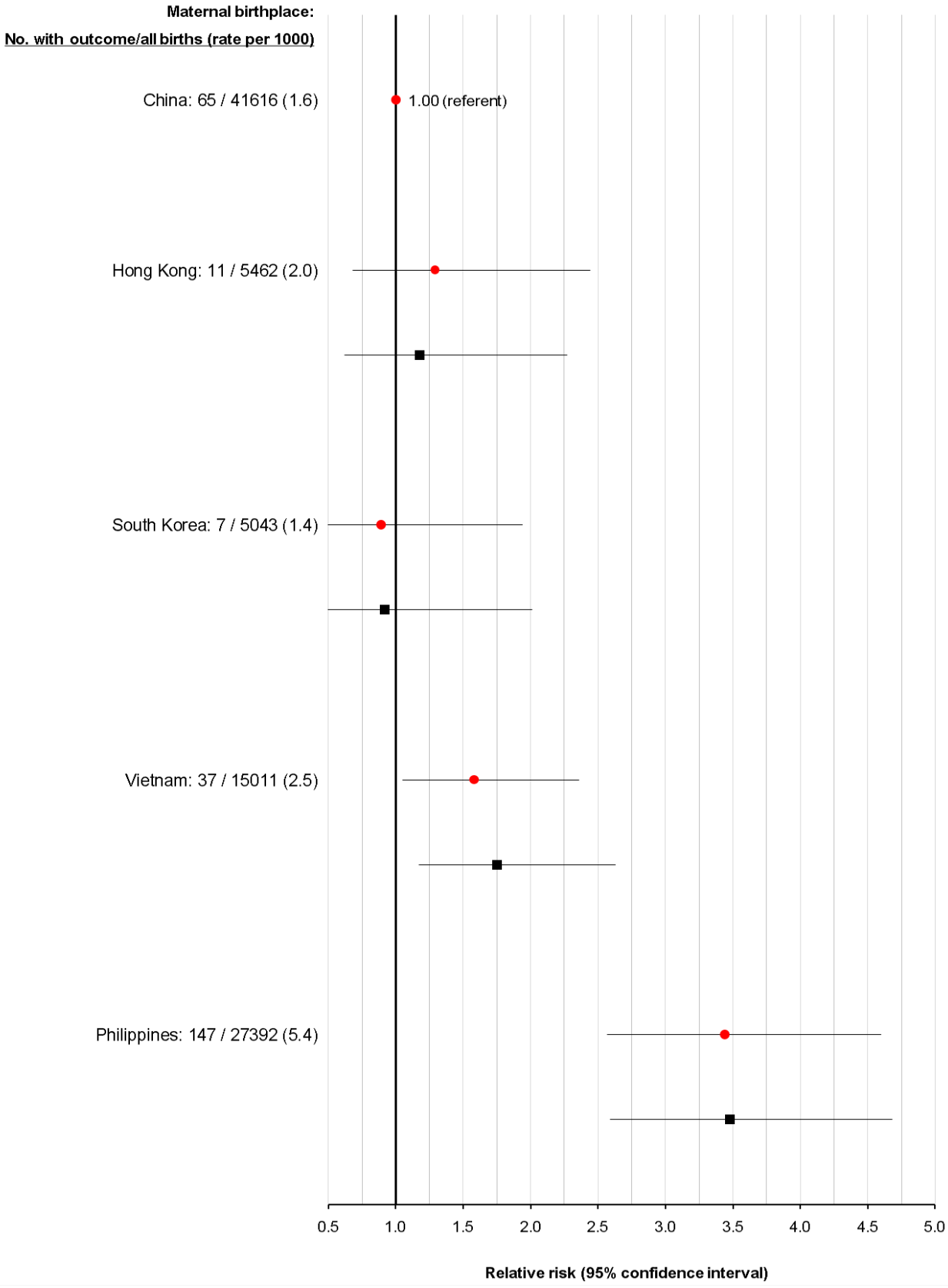
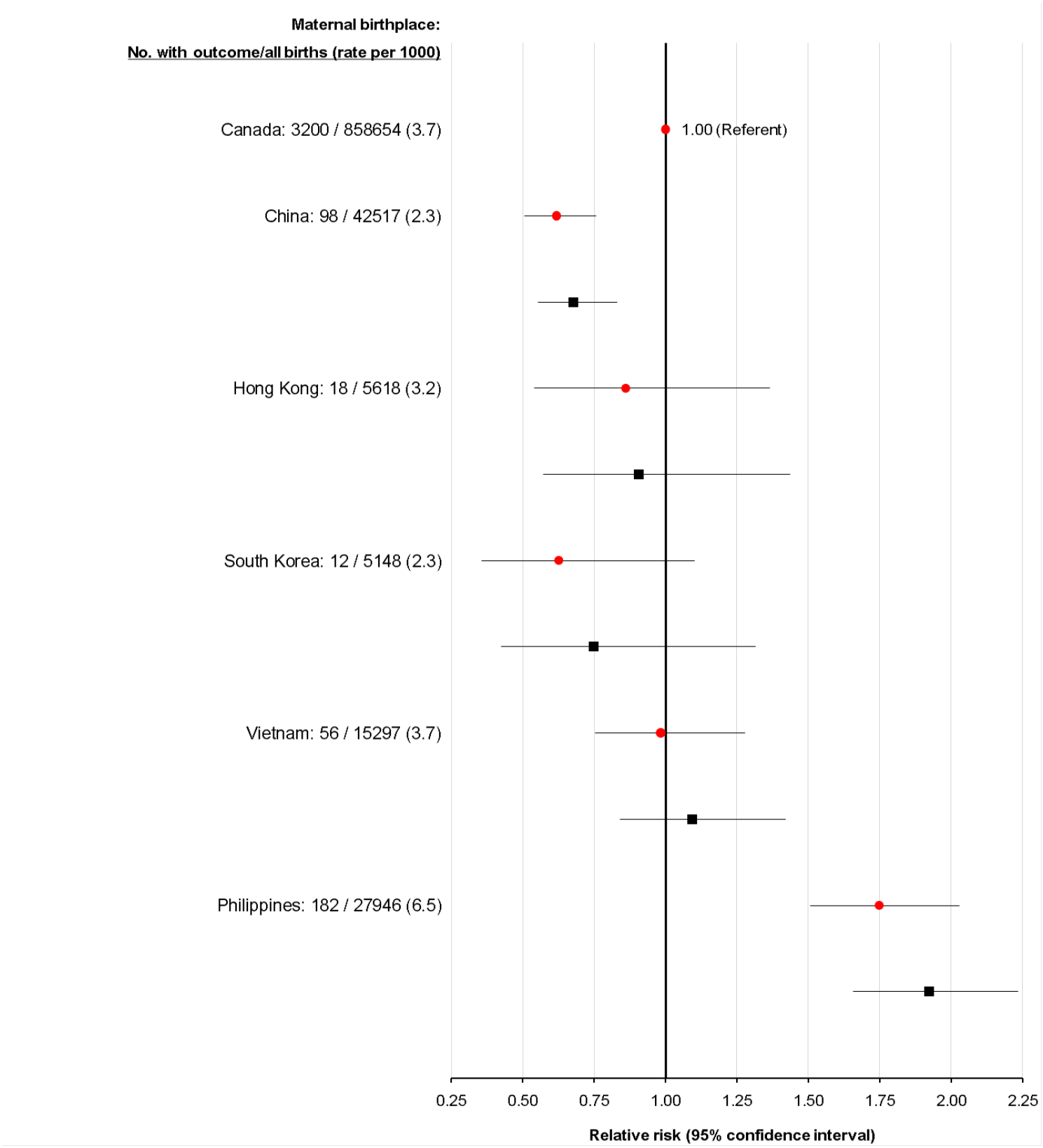
Supplementary file 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn singleton infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown) and infant sex.



Supplementary file 2. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn infants of East Asian-born mothers, each compared to Canadian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.



BMJ Open

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Concomitant preterm birth and severe small-for-gestational age birthweight among infants of immigrant mothers in Ontario originating from the Philippines and East Asia: a population-based study

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Abstract

Objectives: Women from the Philippines form one of the largest immigrant groups to North America. Their newborns experience higher rates of preterm birth (PTB), and separately, small-for-gestational age (SGA) birthweight, compared to other East Asians. It is not known if Filipina women are at elevated risk of concomitant PTB and severe SGA (PTB-SGA), a pathological state likely reflective of placental dysfunction and neonatal morbidity.

Methods: We conducted a population-based study of all singleton or twin livebirths in Ontario, from 2002 to 2011, among immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) and China (N = 42,517). We used modified Poisson regression to generate relative risks (RR) of PTB-SGA, defined as a birth < 37 weeks' gestation and a birthweight < 5th percentile. RRs were adjusted for maternal age, parity, marital status, income quintile, infant sex and twin births.

Results: Relative to mothers from China (2.3 per 1000), the rate of PTB-SGA was significantly higher among infants of mothers from the Philippines (6.5 per 1000; RR 2.91, 95% CI 2.27-3.73), and those from Vietnam (3.7 per 1000; RR 1.68, 95% CI 1.21-2.34). The RR of PTB-SGA was not higher for infants of mothers from Hong Kong or South Korea.

Interpretation: Among infants born to immigrant women from five East Asian birthplaces, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.

Keywords: Preterm birth; small for gestational age birthweight; ethnicity; race; immigrant; East Asia; Philippines; Filipina; Viet Nam.

Article summary: Strengths and limitations of this study

- We conducted a population-based study of all livebirths in Ontario, capturing the entire population of immigrants to Ontario who have birth between 2002 and 2011.
- We accounted for some risk factors for preterm birth (PTB) and small-for-gestational age birthweight (SGA), such as maternal age, infant sex, parity, income level and marital status.
- We lacked data on skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth.
- We also did not possess information on parental height or weight – which may influence newborn weight.
- We excluded stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA.

Background

A pregnancy resulting in a preterm birth (PTB) and concomitant small for gestational age birthweight (SGA) – "PTB-SGA" – is thought to be most pathological, in terms of both being due to placental dysfunction[1 2] and their adverse sequelae for the newborn infant[3 4]. Relative to infants born either PTB alone or SGA alone, those affected by PTB-SGA are 15 times more likely to die in the first month of life[3].

PTB[5] and SGA[6] are each more frequent in women from the Philippines. Chronic hypertension[7] and preterm onset of preeclampsia[8] are each risk factors for provider-initiated ("iatrogenic") PTB and SGA, and they are significantly more likely to present in Filipina women than Caucasian or other East Asian women. What remains unknown is whether the risk of PTB-SGA is higher among Filipina women than their counterparts from other East Asian regions.

Herein, we performed a study in Ontario, Canada, where foreign-born individuals comprise 20% of the population and nearly 35% of all births, the highest proportion of G8 countries.[9] We compared the risk of PTB-SGA among five East Asian groups, using a < 5th percentile cut-off to define severe SGA, which is more predictive of adverse perinatal outcomes than a < 10th percentile cut-off[10].

Methods

Study sample

This population-based study comprised all live singletons and twin births in Ontario between 2002 and 2011. Data were retrieved from livebirth records provided by Vital Statistics. We excluded stillbirths, as information on parental place of birth is missing for 12% of records[11]. As all records were de-identified, a given woman may have contributed more than one birth during the study period, but we adjusted for parity, as described below. All pregnancy and newborn care is universally covered under Ontario's Health Insurance Plan. Approximately 95% of Ontarian women undergo prenatal ultrasonography before 20 weeks gestation, enhancing accuracy of gestational age determined at birth.[12]

Exposures and outcomes

The main exposure was maternal place of birth, which was self-reported on the infant's birth record. Each newborn was then assigned to one of five maternal East Asian birthplaces: (1) China (the referent), (2) Hong Kong, (3) South Korea, (4) Vietnam, and (5) the Philippines. Women from China were chosen as the reference group as they are the largest East Asian immigrant group in Ontario[9], and are have relatively lower rates of PTB and SGA[5 6]. The main study outcome was PTB-SGA, defined as PTB < 37 weeks and severe SGA < 5th percentile[10]. The birthweight percentile curves used herein were those for all livebirths in Ontario, and were not otherwise customized by maternal ethnicity or other factors (6,11). Reasons for the latter were that we restricted our cohort solely to births of East Asian mothers, and that defining severe SGA at < 5th percentile is a cut-off that reflects pathological intrauterine growth restriction (10). Secondary outcomes were PTB without severe SGA, and severe SGA without PTB.

Data analysis

We used modified Poisson regression models to estimate relative risks (RR) and 95% confidence intervals (CI) for each study outcome in association with maternal place of birth. RR were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown)[13], infant sex, and twin births. The "unknown" categories of marital status and residential income quintile were included in the multivariable models. However, for maternal age and parity, we excluded those pregnancies with "unknown" status, given the rarity of this situation and the need to allow model convergence, accordingly.

For the main outcome of PTB-SGA, we additionally performed stratified analyses to examine potential effect measure modification by parity (nulliparous vs. parous) and by maternal age (< 35 years vs. ≥ 35 years).

As the study focus was to compare immigrants from different East Asian birthplaces, Canadian-born mothers were not included in main regression models. However, for comparative purposes, we described the characteristics of Canadian-born mothers and their

infants, and ran an additional analysis of the main model of PTB-SGA with Canadian-born mothers as the referent.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary NC). Ethics approval was provided by the Research Ethics Board of St. Michael's Hospital, Toronto, Ontario.

Results

Between 2002 and 2011, there were 956,994 liveborn singleton or twin births in Ontario to mothers born in Canada, China, Hong Kong, South Korea, Vietnam or the Philippines. We excluded 893 infants (0.09%) whose gestational age was < 24 or > 42 weeks, and 487 infants (0.05%) whose gestational age at birth was unknown. We further excluded infants whose birthweight was unknown (n = 31) or < 500 g (n = 55), whose sex was unknown (n = 1), or in which maternal age (n = 108) or parity (n = 239) were unknown.

The final cohort comprised 42,517 births to mothers from China, 5,618 from Hong Kong, 5,148 from South Korea, 15,297 from Vietnam, and 27,946 from the Philippines. The remainder were newborns of mothers from Canada (Table 1). In general, mothers from East Asia tended to be older than Canadian-born women, but of similar parity. Filipina-born mothers were similar in age, marital status and income to Chinese-born mothers (Table 1).

Compared to mothers from China, the outcomes of PTB without severe SGA, and severe SGA without PTB, were significantly more prevalent among newborns of mothers from Hong Kong, Vietnam and the Philippines, but not South Korea (Figure 1). The more severe outcome of PTB-SGA was significantly more common among newborns of mothers from Vietnam (3.7 per 1000; aRR 1.68 95% CI 1.21 to 2.34), compared to those of mothers from China (2.3 per 1000) (Figure 1). For newborns of Filipina women, the rate (6.5 per 1000) and aRR (2.91, 95% CI 2.27 to 3.73) were even higher (Figure 1).

In our stratified analyses, the risk of PTB-SGA was somewhat more pronounced among Filipina women aged ≥ 35 years or older (Figure 2, upper) and those who were nulliparous (Figure 2, lower).

Limiting the dataset to singleton births did not appreciably change the RR of PTB-SGA, even heightening the RR among Filipina women (Supplementary file 1).

Re-running the main model of PTB-SGA, with Canadian-born mothers as the referent, showed that only the offspring of Filipina mothers were at higher risk of PTB-SGA (Supplementary file 2).

Interpretation

Newborns of mothers from the Philippines were most vulnerable to PTB-SGA, especially among women ≥ 35 years, who comprised 37% of all Filipina mothers, and in whom the rate of PTB-SGA was nearly 1%.

Strengths and limitations

We evaluated nearly 100,000 livebirths among women born in five East Asian regions, which are major sources of immigrants to Ontario, in a setting of universal healthcare. Infants of Chinese-born women provided an ideal reference group, as China is the largest source of immigrants from East Asia to Ontario, and they have a low incidence of adverse neonatal and maternal outcomes[5, 14]. The < 5th percentile cut-off used to define severe SGA reflects a degree of smallness that is more likely to be pathological, rather than constitutional[10]. Still, the outcome of PTB-SGA was not rare – occurring in 6.5 per 1000 infants of Filipina mothers. Through our analysis, we were able to account for some previously noted risk factors for PTB or SGA, such as maternal age, infant sex, parity, income level and marital status.

A limitation of this study was the exclusion of stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA[15, 16]. We lacked data on factors associated with the so-called "healthy immigrant effect"[17], such as skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight – which may influence newborn weight – or conditions such as maternal chronic hypertension and diabetes mellitus, or maternal behavioural risk factors (e.g. smoking, drug or substance use). However, Filipina women of reproductive age living in Canada have a rate of smoking under 6.0%, comparable to that of their East Asian counterparts[7], and the corresponding rate in pregnancy would be expected to be even lower. The body mass index (BMI) of Filipina women of reproductive age tends to be higher than that of other East Asians[7]. It is unlikely that access to prenatal care

explains the current findings, as 88% of Filipina women and 85% of other East Asian women in Canada have a regular medical doctor[7]. Finally, we could not identify the specific causes of PTB-SGA from the dataset used herein, which is certainly worthy of a focused study focused on differentiating spontaneous vs. provider-initiated PTB.

Implications

In 2011, 13.1% of all newcomers to Canada were from the Philippines[9]. Women from the Philippines were at exceptionally high risk of PTB-SGA, peaking at nearly 1% among those aged 35 years and older, and who represent one-third of all Filipina women giving birth in Ontario. From a public health perspective, there is value in reducing the incidence of PTB-SGA, and such a strategy might start with Filipina women. For healthcare providers – including family doctors, obstetricians, or midwives – the priority would be to address risk factors in these women. This can be done at several time points – before becoming pregnant, during pregnancy, and at the time of delivery. Before pregnancy, providers can counsel Filipina women, especially those women older than 35 years of age, on the possibility of adverse perinatal outcomes. During the pregnancy, risk factors can be identified and managed. Chronic hypertension is one important risk factor for both PTB[18] and SGA[19 20], and also for preeclampsia[21], which can give rise to PTB-SGA[22]. Chronic hypertension is highly prevalent among Filipina women in Ontario[7]; therefore, efforts to regulate blood pressure and prevent preeclampsia may help reduce the risk of SGA-PTB among Filipina women, and also those from Vietnam. Such interventions include aspirin[23-25] and early pregnancy blood pressure assessments[26]. By the third trimester of pregnancy, periodic sonographic assessment of fetal growth and well-being should be considered, as there is evidence that this helps the clinician identify SGA infants and balance the risks of prematurity against a worsening intrauterine environment[27 28].

Conclusions

What differentiates a Filipina woman from another East Asian woman is her heightened risk of having a liveborn affected by PTB-SGA, a severe pathological state. For Filipina immigrant women, appropriate cautionary measures should be taken to ensure that mother and baby

remain healthy throughout the pregnancy and delivery. Future research should aim to identify specific, and ideally modifiable, traits of Filipina women that increase the risk of PTB-SGA during pregnancy. Specifically, it would be worthwhile to evaluate whether the rates of smoking, high BMI, or other socioeconomic indicators differ between pregnant Filipina women and those women from other East Asian birthplaces.

Authors contributions: Bartsch contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision and approval of final version. Ray contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Park contributed to the analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Jairam contributed to the interpretation of the data and approval of final version.

Data sharing statement: No additional data available.

Details of ethics approval: Ethics approval was granted by the Research Ethics Board of St. Michael's Hospital in Toronto, Ontario, Canada.

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Competing interests: None.

FIGURE LEGENDS

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Table 1. Characteristics of live singleton and twin births and their mothers, who delivered at 24 to 42 weeks' gestation in Ontario, 2002 to 2011. All data are presented as a number (%) unless otherwise indicated.

	East Asian maternal place of birth					
Characteristic	**China (n = 42,517)**	**Hong Kong (n = 5618)**	**South Korea (n = 5148)**	**Vietnam (n = 15,297)**	**Philippines (n = 27,946)**	**Canadian maternal country of birth (n = 858,654)**
Of the mother						
Mean (*SD*) age, years	32.3 (4.7)	33.5 (4.3)	32.1 (3.9)	31.4 (4.8)	32.6 (5.4)	29.5 (5.5)
Age category, years						
< 20	81 (0.2)	17 (0.3)	7 (0.1)	68 (0.4)	353 (1.3)	38920 (4.5)
20-34	28163 (66.2)	3346 (59.6)	3801 (73.8)	11178 (73.1)	17042 (61.0)	662500 (77.2)
≥ 35	14273 (33.6)	2255 (40.1)	1340 (26.0)	4051 (26.5)	10551 (37.8)	157234 (18.3)
Parity	1 (0-1)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
0	21160 (49.8)	3104 (55.3)	2552 (49.6)	6809 (44.5)	12698 (45.4)	389635 (45.4)
1	17836 (42.0)	2023 (36.0)	1990 (38.7)	5984 (39.1)	9905 (35.4)	304847 (35.5)
2	3012 (7.1)	413 (7.4)	505 (9.8)	1896 (12.4)	3921 (14.0)	111814 (13.0)
3	410 (1.0)	59 (1.1)	78 (1.5)	470 (3.1)	1047 (3.7)	33591 (3.9)
≥ 4	99 (0.2)	19 (0.3)	23 (0.4)	138 (0.9)	375 (1.3)	18767 (2.2)
Marital status						
Married/common-law	36668 (86.2)	5205 (92.6)	4829 (93.8)	10899 (71.2)	22304 (79.8)	578402 (67.4)
Unmarried	3764 (8.9)	236 (4.2)	107 (2.1)	2388 (15.6)	3125 (11.2)	132698 (15.5)
Unknown	2085 (4.9)	177 (3.2)	212 (4.1)	2010 (13.1)	2517 (9.0)	147554 (17.2)
Residential income quintile (*Q*)						
Q1 (lowest)	12391 (29.1)	512 (9.1)	1183 (23.0)	4091 (26.7)	8992 (32.2)	150194 (17.5)
Q2	11092 (26.1)	1119 (19.9)	976 (19.0)	3454 (22.6)	6770 (24.2)	159370 (18.6)
Q3	7328 (17.2)	1193 (21.2)	1021 (19.8)	3336 (21.8)	5445 (19.5)	177349 (20.7)
Q4	6236 (14.7)	1487 (26.5)	1021 (19.8)	2526 (16.5)	4183 (15.0)	192726 (22.4)
Q5 (highest)	3971 (9.3)	1148 (20.4)	852 (16.6)	1387 (9.1)	2342 (8.4)	166173 (19.4)
Unknown	1499 (3.5)	159 (2.8)	95 (1.8)	503 (3.3)	214 (0.8)	12842 (1.5)
Of the newborn infant						
Female sex	20519 (48.3)	2703 (48.1)	2444 (47.5)	7381 (48.3)	13491 (48.3)	418726 (48.8)
Twin births	901 (2.1)	156 (2.8)	105 (2.0)	286 (1.9)	554 (2.0)	29075 (3.4)

SD Standard deviation

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

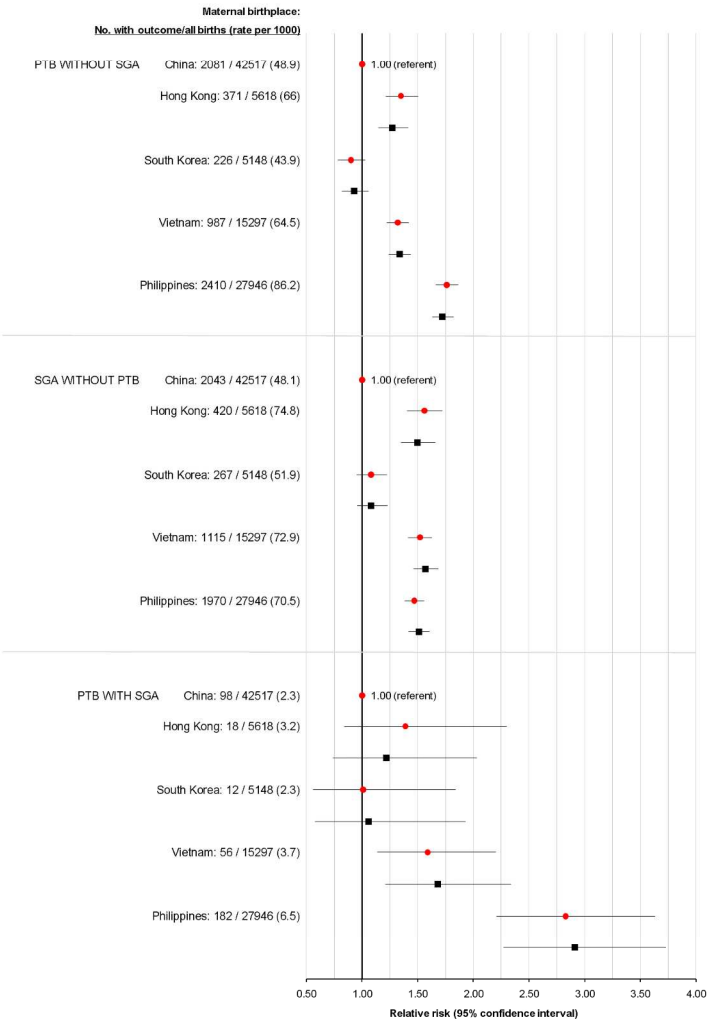

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots).
Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

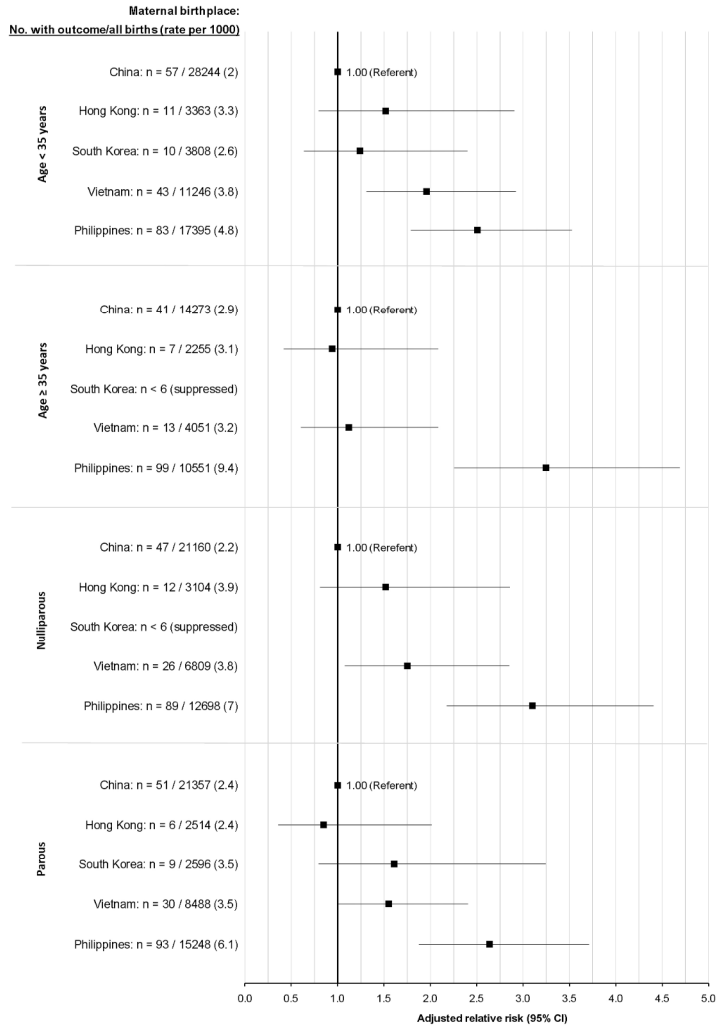
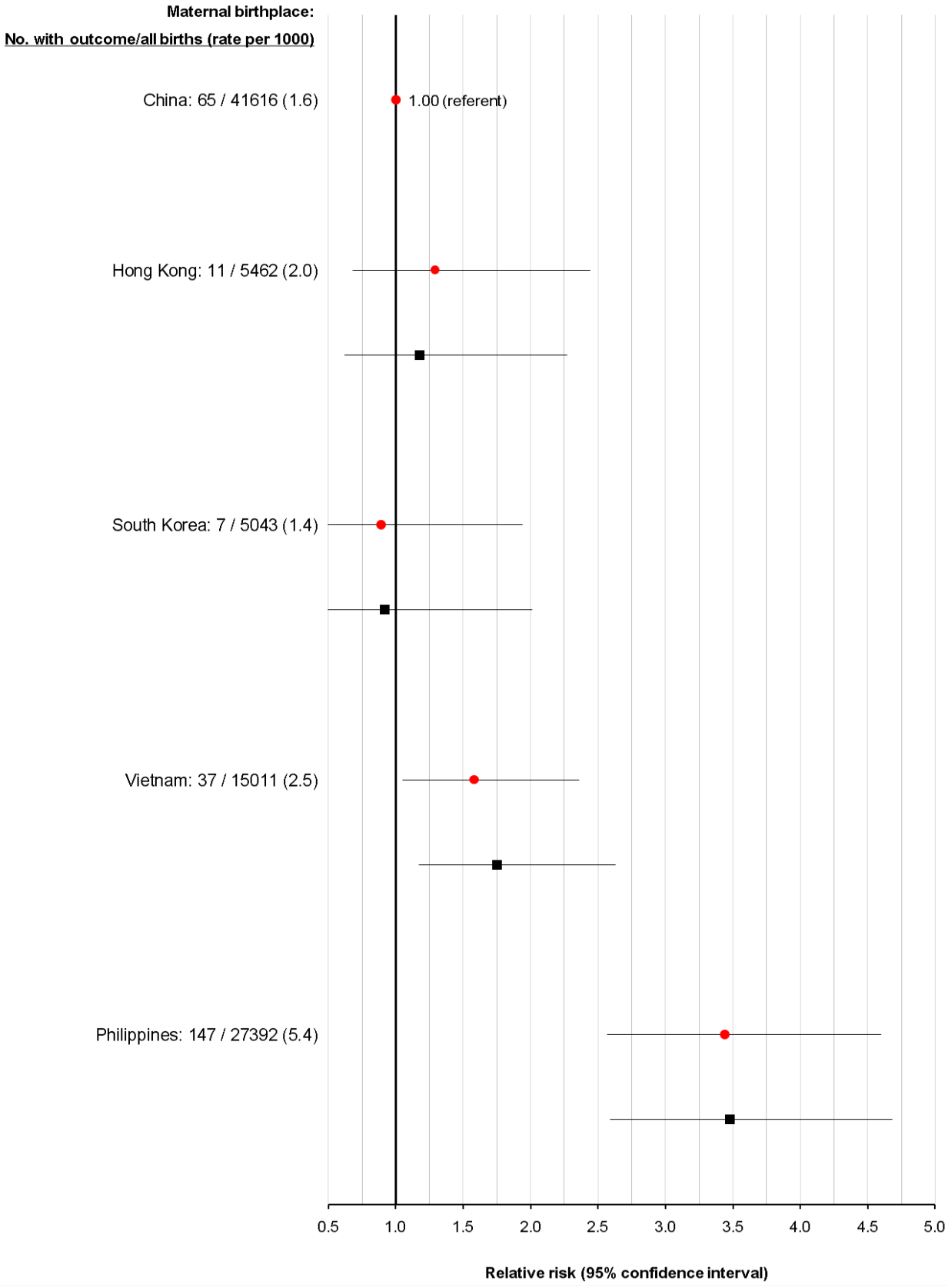


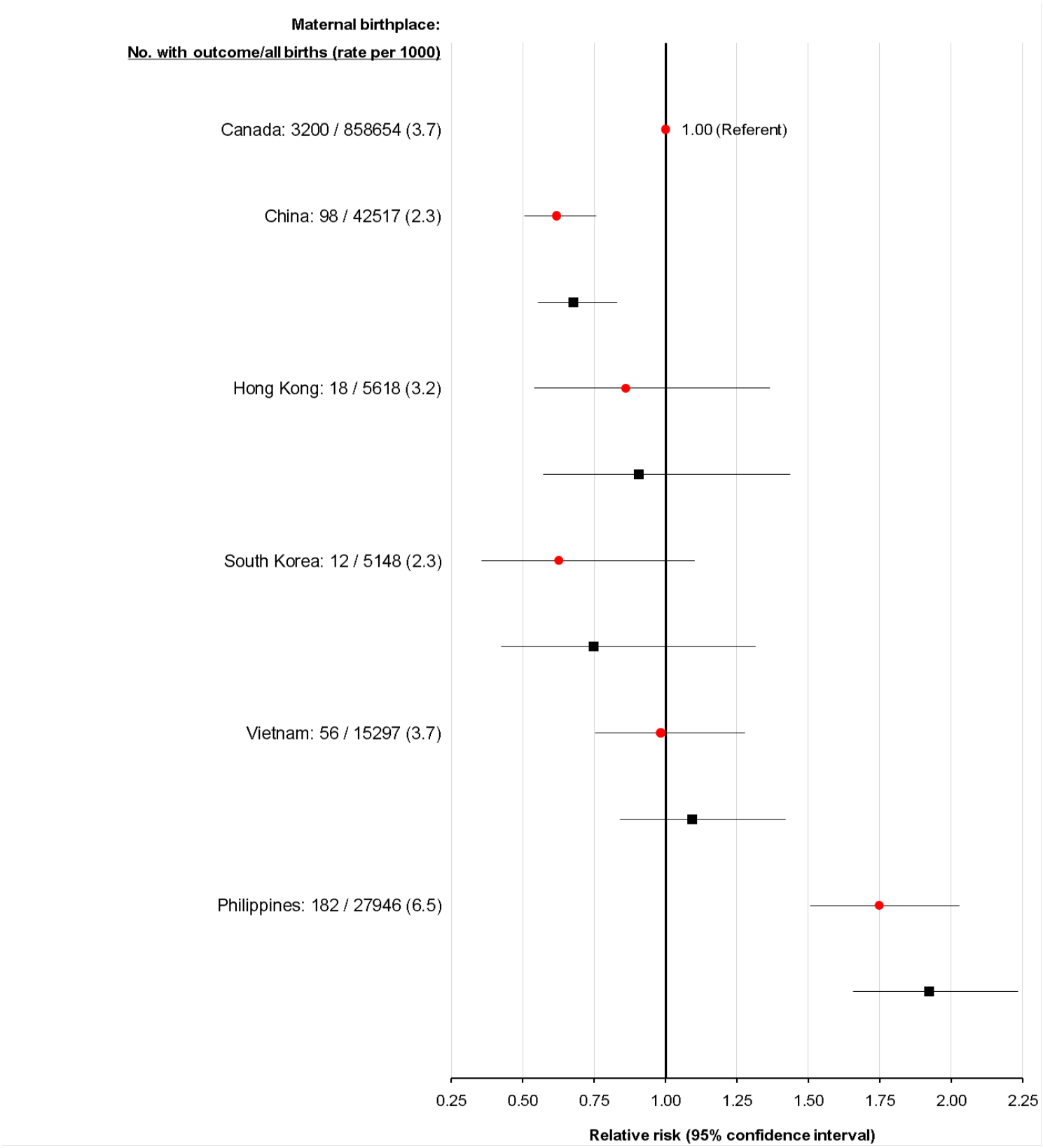
Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

279x361mm (300 x 300 DPI)

Supplementary file 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn singleton infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown) and infant sex.



Supplementary file 2. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn infants of East Asian-born mothers, each compared to Canadian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.



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Concomitant preterm birth and severe small-for-gestational age birthweight among infants of immigrant mothers in Ontario originating from the Philippines and East Asia: a population-based study

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Concomitant preterm birth and severe small-for-gestational age birthweight among infants of immigrant mothers in Ontario originating from the Philippines and East Asia: a population-based study

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Abstract

Objectives: Women from the Philippines form one of the largest immigrant groups to North America. Their newborns experience higher rates of preterm birth (PTB), and separately, small-for-gestational age (SGA) birthweight, compared to other East Asians. It is not known if Filipina women are at elevated risk of concomitant PTB and severe SGA (PTB-SGA), a pathological state likely reflective of placental dysfunction and neonatal morbidity.

Methods: We conducted a population-based study of all singleton or twin livebirths in Ontario, from 2002 to 2011, among immigrant mothers from the Philippines (N = 27,946), Vietnam (N = 15,297), Hong Kong (N = 5618), South Korea (N = 5148) and China (N = 42,517). We used modified Poisson regression to generate relative risks (RR) of PTB-SGA, defined as a birth < 37 weeks' gestation and a birthweight < 5th percentile. RRs were adjusted for maternal age, parity, marital status, income quintile, infant sex and twin births.

Results: Relative to mothers from China (2.3 per 1000), the rate of PTB-SGA was significantly higher among infants of mothers from the Philippines (6.5 per 1000; RR 2.91, 95% CI 2.27-3.73), and those from Vietnam (3.7 per 1000; RR 1.68, 95% CI 1.21-2.34). The RR of PTB-SGA was not higher for infants of mothers from Hong Kong or South Korea.

Interpretation: Among infants born to immigrant women from five East Asian birthplaces, the risk of PTB-SGA was highest among those from the Philippines. These women and their fetuses may require additional monitoring and interventions.

Keywords: Preterm birth; small for gestational age birthweight; ethnicity; race; immigrant; East Asia; Philippines; Filipina; Viet Nam.

Article summary: Strengths and limitations of this study

- We conducted a population-based study of all livebirths in Ontario, capturing the entire population of immigrants to Ontario who have birth between 2002 and 2011.
- We accounted for some risk factors for preterm birth (PTB) and small-for-gestational age birthweight (SGA), such as maternal age, infant sex, parity, income level and marital status.
- We lacked data on skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth.
- We also did not possess information on parental height or weight – which may influence newborn weight.
- We excluded stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA.

Background

A pregnancy resulting in a preterm birth (PTB) and concomitant small for gestational age birthweight (SGA) – "PTB-SGA" – is thought to be most pathological, in terms of both being due to placental dysfunction[1 2] and their adverse sequelae for the newborn infant[3 4]. Relative to infants born either PTB alone or SGA alone, those affected by PTB-SGA are 15 times more likely to die in the first month of life[3].

PTB[5] and SGA[6] are each more frequent in women from the Philippines. Chronic hypertension[7] and preterm onset of preeclampsia[8] are each risk factors for provider-initiated ("iatrogenic") PTB and SGA, and they are significantly more likely to present in Filipina women than Caucasian or other East Asian women. What remains unknown is whether the risk of PTB-SGA is higher among Filipina women than their counterparts from other East Asian regions.

Herein, we performed a study in Ontario, Canada, where foreign-born individuals comprise 20% of the population and nearly 35% of all births, the highest proportion of G8 countries.[9] We compared the risk of PTB-SGA among five East Asian groups, using a < 5th percentile cut-off to define severe SGA, which is more predictive of adverse perinatal outcomes than a < 10th percentile cut-off[10].

Methods

Study sample

This population-based study comprised all live singletons and twin births in Ontario between 2002 and 2011. Data were retrieved from livebirth records provided by Vital Statistics. We excluded stillbirths, as information on parental place of birth is missing for 12% of records[11]. As all records were de-identified, a given woman may have contributed more than one birth during the study period, but we adjusted for parity, as described below. All pregnancy and newborn care is universally covered under Ontario's Health Insurance Plan. Approximately 95% of Ontarian women undergo prenatal ultrasonography before 20 weeks gestation, enhancing accuracy of gestational age determined at birth.[12]

Exposures and outcomes

The main exposure was maternal place of birth, which was self-reported on the infant's birth record. Each newborn was then assigned to one of five maternal East Asian birthplaces: (1) China (the referent), (2) Hong Kong, (3) South Korea, (4) Vietnam, and (5) the Philippines. Women from China were chosen as the reference group as they are the largest East Asian immigrant group in Ontario[9], and are have relatively lower rates of PTB and SGA[5 6]. The main study outcome was PTB-SGA, defined as PTB < 37 weeks and severe SGA < 5th percentile[10]. The birthweight percentile curves used herein were those for all livebirths in Ontario, and were not otherwise customized by maternal ethnicity or other factors (6,11). Reasons for the latter were that we restricted our cohort solely to births of East Asian mothers, and that defining severe SGA at < 5th percentile is a cut-off that reflects pathological intrauterine growth restriction (10). Secondary outcomes were PTB without severe SGA, and severe SGA without PTB.

Data analysis

We used modified Poisson regression models to estimate relative risks (RR) and 95% confidence intervals (CI) for each study outcome in association with maternal place of birth. RR were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown)[13], infant sex, and twin births. The "unknown" categories of marital status and residential income quintile were included in the multivariable models. However, for maternal age and parity, we excluded those pregnancies with "unknown" status, given the rarity of this situation and the need to allow model convergence, accordingly.

For the main outcome of PTB-SGA, we additionally performed stratified analyses to examine potential effect measure modification by parity (nulliparous vs. parous) and by maternal age (< 35 years vs. ≥ 35 years).

As the study focus was to compare immigrants from different East Asian birthplaces, Canadian-born mothers were not included in main regression models. However, for comparative purposes, we described the characteristics of Canadian-born mothers and their

infants, and ran an additional analysis of the main model of PTB-SGA with Canadian-born mothers as the referent.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary NC). Ethics approval was provided by the Research Ethics Board of St. Michael's Hospital, Toronto, Ontario.

Results

Between 2002 and 2011, there were 956,994 liveborn singleton or twin births in Ontario to mothers born in Canada, China, Hong Kong, South Korea, Vietnam or the Philippines. We excluded 893 infants (0.09%) whose gestational age was < 24 or > 42 weeks, and 487 infants (0.05%) whose gestational age at birth was unknown. We further excluded infants whose birthweight was unknown (n = 31) or < 500 g (n = 55), whose sex was unknown (n = 1), or in which maternal age (n = 108) or parity (n = 239) were unknown.

The final cohort comprised 42,517 births to mothers from China, 5,618 from Hong Kong, 5,148 from South Korea, 15,297 from Vietnam, and 27,946 from the Philippines. The remainder were newborns of mothers from Canada (Table 1). In general, mothers from East Asia tended to be older than Canadian-born women, but of similar parity. Filipina-born mothers were similar in age, marital status and income to Chinese-born mothers (Table 1).

Compared to mothers from China, the outcomes of PTB without severe SGA, and severe SGA without PTB, were significantly more prevalent among newborns of mothers from Hong Kong, Vietnam and the Philippines, but not South Korea (Figure 1). The more severe outcome of PTB-SGA was significantly more common among newborns of mothers from Vietnam (3.7 per 1000; aRR 1.68 95% CI 1.21 to 2.34), compared to those of mothers from China (2.3 per 1000) (Figure 1). For newborns of Filipina women, the rate (6.5 per 1000) and aRR (2.91, 95% CI 2.27 to 3.73) were even higher (Figure 1).

In our stratified analyses, the risk of PTB-SGA was somewhat more pronounced among Filipina women aged ≥ 35 years or older (Figure 2, upper) and those who were nulliparous (Figure 2, lower).

Limiting the dataset to singleton births did not appreciably change the RR of PTB-SGA, even heightening the RR among Filipina women (Supplementary file 1).

Re-running the main model of PTB-SGA, with Canadian-born mothers as the referent, showed that only the offspring of Filipina mothers were at higher risk of PTB-SGA (Supplementary file 2).

Discussion

Newborns of mothers from the Philippines were most vulnerable to PTB-SGA, especially among women ≥ 35 years, who comprised 37% of all Filipina mothers, and in whom the rate of PTB-SGA was nearly 1%.

Strengths and weaknesses

We evaluated nearly 100,000 livebirths among women born in five East Asian regions, which are major sources of immigrants to Ontario, in a setting of universal healthcare. Infants of Chinese-born women provided an ideal reference group, as China is the largest source of immigrants from East Asia to Ontario, and they have a low incidence of adverse neonatal and maternal outcomes[5, 14]. The < 5th percentile cut-off used to define severe SGA reflects a degree of smallness that is more likely to be pathological, rather than constitutional[10]. Still, the outcome of PTB-SGA was not rare – occurring in 6.5 per 1000 infants of Filipina mothers. Through our analysis, we were able to account for some previously noted risk factors for PTB or SGA, such as maternal age, infant sex, parity, income level and marital status.

A limitation of this study was the exclusion of stillbirths, who are potentially the most pathological group of fetuses, and who are at risk of PTB-SGA[15, 16]. We lacked data on factors associated with the so-called "healthy immigrant effect"[17], such as skillset and level of education at immigration, immigration class, and duration of residence at the time of the index birth. We also did not possess information on parental height or weight – which may influence newborn weight – or conditions such as maternal chronic hypertension and diabetes mellitus, or maternal behavioural risk factors (e.g. smoking, drug or substance use). However, Filipina women of reproductive age living in Canada have a rate of smoking under 6.0%, comparable to that of their East Asian counterparts[7], and the corresponding rate in pregnancy would be expected to be even lower. The body mass index (BMI) of Filipina women of reproductive age tends to be higher than that of other East Asians[7]. It is unlikely that access to prenatal care

explains the current findings, as 88% of Filipina women and 85% of other East Asian women in Canada have a regular medical doctor[7]. Finally, we could not identify the specific causes of PTB-SGA from the dataset used herein, which is certainly worthy of a focused study focused on differentiating spontaneous vs. provider-initiated PTB. Thus, while our findings represent a large cohort of immigrants to Canada, they may not be generalizable to other countries with a large number of first- or second-generation Eaat Asian immigrants.

Meaning of the study for clinicians and policy makers

In 2011, 13.1% of all newcomers to Canada were from the Philippines[9]. Women from the Philippines were at exceptionally high risk of PTB-SGA, peaking at nearly 1% among those aged 35 years and older, and who represent one-third of all Filipina women giving birth in Ontario. From a public health perspective, there is value in reducing the incidence of PTB-SGA, and such a strategy might start with Filipina women. For healthcare providers – including family doctors, obstetricians, or midwives – the priority would be to address risk factors in these women. This can be done at several time points – before becoming pregnant, during pregnancy, and at the time of delivery. Before pregnancy, providers can counsel Filipina women, especially those women older than 35 years of age, on the possibility of adverse perinatal outcomes. During the pregnancy, risk factors can be identified and managed. Chronic hypertension is one important risk factor for both PTB[18] and SGA[19 20], and also for preeclampsia[21], which can give rise to PTB-SGA[22]. Chronic hypertension is highly prevalent among Filipina women in Ontario[7]; therefore, efforts to regulate blood pressure and prevent preeclampsia may help reduce the risk of SGA-PTB among Filipina women, and also those from Vietnam. Such interventions include aspirin[23-25] and early pregnancy blood pressure assessments[26]. By the third trimester of pregnancy, periodic sonographic assessment of fetal growth and well-being should be considered, as there is evidence that this helps the clinician identify SGA infants and balance the risks of prematurity against a worsening intrauterine environment[27 28].

Unanswered questions and future research

What differentiates a Filipina woman from another East Asian woman is her heightened risk of having a liveborn affected by PTB-SGA, a severe pathological state. For Filipina immigrant women, appropriate cautionary measures should be taken to ensure that mother and baby remain healthy throughout the pregnancy and delivery. Future research should aim to identify specific, and ideally modifiable, traits of Filipina women that increase the risk of PTB-SGA during pregnancy. Specifically, it would be worthwhile to evaluate whether the rates of smoking, high BMI, or other socioeconomic indicators differ between pregnant Filipina women and those women from other East Asian birthplaces.

Authors contributions: Bartsch contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision and approval of final version. Ray contributed to the study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Park contributed to the analysis and interpretation of the data, drafting of manuscript, manuscript revision, and approval of final version. Jairam contributed to the interpretation of the data and approval of final version.

Data sharing statement: No additional data available.

Details of ethics approval: Ethics approval was granted by the Research Ethics Board of St. Michael's Hospital in Toronto, Ontario, Canada.

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Competing interests: None.

FIGURE LEGENDS

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots). Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

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Table 1. Characteristics of live singleton and twin births and their mothers, who delivered at 24 to 42 weeks' gestation in Ontario, 2002 to 2011. All data are presented as a number (%) unless otherwise indicated.

	East Asian maternal place of birth					
Characteristic	**China (n = 42,517)**	**Hong Kong (n = 5618)**	**South Korea (n = 5148)**	**Vietnam (n = 15,297)**	**Philippines (n = 27,946)**	**Canadian maternal country of birth (n = 858,654)**
Of the mother						
Mean (*SD*) age, years	32.3 (4.7)	33.5 (4.3)	32.1 (3.9)	31.4 (4.8)	32.6 (5.4)	29.5 (5.5)
Age category, years						
< 20	81 (0.2)	17 (0.3)	7 (0.1)	68 (0.4)	353 (1.3)	38920 (4.5)
20-34	28163 (66.2)	3346 (59.6)	3801 (73.8)	11178 (73.1)	17042 (61.0)	662500 (77.2)
≥ 35	14273 (33.6)	2255 (40.1)	1340 (26.0)	4051 (26.5)	10551 (37.8)	157234 (18.3)
Parity	1 (0-1)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
0	21160 (49.8)	3104 (55.3)	2552 (49.6)	6809 (44.5)	12698 (45.4)	389635 (45.4)
1	17836 (42.0)	2023 (36.0)	1990 (38.7)	5984 (39.1)	9905 (35.4)	304847 (35.5)
2	3012 (7.1)	413 (7.4)	505 (9.8)	1896 (12.4)	3921 (14.0)	111814 (13.0)
3	410 (1.0)	59 (1.1)	78 (1.5)	470 (3.1)	1047 (3.7)	33591 (3.9)
≥ 4	99 (0.2)	19 (0.3)	23 (0.4)	138 (0.9)	375 (1.3)	18767 (2.2)
Marital status						
Married/common-law	36668 (86.2)	5205 (92.6)	4829 (93.8)	10899 (71.2)	22304 (79.8)	578402 (67.4)
Unmarried	3764 (8.9)	236 (4.2)	107 (2.1)	2388 (15.6)	3125 (11.2)	132698 (15.5)
Unknown	2085 (4.9)	177 (3.2)	212 (4.1)	2010 (13.1)	2517 (9.0)	147554 (17.2)
Residential income quintile (*Q*)						
Q1 (lowest)	12391 (29.1)	512 (9.1)	1183 (23.0)	4091 (26.7)	8992 (32.2)	150194 (17.5)
Q2	11092 (26.1)	1119 (19.9)	976 (19.0)	3454 (22.6)	6770 (24.2)	159370 (18.6)
Q3	7328 (17.2)	1193 (21.2)	1021 (19.8)	3336 (21.8)	5445 (19.5)	177349 (20.7)
Q4	6236 (14.7)	1487 (26.5)	1021 (19.8)	2526 (16.5)	4183 (15.0)	192726 (22.4)
Q5 (highest)	3971 (9.3)	1148 (20.4)	852 (16.6)	1387 (9.1)	2342 (8.4)	166173 (19.4)
Unknown	1499 (3.5)	159 (2.8)	95 (1.8)	503 (3.3)	214 (0.8)	12842 (1.5)
Of the newborn infant						
Female sex	20519 (48.3)	2703 (48.1)	2444 (47.5)	7381 (48.3)	13491 (48.3)	418726 (48.8)
Twin births	901 (2.1)	156 (2.8)	105 (2.0)	286 (1.9)	554 (2.0)	29075 (3.4)

SD Standard deviation

Figure 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth (PTB) without severe small for gestational age (SGA [upper]), SGA without PTB (middle), and PTB with SGA (PTB-SGA [lower]) for liveborn infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.

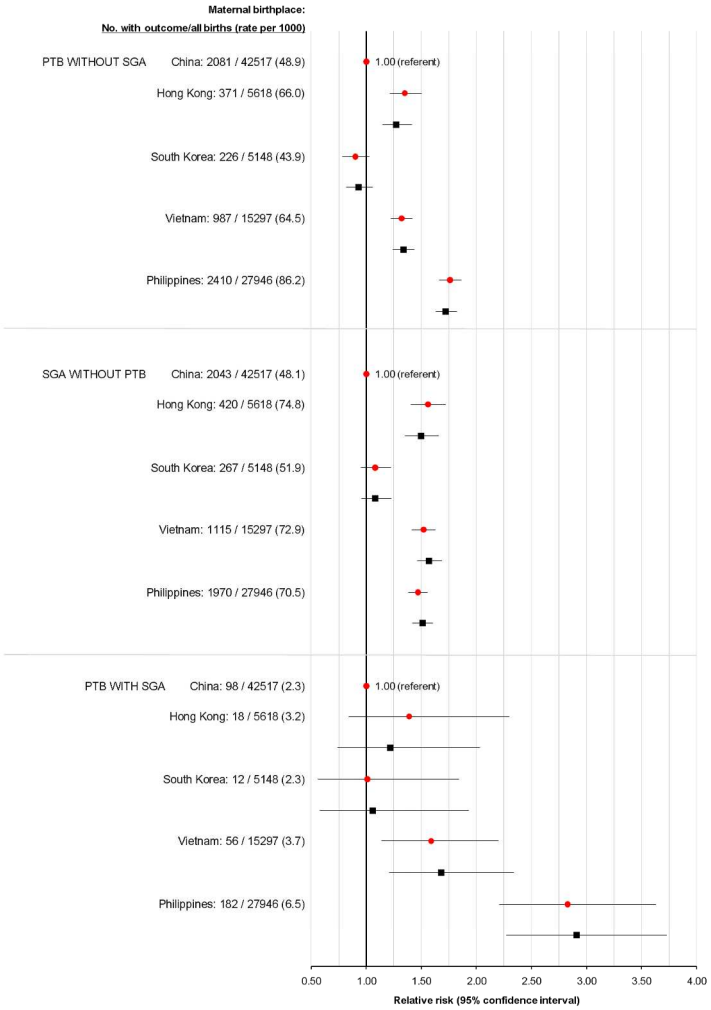

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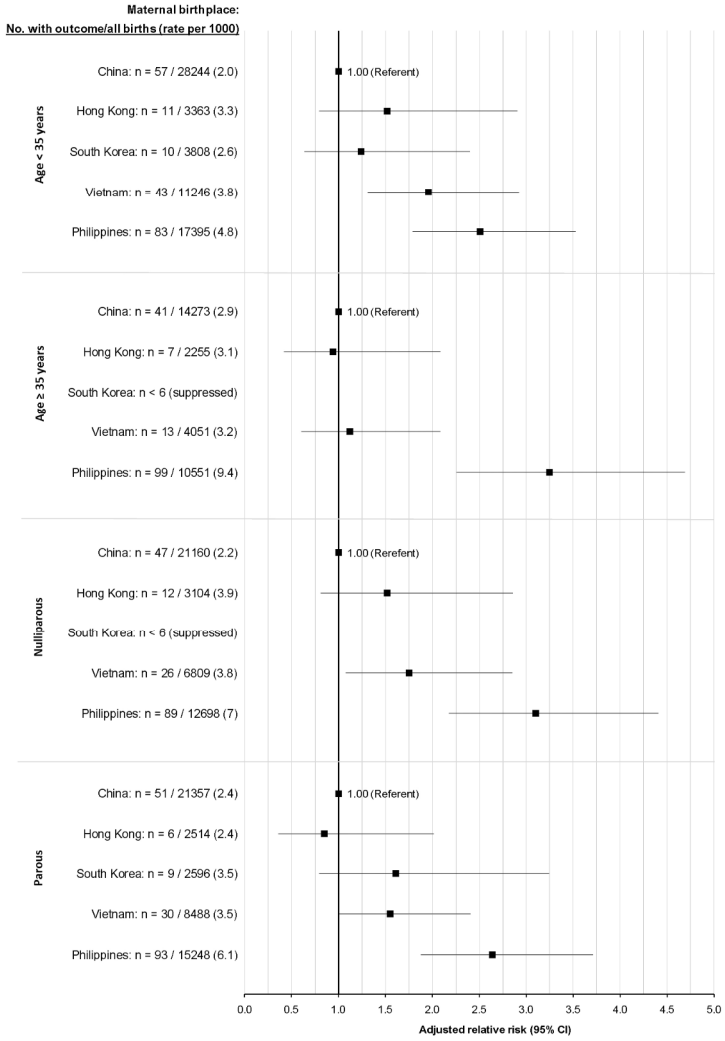
Figure 2. Rate and adjusted relative risk of preterm birth (PTB) with severe small for gestational age (SGA) – PTB-SGA – for liveborn infants of East Asian-born mothers, stratified by age (upper two plots) and parity (lower two plots).
Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.



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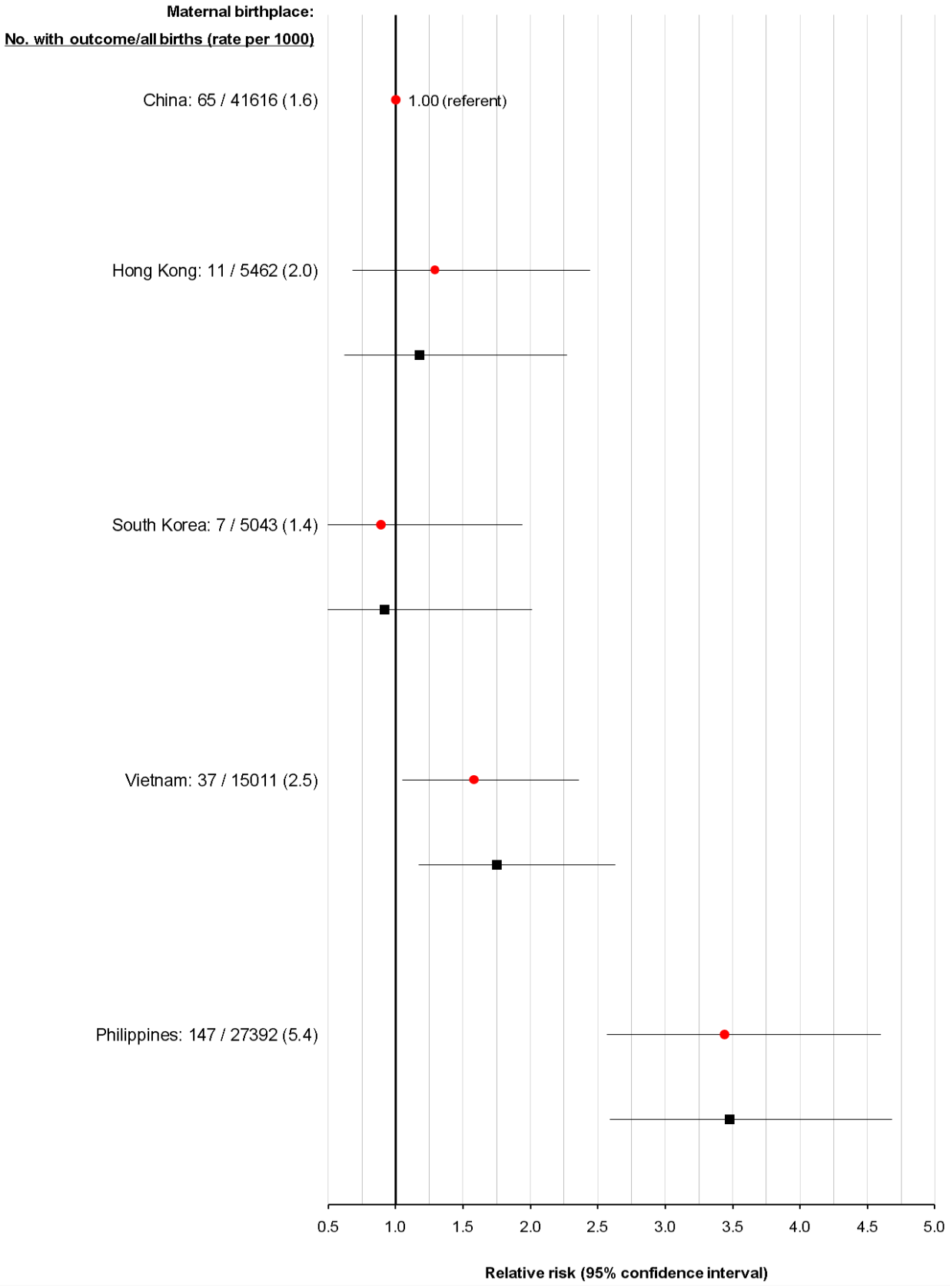
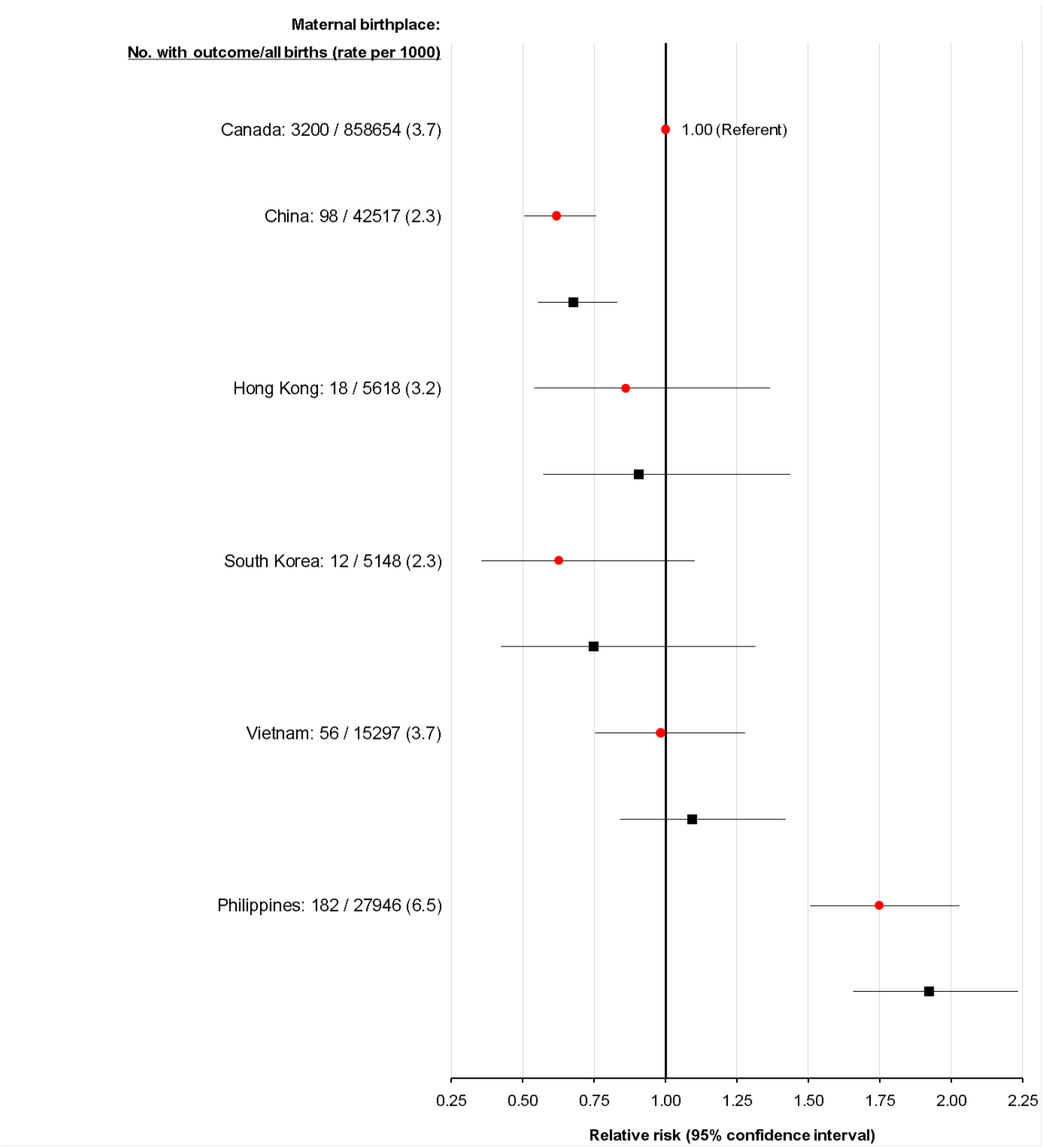
Supplementary file 1. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn singleton infants of East Asian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown) and infant sex.



Supplementary file 2. Rate and crude (red circles) and adjusted (black squares) relative risk of preterm birth with severe small for gestational age birthweight for liveborn infants of East Asian-born mothers, each compared to Canadian-born mothers. Relative risks were adjusted for maternal age (< 20, 20–34, ≥ 35 years), parity (0, 1, 2, 3, ≥ 4), marital status (married/common-law, unmarried, unknown), residential income quintile (Q1 [lowest] to Q5 [highest], unknown), infant sex, and twin birth.



STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3,4
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	3
		(*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	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4,5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4,6
		(*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 sampling strategy	4,6
		(*e*) Describe any sensitivity analyses	5

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, 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	5, Table 1, Figure 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	All Figures
		(*b*) Report category boundaries when continuous variables were categorized	All Figures
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	5
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	6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6,7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.