Global Prevalence of Aspirin Use for Primary Prevention of Cardiovascular Disease: A Cross-Sectional Study of Nationally Representative, Individual-Level Data

## **RESEARCH LETTER**

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The role of aspirin in the primary prevention of atherosclerotic cardiovascular disease (CVD) is not clear, with recent clinical trials evaluating aspirin for primary prevention demonstrating both modest benefits and risks associated with its use [1]. Aspirin is not routinely recommended for primary prevention of CVD. Understanding patterns of aspirin use can inform strategies to promote guideline-concordant therapy, including de-implementation strategies to reduce unnecessary aspirin use. This study seeks to provide an updated estimate of worldwide aspirin use for primary prevention of CVD.

# **METHODS**

We analyzed pooled individual-participant data from nationally representative health surveys conducted in 49 countries between 2013 and 2020. Details of the study design, data sources, and sample population have been described (Figure 1) [2].

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Figure 1 A) Survey inclusion flow chart. HPACC refers to The GHP Project on Access to Care for Cardiometabolic Diseases Collaboration. STEPS refers to STEPwise approach to NCD risk factor surveillance surveys. B) Use of aspirin for primary prevention of cardiovascular disease by income group, age, sex, education, and rurality. Estimates are weighted by each country's 2019 population of individuals aged 40 to 69 years. Income group refers to World Bank per capita income categories in the year the survey was conducted. <sup>a</sup>Education was unavailable in the survey from Tokelau. <sup>b</sup>Urban vs rural residence was unavailable in the surveys from Bermuda, Botswana, Brunei, Ecuador, Eswatini, Kiribati, Kuwait, Lebanon, Myanmar, Nauru, Solomon Islands, Sri Lanka, St Vincent and the Grenadines, Tajikistan, Timor-Leste, Tokelau, Tuvalu, and the US. C) CVD risk categories of individuals using aspirin for primary prevention by income group. Estimates are weighted by each country's 2019 population of individuals aged 40 to 69 years. Income group refers to World Bank per capita income categories in the year the survey was conducted. Categories of 10-year predicted CVD risk are calculated using the 2019 regionally calibrated WHO laboratory-based riskprediction models.

The primary outcome was the use of aspirin for primary prevention of CVD. We defined primary prevention as the population without a self-reported history of myocardial infarction, stroke, or angina. We classified participants using aspirin for primary prevention into categories based on 10-year predicted CVD risk: <5%, 5–10%, 10–20%, and >20%, aligning with established guidelines [1]. The analysis used the 2019 regionally calibrated WHO laboratory-based risk-prediction models, which includes input variables of age, sex, smoking status, systolic blood pressure, history of diabetes, and total cholesterol [3].

We estimated the proportion of individuals using aspirin for the primary prevention of CVD by World Bank per-capita income categories [4]. We accounted for the complex survey design in analyses and used sampling weights rescaled in proportion to each country's 2019 population. We conducted our analysis in Stata version 17.0 (StataCorp) and R version 4.2.2 (R Foundation). Our study was considered exempt from regulation by the institutional review board at the University of Michigan (HUM00201307).

# RESULTS

The dataset encompassed 96,914 individuals from 49 countries, with 88,340 categorized as belonging to the primary prevention group (Figure 1). Among individuals without a self-reported history of CVD, aspirin use in the overall pooled sample was 9.2% (95% CI: 8.4%–10.0%). The prevalence of aspirin use varied significantly by income group, with estimates of 0.6% (95% CI: 0.4%–0.8%) in low-income countries, 1.2% (95% CI: 1.1%–1.4%) in lower-middle-income countries, 11.7% (95% CI: 11.2%–12.2%) in upper-middle-income countries, and 17.7% (95% CI: 15.9%–19.6%) in high-income countries (Figure 1).

A substantial proportion of individuals in higher-income countries who used aspirin for primary prevention had low predicted CVD risk. For example, among those using aspirin for primary prevention in high-income countries, 59.6% (95 CI: 55.3%–63.7%) had 10-year CVD risk less than 10% (Figure 1). The median 10-year CVD risk among individuals using aspirin for primary prevention in high-income countries was 6.2% (IQR: 3.3%–10.2%).

# DISCUSSION

In a diverse sample of nationally representative surveys conducted between 2013-2020, we found many people using aspirin for primary CVD prevention across the world. Particularly in upper-middle-income and high-income countries, people using aspirin for primary CVD prevention have low CVD risk. This study offers the most extensive and contemporary understanding of global aspirin use among individuals without a prior history of CVD. The finding is in contrast to evidence that questions the routine use of aspirin in populations effectively managed with cholesterol and blood pressure-lowering medications [5]. A modeling study suggested that primary prevention aspirin users who are at low risk or aged greater than 60 years experience minimal or even negative lifetime net benefit as measured by qualityadjusted life-years and total life-years [6]. In this context, the current study suggests overuse of aspirin among populations without a history of CVD is an important worldwide public health problem with particular salience in upper-middle-income and high-income countries where resources may be limited and greater health system efficiency could be achieved. However, the use of aspirin for primary prevention should be contextualized within individual health systems, considering factors such as population-level CVD risk and the accessibility of cholesterol and blood pressure-lowering medications and aspirin.

Limitations of the study include the use of self-reported data on aspirin use and CVD history and the incorporation of some surveys completed before the release of recent aspirin primary prevention trials. Nevertheless, the data remain relevant, as it takes decades for medical practices to change with the evolving evidence regarding the role of aspirin in prevention [7]. Additionally, it was not possible to define with certainty whether an individual's aspirin use was appropriate. For primary prevention, we assumed individuals to be at low CVD risk using a 10-year threshold of <10%. Finally, the 2019 WHO CVD risk equations used in our analysis are the most updated risk-prediction model for worldwide use, but the models have not been externally validated in all countries, given a paucity of CVD cohorts outside of high-income countries.

# **CONCLUSIONS**

Aspirin use for primary prevention varies widely globally. Strategies aimed at de-prescribing aspirin in populations unlikely to benefit should be developed, evaluated, and implemented to mitigate the potential harms associated with unnecessary aspirin use.

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# **COMPETING INTERESTS**

The authors have no competing interests to declare.

# **AUTHOR CONTRIBUTIONS**

Funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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6