Increasing Prevalence and Incidence of Atherosclerotic Cardiovascular Disease in Adult Patients in Ontario, Canada From 2002 to 2018

Erin S. Mackinnon, PhD,a Ron Goeree, BA, MA,b,c Shaun G. Goodman, MD, MSc,d Raina M. Rogoza, MSc,a Millicent Packalen, BSc(Hons),a Louisa Pericleous, PhD,a Ponda Motsepe-Ditshego, MD,a and Paul Oh, MD, MSc, FRCPCe

a Amgen Canada Inc, Mississauga, Ontario, Canada
b Goeree Consulting Ltd, Hamilton, Ontario, Canada
c Professor Emeritus, McMaster University, Hamilton, Ontario, Canada
d St. Michael’s Hospital, University of Toronto, Toronto, Ontario, Canada
e Toronto Rehabilitation Institute, Toronto, Ontario, Canada

ABSTRACT

Background: Cardiovascular disease is the leading cause of death in Canada. However, limited data are available on the prevalence of atherosclerotic cardiovascular disease (ASCVD) in Canada. The study objective was to describe the incidence and prevalence of ASCVD in adult patients in Ontario, Canada, and to evaluate temporal trends for subsequent ASCVD events among those with new-onset ASCVD.

Methods: This retrospective, observational study identified ASCVD incidence and prevalence data from the Institute for Clinical Evaluative Sciences Data Repository for adults from Ontario. Overall prevalence was established for the period from 2002 to 2018. Incident cases from April 1, 2005 to March 2016 were then identified, and followed

Cardiovascular disease (CVD) is the leading cause of death worldwide; an estimated 17.9 million people died from CVD in 2016, representing 31% of all global mortality.1 Atherosclerotic cardiovascular disease (ASCVD) typically encompasses a range of cerebral, cardiac, and peripheral vascular diagnoses, events, and revascularization procedures.2,3 Of these, myocardial infarction (MI) is highly prevalent and is one of the predominant causes of all inpatient hospitalizations in Canada.4,5 Patients with ASCVD have a high risk of cardiovascular events and recurrent events.6-8 Indeed, atherosclerosis is responsible for ischemic heart disease and stroke, which were identified as the leading causes of mortality after cancer in Canada and accounted for approximately 1 of 4 deaths in 2018.9

Globally over the past few decades, CVD event and mortality rates have decreased.10,11 In Canada, although the mortality rate due to ischemic heart disease has been steadily decreasing since 2000, the age-standardized prevalence of diagnosed ischemic heart disease has remained stable, being 7.1% in 2000 and 7.8% in 2015.12 A study conducted by the Cardiovascular Health in Ambulatory Care Research Team (CANHEART) initiative in Ontario, Canada, showed that despite improvements in ASCVD diagnosis and treatment guidelines, the average decline in annual rates during 1994-2012 in hospitalizations and deaths due to major
up to 2018. Primary outcomes were date and type of index event/procedure, patient characteristics/baseline demographics, and comorbidities. Secondary outcomes assessed were time from first to second ASCVD event, subsequent event(s) and/or mortality, and type of subsequent event(s) relative to the type of index/primary event.

Results: A total of 1,042,621 eligible prevalent ASCVD cases were identified; of these, 743,309 patients (69%) were newly diagnosed with incident ASCVD. The 10-year prevalence rates for all ASCVD subtypes increased over the study period. Overall event incidence rates per 1000 person-years were mostly stable or increased. Among incident cases, 50% experienced subsequent events over the study period.

Conclusions: This observational study demonstrated increasing prevalence and high incidence of new ASCVD diagnoses in adults from Ontario, over the study period. These data, together with the substantial number of subsequent events in ASCVD patients, demonstrate significant clinical burden of this disease in Ontario.

Materials and Methods

Study design, population, and data source

This retrospective, observational study used administrative health data from the province of Ontario, Canada maintained at the Institute for Clinical Evaluative Sciences (ICES) Data Repository (Supplemental Table S1). This study focused on identification and characterization of prevalence and incidence data of ASCVD events and procedures.

Incidence data for all adult patients with an initial (index) ASCVD event between April 1, 2005 and March 31, 2016 (Supplemental Fig. S1) were identified from the ICES database and included in this analysis. To determine if these were new (incident) events, patients with a diagnostic code for an ASCVD event within a 2-year lookback period (from April 1, 2003) were excluded from the incident cases. This exclusion was used to ensure that only index events (ie, first ASCVD event) were included; it also provided patient baseline characteristics for this cohort. ASCVD incidence was then calculated for the time period 2005 to 2016. The incidence of ASCVD was described by year as the number of new cases of ASCVD identified from April 1 to March 31 of the following year as a proportion of the population present within the ICES database (adults in Ontario aged ≥ 18 years) who did not have ASCVD. Follow-up on these incident cases was done until 2018, to gain an understanding of subsequent ASCVD events.

Overall prevalence for the study cohort was established by identification of patients given a diagnosis of ASCVD between April 1, 2002 and March 31, 2018 (Supplemental Figure S1). Prevalent ASCVD cases were then assessed and reported as 5- and 10-year prevalence. The overall prevalence over time of ASCVD was described by the number of new cases of ASCVD identified from April 1 to March 31 (numerator) of the given period as a proportion of the population present within the entire ICES database (adults in Ontario aged ≥ 18 years; denominator).

Based on the definition in the 2016 Canadian Cardiovascular Society (CCS) dyslipidemia management guidelines, in this study, ASCVD included coronary, cerebrovascular, and peripheral events. Coronary events included MI, PCI, and coronary artery bypass graft surgery (CABG), as well as a hospitalization or emergency room visit for unstable angina. Cerebrovascular events included ischemic stroke, transient ischemic attack (TIA), and carotid endarterectomy/stenting. Peripheral events included symptomatic peripheral artery
disease (PAD), peripheral artery angioplasty/stenting, peripheral artery bypass surgery, peripheral artery endarterectomy, and aortic aneurysm.

**Study variables and outcomes**

Variables of interest were extracted from the ICES databases up to 2 years prior to the date of the index event. Date and type of event were identified using diagnostic codes from the International Classification of Diseases, versions 9 and 10 (ICD-9 and -10; Supplemental Table S2). Patient characteristics at the time of hospitalization for events were collected, including average age at the time of the index event/procedure, gender, and LDL-C test results. Diabetes, hypertension, and hypercholesterolemia comorbidities were identified by ICD coding and ICES predefined cohorts/databases; respective Charlson Comorbidity Index (CCI) scores were extracted.

Secondary outcomes assessed were the time from the first ASCVD event to the second event, subsequent event(s) and/or mortality, and type of second and/or subsequent event(s) relative to the type of index/primary event. Event types within each of the groups (coronary, cerebrovascular, and peripheral events/procedures) were considered related. Related events occurring within 30 days were counted as one event, with precedence given to the event that came first in the hierarchical order listed above. For instances in which unrelated events occurred within 30 days of each other, both events were counted (the first was recorded as the index event, and the second as a subsequent event). Data were collected for deaths occurring within the given study period. For patients with a date of death, the time from the index event to the date of death was recorded. Deaths (all-cause mortality) were extracted as subsequent events only. Deaths that occurred within 30 days of an MI, aortic aneurysm, or ischemic stroke were considered related to those events and were not counted as a subsequent event. Deaths that occurred more than 30 days after these related events, and deaths that occurred within 30 days of unrelated events, were counted as subsequent events.

**Statistical methods and ethics approval**

Descriptive statistics were used to describe the study outcomes, including means, medians, and ranges. Event rates were calculated per 1000 person-years. No statistical analyses were performed to assess significance. The study protocol was reviewed and approved by the Advarra Institutional Review Board.

**Results**

**Description of study cohort**

A schematic overview of the patients described in this study is presented in Figure 1. Based on ICD diagnostic codes, 1,042,621 eligible prevalent cases were identified from the ICES database with a diagnosis of ASCVD between April 1, 2002 and March 31, 2018, providing a strong sense of overall ASCVD prevalence in this population. Of these, 743,309 patients (69%) were newly diagnosed with incident ASCVD between April 1, 2005 and March 31, 2016. These latter incidence data were analyzed separately to describe annual outcomes relative to the index event.

**Patient characteristics**

Characteristics of patients included in this study are described in Table 1. The majority of patients who experienced an ASCVD event were ≥ 65 years of age, among both prevalent cases (634,928 of 1,042,621 [61%]) and incident cases (458,569 of 743,309 [62%]). Among the incident ASCVD cases, the majority were male (59%), the median age was 69 years (interquartile range [IQR]: 59-79 years), and the most frequent events/procedures were MI (30%), unstable angina (17%), TIA (16%), stroke (11%), PCI (9%), PAD (5%), and CABG (5%). Similar data were reported for the prevalent ASCVD cases, shown in Table 1. Concomitant hypertension (71%-73%) and/or diabetes (31%-32%) were common among both the prevalent and incident ASCVD cases.

**Incidence of ASCVD subtypes in Ontario**

The overall event IRs per 1000 person-years (IRs) were calculated for each ASCVD subtype over the study period; IRs for all events ranged from 7.2 to 8.8 over the study period (Fig. 2; Supplemental Fig. S2). The IRs for MI, PAD, and aortic aneurysm remained stable at approximately 2.5, 0.7, and 0.4, respectively, over the study period; however, the IRs increased steadily for PCI/CABG (from 2.5 in 2005 to 3.0 in 2016), TIA (from 0.9 in 2005 to 1.5 in 2016), and stroke (from 0.7 in 2005 to 1.5 in 2016) every year across the study period (Fig. 2). IRs for unstable angina decreased over the course of the study period (from 3.3 in 2005 to 1.7 in 2016).

The annual IR for the first event was calculated per 1000 individuals and analyzed for the total incident cases and stratified by age (< 65 years and ≥ 65 years; Fig. 3; Supplemental Fig. S3). The IRs for the first event were higher among patients aged ≥ 65 years than those aged < 65 years; however, the trends were largely similar in the 2 age groups. The IRs of index MI were consistently higher than those for other ASCVD subtypes across the 11-year study period (Fig. 3). Of note, the annual incidence of index MI events was nearly halved in older patients aged ≥ 65 years (from 8.4 per 1000 individuals in 2005 to 4.8 per 1000 individuals in 2015; Fig. 3B), whereas in patients aged < 65 years, it remained stable (1.0 per 1000 individuals in 2005 to 0.9 per 1000 individuals in 2015; Fig. 3C). The annual IR for index unstable angina also decreased substantially in patients aged ≥ 65 years (from 7.5 per 1000 individuals in 2005 to 2.1 per 1000 individuals in 2015; Fig. 3B), as well as in patients aged < 65 years (from 0.9 per 1000 individuals in 2005 to 0.4 per 1000 individuals in 2015; Fig. 3C). However, IRs doubled for index TIA (from 0.26 per 1000 individuals in 2005 to 0.5 per 1000 individuals in 2015) and stroke (from 0.2 per 1000 individuals in 2005 to 0.4 per 1000 individuals in 2015) in patients aged < 65 years (Fig. 3C).

**Prevalence of ASCVD subtypes in Ontario**

The 10-year prevalence rates for all ASCVD subtypes increased over the study period (Fig. 4; Supplemental Fig. S4). The highest rates were seen for PCI/CABG, MI, and unstable angina, which respectively increased from 24.5 to 31.8, 23.5...
to 26.9, and 22.1 to 23.7 per 1000 individuals, between the periods 2004-2013 and 2008-2017 (Fig. 4). The 10-year prevalence rates for all events changed from 64.2 per 1000 individuals to 75.5 per 1000 individuals, respectively (data not shown). The prevalence of ASCVD per 1000 individuals in Ontario for the period 2004-2017 was 78.2 (95% confidence interval [CI]; 78.1, 78.4; Supplemental Table S3). The prevalence per 1000 individuals was greater for coronary events (eg, MI, unstable angina, PCI) and cerebrovascular events (eg, TIA, stroke), compared with that of peripheral artery events. Similarly, 5-year prevalence rates for all ASCVD subtypes increased over the study period, changing from 43.7 per 1000 individuals for the period 2004-2008 to 67.1 per 1000 individuals for the period 2012-2016 and 69.1 per 1000 individuals for the period 2013-2017 (data not shown).

Subsequent events and mortality after index incident ASCVD event

Half (374,715 of 743,309) of all incident cases experienced only one event over the study period, whereas 33% (242,698 of 743,309) had 2 ASCVD events, and 17% (125,896 of 743,309) had 3 or more ASCVD events (Table 2). Analysis of index cerebrovascular or coronary events revealed that approximately half of all patients had a subsequent event within the study period for the following subtypes by index event: MI (48%; 106,057 of 221,429); unstable angina (53%; 68,459 of 128,490); TIA (44%; 51,903 of 117,421); and stroke (48%; 40,368 of 84,739; Fig. 5, A and B). Overall, 19% (143,649 of 743,309) of patients died following their index ASCVD event within the study period (data not shown).

Table 1. Characteristics of patients in the study

| Characteristic                              | ASCVD prevalence (N = 1,042,621) | ASCVD incidence (N = 743,309) |
|--------------------------------------------|----------------------------------|-------------------------------|
| Female sex                                 | 432,300 (41.5)                   | 306,954 (41.3)                |
| Age at index/primary ASCVD event, y*       |                                   |                               |
| Median (IQR)                               | 69 (58–79)                       | 69 (59–79)                    |
| 18–64                                      | 407,693 (39.1)                   | 284,740 (38.3)                |
| 65–74                                      | 260,454 (25.0)                   | 181,780 (24.5)                |
| 75–84                                      | 249,886 (24.0)                   | 180,756 (24.3)                |
| ≥ 85                                       | 124,588 (11.9)                   | 96,033 (12.9)                 |
| Selected comorbidities                     |                                   |                               |
| Hypertension                               | 738,861 (70.9)                   | 539,788 (72.6)                |
| Diabetes                                   | 322,926 (31.0)                   | 239,529 (32.2)                |
| Index ASCVD event*                         |                                   |                               |
| MI                                         | 304,326 (29.2)                   | 221,429 (29.8)                |
| Unstable angina                            | 197,481 (18.9)                   | 128,490 (17.3)                |
| PCI/CABG surgery                           | 138,494 (13.3)                   | 100,590 (13.5)                |
| Aortic aneurysm                            | 42,632 (4.1)                     | 30,878 (4.2)                  |
| PAD                                        | 57,247 (5.5)                     | 39,543 (5.3)                  |
| Peripheral artery angioplasty/ stenting    | 12,001 (1.2)                     | 9241 (1.2)                    |
| Peripheral artery bypass surgery           | 4483 (0.4)                       | 3357 (0.5)                    |
| Peripheral artery endarterectomy           | 1283 (0.1)                       | 952 (0.1)                     |
| TIA                                        | 157,066 (15.1)                   | 117,421 (15.8)                |
| Stroke                                     | 118,015 (11.3)                   | 84,739 (11.4)                 |
| Carotid endarterectomy/stenting            | 9593 (0.9)                       | 6669 (0.9)                    |

Values are n (%), unless otherwise indicated. Study methods used precluded statistical comparisons being performed.

ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery bypass graft; IQR, interquartile range; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

* An event was considered an index event if it occurred in a patient aged ≥ 18 years, from April 1, 2005 to March 31, 2016.

1 Proportion of patients aged ≥ 65 years: 61% (634,928 of 1,042,621) with prevalent ASCVD; 62% (458,569 of 743,309) with incident ASCVD.
shown). Rates of mortality as a second event were highest for those with index events of PAD (26.8%; n = 10,589), stroke (27.1%; n = 22,990), unstable angina (18.3%; n = 23,478), and MI (17.8%; n = 39,320).

Type of subsequent event relative to index event

Second ASCVD events were most common among patients whose index event was MI (n = 106,057), followed by unstable angina (n = 68,459), TIA (n = 51,903), stroke (n = 40,368), and PAD (n = 27,151; Supplemental Fig. S5). Subtypes of subsequent events are reported in Supplemental Figure S6, A-C. In general, index events commonly led to subsequent coronary events; of note, experiencing an incident cerebrovascular or peripheral event conferred a risk of having a second coronary event. For example, among those with a peripheral index procedure, 12.2% had a subsequent coronary event. Analysis by individual subtype revealed that patients most frequently had an identical diagnosis for both first and second events (data not shown).

Time to event/death

Of the incident cases, the median time between the index and second event was 1.66 years (IQR: 0.35-4.16 years; 368,594 of 743,309 patients); the median time between the second and third event was 1.10 years (IQR: 0.29-3.00 years; 125,896 of 743,309 patients) (Supplemental Fig. S7). The median time between the index event and death (including deaths occurring after the third event) was 2.16 years (IQR: 0.25-5.11 years), and between the last event and death, it was 2.08 years (IQR: 0.55-4.57 years).

Figure 2. Incident atherosclerotic cardiovascular disease event rate per 1000 person-years (PY) in Ontario (2005/2006 to 2016/2017; for subtypes > 5% of all cases). CABG, coronary bypass graft; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Figure 3. Annual incidence of index atherosclerotic cardiovascular disease event per 1000 individuals in Ontario (2005/2006 to 2015/2016; for subtypes > 5% of all cases), for (A) all incident cases; (B) patients aged ≥ 65 years; (C) patients aged < 65 years. CABG, coronary bypass graft; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.
Discussion

This is the first comprehensive analysis of ASCVD prevalence and incidence in a cohort of adult patients in Ontario, Canada. This study spans a substantial period of time, demonstrating the progression of 12 subtypes of ASCVD events and procedures that have not been reported to date in Ontario. Further, the findings of this study demonstrate increased 10-year prevalence rates over time for all ASCVD subtypes, with stable or increased annual IRs observed for most events. A recent cohort study of adult patients within a large, diverse US healthcare system demonstrated an ASCVD IR of 8.67 (95% confidence interval 8.61-8.74) per 1000 person-years, similar to the observed range of ASCVD incidence in this study (7.2-8.8 per 1000 person-years). In the present study, 10-year prevalence rates increased from 64.2 per 1000 individuals in 2004-2013 to 75.5 per 1000 individuals in 2008-2017, which represents a 17.6% increase. The trend of increased ASCVD prevalence over time mirrors that of another recent Canadian study that showed a 21.4% increase in the age-standardized prevalence of vascular diseases between 2000 and 2015.

The rate of subsequent events among the incident cases over the follow-up period was approximately 50% those with ASCVD and additional cardiovascular risk enhancers, including polyvascular disease, symptomatic PAD, history of MI, MI in the past 2 years, and previous CABG surgery, per the 2021 CCS Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. In our study, the second event was more likely to be of the same class as the first (ie, coronary, cerebrovascular, peripheral). However, regardless of the index event, these patients had a substantial risk of having a subsequent coronary or cerebrovascular event, further supporting their classification as very high risk, as outlined by the CCS. Overall, 1 in 5 patients diagnosed with ASCVD in the incidence cohort died over the study period. Of the 143,649 deaths, 1 in 4 occurred within 3 months of the patient’s first ASCVD event. In line with CCS and other global guidelines, these findings indicate that patients who experience an event are at increased risk of death (especially within the first 3 months after the event), and survivors are at risk of further subsequent events. Of note, patients who experienced peripheral events/procedures had the greatest risk of subsequent ASCVD diagnoses or death, highlighting a care gap that requires urgent attention. The median time between the index event and death was approximately 2.2 years, whereas the median time between the last event and death was approximately 2.1 years. This increased risk of mortality within 2 years post—ASCVD event is consistent with that found in other real-world analyses, and it reinforces the urgency of treating these patients using guideline-recommended targets. Over the 11-year study period, MI was the most common index event, followed by unstable angina, TIA, stroke, PCI, and PAD. Patients with an index MI event had the greatest

Table 2. Number of ASCVD events reported over the study period, by age group

| Characteristic          | All events (N = 743,309) | 1 event1 (n = 374,715) | 2 events2 (n = 242,698) | ≥ 3 events3 (n = 125,896) |
|-------------------------|--------------------------|------------------------|-------------------------|---------------------------|
| Female sex              | 306,954 (41.3)           | 153,622 (41.0)         | 104,115 (42.9)          | 49,217 (39.1)             |
| Age at the time of index ASCVD event, y |                       |                        |                         |                           |
| Median (IQR)            | 69 (59-79)               | 65 (55-75)             | 75 (64-83)              | 72 (62-80)                |
| 18–64                   | 284,740 (38.3)           | 184,628 (49.3)         | 62,938 (25.9)           | 37,174 (29.5)             |
| 65–74                   | 181,780 (24.5)           | 92,374 (24.7)          | 55,775 (23.0)           | 33,631 (26.7)             |
| 75–84                   | 180,756 (24.3)           | 67,893 (18.1)          | 74,364 (30.6)           | 38,499 (30.6)             |
| ≥ 85                    | 96,033 (12.9)            | 29,820 (8.0)           | 49,621 (20.4)           | 16,592 (13.2)             |

Values are n (%), unless otherwise indicated.
ASCVD, atherosclerotic cardiovascular disease; IQR, interquartile range.

1 For the period from 2005/2006 to 2015/2016.
2 For the period from 2005/2006 to 2017/2018.
number of second and third events of any type, and the mortality rate was 17.8% (39,320 of 221,429). These findings are consistent with a recent study demonstrating that almost one-third of patients with a first event had a subsequent event; in those with an initial MI, subsequent MI was the most common secondary event. Furthermore, these findings support previous real-world evidence of increased cardiovascular risk in patients post-MI, and they emphasize the burden of disease and the importance of addressing MI with aggressive treatment. CCS guideline-recommended treatment strategies can be implemented using LDL-C levels to guide therapeutic goals, as well as other secondary prevention strategies. Of note, higher annual MI incidence was observed in earlier years for the patients aged ≥ 20 years. However, this measure only captured index MI events; as a result, those patients who had greatest residual risk and went on to have further events were excluded from this analysis. The lower incidence in MI events in younger patients may be explained by the fact that events likely are not as common in the younger group, and many of these patients may experience single events only.

Limitations

Limitations of this retrospective study include the quality and accuracy issues inherently associated with collecting data in a real-world setting. In addition, patient data may be incomplete due to their relocation to other provinces and/or countries; consequently, the study may not have included data for all eligible Ontario residents. Similarly, the incidence and prevalence of ASCVD in Ontario may be under-represented due to missed events if a patient with ASCVD did not present to a hospital or visit a physician. The data collection for the index ASCVD event began in 2005, with a lookback of 2 years for prior events; however, the index events herein are not guaranteed to be the first events for each patient. When describing the incidence of index ASCVD event by type, patients are limited to a single “first event,” with more common events such as unstable angina potentially limiting the reporting of other subsequent ASCVD event types, due to their hierarchical order (as outlined in the Materials and Methods section), and death was excluded as an index event. Patients who were not as healthy could experience these initial first events early in the study time period, and hence, they were removed from the pool of patients able to have first ASCVD events, and potentially events of greater severity, in subsequent years. ASCVD event rates were calculated per 1000 person-years, but they were not standardized for age, which may lead to inaccuracies in reporting trends over time. Finally, the comparisons performed in this study are descriptive in nature.

Conclusions

This retrospective, observational study explored the prevalence and incidence of ASCVD in Ontario, Canada in patients aged ≥ 18 years throughout 2002-2018, demonstrating a prevalence of more than 1 million cases of ASCVD. Prevalence rates are increasing, and there is a high IR for new ASCVD diagnoses, highlighting opportunities to continue to close the care gap and improve outcomes in ASCVD patients in Canada.

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**Supplementary Material**

To access the supplementary material accompanying this article, visit **CJC Open** at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2021.10.003.