The Incidence of Major Cardiovascular Events in Immigrants to Ontario, Canada: The CANHEART Immigrant Study

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Abstract

Background—Immigrants from ethnic minority groups represent an increasing proportion of the population in many high-income countries but little is known about the causes and amount of variation between various immigrant groups in the incidence of major cardiovascular events.

Methods and Results—We conducted the Cardiovascular Health in Ambulatory Care Research Team (CANHEART) Immigrant study, a big data initiative, linking information from Citizenship and Immigration Canada’s Permanent Resident database to nine population-based health databases. A cohort of 824,662 first-generation immigrants aged 30 to 74 as of January 2002 from eight major ethnic groups and 201 countries of birth who immigrated to Ontario, Canada between 1985 and 2000 were compared to a reference group of 5.2 million long-term residents. The overall 10-year age-standardized incidence of major cardiovascular events was 30% lower among immigrants compared with long-term residents. East Asian immigrants (predominantly ethnic Chinese) had the lowest incidence overall (2.4 in males, 1.1 in females per 1000 person-years) but this increased with greater duration of stay in Canada. South Asian immigrants, including those born in Guyana had the highest event rates (8.9 in males, 3.6 in females per 1000 person-years), along with immigrants born in Iraq and Afghanistan. Adjustment for traditional risk factors reduced but did not eliminate differences in cardiovascular risk between various ethnic groups and long-term residents.

Conclusions—Striking differences in the incidence of cardiovascular events exist among immigrants to Canada from different ethnic backgrounds. Traditional risk factors explain part but not all of these differences.

Key words: cardiovascular disease risk factors, ethnicity, myocardial infarction, stroke, immigrants
Introduction

The increasing frequency of global migration to high-income countries such as Canada has highlighted the need for more information on cardiovascular risk factors and diseases in migrant populations from different ethnic backgrounds and regions of the world. Cardiovascular diseases (including stroke) are the leading cause of death globally and many immigrants to Canada come from low- and middle-income countries, which have the greatest absolute burden of cardiovascular deaths. A systematic review of 12 studies of cardiovascular disease in immigrant populations demonstrated that the burden of ischemic heart disease and stroke is higher in many immigrant populations compared with the host population in those countries. However, most previous studies have focussed on one or a limited number of immigrant groups, only include data derived from death certificates or hospitalizations, and have not studied the causes of variations in cardiovascular disease burden among different immigrant groups.

Among high-income countries, Canada is the most ethnically and culturally diverse, and represents an ideal setting in which to conduct research on cardiovascular diseases in multi-ethnic migrant populations. Canada has one of the highest per-capita rates of immigration of any high-income country, with approximately 250 000 immigrants (0.8% of population) arriving annually from countries around the world. Of these, the greatest proportion settles in Ontario, Canada’s most populous province (13 million in 2011). The CARDiovascular HEalth in Ambulatory care Research Team (CANHEART) is a “big data” research initiative aimed at measuring and improving the cardiovascular health of all Canadians. The objectives of this CANHEART Immigrant study were to determine the prevalence of traditional cardiovascular risk factors and the 10-year incidence rates of major cardiovascular events in a large multi-ethnic cohort of first-generation immigrants who immigrated to Ontario between 1985 and 2000. We
sought to determine whether significant differences in cardiovascular event rates exist among immigrants from different major ethnic groups, and if so, how variations in the burden of traditional risk factors contribute to these differences.

Methods

Study design and population

We identified a retrospective population-based cohort of 824,662 immigrants from the Citizenship and Immigration Canada Permanent Resident (CIC) database who arrived in Ontario between 1985 and 2000, aged 30 to 74, and who were living in Ontario as of January 1, 2002. The CIC database contains socio-demographic information such as country of birth, mother tongue, education, and immigration class on all immigrants to Ontario since 1985. Immigrants with hospitalizations for cardiovascular events prior to 2002 were excluded from the study to create a primary prevention cohort. Further details about study inclusion/exclusion criteria and methods used to construct the CANHEART cohort are provided in the Supplemental Material and described in detail elsewhere (www.canheart.ca).\(^8\) A comparison cohort of 5,200,258 long-term residents who were born in Ontario or arrived prior to 1985, meeting the same age, residential, and cardiovascular disease history criteria was identified from the Ontario Registered Persons Database (RPDB). We estimate that the long-term resident cohort consists predominantly of white individuals (>95%) born in (~83%) or who migrated to Canada before 1985 (~17%) (Supplemental Material).

Ethnic groups

Ethnicity has been defined as “the social group a person belongs to, and either identifies with or is identified with by others, as a result of a mix of cultural and other factors including language,
diet, religion, ancestry and physical features traditionally associated with race." It is often defined at the ethnic group level or by country of birth. In this study, we chose to categorize each immigrant into one of eight major ethnic groups derived from Canada’s officially recognized visible minority groups using two validated algorithms that identify an immigrant’s most likely ethnic background based on a combination of their country of birth, mother tongue, and surname (for Chinese and South Asians). These major ethnic groups were: 1) East Asian (e.g., Chinese, Korean); 2) Southeast Asian (e.g., Filipino, Vietnamese); 3) Black – from Sub-Saharan Africa and the Caribbean; 4) West Asian/Arab – from the Middle East, West Asia and some former republics of the USSR; 5) Latin American – from Central and South America; 6) South Asian (e.g., Pakistani, Indian, Sri Lankan); and White immigrants subdivided into those of 7) White-Eastern European and 8) White-Western European origin. The latter category also included immigrants from non-European countries from which most immigrants are of White-Western European origins (e.g., the United States, Australia, New Zealand, and South Africa).

We also conducted subgroup analyses by country of birth as a secondary approach to ethnic classification.

Data sources and linkage

The immigrant and long-term resident cohorts created from the CIC and RPDB databases were linked to nine population-based health databases using unique, encoded identifiers to obtain information on the prevalence of traditional cardiac risk factors (smoking, hypertension, diabetes, lipid levels) and cardiovascular event rates (Supplemental Material). Databases used to identify these risk factors and clinical events (including the relevant ICD-9 and ICD-10 codes) are shown in the Supplemental Material. Mean body mass index (BMI) and the prevalence of obesity (BMI ≥ 30 kg/m²) were also determined, but not used in calculation of a cardiac risk factor...
score (see below) since the effect of obesity on cardiovascular risk is felt to be mediated through its effect on the other traditional risk factors. However, adjustment for BMI was included as a sensitivity analysis in regression analyses (see below).

**CANHEART cardiac risk factor score**

To quantify the relative combined burden of four traditional modifiable cardiac risk factors (smoking, diabetes, hypertension, and hyperlipidemia) in each ethnic group, we developed a points-based cardiac risk factor score using the methods originally described by Sullivan et al in creating the points-based Framingham risk score (Supplemental Material). A cardiac risk factor score was calculated for each immigrant and long-term resident by assigning points based on the presence or absence of each traditional risk factor. The age-standardized mean score for each ethnic group represents the group’s relative burden of risk factors with higher scores indicating a higher burden. Missing lipid and smoking data were imputed using multiple imputation methods (Supplemental Material).

**Outcomes**

The primary study outcome of a major cardiovascular event was a composite measure defined as the incidence of hospitalization for either acute myocardial infarction (AMI), stroke, revascularization with either percutaneous coronary intervention or coronary artery bypass graft surgery, or death from ischemic heart diseases or cerebrovascular diseases (Supplemental Material). The ratio of AMI/stroke rates was determined to compare the relative incidence of these conditions in each group. Revascularization/AMI ratios in each group were also calculated to determine whether access to revascularization procedures was equitable across ethnic groups. To determine the impact of acculturation, we also calculated the event rate comparing immigrants who had lived in Canada for less than 10 years with immigrants who had lived in
Canada for at least 10 years prior to study period inception.

Statistical analyses

Descriptive statistics (means, proportions) were calculated for socio-demographic and outcome variables with 95% confidence intervals. Sex-specific, age-standardized 10-year incidence rates per 1000 person-years follow-up were calculated for each ethnic group and the long-term resident cohort using the 2006 Ontario population aged 30 to 74 as the standard population. We also conducted sex-stratified subgroup analyses by country of birth for those 29 countries with at least 5000 immigrants to Ontario. Pearson correlation coefficients were calculated to examine the ecological association between the mean ethnic-group specific cardiac risk factor score and the ethnic-group specific incidence rate of cardiovascular events. Sex-stratified, sequential Cox proportional hazard modelling was performed to investigate differences in the primary outcome between ethnic groups and the long-term resident cohort after adjusting for individual-level differences in age, socioeconomic status (SES) measured by neighbourhood income quintile, prevalence of traditional cardiovascular risk factors, and BMI (see Supplemental Material).

Individuals who emigrated from Ontario were censored at the time of departure. Data analyses were conducted using SAS version 9.3 (SAS Institute, Cary NC) and R software version 2.15.1, and analyzed at the Institute for Clinical Evaluative Sciences. Results are presented in order of increasing incidence of the primary outcome by ethnicity among male immigrants. This study was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre. Informed consent from Canadian Community Health Survey participants was obtained by Statistics Canada for record linkage to administrative databases.
Results

Baseline characteristics of immigrant cohort

Figure 1 provides a global map showing the distribution of the 824,662 immigrants in our study population by country of birth. The map demonstrates the wide diversity of Ontario immigrants with 201 countries (and 179 mother tongues) represented, covering all inhabited continents and nearly all countries in the world. Table 1 shows baseline socio-demographic information of the immigrant cohort by ethnic group and long-term residents. At study initiation, the mean age of the immigrant cohort was 44 years and their mean duration in Canada was 8.6 years. Economic immigrants (i.e., skilled workers selected via a points system) comprised 43.0% of immigrants, 40.1% were family class immigrants (sponsored by a relative already in Canada) and 15.2% were refugees. All immigrant groups were more likely to live in low-income neighbourhoods in Ontario compared with long-term residents. Overall, 21.7% of immigrants were from other high-income countries, 56.9% from middle-income countries, and 21.4% from low-income countries.14

Cardiovascular disease risk factors

Table 2 shows the prevalence of traditional cardiac risk factors in each ethnic group and among long-term residents. Smoking rates were lower in all female and most male ethnic groups (except White-Eastern European and West Asian/Arab males) compared with long-term residents. The overall prevalence of obesity and hypertension was also lower among immigrants. Black and Southeast Asian immigrants had particularly high rates of hypertension, while South Asian and Black immigrants had the highest rates of diabetes. The total/high density lipoprotein (HDL) cholesterol ratio was highest in South Asian immigrants and lowest in East Asian and Black (males only) immigrants. The mean cardiac risk factor score varied widely among ethnic groups,
but was lower among immigrants overall compared with long-term residents. The mean cardiac risk factor score was also lower among immigrants who left Ontario (12.1% of males, 10.4% of females) before the end of the 10-year study period (1.92 in males, 1.51 in females) compared with immigrants followed for the entire study (2.20 in males, 1.81 in females).

**Ten-year incidence rates of cardiovascular events**

Overall, 19 127 events occurred over 7 674 691 person-years of follow up in the immigrant cohort (mean 9.3 years of follow-up). The overall incidence of major events was 30% lower (31% in males, 29% in female) in immigrants compared with long-term residents. The age-standardized 10-year incidence rate of major cardiovascular events by ethnic group varied four-fold with East Asian male and female immigrants at lowest risk (2.4 and 1.1 per 1000 person-years respectively) and South Asian male and female immigrants at highest risk (8.9 and 3.6 per 1000 person-years respectively) (Table 3). The ratio of AMI/stroke events varied three-fold across ethnic groups with East Asian, Black, and Southeast Asian immigrants having relatively low ratios, indicating relatively fewer AMIs in each of these groups. The revascularization/AMI ratio was similar across ethnic groups, indicating similar access to invasive cardiac procedures.

Comparing immigrants living in Canada for less than 10 years versus 10 or more years, the incidence of events was similar in most ethnic groups. A notable exception was among East Asian immigrants where a 40% and 60% higher incidence was found among males and females respectively, living in Canada for 10 or more years (Table 4).

**Cardiovascular event rates by country of birth**

Results from analysis of age-standardized major cardiovascular event incidence rates in the 29 countries of birth with at least 5000 immigrants to Ontario are shown in Figure 2. Greater variation in cardiovascular event rates by country of birth was observed among male immigrants.
compared with female immigrants. In general, the cardiovascular event rate was similar among different countries of birth within each region of birth, but some exceptions were found. Immigrants born in Iraq and Afghanistan had higher event rates than those born in neighbouring countries. Immigrants from these two countries also had among the highest mean cardiac risk factor scores (Figure 3) and relatively high proportions were refugees (61% from Iraq, 79% from Afghanistan) compared with other immigrants from the Middle East and West Asia (19%). Relatively high incidences of cardiovascular events among immigrants born in Guyana and Trinidad and Tobago were also observed, explained in part by the heavy presence of South Asian diaspora among migrants to Canada from these regions of the world.

Association between CANHEART cardiac risk factor score and cardiovascular event rates

Figure 3 shows the association between the risk factor burden measured using our cardiac risk factor score and the 10-year age-standardized incidence of major cardiovascular events in both ethnic group and country of birth analyses. By ethnicity, the correlation coefficients between the mean cardiac risk factor score and cardiovascular event rate were 0.76 for males and 0.92 for females. By country of birth, the corresponding correlation coefficients were 0.81 for males and 0.75 for females, demonstrating that variation in risk factor burden contributes to the event rate differences found in this study.

Role of socio-demographics and risk factors to event rate variation

A series of sequential sex-specific Cox regression models exploring the contribution of ethnicity, age, SES, traditional cardiovascular risk factors and BMI to individual-level differences in major cardiovascular event rates by ethnic group is shown in Figure 4. Adjustment for age and SES reduced the variation amongst different ethnic groups and the long-term residents, with a further reduction seen after adjustment for traditional risk factors. However, all ethnic groups (except
South Asian males) had persistently lower event rates than long-term residents after adjustment for all socio-demographic and risk factor variables. Significant differences in the hazard ratios between certain ethnic groups also remained, demonstrating that ethnic origin is an independent predictor of cardiovascular events.

Discussion

The CANHEART Immigrant study demonstrates that most immigrant groups to Canada have lower rates of major cardiovascular events than long-term residents of similar age, and that striking variations in the event rates exist between immigrants from different ethnic backgrounds. East Asian immigrants, comprised predominantly of ethnic Chinese, had the lowest burden of cardiac risk factors and events overall, although the event rate increased with greater duration in Canada. We also found certain high-risk groups such as South Asian immigrants, including those born in Guyana and immigrants born in Afghanistan and Iraq had a high burden of traditional risk factors and frequent cardiovascular events. Our findings demonstrate that the four traditional modifiable cardiac risk factors (smoking, lipids, hypertension, diabetes) originally identified from a White Caucasian cohort in the Framingham Heart Study and subsequently confirmed in major multiethnic epidemiological studies (e.g., Seven Countries Study, INTERHEART, INTERSTROKE) are important contributors to variations in cardiovascular event rates in migrant populations from very diverse ethnic backgrounds and countries of the world.\textsuperscript{15-18} However, our study also demonstrates that these factors do not explain all of the observed variation and highlights the need for further research to identify additional factors that contribute to the observed differences.

Our study results provide some new insights into the previously observed “healthy
immigrant” effect, whereby immigrants to some countries such as Canada appear to be relatively healthier at the time of immigration than the host population.19, 20 Contributing to the healthy immigrant effect may be lower smoking rates, which were notably lower in the Canadian immigrant populations compared with their source countries, such as for male immigrants from China and India.19 Obesity rates were also significantly lower in most immigrant groups. Smoking and obesity are important risk factors for other chronic conditions (e.g. cancer) that may have contributed to the poorer outcomes among long-term residents. In the 1960’s, Canada was the first country to use a points-based system to select skilled workers or economic immigrants, where preference is given to those who have experience in selected occupations, higher levels of education, English or French language skills, and are younger adults. Except refugees, all immigrants to Canada also undergo a medical examination pre-migration, and those found to have serious chronic medical conditions may be deemed inadmissible, although relatively few applicants are rejected for health reasons.21 Canada’s immigrant selection criteria and medical screening requirements may deter certain applicants and result in highly-selected migrants who are healthier than the average citizen in both their home and new countries. The lower cardiac risk factor score amongst immigrants who emigrated from Ontario further supports the notion that healthier individuals are more likely to migrate.

Our findings are in contrast to those from several studies in other high-income countries in Europe and the United States where immigrants’ cardiovascular health have been shown to be worse than the host population.5, 22, 23 These discrepancies may reflect differences in the types, region of origin, and lifestyle habits of immigrants migrating to different countries, the proportion of undocumented migrants, the health of the host population, the pre-migration medical screening requirements, and the availability of health care services.24 In the United
States, difficulties accessing health insurance have been frequently noted among legal immigrants, whereas new immigrants to Ontario receive access to its universal health care system within three months of arrival. Canada’s health care system, where no copayments are required to see physicians or visit hospitals, may be particularly important for immigrant populations, many of whom live in low income neighbourhoods, struggle to find employment as they adapt to their new country, and arrive from low and middle income countries with less well-established health care systems. As demonstrated by the similar revascularization/AMI ratio across ethnic groups and long-term residents, the Canadian system provides equitable access to invasive cardiac procedures whereas studies from the United States and the United Kingdom show that racial/ethnic disparities in access to cardiac procedures may exist.

Our findings within ethnic groups are generally consistent with previous studies conducted in other high-income countries. In Europe, Black immigrants have also been found to have high stroke rates, which have been partly attributed to high rates of hypertension and the protective effects of relatively high HDL levels, low smoking rates, and low fibrinogen levels. South Asian immigrants in this and other studies have been found to have a high burden of metabolic syndrome and insulin resistance, as evidenced by high rates of central obesity, diabetes, hypertension, triglycerides, and low HDL levels. The higher incidence of events observed amongst the East Asian immigrants with greater duration of stay in Canada are consistent with the Ni-Hon-San study which showed that Japanese immigrants to California and Hawaii had higher cardiovascular event rates with greater exposure to a Western-lifestyle than those who remained in Japan. Previous studies have also shown that diabetes rates and cholesterol levels are rapidly rising in the Chinese population in both Canada and East Asia from historically low levels which may contribute to the increasing event rates observed in our study.
with greater duration of stay and acculturation to Western diets and lifestyles.\textsuperscript{30,31}

Our study is unique in that it includes a very large sample of immigrants, representing 201 countries from all parts of the world, followed for a decade using linked electronic databases. However, a limitation is that significant residual variation between ethnic groups remains that cannot be completely accounted for by traditional risk factors or neighbourhood socioeconomic differences. Possible contributing factors that warrant additional research include a) variations in dietary practices, alcohol intake, and physical activity levels, b) pre-migration environmental exposures (urbanization, air pollution, second hand smoke, health care access), c) precision in measuring certain risk factors (e.g. measured blood pressure, incomplete smoking and lipid data), d) cultural differences in health-seeking behaviour, e) variations in the proportion and types of immigrants who decide to emigrate back to their home country, and f) genetic factors not yet identified.

In summary, we found striking variations in the burden of cardiac risk factors and incidence of major cardiovascular events amongst a population of over 800 thousand immigrants to Ontario, Canada. Our study provides new information that may assist clinicians and policy makers in developing strategies to prevent cardiovascular diseases in immigrant populations. A focus on the prevention, early identification and management of the classical cardiac risk factors coupled with provision of equitable access to health care services could potentially prevent many cardiovascular events. Additional studies to identify other modifiable risk factors contributing to outcome differences between immigrant populations are also warranted.

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Table 1. Baseline Characteristics of Ontario Immigrants and Long-term Residents

| Demographics                          | East Asian (N=174 167) | Black (N=84 914) | White-Western European (N=82 998) | Southeast Asian (N=68 239) | Latin American (N=55 173) | West Asian/Arab (N=71 770) | White-Eastern European (N=121 912) | South Asian (N=165 489) | All Immigrants (N=824 662) | Long-term Residents (N=5 200 258) |
|---------------------------------------|------------------------|------------------|-----------------------------------|-----------------------------|---------------------------|---------------------------|------------------------------------|--------------------------|-------------------------------|------------------------------|
| Age on arrival, years                 | 37.7 (11.4)            | 32.7 (10.0)      | 33.5 (10.3)                       | 35.6 (11.1)                 | 33.8 (10.6)               | 35.2 (10.7)               | 35.4 (9.8)                         | 36.8 (11.7)               | 35.6 (11.0)                    | na                           |
| Age on Jan 1, 2002, years             | 45.4 (11.6)            | 42.0 (9.5)       | 43.8 (10.1)                       | 44.4 (10.7)                 | 43.5 (10.3)               | 43.1 (10.3)               | 43.7 (9.5)                         | 44.2 (11.4)               | 44.0 (10.7)                    | 48.7 (11.8)                   |
| Female sex                            | 52.0%                  | 50.6%            | 50.1%                             | 60.2%                       | 48.9%                     | 42.3%                     | 49.9%                             | 46.7%                     | 49.9%                         | 52.2%                        |
| Education                              |                        |                  |                                   |                             |                           |                           |                                    |                          |                               |                               |
| ≤12 years of schooling                 | 47.5%                  | 64.2%            | 49.2%                             | 46.2%                       | 61.2%                     | 46.8%                     | 30.4%                             | 52.6%                     | 48.8%                         | na                           |
| Some post-secondary                    | 26.3%                  | 27.5%            | 31.4%                             | 25.5%                       | 26.4%                     | 21.5%                     | 38.5%                             | 19.3%                     | 27.0%                         | na                           |
| Completed university                   | 26.2%                  | 8.3%             | 19.4%                             | 28.3%                       | 12.3%                     | 31.7%                     | 31.1%                             | 28.0%                     | 24.2%                         |                              |
| Immigration class                      |                        |                  |                                   |                             |                           |                           |                                    |                          |                               |                               |
| Economic                               | 58.0%                  | 29.7%            | 56.5%                             | 43.2%                       | 30.3%                     | 42.9%                     | 33.5%                             | 39.5%                     | 43.0%                         |                              |
| Family class                           | 34.2%                  | 52.1%            | 42.0%                             | 46.9%                       | 46.2%                     | 27.3%                     | 29.3%                             | 47.5%                     | 40.1%                         | na                           |
| Refugee                               | 3.1%                   | 17.5%            | 0.4%                              | 9.7%                        | 22.8%                     | 28.8%                     | 36.8%                             | 12.5%                     | 15.2%                         |                               |
| Years in Ontario (up to Jan 1, 2002)   | 8.1                    | 9.5              | 10.5                              | 8.9                        | 9.9                       | 8.1                       | 8.5                                | 7.6                       | 8.6                            | na                           |
| Low-income neighbourhood               | 42.7%                  | 68.0%            | 38.4%                             | 60.2%                       | 63.9%                     | 51.8%                     | 53.1%                             | 58.1%                     | 52.9%                         | 35.8%                        |
| Country of birth income group          |                        |                  |                                   |                             |                           |                           |                                    |                          |                               |                               |
| High                                  | 43.6%                  | 19.9%            | 92.5%                             | 0.3%                        | 0.1%                      | 5.7%                      | 0.7%                              | 3.1%                      | 21.7%                         |                               |
| Middle                                | 49.9%                  | 46.4%            | 7.3%                              | 79.7%                       | 99.9%                     | 83.7%                     | 99.3%                             | 28.6%                     | 56.9%                         | na                           |
| Low                                   | 6.5%                   | 33.7%            | 18.2%                             | 19.9%                       | 0%                        | 10.6%                     | 0%                                | 68.3%                     | 21.4%                         |                               |

Data are mean (SD) or as labelled. Values are age- and sex-standardized to the 2006 Ontario census population (except age on arrival, age on January 1, 2002 and females), and ordered by male ranking on the primary outcome measure (See Table 3). Education is at the time of application for immigration. Family class includes immigrants who arrived as spouses, partners, parents, grandparents, or children of a Canadian citizen or permanent resident; Economic class includes skilled workers, entrepreneurs, the self-employed, live-in caregivers, investors and their dependents (e.g. spouses, parents and children). Columns do not add up to 100% because immigrants outside these classes (e.g., humanitarian and compassionate cases) are not shown (<1.7% of all immigrants). Low income neighbourhood is defined as neighbourhood income quintile=1 or 2, where quintile 1 has the lowest income. Country of birth income group is based on the World Bank’s 2006 classification. * na indicates not applicable.
## Table 2. Age-standardized Baseline Risk Factors for Cardiovascular Disease Among Ontario Immigrants and Long-term Residents

|                     | East Asian | Black              | White-Western European | Southeast Asian | Latin American | West Asian/Arab | White-Eastern European | South Asian | All Immigrants | Long-term Residents |
|---------------------|------------|--------------------|------------------------|----------------|----------------|------------------|------------------------|-------------|---------------|---------------------|
| **Males**           |            |                    |                        |                |                |                  |                        |             |               |                     |
| Current cigarette smoker, % | 23.3 (17.7-28.9) | 16.0 (10.8-22.7) | 24.7 (17.8-33.0) | 21.1 (16.3-27.5) | 26.1 (17.2-35.7) | 39.4 (23.4-50.3) | 32.7 (25.4-40.3) | 39.4 (25.4-40.3) | 16.5 (12.9-20.8) | 24.5 (22.0-27.0) |
| Hypertension, %     | 14.2 (13.9-14.6) | 23.2 (22.4-24.0) | 14.2 (13.7-14.7) | 24.9 (24.1-25.6) | 18.3 (17.6-19.1) | 15.8 (15.3-16.4) | 15.9 (15.4-16.5) | 15.9 (15.4-16.5) | 21.4 (21.0-21.8) | 17.9 (17.7-18.1) |
| Diabetes, %         | 6.2 (6.0-6.4) | 12.3 (11.7-12.9) | 4.7 (4.4-5.0) | 8.8 (8.4-9.3) | 9.8 (9.2-10.3) | 8.5 (8.1-9.0) | 4.6 (4.3-4.9) | 15.0 (14.7-15.3) | 8.8 (8.6-8.9) | 7.3 (7.3-7.4) |
| Mean cholesterol, mmol/L |              |                    |                        |                |                |                  |                        |             |               |                     |
| Total               | 5.21 (5.19-5.22) | 5.20 (5.17-5.22) | 5.46 (5.43-5.49) | 5.37 (5.34-5.39) | 5.40 (5.38-5.43) | 5.18 (5.16-5.20) | 5.45 (5.43-5.47) | 5.24 (5.22-5.25) | 5.29 (5.29-5.30) | 5.34 (5.34-5.34) |
| High density lipoprotein | 1.34 (1.34-1.35) | 1.35 (1.34-1.36) | 1.33 (1.32-1.34) | 1.28 (1.28-1.29) | 1.24 (1.23-1.25) | 1.19 (1.19-1.20) | 1.32 (1.31-1.32) | 1.18 (1.18-1.19) | 1.27 (1.27-1.28) | 1.29 (1.29-1.29) |
| Mean total cholesterol/high density lipoprotein ratio | 4.08 (4.06-4.09) | 4.07 (4.05-4.10) | 4.35 (4.31-4.38) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) | 4.38 (4.35-4.41) |
| Mean body-mass index (BMI), kg/m² | 23.5 (23.1-23.8) | 25.6 (24.8-26.3) | 27.5 (26.1-29.5) | 25.2 (24.3-26.0) | 26.9 (26.3-27.5) | 26.3 (26.6-27.5) | 25.4 (25.3-26.8) | 25.4 (25.3-26.8) | 27.1 (27.1-27.3) | 21.5 (21.0-22.0) |
| Obesity (BMI ≥30kg/m²), % | 2.4 (1.2, 4.1) | 12.4 (6.9, 21.1) | 14.7 (8.9, 21.1) | 10.6 (4.2, 18.0) | 15.8 (7.8, 25.2) | 9.5 (4.6, 15.3) | 16.2 (10.6, 22.1) | 8.6 (5.9, 11.8) | 10.2 (8.8, 11.7) | 21.5 (21.0, 22.0) |
| Cardiac risk factor score | 1.73 (1.72-1.75) | 2.06 (2.03-2.09) | 2.11 (2.09-2.13) | 2.32 (2.30-2.35) | 2.41 (2.38-2.44) | 2.52 (2.50-2.54) | 2.31 (2.29-2.33) | 2.36 (2.35-2.37) | 2.18 (2.17-2.18) | 2.28 (2.28-2.29) |
| **Females**         |             |                    |                        |                |                |                  |                        |             |               |                     |
| Current cigarette smoker, % | 1.7 (0.8-2.9) | 2.8 (1.3-4.8) | 13.3 (8.7-18.6) | 4.0 (1.7-7.0) | 7.9 (4.1-13.6) | 19.3 (12.2-29.0) | 20.9 (16.2-26.9) | 2.5 (1.3-4.2) | 8.6 (7.6-9.8) | 23.8 (23.3-24.4) |
| Hypertension, %     | 16.2 (15.9-16.6) | 31.3 (30.6-32.1) | 15.9 (15.4-16.4) | 25.8 (25.1-26.4) | 21.7 (20.1-22.4) | 17.4 (16.8-18.1) | 17.9 (17.4-18.4) | 21.7 (21.3-22.1) | 20.3 (20.2-20.5) | 21.3 (21.3-21.4) |
| Diabetes, %         | 5.8 (5.6-6.0) | 13.3 (12.8-13.8) | 4.4 (4.1-4.6) | 8.3 (8.0-8.7) | 10.2 (9.7-10.7) | 7.8 (7.4-8.2) | 3.6 (3.4-3.8) | 13.1 (12.8-13.4) | 8.2 (8.1-8.3) | 6.0 (5.9-6.0) |
| Mean cholesterol, mmol/L |              |                    |                        |                |                |                  |                        |             |               |                     |
| Total               | 5.13 (5.12-5.14) | 5.14 (5.12-5.14) | 5.34 (5.31-5.36) | 5.25 (5.23-5.27) | 5.28 (5.26-5.30) | 5.18 (5.16-5.20) | 5.36 (5.35-5.38) | 5.10 (5.09-5.12) | 5.20 (5.19-5.20) | 5.35 (5.35-5.36) |
| High density lipoprotein | 1.63 (1.63-1.64) | 1.56 (1.56-1.57) | 1.61 (1.60-1.62) | 1.55 (1.54-1.56) | 1.48 (1.47-1.49) | 1.48 (1.47-1.49) | 1.64 (1.63-1.65) | 1.38 (1.38-1.38) | 1.54 (1.54-1.54) | 1.60 (1.60-1.60) |
|                  | Mean total cholesterol/high density lipoprotein ratio | Mean body-mass index (BMI), kg/m² | Obesity (BMI ≥30kg/m²), % | Cardiac risk factor score |
|------------------|------------------------------------------------------|----------------------------------|---------------------------|--------------------------|
|                  | 3.31 (3.30-3.32)                                     | 22.2 (21.9-22.5)                 | 2.5 (1.1, 4.2)            | 1.49 (1.48-1.50)         |
|                  | 3.46 (3.44-3.48)                                     | 26.7 (25.9-28.0)                 | 23.8 (18.3, 32.8)         | 1.88 (1.86-1.90)         |
|                  | 3.52 (3.49-3.54)                                     | 26.0 (25.1-26.9)                 | 19.6 (12.1, 26.2)         | 1.64 (1.62-1.66)         |
|                  | 3.56 (3.54-3.58)                                     | 23.8 (23.2-24.5)                 | 6.9 (2.5, 12.2)           | 1.86 (1.84-1.88)         |
|                  | 3.76 (3.73-3.78)                                     | 26.3 (25.4-27.0)                 | 17.6 (10.6, 26.0)         | 1.97 (1.94-1.99)         |
|                  | 3.69 (3.67-3.72)                                     | 25.8 (24.8-26.7)                 | 15.4 (6.4, 24.6)          | 2.00 (1.98-2.02)         |
|                  | 3.46 (3.44-3.48)                                     | 25.2 (24.6-26.0)                 | 16.4 (12.1, 22.5)         | 1.75 (1.73-1.76)         |
|                  | 3.88 (3.86-3.89)                                     | 25.2 (24.4-25.7)                 | 10.7 (7.4, 14.2)          | 2.02 (2.01-2.03)         |
|                  | 3.57 (3.56-3.57)                                     | 24.7 (24.4-25.0)                 | 11.3 (9.7, 13.0)          | 1.79 (1.78-1.80)         |
|                  | 3.55 (3.55-3.56)                                     | 26.0 (25.9-26.0)                 | 18.5 (18.0, 18.9)         | 2.09 (2.09-2.09)         |

Data are mean or % with 95% confidence intervals unless otherwise stated. Smoking status is as of January 1, 2002 and is based on 8416 immigrants and 130 975 long-term residents surveyed in the 2000-2012 Canadian Community Health Surveys (CCHS) (with the exception of White-Western and Eastern Europeans where results were calculated from a study sub-population linkable to the CCHS; n=664 for Western Europeans and n=818 for Eastern Europeans). Lipid testing results were available for 272 399 (33%) immigrants and 1 478 632 (28%) long-term residents. The cardiac risk factor score is a measure of the traditional risk factor burden with higher scores indicating higher risk. See Supplemental Material for further details.
Table 3. Age-standardized Incidence of Major Cardiovascular Events by Ethnicity.

| Event                                                   | East Asian | Black | White-Western European | Southeast Asian | Latin American | West Asian/Arab | White-Eastern European | South Asian | All Immigrants | Long-term Residents |
|---------------------------------------------------------|------------|-------|-------------------------|-----------------|----------------|---------------------|------------------------|-------------|----------------|---------------------|
| Acute myocardial infarction (AMI)                       | N=83535    | N=41907| N=41434                 | N=27159         | N=28176        | N=41407            | N=61096                | N=88161     | N=412875       | N=2484554           |
| Stroke                                                  | 0.7 (0.6-0.8) | 1.5 (1.3-1.8) | 1.8 (1.6-2) | 1.9 (1.6-2) | 2.4 (2.1-2.7) | 2.5 (2.3-2.8) | 2.5 (2.3-2.7) | 3.5 (3.3-3.7) | 2.1 (2.0-2.1) | 3.0 (2.9-3.0) |
| AMI/Stroke ratio                                         | 0.7 (0.6-0.8) | 1.5 (1.3-1.8) | 0.9 (0.8-1.1) | 1.5 (1.3-1.7) | 1.3 (1.1-1.6) | 0.8 (0.7-0.9) | 1.3 (1.1-1.5) | 1.2 (1.1-1.3) | 1.0 (1.0-1.1) | 1.3 (1.3-1.3) |
| Revascularization                                       | 1.0 (1.0-1.2) | 1.0 (0.8-1.3) | 1.9 (1.6-2.4) | 1.2 (1.0-1.5) | 1.8 (1.5-2.3) | 3.2 (2.6-4.0) | 1.9 (1.7-2.3) | 3.0 (2.7-3.3) | 2.0 (1.9-2.1) | 2.3 (2.2-2.3) |
| Revascularization/AMI ratio                             | 1.8 (1.6-2.1) | 1.5 (1.3-1.9) | 1.6 (1.4-1.8) | 1.6 (1.4-1.9) | 1.4 (1.2-1.6) | 1.9 (1.7-2.1) | 1.8 (1.6-2.0) | 1.8 (1.7-1.9) | 1.7 (1.7-1.8) | 1.6 (1.6-1.6) |
| Cardiovascular death                                     | 0.4 (0.4-0.5) | 0.7 (0.6-0.9) | 0.8 (0.7-1.0) | 0.7 (0.6-0.9) | 0.7 (0.5-0.9) | 0.7 (0.6-0.9) | 1.2 (1.0-1.3) | 1.1 (1.0-1.2) | 0.8 (0.7-0.8) | 1.5 (1.5-1.5) |
| Either AMI, stroke, revascularization or cardiovascular death | 2.4 (2.2-2.5) | 4.7 (4.3-5.2) | 4.8 (4.5-5.1) | 5.4 (5.0-5.9) | 5.6 (5.2-6.1) | 6.7 (6.3-7.1) | 7.2 (6.8-7.5) | 8.9 (8.7-9.2) | 5.6 (5.5-5.7) | 8.1 (8.1-8.1) |

Data are per 1000 person-years (95% confidence interval) unless otherwise stated. Revascularization procedures include percutaneous coronary intervention or coronary artery bypass graft surgery. Cause of death is known for 96% of immigrants and 99% of long-term residents with cardiovascular death defined as death due to ischemic heart disease or stroke and unknown causes considered non-cardiovascular.
Table 4. Age-standardized Incidence of a Major Cardiovascular Event by Ethnicity and Length of Stay in Ontario, Canada Prior to Study Inception

| Length of stay in Ontario, Canada prior to study inception | Incidence of a major cardiovascular event |
|-----------------------------------------------------------|------------------------------------------|
|                                                           | East Asian | Black | White-Western European | Southeast Asian | Latin American | West Asian/Arab | White-Eastern European | South Asian | All immigrants  |
| Males <10 years                                           | 2.1 (1.9-2.3) | 4.7 (4.2-5.3) | 4.5 (4.0-5.0) | 5.0 (4.5-5.5) | 5.7 (5.1-6.4) | 6.7 (6.2-7.2) | 6.7 (6.2-7.2) | 8.5 (8.2-8.8) | 5.4 (5.3-5.5) |
| <10 years                                                | 2.9 (2.7-3.2) | 4.4 (3.8-5.0) | 4.8 (4.4-5.2) | 6.3 (5.6-7.1) | 5.2 (4.7-5.9) | 6.5 (5.9-7.1) | 7.2 (6.6-7.8) | 9.6 (9.1-10.2) | 5.7 (5.6-5.9) |
| 10+ years/10 years ratio                                 | 1.4 (1.2-1.6) | 0.9 (0.8-1.1) | 1.1 (0.9-1.2) | 1.3 (1.1-1.5) | 0.9 (0.8-1.1) | 1.0 (0.9-1.1) | 1.1 (1.0-1.2) | 1.1 (1.1-1.2) | 1.1 (1-1.1) |
| Females <10 years                                        | 1.0 (0.9-1.1) | 2.5 (2.2-2.8) | 2.0 (1.7-2.4) | 1.9 (1.7-2.1) | 2.7 (2.3-3.1) | 2.9 (2.6-3.3) | 2.4 (2.2-2.6) | 3.4 (3.3-3.6) | 2.3 (2.2-2.3) |
| <10 years                                                | 1.5 (1.4-1.7) | 3.0 (2.6-3.4) | 2.1 (1.8-2.3) | 2.3 (2.0-2.7) | 3.0 (2.6-3.4) | 2.6 (2.2-3.1) | 2.5 (2.2-2.8) | 3.6 (3.3-3.9) | 2.5 (2.4-2.6) |
| 10+ years/10 years ratio                                 | 1.6 (1.4-1.8) | 1.2 (1.0-1.4) | 1.0 (0.8-1.2) | 1.2 (1.0-1.5) | 1.1 (0.9-1.4) | 0.9 (0.7-1.1) | 1.0 (0.9-1.2) | 1.0 (0.9-1.2) | 1.1 (1.1-1.2) |

Data are per 1000 person-years (95% confidence interval) unless otherwise stated.
Figure Legends:

**Figure 1.** Countries of birth of 824,662 immigrants to Ontario, Canada (1985-2000) in the CANHEART immigrant study cohort.

**Figure 2.** Age-standardized incidence of a major cardiovascular event by country and region of birth among 29 countries of birth with at least 5000 immigrants, 2002-2011.

**Figure 3.** Age-standardized cardiac risk factor score versus incidence of a major cardiovascular event by ethnicity and country of birth, 2002-2011. Cardiac risk factor scores are a measure of the traditional cardiac risk factor burden in each group (see Supplemental Material for more details). Results by country of birth are among 29 countries with at least 5000 immigrants.

**Figure 4.** Relative risk of a major cardiovascular event using Cox proportional hazard modelling, 2002-2011. Independent variables were added sequentially from models A to E. The $R^2$ for each model indicates the proportion of variation in outcomes explained by each model. BMI indicates body mass index; CI, confidence interval; DM, diabetes mellitus; HDL, high density lipoprotein cholesterol; HTN, hypertension; and TC, total cholesterol.
Figure 1
Figure 2

Long-term Residents

East Asia

Western Europe/
United States

Sub-Saharan Africa/
Caribbean

Southeast Asia

Latin America

Middle East/West Asia

Eastern Europe

South Asia

Incidence, per 1000 person-years (95% CI)

Taiwan
Hong Kong
China
South Korea

United States
Portugal
United Kingdom

Ghana
Somalia
Ethiopia
Jamaica
Trinidad & Tobago

Vietnam
Philippines

Iran
Lebanon
Egypt
Afghanistan
Iraq

Romania
Yugoslavia
Russia
Poland

India
Bangladesh
Pakistan
Sri Lanka

Incidence, per 1000 person-years (95% CI)

Taiwan
Hong Kong
China
South Korea

United States
Portugal
United Kingdom

Ethiopia
Somalia
Ghana
Jamaica
Trinidad & Tobago

Vietnam
Philippines

Iran
Lebanon
Egypt
Iraq

Romania
Yugoslavia
Russia
Poland

Sri Lanka
India
Pakistan
Bangladesh
Figure 3
Figure 4
The Incidence of Major Cardiovascular Events in Immigrants to Ontario, Canada: The CANHEART Immigrant Study
Jack V. Tu, Anna Chu, Mohammad R. Rezai, Helen Guo, Laura C. Maclagan, Peter C. Austin, Gillian L. Booth, Douglas G. Manuel, Maria Chiu, Dennis T. Ko, Douglas S. Lee, Baiju R. Shah, Linda R. Donovan, Qazi Zain Sohail and David A. Alter

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SUPPLEMENTAL MATERIAL

The incidence of major cardiovascular events in immigrants to Ontario, Canada: The CANHEART Immigrant study

In addition to the material contained in this appendix, information about the CANHEART initiative and the Immigrant study (including a slide deck) can be found on the study web site at www.canheart.ca.

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Supplemental Methods

a) Data sources

Supplemental Figures 1 and 2 show the data sources used to identify the study population and study variables. A summary of the data sources used follows.

Canadian Immigration and Citizenship Permanent Resident (CIC) Database: Contains information from the application records for 2.9 million immigrants who landed in Ontario between 1985 and 2010. Data include permanent residents' demographic information such as country of birth, mother tongue, landing date, level of education, marital status and immigration category. Linkage to the Institute for Clinical Evaluative Sciences' (ICES) Registered Persons Database (see below) is described elsewhere.¹

Registered Persons Database (RPDB): Provides basic demographic information about anyone who has ever received an Ontario health card number. Key data variables include date of birth, date of death, sex, geographical information and time periods for which an individual was eligible for coverage under the Ontario Health Insurance Plan (OHIP). All health card numbers are encrypted before being linked to other databases.

Canadian Institute for Health Information Discharge Abstract Database (CIHI DAD): Comprises individual-level data from the discharge abstracts of Ontario hospitals for acute, chronic and rehabilitative care from 1988 onwards. Information includes admission and discharge dates, diagnoses, complications, procedures and comorbidities. Prior to April 2002, International Classification of Diseases (ICD)-9 coding was used with up to 16 diagnoses recorded in each abstract. Since April 2002, ICD-10 coding has been used with up to 25 diagnoses recorded.

Ontario Health Insurance Plan (OHIP) Claims Database: This database captures all reimbursement claims made since 1991 by registered health care providers who are eligible to claim under OHIP. This includes fee-for-service physicians (covering 94% of Ontario’s physicians), other health care providers and community-based labs. Excluded are services received in psychiatric hospitals, services provided by alternate funding plans (e.g. private insurance and federal programmes), diagnostic procedures performed on an inpatient basis (e.g. radiology, ECGs) and laboratory services performed in hospitals (inpatient or same day). Information includes encrypted service provider and specialty (if a physician), diagnosis, service provided, date of service and fee paid.

Ontario Hypertension Database (OHD): Validated registry of all Ontarians identified with hypertension since 1988 with demonstrated sensitivity of 73% and specificity of 95% compared with physician-assigned diagnoses identified in chart audits.² An individual is said to have hypertension if he/she has had one hospital admission with a hypertension diagnosis, or an OHIP claim with a hypertension diagnosis followed within two years by either an OHIP claim or a hospital admission with a hypertension diagnosis. The registry also includes the date of diagnosis using the first record of a hypertension diagnosis meeting the above criteria.

Ontario Diabetes Database (ODD): Validated registry of all Ontarians identified as having diabetes since 1991 with demonstrated sensitivity of 86% and specificity of 90% compared with physician-assigned diagnoses identified in chart audits.³ An individual is said to have diabetes if he/she has had two OHIP claims with a diabetes diagnosis, one OHIP service claim for diabetes management or intensive insulin therapy counselling, or one hospitalization for diabetes within two years. The registry also includes the date and source of diagnosis using the first record of a diabetes diagnosis meeting the above the criteria.

Canadian Community Health Survey (CCHS): An ongoing computer-assisted, population-based survey conducted since 2000 that uses a multi-stage cluster sampling design to collect information on self-reported health status,
health determinants and health care utilization for the Canadian population aged 12 and older. The CCHS includes respondents from all ten provinces and three territories in Canada. It is conducted in multiple languages to include non-English and non-French speaking residents, and uses sampling weights in data analyses to be representative of 98% of the Canadian population. Only responses up to 2010 are linkable to other databases because encrypted health card numbers for later respondents were not available at the time of the study.

Office of the Registrar General of Ontario Vital Statistics Database (ORGD): Contains information about all deaths registered in Ontario since 1990. Since health card numbers are not provided in this dataset, records are linked to the RPDB and other health administrative databases by deterministic (79%) and probabilistic (17%) data linkage. Additionally, as deaths prior to 2003 are classified using ICD-9 codes and deaths thereafter are classified using ICD-10, a single cause of death variable in ICD-9 format was created to facilitate analyses using cause of death.

Gamma Dynacare Medical Laboratories (GDML) Database: Provides outpatient results from laboratory tests performed as part of routine clinical care, including fasting lipid profiles and fasting glucose tests from 2002 onwards. GDML is a major commercial laboratory provider in Ontario with geographic distribution across Ontario, but with a higher concentration in the Greater Toronto Area where a majority of immigrants reside. Our analyses indicate that coverage for the Ontario population for lipid and glucose tests is approximately 25-30% with demographic characteristics of people tested at GDML clinics similar to those tested elsewhere. Key variables include test performed, service date, specimen collection time and test result.

Ontario Visible Minority Database: Dataset that uses validated lists of South Asian and Chinese surnames to assign an ethnicity of Chinese or South Asian (Canada’s two largest visible minority groups), or “general” to individuals in the RPDB. Surnames not unique to the South Asian or Chinese populations are purposely excluded from the lists. Specificity is over 99.5% and positive predictive value is 89 to 92%; sensitivity is 50% for South Asians and 80% for Chinese.

Ontario Drug Benefit Database (ODB): Contains information on prescription drug claims covered by and made to the Ontario Drug Benefit programme. This programme primarily covers drug expenses for Ontarians with a valid OHIP card who are 65 years and older or residents of long-term care facilities, but also provides coverage to others such as those receiving social assistance. Key data elements include dispensing date, drug identifier, quantity supplied and whether the recipient is a resident of a long-term care facility.

b) Study variables

A summary of data sources used to develop study variables is provided in Supplemental Figures 1 and 2.

The RPDB was used to obtain data for sex, date of birth, date of death and OHIP eligibility dates. Other socio-demographic information for immigrants, including date of immigration to Ontario, country of birth and mother tongue was obtained from the CIC database. An immigrant’s ethnicity was determined from country of birth, mother tongue and surname (for Chinese and South Asian ethnicity) using validated algorithms. To identify White immigrants of Western European origin versus Eastern European origin, we used classifications from the United Nations Statistics Division and the Organization for Economic Co-operation and Development (OECD). Immigrants from countries of Central and Eastern Europe (Albania, Belarus, Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Republic of Moldova, Romania, Russia, Slovakia, Ukraine, former USSR), Yugoslavia and former republics of Yugoslavia (Bosnia-Herzegovina, Croatia, Macedonia, Montenegro, Serbia, Slovenia) and the Democratic Republic of Germany were classified as White-Eastern European while White immigrants from all other countries were classified as White-Western European. We classified immigrants from
South Africa as White because our analysis of data from the CCHS indicated that 89% of immigrants from South Africa reported their ethnicity as White.

Baseline hypertension and diabetes were defined based on diagnosis occurring prior to January 1, 2002. Individuals with baseline hypertension and diabetes were identified from the OHD and ODD. Smoking status and body mass index (BMI) were estimated from 8416 immigrants and 130 975 long-term residents who responded to the CCHS. Lipid and glucose test results were available for 272 399 (33%) immigrants and 1 478 632 (28%) long-term residents from the GDML database using the first test result available between 2002 and 2011. Tests examined included total cholesterol (TC), low density lipoprotein (LDL) and high density lipoprotein cholesterol (HDL), triglycerides, total to high density lipoprotein cholesterol ratio (TC/HDL) and fasting serum glucose. TC, HDL, and TC/HDL were selected as the primary lipid measures since previous studies and analyses of the CANHEART data identified these to be the best predictors of cardiovascular events. Socio-demographics of the immigrant study population with laboratory data available are similar to the overall study population, while those with CCHS data available are more likely to have completed university than the overall study population (Supplemental Table 1).

Our primary outcome (or clinical endpoint) was defined as a composite measure consisting of either a hospitalization with a most responsible diagnosis of acute myocardial infarction, stroke, revascularization with percutaneous coronary intervention or coronary artery bypass surgery, or death due to ischemic heart disease or cerebrovascular disease. ICD-9 and ICD-10 codes used to define these events are listed in Supplemental Table 2 and have been previously validated using chart reviews. Hospitalization data was obtained from the CIHI DAD while cause of death was determined from the ORGD. Deaths in the study population where cause of death is unknown (4% of immigrants and 1% of long-term residents) were classified as non-cardiovascular deaths.

c) Data analysis

Analyses were conducted comparing eight major ethnic groups and 29 countries of birth with at least 5000 immigrants in the study population. Categorical variables were examined with frequency tables and chi-square tests. Continuous variables were examined using one-way ANOVA. All estimates for socio-demographic characteristics, cardiovascular risk factors, and outcomes were directly age-standardized to the 2006 Ontario census population in five-year age bands (30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74), with the exception of age on landing, age on January 1, 2002 and percentage of females.

For analyses of lipid and glucose levels, the age at the time of the laboratory test was used for standardization (30-34, 35-39, etc., 70-74, 75-84) since the time of testing varied across the cohort. Further details describing the use of CCHS data to obtain smoking prevalence and BMI estimates are provided separately due to the complexity of the methods used. Due to our study’s large sample size, we report 95% confidence intervals as they are more meaningful than p-values.

Sex-stratified, sequential Cox proportional hazard modelling was performed to investigate the incremental contribution of known socio-demographic and traditional cardiovascular risk factors on differences in the primary outcome of a major cardiovascular event between ethnic groups and the long-term resident cohort. Time to our primary outcome was defined in months, and individuals were censored when they emigrated from Ontario or their eligibility for OHIP lapsed (if ineligibility lasted for greater than one continuous year during the 10 year follow-up period). Beginning with an unadjusted model, subsequent models included age first, followed by the addition of socioeconomic status (SES) measured by neighbourhood income quintile, and then the addition of the four traditional cardiovascular risk factors – smoking, hypertension, diabetes, TC and HDL. A final model included BMI. The proportional hazards assumption was tested by including time by ethnic group interaction terms into the
models and examining their significance at p<0.05. In the full risk-adjusted model, the assumption was met for all female ethnic groups and three of eight male ethnic groups (East Asian, South Asian and West Asian/Arab). However, we report hazard ratios as time-averaged effects of ethnicity recognizing that the reason for varying hazards over time observed in some male ethnic groups requires additional research.

d) Smoking and body mass index (BMI) estimates

Data from the CCHS were used to determine smoking prevalence as of the year 2002 and BMI.

Inclusions/Exclusions: Respondents from the 2000-2012 CCHS cycles who reported they arrived in Canada from 1985-2000 and were without a history of heart disease or stroke were included in the analysis. A long-term resident comparison sample included immigrants who arrived in Canada prior to 1985 and individuals who were born in Canada. Responses to a question regarding the cultural/racial background of the respondent were used to classify individuals into ethnic groups (Supplemental Table 3). Individuals reporting multiple ethnic origins were excluded from the analysis. To generate smoking prevalence and mean BMI estimates for White-Western European and White-Eastern European groups, a sub-sample of the CCHS was linked to the CANHEART immigrant cohort based on their country of birth. This sub-sample included 664 White-Western Europeans and 818 White-Eastern Europeans.

Smoking prevalence and mean BMI were calculated by ethnic group and sex, and were weighted using Statistics Canada’s survey weights to generate estimates representative of the Canadian population and directly age-standardized to the Ontario 2006 census population. Due to small cell sizes for certain ethnic groups, we used the Ontario census 2006 population in four age-bands (30-39, 40-49, 50-59, 60-74) as the standard population.

Smoking Prevalence: Smoking status at 2002 was estimated retrospectively among respondents aged 30-74 on January 1, 2002 (7352 immigrants and 126 939 long-term residents) based on respondents’ answers to questions regarding their date of birth, current smoking status at their survey date and when they stopped smoking (if they were a former daily or occasional smoker). Current daily and occasional smokers were classified as smokers at 2002. For individuals who reported being a former daily or occasional smoker, information regarding the date of smoking cessation was used to estimate smoking status at 2002. For example, an individual interviewed in 2011 was classified as a non-smoker in 2002 if they reported quitting nine or more years ago (during or prior to 2000).

Mean BMI: BMI in kg/m² was calculated among respondents aged 30-74 on the survey date (8416 immigrants and 130 975 long-term residents) based on their self-reported height in metres and weight in kilograms at the time of the survey. Individuals who reported being pregnant at the time of the survey were excluded from the BMI analysis.

Main variables used in the analysis of CCHS data (2000-2012)

| Cycle     | Smoking status | Quit smoking | Height    | Weight    |
|-----------|----------------|--------------|-----------|-----------|
| 2000/2001 | smkadsty       | Scaadqui     | hwtdhtm   | hwtdwtk   |
| 2003/2004 | smkcdsty       | Smkcdstp     | hwtdhtm   | hwtdwtk   |
| 2005/2006 | smkedsty       | Smkedstp     | hwtedhtm  | hwtedwtk  |
| 2007/2008 | smkdsty        | Smkdstp      | hwtdhtm   | hwtdwtk   |
| 2009/2010 | smkdsty        | Smkdstp      | hwtdhtm   | hwtdwtk   |
| 2011/2012 | smkdsty        | Smkdstp      | hwtdhtm   | hwtdwtk   |
Development of a CANHEART cardiac risk factor score

To measure the burden of traditional cardiovascular risk factors and as a comparison with the observed 10-year risk of a major cardiovascular event between ethnic groups and long-term residents, we applied a modification of the methodology used to develop the Framingham risk score to our immigrant and long-term resident study populations.\(^\text{10}\)

We developed a CANHEART cardiac risk factor score as a points-based risk score based on results from a multivariate Cox proportional hazards model predicting 10-year risk of the primary study outcome. Predictors in our model were age, baseline smoking, hypertension and diabetes status, and TC and HDL levels. Sex-specific models were developed treating age as a continuous variable while TC and HDL levels were categorized following cut points originally developed by The Adult Treatment Panel III and used in Framingham risk functions predicting 10-year risk of hard coronary artery disease.\(^\text{10}\)

Where TC or HDL test results or smoking status were missing, multiple imputation using complete observations and 5 imputation datasets was conducted. TC and HDL test results were available for 281,397 immigrants and 1,519,084 long-term residents, and smoking status was known for 4080 immigrants and 89,160 long-term residents. Variables used in the imputations for the immigrant cohort were age on January 1, 2002, sex, ethnic group, education, marital status, ability to speak English or French, immigration class, year of arrival in Ontario, Canada, baseline hypertension, baseline diabetes, primary outcome and time to the primary outcome. As variables related to immigration do not apply to or were unavailable for long-term residents, those used for imputations in the long-term resident cohort included: age on January 1, 2002, sex, baseline hypertension, baseline diabetes, primary outcome and time to the primary outcome. These variables were chosen because they were either predictive of TC, HDL or smoking status, were potentially related to our primary outcome, or they could help reduce any participant biases that may be present in our complete data.\(^\text{11}\) Since age, TC, and HDL levels were not normally distributed, they were log transformed in the imputations. We assumed values were missing at random since Gamma Dynacare Medical Laboratories has laboratories all over Ontario and the CCHS is sampled to be representative of the Canadian population. A comparison of observed and imputed mean TC and HDL levels and smoking status by ethnicity demonstrated similar values.

Model coefficients for each risk factor without interactions in each of the sex-specific models are shown in Supplemental Table 4. C-statistics from each of the five imputed datasets were averaged to get an overall sex-specific c-statistic. In each model, the beta coefficient for age was used to determine a constant that is equivalent to a risk increment associated with a five-year increase in age. This constant was considered the number of regression coefficient units equivalent to one point in the scoring system. The difference between the beta coefficient for each risk factor category and that of its reference category, divided by the age-derived constant was calculated to assign a point score for each risk factor category (Supplemental Table 5). The reference category was assigned zero points.

A risk score for each individual in the immigrant and long-term resident cohorts was calculated as the sum of the risk factor points. Individual scores could range from -4 to 14 for males and -3 to 13 for females, with lower scores indicating more favourable risk factors (e.g. youngest age, non-smoke, no hypertension or diabetes, low TC and high HDL) and higher scores indicating less favourable risk factors and higher cardiovascular risk. Individual risk scores were averaged to obtain a mean score for each ethnic group and the long-term resident cohort. Since risk factors such as hypertension and diabetes are associated with age, and age varied across the ethnic groups and the long-term resident cohort, we age-standardized the final mean CANHEART cardiac risk factor scores.

All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA) or R software version 2.15.1.\(^\text{12}\)
**Supplemental Table 1.** Baseline Characteristics of the CANHEART Immigrant Cohort Versus Sub-populations with Lipid Test Results and in the 2000-2012 Canadian Community Health Surveys (CCHS)

|                           | Overall (N=412 875) | With TC/HDL ratio result (N=127 051) | CCHS (N=3451) | Overall (N=411 787) | With TC/HDL ratio result (N=145 348) | CCHS (N=3901) |
|---------------------------|---------------------|--------------------------------------|---------------|---------------------|--------------------------------------|---------------|
| Age on landing, years     | 35.1 (10.5)         | 35.3 (10.4)                          | 33.6 (12.8)   | 36.1 (11.4)         | 36.3 (11.2)                          | 33.8 (16.3)   |
| Age on January 1, 2002, years | 43.5 (10.1)         | 43.9 (10.0)                          | 42.1 (10.9)   | 44.4 (11.2)         | 44.7 (10.9)                          | 42.3 (15.4)   |
| Education                 |                     |                                      |               |                     |                                      |               |
| ≤12 years of schooling    | 39.1%               | 41.9%                                | 26.8%         | 49.7%               | 53.1%                                | 33.4%         |
| Some post-secondary       | 29.2%               | 29.2%                                | 3.3%          | 28.0%               | 27.0%                                | 4.4%          |
| Completed university      | 31.7%               | 29.0%                                | 69.9%         | 22.3%               | 19.9%                                | 62.1%         |
| Marital status,           |                     |                                      |               |                     |                                      |               |
| Single                    | 33.0%               | 31.3%                                | 6.7%          | 24.0%               | 23.2%                                | 8.1%          |
| Married/common-law        | 64.6%               | 66.5%                                | 86.9%         | 68.0%               | 68.7%                                | 76.1%         |
| Separated/divorced/widowed| 2.4%                | 2.2%                                 | 6.3%          | 8.0%                | 8.1%                                 | 15.7%         |
| Unable to communicate in  | 30.1%               | 32.3%                                | Not available | 38.5%               | 41.3%                                | Not available |
| either English or French  |                     |                                      |               |                     |                                      |               |
| Immigration class         |                     |                                      |               |                     |                                      |               |
| Economic                  | 46.7%               | 44.9%                                | Not available | 43.7%               | 42.0%                                | Not available |
| Family class              | 31.6%               | 32.5%                                | 41.8%         | 41.8%               | 42.4%                                |               |
| Refugee                   | 20.3%               | 21.1%                                | 13.2%         | 13.2%               | 14.2%                                |               |
| Other                     | 1.5%                | 1.5%                                 | 1.4%          | 1.4%                |                                      |               |
| Years in Ontario (up to  | 8.5 (4.2)           | 8.6 (4.2)                            | 9.5 (6.7)     | 8.3 (4.0)           | 8.5 (4.0)                            | 9.5 (7.5)     |
| January 1, 2002)          |                     |                                      |               |                     |                                      |               |
| Hypertension              | 12.2%               | 15.8%                                | 15.6%         | 14.1%               | 16.9%                                | 15.8%         |
| Diabetes                  | 5.9%                | 8.2%                                 | 6.8%          | 5.9%                | 7.5%                                 | 6.5%          |

Data are mean (SD) or %. For the overall population and sub-population with TC/HDL results, education is at the time of application for immigration, family class includes immigrants who landed as spouses, partners, parents, grandparents, or children of a Canadian citizen or permanent resident, and economic class includes skilled workers, entrepreneurs, the self-employed, live-in caregivers, investors and their dependents (e.g. spouses, parents and children). Results for the CCHS population are among respondents for whom smoking was calculated, based on responses at the time of survey unless otherwise stated, and are weighted using Statistics Canada’s survey weights with standard deviation determined using bootstrapping. SD indicates standard deviation; TC/HDL, total cholesterol/high density lipoprotein.
**Supplemental Table 2.** International Classification of Diseases Cardiovascular Event Codes

| Cardiovascular Event                                    | ICD-9 (unless otherwise stated) | ICD-10 (unless otherwise stated) |
|---------------------------------------------------------|---------------------------------|---------------------------------|
| Acute myocardial infarction\(^{13}\)                    | 410                             | I21, I22                        |
| Stroke\(^{14}\)                                         | 430, 431, 434, 436, 3623        | I60, I61, I63 (excluding I63.6), I64, H341 |
| Congestive heart failure\(^{15}\)                        | 428                             | I50                             |
| Percutaneous coronary intervention\(^{16}\)             | CCP codes: 4802, 4803, 4809     | CCI codes: 1IJ50, 1IJ57GQ       |
| Coronary artery bypass graft surgery\(^{16}\)           | CCP code 481                    | CCI code 1IJ76                  |
| Death due to cardiovascular disease\(^{5}\)              | 410-414, 430-438                | I20-25, I60-69                  |

CCI indicates Canadian Classification of Health Interventions; CCP, Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures; ICD, International Classification of Disease.
**Supplemental Table 3.** Ethnicity of CANHEART Long-term Residents linked to the 2000-2010 Canadian Community Health Surveys (CCHS)

| Ethnic group         | Arrived in Canada prior to 1985 (N=14 349) | Born in Canada (N=71 666) | Overall (N=86 015) |
|----------------------|---------------------------------------------|---------------------------|-------------------|
| White                | 12 183                                      | 71 219                    | 83 402 (97.0%)    |
| Black                | 561                                         | 121                       | 682 (0.8%)        |
| East Asian           | 522                                         | 248                       | 770 (0.9%)        |
| Southeast Asian      | 306                                         | 16                        | 322 (0.4%)        |
| South Asian          | 534                                         | 26                        | 560 (0.7%)        |
| West Asian/Arab      | 111                                         | 18                        | 129 (0.1%)        |
| Latin American       | 132                                         | 18                        | 150 (0.2%)        |
| **Overall**          | **14 349 (16.7%)**                          | **71 666 (83.3%)**        | **86 015 (100%)** |
**Supplemental Table 4.** Cox Proportional Hazards Model β-Coefficients Underlying the CANHEART Cardiac Risk Factor Score (derived using the Framingham Risk Score methodology)

| Risk Factor                              | Males                      | Females                    |
|------------------------------------------|----------------------------|-----------------------------|
|                                          | β-Coefficient | Hazard Ratio | P-value | β-Coefficient | Hazard Ratio | P-value |
| Age, years                               | 0.07           | 1.07         | <.0001  | 0.08           | 1.08         | <.0001  |
| Hypertension                             | 0.40           | 1.49         | <.0001  | 0.51           | 1.67         | <.0001  |
| Diabetes                                 | 0.59           | 1.81         | <.0001  | 0.84           | 2.31         | <.0001  |
| Total cholesterol, mmol/L (mg/dL)        |                |              |         |                |              |         |
| < 4.14 (< 160)                           | -0.23          | 0.79         | <.0001  | -0.18          | 0.83         | <.0001  |
| **4.14 – 5.15 (160 – 199)**              | N/A            | N/A          | N/A     | N/A            | N/A          | N/A     |
| 5.16 – 6.19 (200 – 239)                   | 0.15           | 1.16         | <.0001  | 0.13           | 1.14         | <.0001  |
| 6.20 – 7.22 (240 – 279)                   | 0.32           | 1.38         | <.0001  | 0.28           | 1.33         | <.0001  |
| ≥ 7.23 (≥ 280)                           | 0.51           | 1.67         | <.0001  | 0.49           | 1.63         | <.0001  |
| HDL cholesterol, mmol/L (mg/dL)          |                |              |         |                |              |         |
| < 1.03 (< 40)                            | 0.26           | 1.29         | <.0001  | 0.25           | 1.28         | <.0001  |
| **1.03 – 1.28 (40 – 49)**                | N/A            | N/A          | N/A     | N/A            | N/A          | N/A     |
| 1.29 – 1.53 (50 – 59)                     | -0.17          | 0.84         | <.0001  | -0.16          | 0.85         | <.0001  |
| ≥ 1.54 (≥ 60)                            | -0.41          | 0.67         | <.0001  | -0.45          | 0.64         | <.0001  |
| Smoking                                  | 0.57           | 1.77         | <.0001  | 0.61           | 1.84         | <.0001  |
| C-statistic                              | 0.78           | 0.82         |         |                |              |         |

Categories in bold are the reference categories.
**Supplemental Table 5. Scoring Algorithm for the CANHEART Cardiac Risk Factor Score**

| Risk Factor                        | Category | Males’ Points | Females’ Points |
|------------------------------------|----------|---------------|-----------------|
| Age (years)                        |          |               |                 |
|                                    | 30-34    | -2            | -2              |
|                                    | 35-39    | -1            | -1              |
| **40-44**                          | 0        | 0             |                 |
|                                    | 45-49    | 1             | 1               |
|                                    | 50-54    | 2             | 2               |
|                                    | 55-59    | 3             | 3               |
|                                    | 60-64    | 4             | 4               |
|                                    | 65-69    | 5             | 5               |
|                                    | 70-74    | 6             | 6               |
| Hypertension                       |          | 1             | 1               |
| Diabetes                           |          | 2             | 2               |
| Total cholesterol mmol/L (mg/dL)   |          |               |                 |
| < 4.14 (< 160)                     | -1       | 0             |                 |
| **4.14 – 5.15 (160 – 199)**        | 0        | 0             |                 |
| 5.16 – 6.19 (200 – 239)            | 0        | 0             |                 |
| 6.20 – 7.22 (240 – 279)            | 1        | 1             |                 |
| ≥ 7.23 (≥ 280)                     | 2        | 1             |                 |
| HDL cholesterol mmol/L (mg/dL)     |          |               |                 |
| < 1.03 (< 40)                      | 1        | 1             |                 |
| **1.03 – 1.28 (40 – 49)**          | 0        | 0             |                 |
| 1.29 – 1.53 (50 – 59)              | -1       | 0             |                 |
| ≥ 1.54 (≥ 60)                      | -1       | -1            | -1              |
| Smoking                            |          | 2             | 2               |

Categories in bold are the reference categories.
Supplemental Figure 1. CANHEART Study Population Selection and Data Sources

A. Immigrant Population Selection

Immigrants arriving in Ontario between 1985 and 2000; have a valid encrypted health card number and known sex (N=1 415 644)

Exclude if on January 1, 2002:
- <30 or >74 years (n=511 557)
- No longer living in Ontario (n=27 417)
- Died or not eligible for OHIP (n=35 139)

Exclude if known hospitalization between January 1, 1990 and December 31, 2001 for AMI, stroke, CHF or revascularization with PCI or CABG surgery (n=9485)

Exclude if:
- Long-term care resident between 1997 and 2001 (n=142)
- Unable to assign ethnicity based on country of birth, mother tongue and surname (n=7242)

Primary prevention cohort of immigrants to Ontario (N=824 662)

Data Sources

- Citizenship and Immigration Canada Permanent Resident Database (CIC) linked to Registered Persons Database (RPDB)
- CIHI Hospital Discharge Abstract Database
- Ontario Drug Benefit Database, Ontario Visible Minority Database and CIC

B. Long-term Resident Population Selection

Residents of Ontario (not in the CIC database) with a valid encrypted health card number and known sex as of January 1, 2002 (N=12 492 449)

Exclude if on January 1, 2002:
- <30 or >74 years (n=5 728 773)
- No longer living in Ontario (n=219 875)
- Died or not eligible for OHIP (n=1 150 036)

Exclude if known hospitalization between January 1, 1990 and December 31, 2001 for AMI, stroke, CHF or revascularization with PCI or CABG surgery (n=186 327)

Exclude if:
- Long-term care resident between 1997 and 2001 (n=7180)

Primary prevention cohort of long-term residents of Ontario (N=5 200 258)

Data Sources

- CIC, RPDB
- CIHI DAD
- Ontario Drug Benefit Database
Supplemental Figure 2. CANHEART Data Sources

- **Socio-demographics**
  - CIC
  - RPDB
  - Ontario Visible Minority Database

- **Cardiovascular Disease Risk Factors**
  - Canadian Community Health Survey
  - Ontario Hypertension Database
  - Ontario Diabetes Database
  - Gamma-Dynacare Medical Laboratories Database

- **Clinical Outcomes**
  - CIHI DAD
  - Registrar General of Ontario Vital Statistics Database

Encrypted health card number / unique identifier
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