ORIGINAL RESEARCH

Prevalence of Acetylsalicylic Acid Use for Primary Prevention of Cardiovascular Disease Amongst Older Adults From 2017—2021: a Retrospective Cross-Sectional Study

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ABSTRACT

Background

Three landmark trials on the use of acetylsalicylic acid (ASA) for primary prevention of cardiovascular disease (CVD) were published in 2018. Since then, major clinical practice guidelines have been updated with recommendations against the routine use of ASA for primary CVD prevention, particularly in older adults. However, little is known about the uptake of this evidence into real world practice. The purpose of this study was to assess the change in ASA usage for primary prevention of CVD in older adults between 2017 and 2021.

Methods

A retrospective cross-sectional study of ASA use for primary prevention in ambulatory older adults without known CVD in an urban Canadian city was conducted.

Results

Seven hundred and fifty-six participants were included. The mean age was 78.9 years (standard deviation 7.9) and 64.8% were female. One hundred and thirty (17.2%) participants used ASA for primary prevention, including 20.3% in 2017, 17.0% in 2018, 21.8% in 2019, 16.3% in 2020, and 11.0% in 2021 (p = .061). Female sex was associated with lower ASA use (odds ratio [OR] 0.44, 95% confidence interval [CI] 0.29-0.68) and hypertension was associated with higher ASA use (OR 2.72, 95% CI 1.73-4.29).

Conclusions

Use of ASA for primary CVD prevention in older Canadians decreased between 2017 and 2021, suggesting an uptake of clinical trial data and practice guideline recommendations. Focusing on deprescribing of ASA for primary CVD prevention continues to be warranted, given the risks associated with ASA in this population.

Key words: aspirin, primary prevention, cardiovascular disease, aged

INTRODUCTION

Acetylsalicylic acid (ASA) has been used for the primary prevention of cardiovascular disease (CVD) for over 30 years.[1] Since then, studies using ASA for primary prevention of CVD have included over 160,000 adults for over 1,000,000 participant-years.[2] Until 2016, major international guidelines, including the American Heart Association, American Diabetes Association, Hypertension Canada, European Society of Cardiology, and the United States Preventive Services Task Force all recommended the use of ASA for primary prevention for at least a subset of adults.[1,3-7] Observational data have demonstrated a modest uptake of these recommendations, with the prevalence of ASA use for primary prevention of CVD ranging from 12–47% of middle-aged or older adults, 45% of those over the age of 70, and 62% of those with diabetes reported using ASA for primary prevention.[8-10]

In 2018, three landmark clinical trials examining the contemporary use of ASA for primary prevention of CVD were published.[11-13] Only one of these studies found that ASA reduced the primary composite cardiovascular outcome, while an increase in hemorrhagic events was demonstrated across all three studies, and one study found an increase in mortality.[11-14] Since then, multiple guidelines have updated their recommendations regarding the use of ASA for primary CVD prevention. The American College of Cardiology/American Heart Association, Canadian stroke best practice recommendations, Hypertension Canada, United States Preventive Services Task Force, and Canadian and American diabetes guidelines now all recommend against the routine use of ASA for primary prevention of CVD, particularly in older adults, but note that ASA may be considered for primary prevention in some younger adults with additional cardiovascular risk

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factors.[15-20] However, little is known about the impact of this evidence and these revised guidelines on the use of ASA for primary prevention.

The purpose of this study was to assess the change in use of ASA for primary prevention of CVD in older adults since the publication of these pivotal trials and guideline statements. The primary objective was to determine the change in prevalence of use of ASA for primary prevention in older adults between 2017 and 2021. The secondary objective was to determine if use of ASA for primary prevention differed based on age, vascular risk factors, cognitive impairment, or frailty.

METHODS

Design and Setting

The study was a retrospective cross-sectional analysis using a convenience sample of older adults referred to an ambulatory geriatrics clinic in an urban centre in British Columbia, Canada. The clinic's interdisciplinary team provides short-term assessment and management of geriatric syndromes to older adults living independently or in assisted-living facilities. It does not provide care to adults living in long-term care or residential facilities.

Participant Selection

Potential participants were identified from a pre-existing database of all individuals referred to the study clinic. Individuals referred to the study clinic between January 1, 2017 and December 31, 2021 who had a best possible medication history documented by a clinical pharmacist were included in the study. Prospective participants were excluded if they had a history of CVD including myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, stable coronary artery disease, stroke, transient ischemic attack, or peripheral artery disease; mechanical or bioprosthetic heart valve; atrial fibrillation or atrial flutter; previous venous thromboembolism; or were on another antiplatelet or anticoagulant agent. For patients referred to the clinic more than once during the study period, only their first admission with a documented best possible medication history was included.

Data Collection

Data were collected from the two electronic health records used by the study clinic (Profile [Intrahealth Canada Ltd, North Vancouver, BC] and Meditech [Medical Information Technology Inc, Westwood, MA]) and entered into REDCap (Research Electronic Data Capture, REDCap Consortium, Nashville, TN), an electronic data capture platform hosted by the University of British Columbia. Data were extracted by two researchers (JP and SL). The principal investigator (JB) extracted data in duplicate for the first 10 participants, followed by every fifth participant. Discrepancies were recorded and resolved by consensus. The following data were collected for each participant: demographics, Rockwood clinical frailty score, medical comorbidities, tobacco and alcohol use, select diagnostic and laboratory tests, and medication use. Frailty was defined as a Rockwood clinical frailty score of 4 to 9.[21] Alcohol use was categorized by no regular alcohol use (less frequent than once weekly) or above or below the Health Canada low-risk drinking guidelines at the time of the study (two or fewer standard drinks per day for women, three or fewer standard drinks per day for men).[22] Medication histories documented in the electronic health records were obtained by pharmacists through interviews with patients and caregivers, and verified against additional sources of information such as PharmaNet, the provincial database of dispensed medications. Use of regularly scheduled low-dose ASA (80–81 mg) taken daily, twice daily, or every two days was categorized as use of ASA for primary CVD prevention.

Statistical Analysis

Categorical data were reported as frequencies with percentages. Continuous data were reported as means with a standard deviation (SD). Ordinal data were reported as medians with an interquartile range (IQR). Baseline characteristics were compared with an independent sample *t*-test for continuous data, Mann-Whitney U test for ordinal data, and chi-squared analysis for categorical data. A chi-squared analysis with a Bonferroni correction for multiple comparisons was used to assess the change in prevalence rates across all years (2017 to 2021). A chi-squared analysis was also used to compare the difference in ASA prevalence rates between 2017 and 2021. A forward stepwise multivariate logistic regression was performed to assess the impact of older age (70 years and older), sex, dementia, and vascular risk factors (hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, tobacco use) on ASA use. Age, sex, and any of the aforementioned factors (dementia, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, tobacco use) with a p value of $< .10$ were included in the logistic regression model. Frailty was originally planned to be included in the regression model but was removed due to the number of missing values for this variable. The missing data points for tobacco use were excluded from the analysis as they made up less than 1% of the overall population. A p value of $< .05$ was considered to be statistically significant. Cohen's kappa was used to assess interrater reliability. IBM SPSS Statistics (version 28, IBM Corporation, Armonk, NY) was used for all statistical analyses.

This study was approved by the clinical research ethics board at the Interior Health Authority (2021-22-112-H).

RESULTS

A total of 1,997 records were screened for eligibility, and 1,513 records met the inclusion criteria. Of 1,513 potential participants, 757 met exclusion criteria. Therefore, 756 participants were included in the analysis (Figure 1). Cohen's kappa was 0.961, indicating very strong interrater reliability.

The mean age of participants was 78.9 years (SD 7.9 years) and 64.8% percent were female (Table 1). Participants had a median clinical frailty score of 5 (IQR 4, 5) and 48.5%,

22.5%, and 14.4% had a recorded diagnosis of hypertension, dyslipidemia, and diabetes mellitus, respectively. Individuals who used ASA were more likely to be male (50% vs. 32.1%, $p < .001$), have a diagnosis of hypertension (67.7% vs. 44.6%, $p < .001$), dyslipidemia (33.1% vs. 20.3%, $p = .001$) and diabetes mellitus (21.5% vs. 12.9%, $p = .011$), and taking HMG-CoA reductase inhibitors (33.1% vs. 17.6%, $p < .001$), beta-blockers (25.4% vs. 10.9%, $p < .001$), and calcium channel blockers (23.8% vs. 13.9%, $p = .004$).

One hundred and thirty (17.2%) participants used ASA for primary prevention. The prevalence was highest in 2019 at 21.8% of participants and lowest in 2021 at 11.0% of participants (Figure 2). Of participants using ASA for primary prevention, 119 (91.5%) used 80–81 mg daily, six (4.6%) used 160–162 mg daily, and five (3.8%) used 80–81 mg every other day. There was no statistically significant difference in the prevalence of ASA use across all years of the study ($p = .061$); however, there was a statistically significant difference between 2017 (20.3%) and 2021 (11.0%) ($p = .024$). Following the forward stepwise multivariate logistic regression, female sex was associated with lower ASA use (odds ratio [OR] 0.44, 95% confidence interval [CI] 0.30–0.66), while a history of hypertension was associated with higher ASA use (OR 2.48, 95% CI 1.65–3.73). Age, also included in the model, was not statistically significant (OR 1.64, 95% CI 0.81, 3.32). No other variables were included in the model.

DISCUSSION

This study sought to explore the utilization of ASA for primary cardiovascular prevention in older Canadians before and after the publication of three landmark clinical trials. In this cohort of relatively healthy older adults, the overall use of ASA for primary prevention was 17%, with a reduction in use from roughly 20% in 2017 to 11% in 2021.

The use of ASA for primary prevention in the present study, prior to the publication of the ASPREE, ARRIVE, and ASCEND trials, was lower than previously published studies. In 2017, data from the National Health Interview Survey (NHIS) in the United States found that 25% of adults 40 years of age and older were taking ASA for primary prevention, including 47% of those 70 years of age and older.[23] The population in the present study was older (mean age 79 years) than that in the NHIS study, and only 20% were using ASA for primary prevention. The downward trend of ASA use for primary prevention from 2017 to 2021 seen in this study was

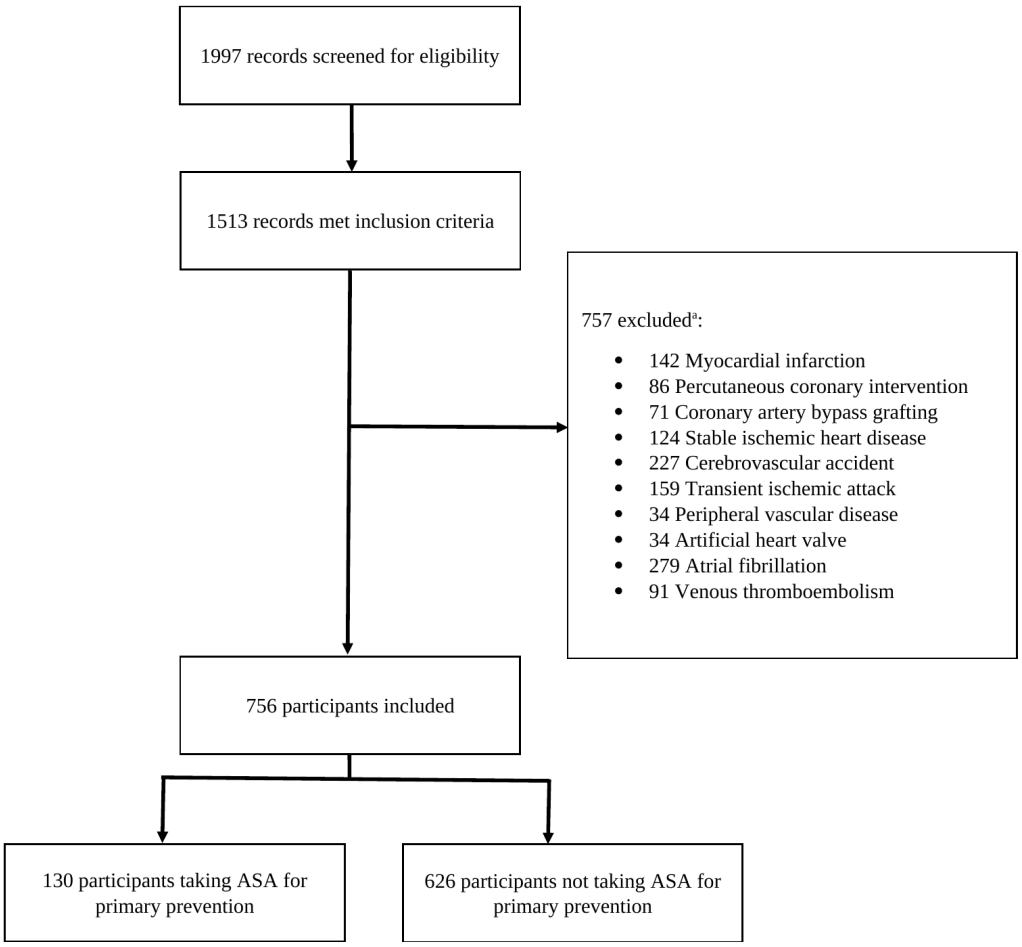


FIGURE 1. Participant flow diagram
[a]325 participants met more than 1 exclusion criteria

TABLE 1.
Participant characteristics

Parameter	*Overall (n=756)*	*ASA Users (n=130)*	*ASA Non-Users (n=626)*	*P value*
Mean age, years (SD)	78.9 ± 7.9	80.0 ± 7.4	78.7 ± 8.0	.082
Female, n (%)	490 (64.8)	65 (50)	425 (67.9)	<.001
Mean BMI, kg/m^2 (SD)[a]	26.0 ± 5.4	26.8 ± 5.2	25.9 ± 5.5	.082
Median Rockwood Frailty Score (IQR)[b]	5 (4, 5)	5 (4, 5)	5 (4, 5)	.078
Tobacco use, n (%)[c]	61 (8.1)	10 (7.9)	51 (8.2)	.903
Alcohol use above low-risk drinking guidelines, n (%)[d]	25 (4.1)	7 (7.1)	18 (3.5)	.242
Mean eGFR, mL/min/1.73 m^2 (SD)[e]	66.1 ± 17.3	66 ± 17.9	66.1 ± 17.2	.941
Comorbidities, n (%)				
Dementia	126 (16.7)	23 (17.7)	103 (16.5)	.730
Hypertension	367 (48.5)	88 (67.7)	279 (44.6)	<.001
Dyslipidemia	170 (22.5)	43 (33.1)	127 (20.3)	.001
Heart failure	14 (1.9)	3 (2.3)	11 (1.8)	.672
Diabetes mellitus	109 (14.4)	28 (21.5)	81 (12.9)	.011
Chronic kidney disease	79 (10.4)	13 (10.0)	66 (10.5)	.854
Previous gastrointestinal bleed	11 (1.5)	1 (0.8)	10 (1.6)	.473
Prior intracranial bleed	7 (0.9)	1 (0.8)	6 (1.0)	.838
Medications, n (%)				
ACE inhibitors	157 (20.8)	35 (26.9)	122 (19.5)	.057
Angiotensin II receptor blockers	86 (11.4)	20 (15.4)	66 (10.5)	.114
Beta-blockers	101 (13.4)	33 (25.4)	68 (10.9)	<.001
Calcium channel blockers	118 (15.6)	31 (23.8)	87 (13.9)	.004
Diuretics	137 (18.1)	22 (16.9)	115 (18.4)	.697
HMG-CoA reductase inhibitors	153 (20.2)	43 (33.1)	110 (17.6)	<.001

[a]BMI data missing for 19 participants.
[b]Rockwood Frailty Score missing for 131 participants.
[c]Tobacco use data missing for 7 participants.
[d]Alcohol use data missing for 142 participants.
[e]eGFR data missing for 88 participants.
eGFR = estimated glomerular filtration rate; NSAID = non-steroidal anti-inflammatory; SD = standard deviation.

similar to the results of the NHIS study, where the use of ASA for primary prevention declined between 2017 to 2021 from 25% to 14% in those aged ≥40 years, and 47% to 26% in those aged ≥70 years.[23] This rate of decline is greater than what was observed in the previous decade. Between 2011 and 2019, the rate of ASA for primary prevention in Americans ≥40 years of age in the Behavioural Risk Factor Surveillance Study only decreased from 31% to 28%.[24] Thus, our data, and that of the NHIS study, support the hypothesis that the 2018 landmark trials and updated guidelines likely influenced real-world ASA use.

This study found a higher rate of ASA use for primary CVD prevention in individuals with hypertension, which aligns with previously published studies.[8-10,24] This finding may be a result of the Hypertension Canada guidelines, which previously recommended the use of ASA for vascular risk reduction in all hypertensive patients aged 50 years and older.[5] The updated version of the Hypertension Canada guidelines no longer recommends ASA use for primary prevention, based on the results of the aforementioned trials.[17] Unlike previous studies, this study did not find an association between ASA use and diabetes or dyslipidemia, despite finding statistically significant differences in these comorbidities in the baseline characteristics.[8-10,24] A small but statistically significant benefit of ASA for primary cardiovascular prevention has been found in clinical trials, albeit at the risk of increased bleeding. The JPAD trial demonstrated reduced fatal atherosclerotic events (though not overall atherosclerotic events) with ASA in patients with diabetes, while the ASCEND trial found a decrease in the primary composite cardiovascular endpoint in diabetes patients using ASA over 7.4 years.[12,25] These data have contributed to the Canadian and American

Diabetes Associations recommending that ASA be considered for primary prevention in individuals with multiple risk factors for CVD, and may have contributed to higher use of ASA in diabetic patients in the literature.[8-10,19,20,24]

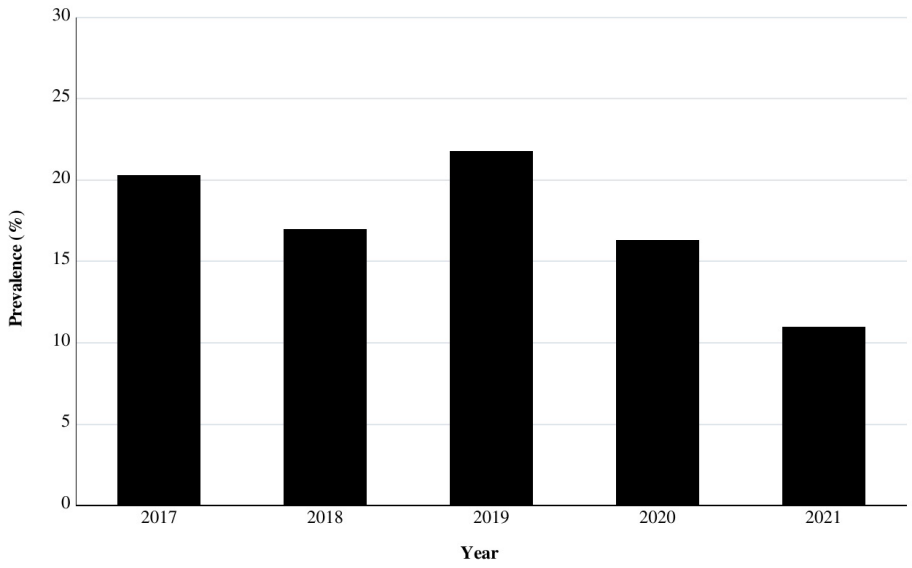
Our study found a lower rate of ASA use for primary prevention in female participants, which aligns with previous research.[8-10,24] This may be an indicator of ongoing sex-based disparity in CVD management. Despite a poorer prognosis after acute cardiovascular events, women are less likely to be screened for, or receive, evidence-based treatment for cardiovascular risk factor modification.[26,27] Given that this study took place across a timeframe when many clinical practice guidelines recommended the use of ASA for primary prevention, this sex-based treatment disparity may be one reason why females were less likely to take ASA for primary prevention. However, ASA is available without a prescription in Canada and self-perception of cardiovascular risk could also contribute to this finding, as not all individuals seek the advice of a health-care provider prior to initiating ASA therapy.[28] While knowledge and awareness of CVD among women has improved over the past several decades, many continue to lack knowledge on CVD prevention.[29] As such, these findings may also support the ongoing need to enhance women's health literacy surrounding cardiovascular health.

While it is promising to see that use of ASA for primary prevention in older adults has decreased, our study did find that 11% of older adults without CVD used ASA in 2021. This usage does not align with most contemporary guidelines that recommend against the use of ASA for primary cardiovascular prevention, particularly in older adults.[15-20] Given increased hemorrhagic risk seen across the ASPREE, ARRIVE, and ASCEND trials, and the increased risk of mortality in older adults in ASPREE, there remain opportunities to further deprescribe ASA in older adults.[11-14]

Our study has limitations that warrant discussion. It was conducted at a single urban centre, and as such, the findings may not be applicable to other sites, particularly rural or remote settings. Because of the retrospective design of this study, we were limited to the data that were recorded in the health-care record of participants. However, the exclusion of participants without a pharmacist-documented best possible medication history increases the confidence in the accuracy of ASA usage in this population. The relatively small sample size of the present study may have impeded the ability to identify risk factors associated with ASA use, such as diabetes or dyslipidemia.

CONCLUSION

In this sample of relatively healthy urban-dwelling older adults, the prevalence of ASA use for primary prevention of CVD decreased from 20% in 2017 to 11% in 2021, suggesting



	2017	2018	2019	2020	2021
No ASA	94 (79.7%)	132 (83.0%)	158 (78.2%)	72 (83.7%)	170 (89.0%)
ASA	24 (20.3%)	27 (17.0%)	44 (21.8%)	14 (16.3%)	21 (11.0%)
Total	118	159	202	86	191
Trend Analysis	$\chi 2=9.017$, df=4, p=0.061				
2017 vs. 2021	$\chi 2=5.119$, df=1, p=0.024				

FIGURE 2. Prevalence of ASA use for primary prevention of cardiovascular disease

uptake of contemporary clinical trial evidence and clinical practice guidelines. A continued focus on deprescribing of ASA for primary cardiovascular prevention is warranted, given the risks of ASA within this population.

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Not applicable.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood the *Canadian Geriatrics Journal's* policy on disclosing conflicts of interest and declare that we have none.

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