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Aspirin for Secondary Prevention of Cardiovascular Disease in 51 Low-, Middle-, and High-Income Countries: A Cross-Sectional Study of Nationally Representative, Individual-Level Data

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KEY POINTS

Question:

What is the prevalence of aspirin use among people with a history of cardiovascular disease in low-, middle- and high-income countries?

Findings:

Among individuals with a self-reported history of cardiovascular disease, aspirin use for secondary prevention was 40.3% (95% CI: 37.6%-43.0%) in the pooled sample and ranged from 16.6% (95% CI: 12.4%-21.9%) in low-income countries to 65.0% (95% CI: 59.1%-70.4%) in high-income countries.

Meaning:

The overall findings suggest suboptimal use of aspirin for secondary prevention of cardiovascular disease in many countries around the world.

ABSTRACT

Importance:

Aspirin is an effective and low-cost option for reducing atherosclerotic cardiovascular disease (CVD) events and improving mortality among individuals with established CVD. To guide efforts to mitigate the global CVD burden, there is a need to understand current levels of aspirin use for secondary prevention of CVD.

Objective:

To report and evaluate aspirin use for secondary prevention of CVD across low-, middle-, and high-income countries.

Design, Setting, Participants

Cross-sectional analysis using pooled, individual-participant data from nationally representative health surveys conducted between 2013-2020 in 51 low-, middle-, and high-income countries. Included surveys contained data on self-reported history of CVD and aspirin use. The sample of participants included non-pregnant adults aged 40-69 years.

Exposures:

Countries' per-capita income levels and world region; individuals' socioeconomic demographics.

Main Outcomes and Measures:

Self-reported use of aspirin for secondary prevention of CVD.

Results:

The overall pooled sample included 124,505 individuals. The median age was 52 (IQR: 45-59) years, and 50.5% (95% CI: 49.9%-51.1%) were women. A total of 10,589 individuals had self-

reported history of CVD (8.1% [95% CI: 7.6%-8.6%]). Among individuals with a prior history of CVD, aspirin use for secondary prevention in the overall pooled sample was 40.3% (95% CI: 37.6%-43.0%). By income group, estimates were 16.6% (95% CI: 12.4%-21.9%) in low-income countries, 24.5% (95% CI: 20.8%-28.6%) in lower-middle-income countries, 51.1% (95% CI: 48.2%-54.0%) in upper-middle-income countries, and 65.0% (95% CI: 59.1%-70.4%) in high-income countries.

Conclusion and Relevance:

Worldwide, aspirin is underused in secondary prevention, particularly in low-income countries. National health policies and health systems must develop, implement, and evaluate strategies to promote aspirin therapy.

Trial Registration:

Not applicable.

INTRODUCTION

Aspirin is widely used for its non-steroidal anti-inflammatory and anti-platelet properties.[1,2] In the prevention of atherosclerotic cardiovascular disease (CVD), aspirin is an effective and low-cost option for reducing CVD events and improving mortality among individuals with established CVD.[3,4] The role of aspirin in the primary prevention of CVD is less clear.[5]

Cardiovascular diseases are the leading cause of global mortality and loss of disability-adjusted life years.[6] To ensure an effective and efficient health system to prevent CVD, it is important to understand whether medication use is commensurate with need.[7] Suboptimal prevention of CVD can have devastating effects on individuals, health systems, and economies. Implementation of evidence-based pharmacotherapy including aspirin is important to achieve Target 3.4 of the United Nations Sustainable Development Goal (SDG), which aims for a one-third reduction in premature mortality from non-communicable diseases (NCDs) including CVD by 2030.[8–10] There also is a need to benchmark progress toward the key 2025 World Health Organization (WHO) target that at least 50% of eligible people receive aspirin for CVD prevention.[11]

The current study aims to provide updated evidence on worldwide aspirin use among individuals with a history of CVD. Using nationally representative health surveys, we estimate aspirin use for secondary prevention of CVD and report its association with individual-level characteristics.

METHODS

Study design and data sources

We conducted a cross-sectional analysis using pooled, individual-participant data from nationally representative health surveys conducted in 51 low-, lower-middle-, upper-middle-, and high-income countries. Details of the systematic processes to pool eligible national health

surveys were reported previously and are summarized in eMethods 1.[12,13] We started with a list of all countries with a World Bank income group classification.[14] Surveys identified in each country were eligible to be included in this study if they (1) used a nationally representative sampling frame, (2) had been conducted in 2013 or after, (3) had availability of individual-participant survey data, and (4) asked respondents questions on the use of aspirin for prevention of CVD. Details on included surveys are provided in eMethods 2-3. We chose 2013 as the initial year of survey eligibility to align with the WHO's release of a new version of the Stepwise Approach to NCD Risk-Factor Surveillance (STEPS) survey containing questions on aspirin use and prior CVD status.[15] All were national household surveys except for the survey in Czech Republic, which sampled from health insurance registries covering 85% of the population.[16] We reported overall response rates according to definitions from the American Association for Public Opinion Research.[17] This study was considered exempt from regulation by the institutional review board at the University of Michigan (HUM00201307), as the research used coded data that the investigators could not link to specific individuals.

Sample

The sample included non-pregnant individuals ages 40-69 years. This age range was chosen to focus on middle-aged and older individuals with a higher likelihood of developing or having CVD and to align with recommended age ranges for monitoring the WHO and SDG targets.[8–11] Exceptions included Burkina Faso, Czech Republic, Kyrgyzstan, Myanmar, and Tokelau, as surveys in these countries had an upper age limit of sample eligibility of 64 years.

Outcome definitions

Our primary outcome was aspirin use for secondary prevention of CVD. Aspirin use was defined by self-report among respondents using the medication to prevent a CVD event (eTable 1). For

example, STEPS surveys ask the following question: “Are you currently taking aspirin regularly to prevent or treat heart disease?”

Secondary prevention of CVD

We defined secondary prevention of CVD among individuals with a self-reported history of prior myocardial infarction, stroke, or angina. For example, STEPS surveys ask the following question: “Have you ever had a heart attack or chest pain from heart disease (angina) or a stroke (cerebrovascular accident or incident)?”[18] Because aspirin is widely recommended for secondary prevention of CVD, we classified all individuals self-reporting prior CVD as eligible for aspirin therapy.[4,19–23]

Statistical analysis

We first harmonized variables needed for this analysis from each survey, as detailed previously.[12,13] We then combined individual-level data from all surveys to construct a pooled dataset. We estimated the proportion of individuals using aspirin for secondary prevention of CVD across the pooled sample, by World Bank per-capita income categories[14] (i.e., low-income, lower-middle-income, upper-middle-income, and high-income), and by country. We also considered each country’s income level as a continuous variable by plotting estimates against per-capita gross national income (eTable 2).[24] To explore individual characteristics associated with aspirin use for secondary prevention of CVD in the pooled sample, we estimated proportions across individual characteristics of age (40-49, 50-59, and 60-69 years), sex, educational attainment (less than primary school, primary school, and secondary school or greater), and urban versus rural residence.

We accounted for complex survey design by considering sampling strata and primary sampling units with appropriate subpopulation specification. To obtain pooled estimates, we rescaled

sample weights in proportion to each country's population aged 40-69 years and ran commands over the pooling unit (i.e., overall or income group).[25] Following this approach, our results can be interpreted as being representative of the population aged 40-69 years across included countries. We report unadjusted estimates, except in our analysis of individual characteristics associated with aspirin use for secondary prevention of CVD, in which we age-standardized to the WHO reference population.[26] A complete case analysis was conducted as missingness was approximately 1% or lower across key variables (eTable 3). We conducted our analysis in Stata version 17.0 and R version 4.2.2.

RESULTS

Survey and sample characteristics

The pooled dataset included nationally representative health surveys conducted from 2013-2020 in 51 countries (Figure 1, eFigure 1, eTables 4-5). By World Bank income group, seven surveys were conducted in low-income countries, 23 in lower-middle-income countries, 14 in upper-middle-income countries, and seven in high-income countries. All but three surveys (Czech Republic, England, and the United States [U.S.]) were conducted as part of the WHO STEPS program.[16,27,28] The median response rate was 85% (interquartile range [IQR]: 70%-95%) in the 50 surveys reporting a response rate (eTable 6). Response rates were lower in high-income countries (median: 57%) than in other income groups (median: 98%, 86%, and 82% in low-income, lower-middle-income, and upper-middle-income countries, respectively).

The overall pooled sample included 124,505 individuals (Table 1). Weighted across surveys, respondents' median age was 52 (IQR: 45-59) years, 50.5% (95% CI: 49.9%-51.1%) were women, and 53.4% (95% CI: 52.0%-54.8%) lived in a rural area. There were 10,589 individuals with a prior history of CVD (weighted 8.1% [95% CI: 7.6%-8.6%]). Further details of the study subpopulation with a prior history of CVD are provided in eTables 7-8.

Aspirin use for secondary prevention of CVD across the pooled sample and by income group

Among individuals with a self-reported history of CVD, aspirin use for secondary prevention in the overall pooled sample was 40.3% (95% CI: 37.6%-43.0%). By income group, estimates were 16.6% (95% CI: 12.4%-21.9%) in low-income countries, 24.5% (95% CI: 20.8%-28.6%) in lower-middle-income countries, 51.1% (95% CI: 48.2%-54.0%) in upper-middle-income countries, and 65.0% (95% CI: 59.1%-70.4%) in high-income countries (Figure 2).

Aspirin use for secondary prevention of CVD across countries

At the country level, 41% of the variation in aspirin use for secondary prevention (R^2=0.41) was accounted for by per-capita income (Figure 3, eTable 9). Countries meeting the WHO target that at least 50% of eligible people receive aspirin for secondary CVD prevention included Belarus, Czech Republic, England, Iran, Iraq, Jordan, Kuwait, Lebanon, Turkmenistan, and the United States.

Aspirin use for secondary prevention of CVD across individual characteristics

In the overall pooled sample, among those with a prior CVD history, greater aspirin use was observed among individuals who were older, male, had higher levels of education, and lived in urban as opposed to rural areas. There were consistent gradients of greater aspirin use in countries with more income within a given individual characteristic (Figure 4, eTables 10-11). In high-income versus low-income countries, the absolute difference in aspirin use for secondary prevention was two to five-fold greater relative use and between 20% to 60% greater absolute use by age, sex, education, or rural versus urban residence (eTable 12-13).

DISCUSSION

In a diverse set of nationally representative surveys from 51 countries, fewer than half of eligible people in the overall pooled sample, including less than one-quarter in low- and lower-middle-income countries, were taking aspirin for secondary prevention of CVD. These results suggest underuse of aspirin use for secondary CVD prevention globally.

To our knowledge, the current study provides the most extensive and updated estimates of the worldwide use of aspirin for secondary prevention of CVD. Our findings revealed marked inequities worldwide, as illustrated by four-fold greater aspirin use for secondary CVD prevention in high-income compared to low-income countries. None of the 30 low- or lower-middle-income countries in our sample achieved the WHO target that at least 50% of eligible individuals with a history of CVD take aspirin. Only about half of upper-middle- and high-income countries included in our analysis achieved this target.[11]

Previously, the Prospective Urban Rural Epidemiology (PURE) cohort study reported on use of secondary prevention drugs in 17 countries. Using data collected from 2003 to 2009, PURE investigators found that use of anti-platelet therapy including aspirin was 11% in low-income countries, 20% in lower-middle-income countries, 27% in upper-middle-income countries, and 64.1% in high-income countries.[29] PURE's findings were generally consistent with other studies conducted in China, Denmark, Italy, Spain, the United Kingdom, and the U.S.[30–32] The current study overcomes the limitations of prior studies by using recent, nationally representative survey data from a larger sample of countries. We find similar results to PURE more than a decade later. Despite considerable international efforts to improve access to CVD medicines, especially in low- and middle-income countries (LMICs), our study reinforces that more work is needed.

There is a need to reflect on the lack of progress over the last decade on use of aspirin and other CVD medicines in LMICs.[13,33] CVD prevention efforts are complex and must be

contextualized to each country, including its patients, clinicians, and health system.[34] For example, countries with a high burden of prevalent CVD may benefit from more aggressive policies to improve evidence-based aspirin use. However, many patients may not understand the role of aspirin in CVD prevention or have variable access to aspirin, whether through prescriptions or over the counter.[35] As highlighted in the current study, an individual country with greater economic resources may find it more feasible to scale-up, sustain, and codify system-level CVD care.

At the same time, some innovations and programs may offer generalizable lessons across countries to address the underuse of aspirin for secondary prevention and, consequently, CVD-related mortality. One innovation is the use of fixed-dose combination therapies ("polypills"), which may include aspirin in addition to anti-hypertensive and statin therapies. Polypills improve patient adherence and are effective in secondary prevention of CVD even in high-income countries with high rates of drug therapy.[36,37] The WHO HEARTS program, launched in 2016, recommends an integrated, multicomponent approach to population-level CVD care, including appropriate use of aspirin.[38] HEARTS has shown excellent results in improving blood pressure control in more than a dozen countries, and future work could assess whether the HEARTS platform can be leveraged to maximize aspirin use for secondary prevention of CVD.[39] Finally, repurposing system-level strategies deployed to manage other chronic conditions such as HIV may help to address CVD medication use.[40]

Limitations

There are several limitations to our study. First, it was not possible to define with certainty whether an individual's aspirin use was appropriate. The appropriateness of aspirin therapy could be confounded by antithrombotic or other antiplatelet therapies that may be a relative contraindication to aspirin due to elevated bleeding risk. Only three surveys captured data on

use of other antithrombotic and other antiplatelet drugs or the specific aspirin dose. Most included surveys did not ask questions that permitted us to distinguish among individuals who had heart disease versus strokes, or whether a stroke was ischemic or hemorrhagic. Second, while the overall median response rate was 85%, response rates tended to be lower in high-income countries. In recent years, many survey programs such as U.S. NHANES have experienced declining response rates that require enhanced weighting adjustments.[41] We used sampling weights adjusted for nonresponse, but it is possible that nonresponse bias could be larger in high-income countries than in other countries in our sample. Third, we used self-reported data on aspirin use and CVD history. Self-reported indicators are recommended in the WHO NCD Monitoring Framework and have been accurate in prior studies.[18,29,42,43] In the case of aspirin use, self-reported data is important as aspirin is obtained over the counter in many countries. Fourth, there were slight variations in survey design across countries, but surveys were comparable in using nationally representative sampling frames. Fifth, included surveys were conducted in different years between 2013 to 2020. Results may not reflect the current use of aspirin in each country. Finally, surveys on aspirin use were not available from some large countries (e.g., India and China) or high-income countries in Asia. Our findings may not be generalizable to countries and regions where surveys were not included. This limitation was balanced by inclusion of surveys from a diverse sample of countries across world regions and a broad spectrum of economic development.

Conclusion

Worldwide, aspirin is underused in secondary prevention, particularly in low-income countries. To meet the goal of reducing premature mortality from NCDs, including CVD, national health policies and health systems must develop, implement, and evaluate strategies to promote evidence-based use of aspirin.

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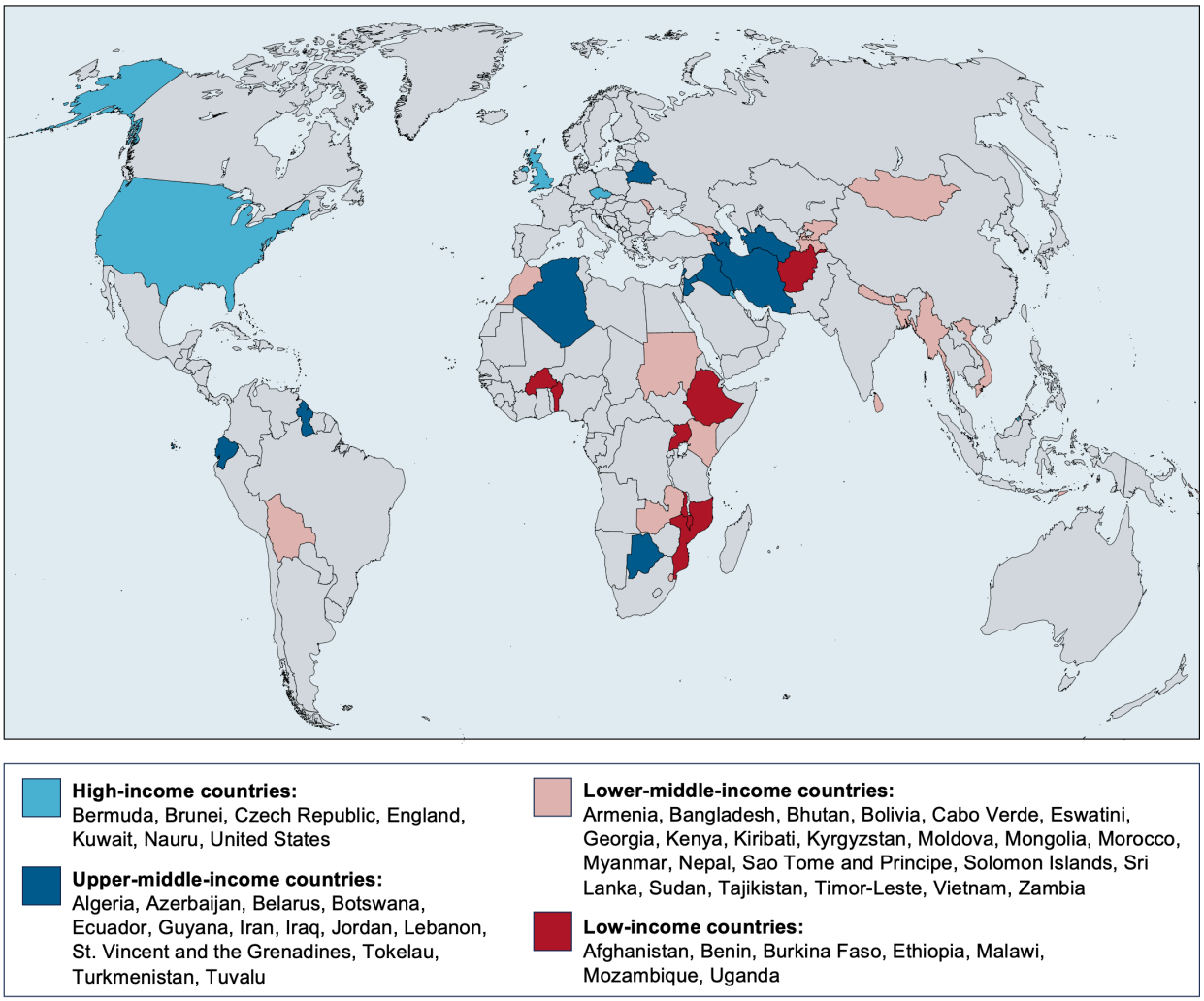
Conflict of Interest Disclosures: None.

Data sharing: Data included in this study are publicly available with registration for 45 of the 51 included country surveys. Further details on accessing data is provided in eMethods 3.

Figure 1: Map of included countries by income group



Colors refer to World Bank per-capita income groups in the year the survey was conducted. Income group thresholds are defined each year based on gross national income per capita in US$ (Atlas methodology, not purchasing power parity-adjusted) from the prior year.[14] Thresholds therefore change slightly each year. During the period the surveys were conducted from 2013-2020, approximate per-capita income thresholds were: low-income countries; <$1,000; lower-middle-income countries, $1,000-$4,000; upper-middle-income countries, $4,000-12,000; high-income countries, >$12,000. The figure was created in MapChart using the Winkel Tripel projection, which minimizes distortions in country land area between the equator and poles.[44] The United Kingdom was shaded though the included survey came only from England.

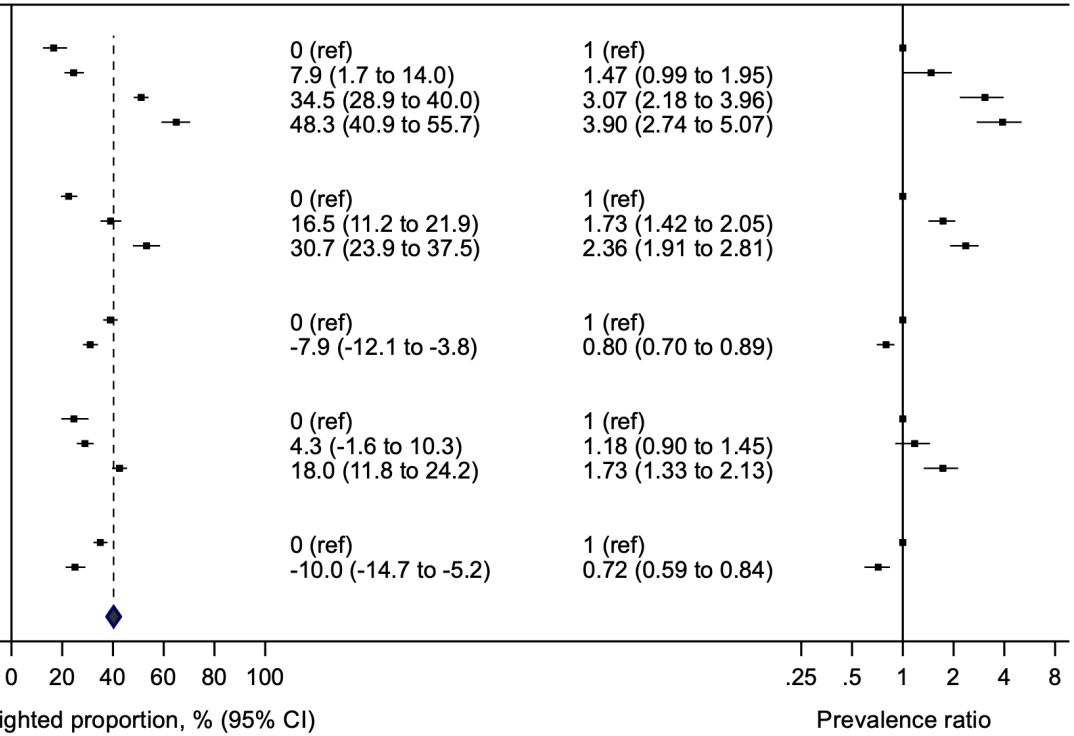
Table 1: Characteristics of study population

Characteristic	Low-income countries	Lower middle-income countries	Upper-middle-income countries	High-income countries	Overall
	n=7 countries	n=23 countries	n=14 countries	n=7 countries	n=51 countries
Total No.	12,637	52,014	39,080	20,774	124,505
Age, median (IQR), years	49 (43-55)	51 (45-58)	51 (45-59)	54 (47-61)	52 (45-59)
Age categories					
40-49 years	49.9 (48.5-51.3)	44.8 (43.8-45.8)	43.7 (43.0-44.4)	34.0 (32.2-35.9)	41.0 (40.2-41.9)
50-59 years	32.8 (31.6-34.1)	32.5 (31.6-33.4)	34.1 (33.4-34.7)	36.3 (34.6-38.1)	34.2 (33.5-35.0)
60-69 years	17.3 (16.2-18.3)	22.7 (21.6-23.8)	22.2 (21.6-22.8)	29.7 (27.6-31.8)	24.7 (23.8-25.6)
Sex					
Male	52.3 (50.5-54.1)	50.5 (49.5-51.5)	48.2 (47.6-48.8)	48.5 (47.4-49.6)	49.5 (48.9-50.1)
Female	47.7 (45.9-49.5)	49.5 (48.5-50.5)	51.8 (51.2-52.4)	51.5 (50.4-52.6)	50.5 (49.9-51.1)
Education[a]					
Total No.	12,602	51,286	38,170	20,531	122,589
No schooling	58.0 (56.0-60.0)	27.9 (26.7-29.1)	16.7 (16.1-17.4)	0.0 (0.0-0.0)	16.1 (15.2-17.0)
Primary	30.4 (28.8-32.1)	32.5 (31.1-33.8)	35.6 (34.8-36.4)	6.8 (5.8-7.9)	21.7 (20.6-22.9)
≥Secondary	11.5 (10.5-12.7)	39.7 (38.3-41.1)	47.7 (46.8-48.5)	93.2 (92.1-94.2)	62.2 (60.4-64.0)
Residence[b]					
Total No.	12,637	37,239	31,070	10,402	91,348
Urban	27.8 (24.8-31.1)	32.4 (31.4-33.4)	69.3 (68.3-70.2)	74.2 (67.7-79.9)	46.6 (45.2-48.0)
Rural	72.2 (68.9-75.2)	67.6 (66.6-68.6)	30.7 (29.8-31.7)	25.8 (20.1-32.3)	53.4 (52.0-54.8)
Prior CVD[c]					
Total No.	12,618	51,825	38,795	20,765	124,003
Yes	8.6 (7.6-9.8)	10.0 (9.2-10.7)	6.6 (6.2-7.0)	7.0 (6.1-8.1)	8.1 (7.6-8.6)
Diabetes[c]					
Total No.	12,618	51,827	38,308	20,768	123,521
Yes	2.7 (2.1-3.3)	7.6 (7.1-8.2)	15.1 (14.6-15.7)	13.1 (11.9-14.4)	10.7 (10.2-11.2)
Hypertension[c]					
Total No.	12,323	51,828	38,609	20,768	123,528
Yes	14.0 (12.8-15.4)	22.7 (21.9-23.6)	31.6 (30.9-32.3)	37.7 (35.5-40.0)	29.8 (28.8-30.9)
Systolic blood pressure, median (IQR), mmHg	125.5 (114.5-140.0)	127.3 (115.7-142.3)	130.0 (119.3-143.7)	124.0 (114.0-136.0)	126.3 (115.7-140.0)
Current smoking					
Total No.	12,632	51,871	38,824	20,742	124,069
Yes	10.1 (9.1-11.1)	24.2 (23.2-25.2)	18.4 (17.9-19.0)	20.9 (19.4-22.5)	20.9 (20.2-21.7)
BMI					
Total No.	12,445	49,591	37,954	18,073	118,063
Median (IQR), kg/m^2	21.6 (19.4-24.8)	23.1 (20.3-26.3)	27.8 (24.8-31.4)	28.8 (25.1-33.3)	25.8 (22.2-30.2)

Values are reported as percentages unless otherwise indicated. Estimates account for survey design and weighting by each country's 2019 population of individuals aged 40-69 years. Values are reported as percentages unless otherwise indicated. Weighted estimates of median (IQR) are calculated using the *ecptile* command in Stata. Income group thresholds are based on gross national income per capita in US$ (Atlas methodology, not purchasing power parity-adjusted) in the year the survey was conducted.[14] Further details on missing data by country are provided in eTable 3. [a]No education is defined as less than primary school or no formal schooling; primary is defined as only primary school completed; secondary is defined as secondary, high school, college, or post-graduate degree. Education was unavailable in the survey from Tokelau. [b]We used each country's definition of rural or urban residence. These definitions are typically set by a country's national statistics office or census bureau.[45] Rural versus urban residence was unavailable in the surveys from Bermuda, Botswana, Brunei, Ecuador, Eswatini, Kiribati, Kuwait, Lebanon, Myanmar, Nauru, Solomon Islands, Sri Lanka, St. Vincent & the Grenadines, Tajikistan, Timor-Leste, Tokelau, Tuvalu, and United States. [c]Based on self-reported diagnosis.

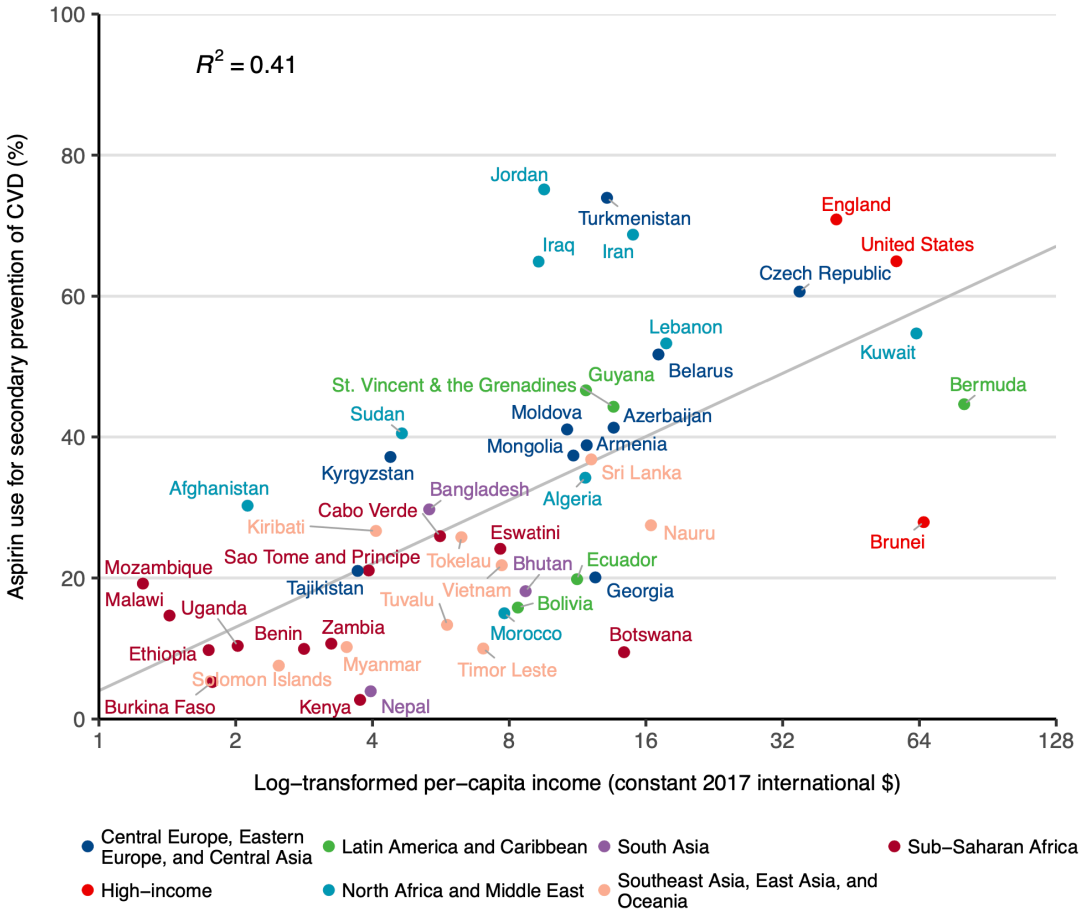
Figure 2: Among those eligible, use of aspirin for secondary prevention of CVD by income group, age, sex, education, and rurality

Characteristic	No. of countries	n/N	Weighted proportion, % (95% CI)	Difference from reference, % (95% CI)	Prevalence ratio, % (95% CI)
Income group					
Low income	7	172/1,037	16.6 (12.4 to 21.9)	0 (ref)	1 (ref)
Lower middle	23	1,522/5,557	24.5 (20.8 to 28.6)	7.9 (1.7 to 14.0)	1.47 (0.99 to 1.95)
Upper middle	14	1,435/2,776	51.1 (48.2 to 54.0)	34.5 (28.9 to 40.0)	3.07 (2.18 to 3.96)
High income	7	661/1,219	65.0 (59.1 to 70.4)	48.3 (40.9 to 55.7)	3.90 (2.74 to 5.07)
Age	51				
40-49 years		676/3,100	22.6 (19.5 to 26.0)	0 (ref)	1 (ref)
50-59 years		1,365/3,812	39.1 (35.1 to 43.3)	16.5 (11.2 to 21.9)	1.73 (1.42 to 2.05)
60-69 years		1,749/3,677	53.3 (47.9 to 58.6)	30.7 (23.9 to 37.5)	2.36 (1.91 to 2.81)
Sex	51				
Male		1,722/4,219	39.0 (36.2 to 41.9)	0 (ref)	1 (ref)
Female		2,068/6,370	31.0 (28.1 to 34.1)	-7.9 (-12.1 to -3.8)	0.80 (0.70 to 0.89)
Education	50				
No schooling		405/1,603	24.6 (19.7 to 30.4)	0 (ref)	1 (ref)
Primary education		991/2,962	29.0 (25.8 to 32.4)	4.3 (-1.6 to 10.3)	1.18 (0.90 to 1.45)
Secondary or above		2,346/5,895	42.6 (39.7 to 45.6)	18.0 (11.8 to 24.2)	1.73 (1.33 to 2.13)
Residence	33				
Urban		1,788/4,203	35.0 (32.3 to 37.8)	0 (ref)	1 (ref)
Rural		1,078/3,526	25.1 (21.4 to 29.1)	-10.0 (-14.7 to -5.2)	0.72 (0.59 to 0.84)
Overall	51	3,790/10,589	40.3 (37.6 to 43.0)		



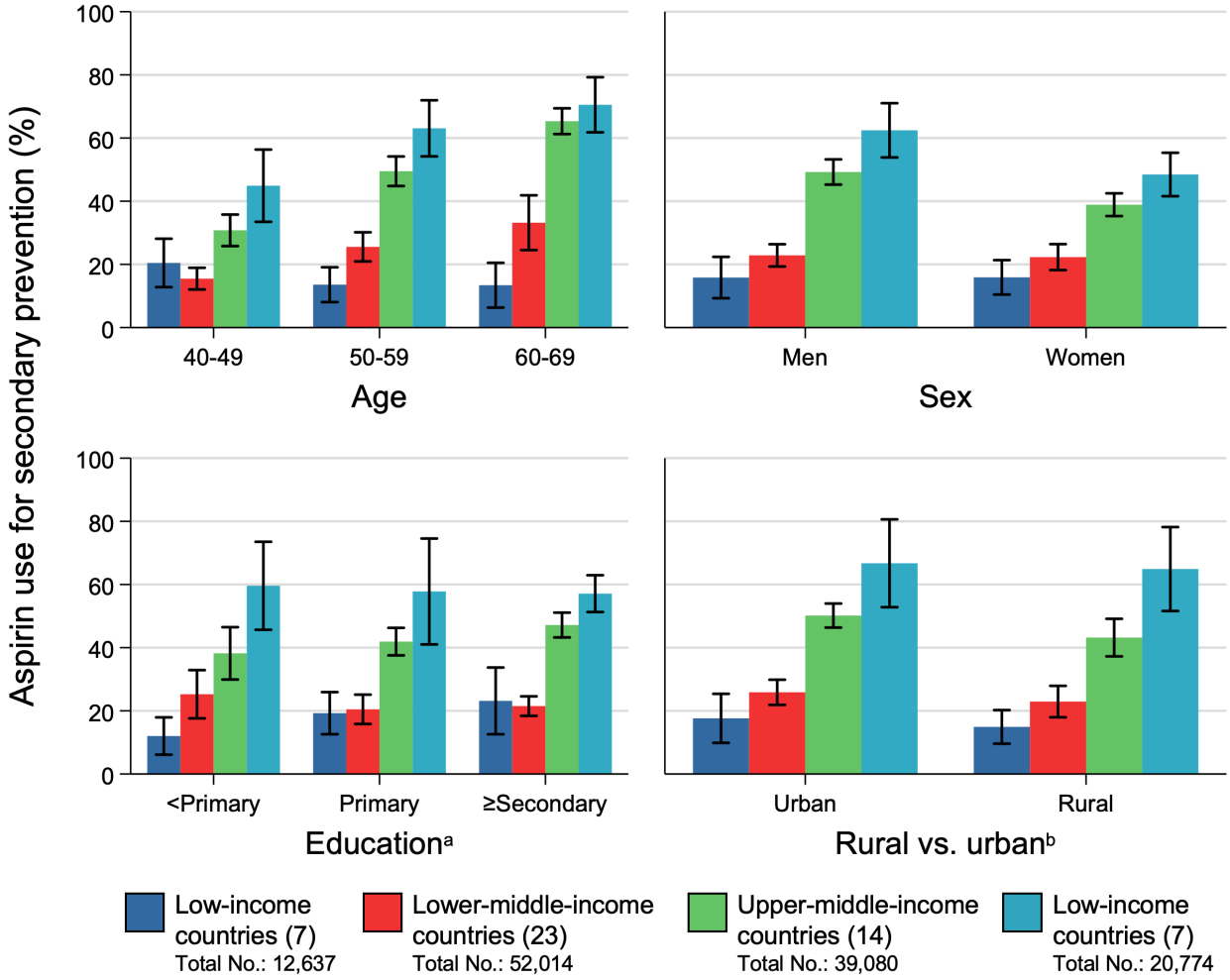
Estimates are weighted by each country's 2019 population of individuals aged 40-69 years. Direct standardization of age to the World Health Organization reference population was used except in the income group and overall estimates. The error bars represent 95% CIs. Income group refers to World Bank per-capita income categories in the year the survey was conducted.[14] Differences from reference and prevalence ratios are calculated using the *lincom* and *nlcom* commands, respectively, in Stata. Education was unavailable in the survey from Tokelau. Rural versus urban residence was unavailable in the surveys from Bermuda, Botswana, Brunei, Ecuador, Eswatini, Kiribati, Kuwait, Lebanon, Myanmar, Nauru, Solomon Islands, Sri Lanka, St. Vincent & the Grenadines, Tajikistan, Timor-Leste, Tokelau, Tuvalu, and United States. Ref: Reference category.

Figure 3: Among those eligible, aspirin use for secondary prevention of CVD by country per-capita income



Colors show each country's super region using the Global Burden of Disease classification system; "high-income" in this classification system is different than the World Bank per-capita income category (eTable 5). Per-capita income is defined as gross national income per capita in purchasing power parity-adjusted dollars (constant 2017 international $) in the year the survey was conducted. Estimates account for survey design and weighting. Underlying estimates and 95% CIs are provided in eTable 9.

Figure 4: Among those eligible, proportion of individuals using aspirin for secondary prevention of CVD by age, sex, education, and rurality across income groups



Estimates account for survey design, direct standardization of age to the World Health Organization reference population, and weighting by each country's 2019 population of individuals aged 40-69 years. The error bars represent 95% CIs. [a]No education is defined as less than primary school or no formal schooling; primary is defined as only primary school completed; secondary is defined as secondary, high school, college, or post-graduate degree. Education was unavailable in the survey from Tokelau. [b]We used each country's definition of rural or urban residence. These definitions are typically set by a country's national statistics office or census bureau.[46] Rural versus urban residence was unavailable in the surveys from Bermuda, Botswana, Brunei, Ecuador, Eswatini, Kiribati, Kuwait, Lebanon, Myanmar, Nauru, Solomon Islands, Sri Lanka, St. Vincent & the Grenadines, Tajikistan, Timor-Leste, Tokelau, Tuvalu, and United States. Underlying data provided in eTables 9-13.

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