

Disparities in pre-eclampsia and eclampsia among immigrant women giving birth in six industrialised countries

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Accepted 13 February 2014. Published Online 24 April 2014.

Objective To assess disparities in pre-eclampsia and eclampsia among immigrant women from various world regions giving birth in six industrialised countries.

Design Cross-country comparative study of linked population-based databases.

Setting Provincial or regional obstetric delivery data from Australia, Canada, Spain and the USA and national data from Denmark and Sweden.

Population All immigrant and non-immigrant women delivering in the six industrialised countries within the most recent 10-year period available to each participating centre (1995–2010).

Methods Data was collected using standardised definitions of the outcomes and maternal regions of birth. Pooled data were analysed with multilevel models. Within-country analyses used stratified logistic regression to obtain odds ratios (OR) with 95% confidence intervals (95% CI).

Main outcome measures Pre-eclampsia, eclampsia and pre-eclampsia with prolonged hospitalisation (cases per 1000 deliveries).

Results There were 9 028 802 deliveries (3 031 399 to immigrant women). Compared with immigrants from Western Europe, immigrants from Sub-Saharan Africa and Latin America & the Caribbean were at higher risk of pre-eclampsia (OR: 1.72; 95% CI: 1.63, 1.80 and 1.63; 95% CI: 1.57, 1.69) and eclampsia (OR: 2.12; 95% CI: 1.61, 2.79 and 1.55; 95% CI: 1.26, 1.91), respectively, after adjustment for parity, maternal age and destination country. Compared with native-born women, European and East Asian immigrants were at lower risk in most industrialised countries. Spain exhibited the largest disparities and Australia the smallest.

Conclusion Immigrant women from Sub-Saharan Africa and Latin America & the Caribbean require increased surveillance due to a consistently high risk of pre-eclampsia and eclampsia.

Keywords Eclampsia, health disparities, immigration, industrialised countries, pre-eclampsia, pregnancy complications.

Please cite this paper as: Urquia ML, Glazier RH, Gagnon AJ, Mortensen LH, Nybo Andersen A-M, Janevic T, Guendelman S, Thornton D, Bolumar F, Río Sánchez I, Small R, Davey M-A, Hjern A, for the ROAM Collaboration. Disparities in pre-eclampsia and eclampsia among immigrant women giving birth in six industrialised countries. BJOG 2014;121:1492–1500.

Introduction

Pre-eclampsia is a major pregnancy complication leading to substantial maternal and perinatal morbidity and mortality

worldwide.^{1,2} Pre-eclampsia is a multi-system disorder with variable clinical manifestations which include hypertension and proteinuria. For the mother, pre-eclampsia is associated with various pregnancy complications, long-term cardiovascular morbidity and maternal death. It is also associated with preterm birth, fetal growth restriction, perinatal death

*ROAM collaboration: see Appendix.

and long-term adult health problems in the offspring.² Pre-eclampsia affects 2–7% of healthy nulliparous women. Although its etiology is poorly understood,³ pre-eclampsia is most common at the extremes of maternal age, in first pregnancies, multi-fetal pregnancies^{2,4,5} and among women with a history of pre-eclampsia.^{6,7} Pre-eclampsia may progress to eclampsia, characterised by life-threatening convulsions that generally occur after mid-pregnancy and around birth.

Rates of pre-eclampsia and gestational hypertension have increased in the USA from 1987 to 2004 by 25% and 184%, respectively, although eclampsia has not.⁸ The contribution of international migration to population estimates of hypertensive disorders in pregnancy and their secular trends in industrialised countries is unknown. According to a recent systematic review, the incidence of pre-eclampsia and eclampsia varies five- and 26-fold worldwide, respectively.⁹ Despite regional variations, few studies have reported variations in pre-eclampsia among immigrants to industrialised countries according to maternal birthplace or ethnic origin and almost none in eclampsia.^{10–14} These studies were based on a single setting, such as a hospital,^{12,13} midwife practices,¹⁵ a city,^{10,11} or a province¹⁴ and used different definitions of the outcomes and migrant groups. Conclusions regarding disparities according to immigrants' maternal birthplace based on single-site studies may not be generalisable to other settings. In contrast, multi-country studies using uniform ascertainment of the outcomes and immigrant groups, such as this one, provide a more robust approach to identifying maternal regions of origin associated with higher (and lower) global risk of pre-eclampsia and eclampsia in receiving countries.

The aim of this study was to assess disparities in pre-eclampsia and eclampsia among immigrants residing in six high-immigration countries according to their maternal region of origin. We compared immigrants from specific regions of the world to Western European immigrants, the sub-population which is ethnically closer to those born in the receiving countries while it shares the experience of migration. We subsequently assessed within-country disparities comparing immigrants from diverse regions of the world to the non-immigrant populations in each of the receiving countries.

Materials and methods

Study design

This is a cross-country comparative study. We used population-based regional or national health data from six countries (Australia, Canada, Denmark, Spain, Sweden and the USA). The study protocol was specified prior to data collection. Participating centres had to meet the following inclusion criteria: (i) ascertainment of pre-eclampsia and eclampsia by either the International Classification of

Diseases, Injuries and Causes of Death, 9th Revision (ICD-9)¹⁶ or the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10);¹⁷ (ii) categorisation of maternal region of origin according to pre-specified groupings by maternal country of birth; (iii) provision of population-based aggregated data (number of cases and non-cases) stratified by maternal region of birth, parity and maternal age groups.

Study populations and data sources

The study population was composed of any obstetrical delivery (including live births and stillbirths) of immigrants and non-immigrants occurring within the most recent 10-year period available to each participating centre (Table S1), although not all centres contributed 10 years of data. The study populations included deliveries from Australia (the state of Victoria), Canada (province of Ontario), Denmark and Sweden (national data), Spain (provinces of Catalonia and Valencia) and the USA (California, New Jersey and New York City). Population health data were obtained from perinatal data collections, health care registers and birth certificates linked to hospital records. These databases have been previously used for perinatal research and have been found to be of good quality.^{18–25} Each participating centre was responsible for assessing the internal consistency and quality of the definitions in the data sets across years and jurisdictions and to obtain ethical approval to share the data for pooled analyses. The study protocol was approved by the Research Ethics Board of the St. Michael's Hospital, Toronto, Canada.

Outcome measures

We defined pre-eclampsia based on the International Classification of Diseases (ICD) criteria available to each participating country. Spain and the USA used the ICD-9 codes 642.4 (Mild or unspecified pre-eclampsia), 642.5 (Severe pre-eclampsia) and 642.6 (Eclampsia), and the remaining countries used the ICD-10 codes O11 (Pre-existing hypertensive disorder with superimposed proteinuria), O14 [Gestational (pregnancy-induced) hypertension with significant proteinuria, including moderate, severe and unspecified pre-eclampsia and HELLP syndrome] and O15 (Eclampsia).

Pre-eclampsia with prolonged hospital stay (PPHS) was defined as any pre-eclampsia with a length of hospital stay greater than or equal to 7 days, as a proxy for more serious cases of pre-eclampsia associated with a higher burden on health care services. PPHS was not reported for Denmark due to data quality concerns and for Sweden due to the unavailability of data.

Maternal region of birth

Information on maternal country of birth was used to create maternal world regions of origin, based on the United

Nations subregions.²⁶ Groups were as follows: Eastern Europe, Western Europe, Latin America & the Caribbean, North Africa & Middle East, Sub-Saharan Africa, South Asia, and East-Southeast Asia. North America and Oceania were not included because of small numbers of immigrants from these regions. Two comparison groups were used. To assess differences according to immigrants' region of origin in analyses restricted to immigrants, Western Europeans were the reference group. This approach allows quantification of the variation in the outcomes that exists among immigrant groups. To assess disparities within each receiving country, the reference group was composed of the receiving country-born: USA-born in the USA, Australian-born in Australia, and so on. This approach is more appropriate to assess how different immigrant groups fare compared with the majority non-immigrant populations of the respective receiving countries.

Covariates

We included maternal age and parity as potential confounders. Because maternal age has a J- or U-shape association with severe maternal morbidity^{5,27} we created two groupings to capture the excess risk associated with the extremes of the maternal age distribution: <20 years or ≥35 years versus 20–34 years as the reference group. Parity was dichotomised in primiparous versus multiparous women as the reference group. Inclusion of additional covariates or more detailed strata of maternal age and parity were not feasible due to restrictions on disclosing small cell sizes in some participating countries.

Statistical analyses

Count data (number of cases and non-cases of each outcome) were provided by each participating centre by strata of maternal region of origin, maternal age and parity in a spreadsheet. These count data were merged into a single data set per outcome with the addition of a receiving country identifier. Each resulting data set was then imported into and analysed with SAS 9.3© (SAS Institute, Cary, NC, USA).

It has been suggested that international comparisons of *absolute population rates* of pre-eclampsia and eclampsia may not be meaningful because of different diagnostic criteria and methods of data collection.^{5,28} However, comparing *relative rates* between different immigrant groups and the non-immigrant population across countries of destination overcomes the limitations of comparing absolute rates, assuming that the probability of being diagnosed does not substantially differ according to immigration status.

We performed two analyses. The first analysis was restricted to immigrants to assess the variability in pre-eclampsia and eclampsia according to maternal region of origin. We used a two-level logistic regression model

with deliveries (first level) nested within receiving countries (second level). The model included random intercepts to account for the variability of the outcome between receiving countries. This model is similar to a meta-analysis in which jurisdictions occupy the place of studies.^{29,30} California, New Jersey and New York City were treated as distinct second-level clusters to account for differences between these jurisdictions. This was not possible for the provinces of Catalonia and Valencia, as the Spanish data were not disaggregated by province. Heterogeneity of outcome rates between receiving countries was assessed by the median odds ratio (MOR).³¹ The MOR translates the country-level variance into the widely used odds ratio scale, which is easier to interpret. Here, the MOR shows the extent to which a woman's risk of pre-eclampsia is determined by the receiving countries. The MOR can be conceptualised as the increased risk that (in median) a woman would have if moving to another country with a higher risk. In addition, one-sided Wald tests were used to obtain *P*-values for the significance of the variances.

The second set of analyses compared different immigrant groups with the non-immigrant population within each receiving country. For this purpose we used ordinary logistic regression stratified by receiving country to obtain within-country estimates and a two-level model with deliveries nested within receiving countries to obtain a pooled estimate across countries. Regression models were run before and after adjustment for maternal age and parity. Effect estimates were odds ratios with 95% confidence intervals. In post-hoc analyses, we assessed the extent of the disparities according to world region of origin by calculating odds ratios between the group with the highest incidence versus the group with the lowest incidence within each country.

Finally, we performed sensitivity analyses using detailed Ontario individual data. The purpose was twofold; to disaggregate Caribbean, Central American and South American women as three different groups, and to explore the potential impact of unmeasured confounders in the pooled estimates, by considering a more complete set of maternal characteristics, including those associated with migration (knowledge of official Canadian languages, maternal education at migration, marital status, refugee status and duration of residence in Canada).

Results

There were 9 028 802 deliveries across the six receiving countries, 3 031 399 (33.6%) of which were to immigrant women (Table S2). The proportion of deliveries to immigrant women varied across countries, from 12.6% in Denmark to 43.5% in the USA, mainly driven by 1 187 393 Latin Americans in California, mostly of Mexican origin.

The occurrence of pre-eclampsia varied from 12.3 per 1000 deliveries in Ontario, Canada, to 32.1 per 1000 in Victoria, Australia, and that of eclampsia varied from 0.4 cases per 1000 deliveries in Denmark and Spain to 1.1 per 1000 in the USA (California, New Jersey and New York City). The proportion of women of extreme maternal age ranged from 19.2% in Denmark to 26.7% in Spain and 26.6% in the USA and of primiparous women from 39.9% and 40.2% in these two countries to 45.6% in Ontario, Canada. The distribution of deliveries by maternal birthplace also varied markedly across countries, reflecting different migration patterns.

Disparities between maternal regions of birth

A multilevel model combining data from all six countries (deliveries as first level units and receiving countries as second level units) and restricted to immigrant women (Table 1) showed that, compared with their Western European counterparts, women from Latin America and the Caribbean and Sub-Saharan Africa had higher odds of pre-eclampsia [OR 1.52 (95% CI 1.46, 1.58) and OR 1.52 (95% CI 1.45, 1.60), respectively], PPHS [OR 1.62 (95% CI 1.47, 1.79) and OR 2.08 (95% CI 1.85, 2.34), respectively], and eclampsia [OR 1.40 (95% CI 1.14, 1.73) and OR 1.85 (95% CI 1.40, 2.43), respectively]. The associations became stronger after controlling for maternal age and parity. Women from East-Southeast Asia and North Africa and Middle East had lower odds of pre-eclampsia and those from Eastern Europe lower odds of eclampsia and PPHS. To test whether differences between world regions varied between receiving countries, we further included region of origin as random slopes in a subsequent model (not shown). A statistically significant variance of the slopes, although small, suggested that disparities according to maternal region of origin varied between receiving countries, which justifies the assessment of disparities within each receiving country (Table S3). The MOR was 1.4 for pre-eclampsia and 1.5 for eclampsia, indicating moderate heterogeneity between receiving countries, which did not reach statistical significance according to the Wald test. The Wald test was only significant for PPHS, which had an MOR of 1.8, suggesting slightly higher heterogeneity. However, this model was also based on a smaller sample, as it did not include Denmark or Sweden, making it less stable.

Disparities within receiving countries

Table S3 shows the results of separate ordinary logistic regression analyses conducted within strata of receiving countries. Here the reference group is the majority non-immigrant population of each receiving country. The excess risk of women from Latin America and the Caribbean and Sub-Saharan Africa was not observed equally in all countries when compared with that in women born in

the receiving country. Women from Sub-Saharan Africa had a higher risk of pre-eclampsia and PPHS in all countries, the only exception being Australia. The higher risk of eclampsia among women from Sub-Saharan Africa was also observed in all countries but only reached statistical significance in Spain and Sweden. A comparable pattern was observed for women from Latin America and the Caribbean, although not in Sweden. Immigrants from that region were at lower risk of pre-eclampsia in Denmark. The remaining maternal regions of origin were associated with lower odds than receiving-country women in all countries except Spain, where only Western European women had lower odds than Spanish-born women. Pooled analyses show that, compared with women born in the receiving country, Sub-Saharan Africans and those from Latin America & the Caribbean were at consistently higher risk of the three outcomes. Conversely, the remaining migrant groups were at lower risk than locally born women.

The magnitude of disparities within countries, however, was in part affected by the baseline risk of the locally born reference group in each country. To better reflect the extent of disparities by maternal birthplace in each country we also compared the groups with the highest versus the lowest level of the outcomes. Spain exhibited the highest disparities according to maternal region of birth, with odds ratios between the groups with the highest versus the lowest incidence ranging from 4.6 for pre-eclampsia to 12.9 for eclampsia. Australia had the lowest disparities, with odds ratios between the groups with the highest versus the lowest incidence in the range of 1.5–2.0.

Sensitivity analyses using Ontario data (Table S4) show that associations were stronger for women from the Caribbean and Central America than for women from South America, whose outcome rates were not higher than those of Western Europeans. Inclusion of additional maternal characteristics, including immigration characteristics, did not substantially alter the observed associations. Interestingly, time since immigration was positively associated with pre-eclampsia (adjusted 10-year OR 1.14, 95% CI 1.06, 1.23) but negatively associated with eclampsia (adjusted 10-year OR 0.79, 95% CI 0.59, 1.05), although the latter did not reach statistical significance.

Discussion

Main findings

Our main finding is that women from Sub-Saharan Africa had the highest risk of pre-eclampsia and eclampsia in all six participating countries, followed by women from Latin America & the Caribbean. The remaining maternal regions of birth were not associated with increased risk of the outcomes, and some exhibited lower risk than in women born in the respective receiving countries.

Table 1. Odds ratios with 95% confidence intervals of the association between immigrants' maternal region of birth and adverse maternal outcomes in the six receiving countries combined (Australia, Canada, Denmark, Spain, Sweden and the USA)

	Pre-eclampsia (n = 3 031 399)			Pre-eclampsia with prolonged hospital stay (n = 2 774 517)**			Eclampsia (n = 3 031 399)		
	Cases per 1000 deliveries	OR (95% CI)*	AOR (95% CI)*	Cases per 1000 deliveries	OR (95% CI)*	AOR (95% CI)*	Cases per 1000 deliveries	OR (95% CI)*	AOR (95% CI)*
Fixed effects Maternal birthplace									
Western Europe	18.4	1.00	1.00	3.0	1.00	1.00	0.5	1.00	1.00
Eastern Europe	18.5	1.01	0.99	2.7	0.84	0.85	0.3	0.62	0.61
Latin America & Caribbean	27.7	1.52	1.63	5.2	1.62	1.76	0.7	1.40	1.55
South Asia	17.8	0.97	1.01	3.3	1.04	1.12	0.4	1.02	1.07
East-Southeast Asia	17.2	0.93	0.90	3.2	0.98	0.97	0.5	0.82	0.80
North Africa & Middle East	13.8	0.75	0.83	2.7	0.84	0.96	0.5	0.95	1.09
Sub-Saharan Africa	27.7	1.52	1.72	6.7	2.08	2.35	1.0	1.85	2.12
Maternal age <20 years or ≥35 years									
Primiparity		–	1.47		–	1.69		–	1.43
			(1.44, 1.49)			(1.63, 1.75)			(1.36, 1.50)
Random effects									
Intercept variance		0.149	0.145		0.403	0.398		0.201	0.186
'Receiving country' (SE)		(0.079)****	(0.077)****		(0.255)***	(0.252)***		(0.108)****	(0.101)****
MOR		1.44	1.44		1.83	1.83		1.53	1.51
			(2.17, 2.23)			(2.24, 2.42)			(2.44, 2.67)

AOR, adjusted odds ratio (adjusted for parity and maternal age); CI, confidence interval; MOR, median odds ratio; OR, odds ratio; SE, standard error.

*Based on a two-level logistic regression model, with deliveries nested within receiving countries

**Defined as pre-eclampsia or eclampsia with hospital stay ≥ 7 days. Denmark and Sweden not included.

***P > 0.05.

****P > 0.05; one-sided.

We also found that disparities between maternal regions of birth varied substantially between receiving countries, being lowest in Victoria, Australia, and highest in Catalonia/Valencia, Spain. The non-immigrant populations generally had incidence rates somewhere in the middle of the continuum of risk.

Strengths and limitations

Study strengths include the use of large population-based data sets, the combination of data collected from six high-immigration countries and the use of standardised definitions of outcomes and migrant groups.

Limitations illustrate the challenges faced by cross-country comparative studies. We relied on perinatal data collections, health care registers and linked databases from different countries, which differ in some characteristics that may impact the absolute rates of the outcomes. However, as our analyses are based on the relative disparities according to maternal region of birth, variations in absolute rates are of less concern.

Whereas reporting systems in Australia, Canada, Denmark and Sweden used the ICD-10, Spain and the USA used the ICD-9. This difference in coding schemes did not result in different incidence rates. The incidence rates of pre-eclampsia and eclampsia in the countries using the ICD-9 (Spain and the USA) were within the range observed in the countries using the ICD-10.

Our assumption that the probability of being diagnosed does not substantially differ according to immigration status may not hold equally true in all participating countries, some of which do not have universal health care coverage, such as the USA. Although we controlled for extreme maternal age and parity, we could not include other covariates such as multiple pregnancies, history of pre-eclampsia, health care access and socioeconomic indicators or health behaviours, due to either lack of information or to restrictions on reporting low event counts in some countries. However, our sensitivity analyses based on Ontario data suggest that inclusion of a larger set of additional covariates, including maternal education, official language ability and neighbourhood income, would not explain the observed associations. Moreover, adjustment for mediators such as health behaviours or social position in the receiving society may not be appropriate and may result in overcontrol. In the same vein, the ability to create more detailed groupings of maternal origin, ideally at country level, was hampered by sample size considerations and consistency across participating countries. Different distribution of countries within maternal world regions may be responsible in part for the differences observed between receiving countries. In addition, most participating countries do not collect data on ethnicity and generational status, which may have unveiled more complex disparities, particularly

among the more ethnically diverse non-immigrant populations. National data were only available for Denmark and Sweden; therefore the findings for the remaining countries, although regionally valid, may not necessarily be representative of the country as a whole.

Interpretation

Despite these limitations, our findings provide robust evidence of an increased global risk of pre-eclampsia and eclampsia among immigrants from Sub-Saharan Africa and Latin America and the Caribbean.

Disparities between maternal regions of birth

The excess risk found among Sub-Saharan Africans may be a reflection of background risks in the source countries. In fact, Sub-Saharan Africans exhibit the highest rates of pre-eclampsia, eclampsia⁹ and maternal mortality worldwide,³² and migrants may carry over their higher susceptibility post-migration. Generalisation regarding Sub-Saharan Africans to other Western countries is supported not only by our findings but also by studies conducted in Belgium,¹¹ the Netherlands¹⁵ and Italy.³³ However, generalisations should be made with caution, as unique processes may occur in different immigration settings. The exception of Victoria, Australia, in the case of pre-eclampsia may be an example. Potential factors that may help explain it include the impact of selective admission policies, which may have excluded less healthy individuals who might otherwise have inflated the numerators,^{34,35} a pool of immigrants different from those of the other countries and the existence of a more equitable socioeconomic environment.

Immigrants from Latin America & the Caribbean had lower odds of pre-eclampsia in Denmark and similar odds in Sweden. The relatively lower incidence of pre-eclampsia in these countries may be due to a different composition of specific countries of origin. In fact, Denmark and Sweden have mainly received immigrants from South America; countries from South America, like Argentina, have been shown to be associated with lower rates of pre-eclampsia compared with those of Central America and the Caribbean.¹⁰ Our sensitivity analyses using Ontario data, showing increased risks for Caribbean and Central American women but not for South American women, are consistent with these previous findings. Therefore, generalisation regarding Latin American and Caribbean women must be cautious and attention must be paid to the composition of specific source-countries in a given receiving setting. Although unexplored, proximity of country of origin to country of delivery may be a factor influencing selective migration patterns. For example, geographical proximity may favour less selected migration of Mexicans into the USA, including undocumented migrants, compared with Mexicans migrating overseas. The same may apply to

Africans in Spain compared with Africans settling in North America.

The remaining immigrant groups from Europe, Asia and North Africa & Middle East had a similar or lower incidence of pre-eclampsia and eclampsia than Western Europeans and noticeably lower incidence than the non-immigrant populations; this pattern being consistent with the healthy migrant effect.³⁶

Disparities within receiving countries

Within-country analyses also provide evidence of a higher vulnerability of Sub-Saharan African women in most countries, followed by those of Latin America and the Caribbean. Interestingly, Europeans, North Africans and Asians had lower incidence of pre-eclampsia and eclampsia than some locally born populations, which had intermediate risk of the outcomes.

Because the varying baseline risk of locally born women in each receiving country affects the comparison of disparities between countries, we also compared the groups at the extremes of the continuum of risk and found the greatest disparities in Catalonia/Valencia, Spain, and the smallest in Victoria, Australia.

The high disparities in Catalonia/Valencia may be due to contrasting influxes of better-off, and therefore healthier, Western Europeans on one end of the continuum of risk and immigrants from poor regions in the other end, including many Latin Americans and North and Sub-Saharan Africans in irregular situations and living in marginalised conditions, thus increasing the differences.^{37,38} Spain has witnessed an immigration boom at the turn of the 21st century,³⁹ implying that many immigrants to Spain are newcomers who may not be familiar with the local environment and health care system. It is possible that some Western Europeans with complicated pregnancies may have chosen to deliver in the more supportive environment of their home countries, which may be facilitated by low travel costs within Europe and easier access to high quality health care. If supported by empirical evidence, this phenomenon would represent a particular case of the 'salmon bias', by which some immigrants groups appear to be healthier than they really are because ill individuals who return to their birthplace for treatment no longer contribute to the numerators.³⁶ On the other hand, Spain also hosts a sizeable undocumented immigrant population, estimated at around 25% among female immigrants aged 20–40 years.⁴⁰ An undocumented status may expose women to exploitation and stress, and hamper their ability to seek and properly utilise health care.⁴¹ However, illegal stay cannot be the only explanation as it occurs in varying degrees in all countries. Finally, discrimination adds another layer of disadvantage that might contribute to higher disparities, particularly among racialised groups.⁴²

The lowest disparities observed in Victoria are puzzling and may be due to factors operating simultaneously. First, selective migration policies may have contributed to flattening the disparities via a healthy migrant effect.³⁶ The Australian Humanitarian Program admits many African refugees only after medical and security checks but admits relatively few asylum seekers from Africa.³⁴ The General Skilled Migration Program selects immigrants on the basis of skills and qualifications in demand in the Australian job market.³⁵ Such selective admission policies may result in the exclusion of less healthy women who otherwise may have contributed to increased rates of pre-eclampsia and eclampsia. It is also possible that narrower material deprivation gradients observed among Australian immigrants⁴³ could account for less disparity in the Victorian findings, compared with other receiving regions with wider income disparities related to migrant status, such as Canada.⁴⁴ Interestingly, the Ontario data show that the risk of pre-eclampsia increased with duration of residence but that of eclampsia decreased. Increases in pre-eclampsia may be due to deterioration of health status following migration, a process already observed for preterm delivery,⁴⁵ whereas decreases in eclampsia may reflect that more cases of eclampsia were prevented over time by timely health care, probably parallel to increased integration of immigrants in the local society.

Conclusion

Our findings provide robust evidence of an increased global risk of pre-eclampsia and eclampsia among Sub-Saharan African immigrants and some Latin American or Caribbean groups. Clinicians are encouraged to consider these high-risk groups for pre-eclampsia and eclampsia in need of enhanced surveillance and culturally sensitive peripartum care.

Future research aimed at generating global evidence about immigrants' determinants of health would benefit from adopting an international comparative approach, based on standardised measurements and more detailed individual data to unveil the mechanisms behind the associations, including access to and health care utilisation, particularly for at-risk pregnancies. Ideally, although challenging, research should also use longitudinal data and include pre-migration measurements to account for selective migration and assess changes in the receiving countries.

Disclosure of interests

Authors declare they have no competing interests.

Contribution to authorship

MU conceived the study, analysed the data and led the writing of the manuscript. RG, LM, AN, TJ, SG, DT, FB, IR, RS, MD

and AH participated in the data collection. LM participated in data analysis. All authors contributed to the study design, writing of the manuscript and approved the final version.

Details of ethics approval

The study protocol was approved by the Research Ethics Board of St. Michael's Hospital in Toronto on April 11, 2012 (REB# 12-087).

Funding

No funding was originally sought for this study. The study was partially funded by a grant of the Canadian Institutes of Health Research (MOP-123267). All authors were supported by their respective institutions.

Acknowledgements

We are grateful to the Consultative Council on Obstetric and Paediatric Mortality and Morbidity, and the Clinical Councils Unit, Department of Health, for providing Australian data from the Victorian Perinatal Data Collection. The study was possible thanks to the Institute for Clinical Evaluative Sciences (ICES), which is supported by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred.

Appendix

ROAM (Reproductive Outcome And Migration) – an international research collaboration; active members (at the time of this project): Sophie Alexander and Judith Racapé (Université libre de Bruxelles, Belgium), Anne-Marie Nybo Andersen and Laust Mortensen (University of Copenhagen, Denmark), Henrique Barros (University of Porto, Portugal), Béatrice Blondel (INSERM, France), Simone Buitendijk (TNO Institute – Prevention and Health, the Netherlands), Cindy-Lee Dennis (University of Toronto), Birgitta Essén (Uppsala University, Sweden), Anita J Gagnon and Lisa Merry (McGill University and McGill University Health Centre Research Institute, Canada), Mika Gissler (National Institute for Health and Welfare, Finland), Richard Glazier (Institute for Clinical Evaluative Sciences, Canada), Maureen Heaman (University of Manitoba, Canada), Russell Kirby (University of South Florida, US), Dineke Korfker and Ashna Mohangoo (TNO Institute – Prevention and Health, the Netherlands), Alison Macfarlane and Christine McCourt (City University of London, UK), Edward Ng (Statistics Canada), Carolyn Roth (Keele University, UK), Rhonda Small and Mary-Ann Davey (La Trobe University, Australia), Mridula Bandyopadhyay (Victoria University, Australia), Erika Sievers (Akademie für öffentliches Gesundheitswesen, Dusseldorf, Germany), Marcelo Urquia (Institute for Clinical Evaluative Sciences, Canada), Teresa Janevic (Rutgers University, USA), Sylvia Guendelman and Dorothy Thornton (University of California at Berkeley, USA), Francisco Bolumar (Universidad de Alcalá, Spain), María Isabel Río Sánchez (National Centre of Epide-

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Characteristics of the study populations and data sets

Table S2. Outcome measures and characteristics of the study population, by immigrants' place of residence at delivery.

Table S3. Odds ratios with 95% confidence intervals of the association between maternal region of birth and adverse outcomes, by immigrants' place of residence at delivery

Table S4. Odds ratios with 95% confidence intervals of the association between maternal region of origin and adverse maternal outcomes in Ontario, Canada ■

References

- Schutte JM, Steegers EA, Schuitemaker NW, Santema JG, de BK, Pel M, et al. Rise in maternal mortality in the Netherlands. *BJOG* 2010;117:399–406.
- Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. *Lancet* 2005;365:785–99.
- Trogstad L, Magnus P, Stoltenberg C. Pre-eclampsia: risk factors and causal models. *Best Pract Res Clin Obstet Gynaecol* 2011;25:329–42.
- Duley L. The global impact of pre-eclampsia and eclampsia. *Semin Perinatol* 2009;33:130–7.
- Roberts JM, Pearson G, Cutler J, Lindheimer M. Summary of the NHLBI working group on research on hypertension during pregnancy. *Hypertension* 2003;41:437–45.
- Hernandez-Diaz S, Toh S, Cnattingius S. Risk of pre-eclampsia in first and subsequent pregnancies: prospective cohort study. *BMJ* 2009;338:b2255.
- Klungsoyr K, Morken NH, Irgens L, Vollset SE, Skjaerven R. Secular trends in the epidemiology of pre-eclampsia throughout 40 years in Norway: prevalence, risk factors and perinatal survival. *Paediatr Perinat Epidemiol* 2012;26:190–8.
- Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of pre-eclampsia, eclampsia, and gestational hypertension, United States, 1987–2004. *Am J Hypertens* 2008;21:521–6.
- Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of pre-eclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2013;170:1–7.
- Gong J, Savitz DA, Stein CR, Engel SM. Maternal ethnicity and pre-eclampsia in New York City, 1995–2003. *Paediatr Perinat Epidemiol* 2012;26:45–52.
- Haelterman E, Qvist R, Barlow P, Alexander S. Social deprivation and poor access to care as risk factors for severe pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol* 2003;111:25–32.
- Margioulou-Siarkou C, Petousis S, Kalogiannidis I, Dagklis T, Traianos V, Goutzioulis M, et al. Immigrants present improved obstetric and neonatal outcomes compared to native women. A northern Greek population analysis. *J Immigr Minor Health* 2013;15: 249–54.

- 13 Salim R, Mfra A, Garmi G, Shalev E. Comparison of intrapartum outcome among immigrant women from Ethiopia and the general obstetric population in Israel. *Int J Gynaecol Obstet* 2012;118:161–5.
- 14 Urquia ML, Ying I, Glazier R, Berger H, De Souza L, Ray JG. Serious pre-eclampsia among different immigrant groups. *J Obstet Gynaecol Can* 2012;34:348–52.
- 15 Knuist M, Bonsel GJ, Zondervan HA, Treffers PE. Risk factors for pre-eclampsia in nulliparous women in distinct ethnic groups: a prospective cohort study. *Obstet Gynecol* 1998;92:174–8.
- 16 World Health Organization. *International Classification of Diseases, Injuries and Causes of Death*, 9th Revision. Geneva: WHO, 1979.
- 17 World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*, 10th Revision. Geneva: WHO, 2003.
- 18 Baumeister L, Marchi K, Pearl M, Williams R, Braveman P. The validity of information on 'race' and 'Hispanic ethnicity' in California birth certificate data. *Health Serv Res* 2000;35:869–83.
- 19 Davey MA, Sloan ML, Palma S, Riley M, King J. Methodological processes in validating and analysing the quality of population-based data: a case study using the Victorian Perinatal Data Collection. *HIM J* 2013;42:12–19.
- 20 Joseph KS, Fahey J. Validation of perinatal data in the Discharge Abstract Database of the Canadian Institute for Health Information. *Chronic Dis Can* 2009;29:96–100.
- 21 Juarez S, Alonso OT, Ramiro-Farinas D, Bolumar F. The quality of vital statistics for studying perinatal health: the Spanish case. *Paediatr Perinat Epidemiol* 2012;26:310–15.
- 22 Lohse SR, Farkas DK, Lohse N, Skouby SO, Nielsen FE, Lash TL, et al. Validation of spontaneous abortion diagnoses in the Danish National Registry of Patients. *Clin Epidemiol* 2010;2:247–50.
- 23 Reichman NE, Schwartz-Soicher O. Accuracy of birth certificate data by risk factors and outcomes: analysis of data from New Jersey. *Am J Obstet Gynecol* 2007;197:32–8.
- 24 Roohan PJ, Josberger RE, Acar J, Dabir P, Feder HM, Gagliano PJ. Validation of birth certificate data in New York State. *J Community Health* 2003;28:335–46.
- 25 Swedish Centre for Epidemiology. *The Swedish Medical Birth Register. A summary of content and quality*. www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/10655/2003-112-3_20031123.pdf. 2003. Sweden: National Board of Health and Welfare.
- 26 United Nations Statistics Division. Composition of macro geographical (continental) regions, geographical sub-regions, and selected economic and other groupings. www.unstats.un.org/. 2011. United Nations. 3-16-2011.
- 27 Joseph KS, Liu S, Rouleau J, Kirby RS, Kramer MS, Sauve R, et al. Severe maternal morbidity in Canada, 2003 to 2007: surveillance using routine hospitalization data and ICD-10CA codes. *J Obstet Gynaecol Can* 2010;32:837–46.
- 28 Roberts CL, Ford JB, Algert CS, Antonsen S, Chalmers J, Cnattingius S, et al. Population-based trends in pregnancy hypertension and pre-eclampsia: an international comparative study. *BMJ Open* 2011;1:e000101.
- 29 Raudenbush S, Bryk A. *Hierarchical Linear Models. Applications and Data Analysis Methods*, 2nd edn. Thousand Oaks, CA: Sage Publications, 2002.
- 30 Thompson SG, Turner RM, Warn DE. Multilevel models for meta-analysis, and their application to absolute risk differences. *Stat Methods Med Res* 2001;10:375–92.
- 31 Larsen K, Merlo J. Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol* 2005;161:81–8.
- 32 World Health Organization. *Maternal Mortality in 2005. Estimates developed by WHO, UNESCO, UNFPA and the World Bank*. Geneva: WHO, 2007.
- 33 Salvador S, Bertozzi S, Londero AP, Driul L, Da RR, Marchesoni D. [Outcome of pregnancy for immigrant women: a retrospective study]. *Minerva Ginecol* 2010;62:277–85.
- 34 Australia's Humanitarian Program. Information Paper. April 2011. 2011. Australian Government. Department of Immigration and Citizenship. 3-7-2013.
- 35 Fact Sheet 22—The Health Requirement. 2013. Australian Government. Department of Immigration and Citizenship.
- 36 Urquia ML, Gagnon AJ. Glossary: migration and health. *J Epidemiol Community Health* 2011;65:467–72.
- 37 Rio I, Castello A, Jane M, Prats R, Barona C, Mas R, et al. [Reproductive and perinatal health indicators in immigrant and Spanish-born women in Catalonia and Valencia (2005-2006)]. *Gac Sanit* 2010;24:123–7.
- 38 Rio SI, Bosch SS, Castello PA, Lopez-Maside A, Garcia SC, Zurriaga LO, et al. [Perinatal mortality assessment in native and immigrant women: influence of exhaustiveness and quality of the registries]. *Gac Sanit* 2009;23:403–9.
- 39 Garcia-Subirats I, Perez G, Rodriguez-Sanz M, Salvador J, Jane M. Recent immigration and adverse pregnancy outcomes in an urban setting in Spain. *Matern Child Health J* 2011;15:561–9.
- 40 Sousa E, Agudelo-Suarez A, Benavides FG, Schenker M, Garcia AM, Benach J, et al. Immigration, work and health in Spain: the influence of legal status and employment contract on reported health indicators. *Int J Public Health* 2010;55:443–51.
- 41 Benach J, Muntaner C, Delclos C, Menendez M, Ronquillo C. Migration and 'low-skilled' workers in destination countries. *PLoS Med* 2011;8:e1001043.
- 42 Llacer A, Amo JD, Garcia-Fulgueiras A, Ibanez-Rojo V, Garcia-Pino R, Jarrin I, et al. Discrimination and mental health in Ecuadorian immigrants in Spain. *J Epidemiol Community Health* 2009;63:766–72.
- 43 Lansakara N, Brown SJ, Gartland D. Birth outcomes, postpartum health and primary care contacts of immigrant mothers in an Australian nulliparous pregnancy cohort study. *Matern Child Health J* 2010;14:807–16.
- 44 Urquia ML, O'Campo PJ, Heaman MI. Revisiting the immigrant paradox in reproductive health: the roles of duration of residence and ethnicity. *Soc Sci Med* 2012;74:1610–21.
- 45 Urquia ML, Frank JW, Moineddin R, Glazier RH. Immigrants' duration of residence and adverse birth outcomes: a population-based study. *BJOG* 2010;117:591–601.