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Short Report

US population qualifying for aspirin use for primary prevention of cardiovascular disease

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HIGHLIGHTS

- 7 % of US adults 40–59 years are eligible for primary prevention aspirin by USPSTF.
- Higher proportional eligibility among men, older age (50–59 years), Black race.
- 30 % of individuals potentially eligible meet increased bleeding risk criteria.
- Limited role of primary prevention aspirin in modern era under USPSTF guidelines.

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ABSTRACT

Objective: Aspirin has been used for primary prevention of atherosclerotic cardiovascular disease (ASCVD) for decades, but this indication has become controversial with recent trial data. The 2022 US Preventive Services Task Force (USPSTF) provided a recommendation to consider aspirin use for primary prevention in adults 40–59 years with a 10-year ASCVD risk ≥10 % and not at increased risk of bleeding, yet population estimates for the impact of this recommendation are unknown. The objective of this study is to determine the prevalence and demographics of the US population who meet eligibility criteria for aspirin under the new 2022 USPSTF guidelines.

Methods: This is a serial cross-sectional study using data from the 2011-March 2020 National Health and Nutrition Examination Survey (NHANES) database. Individuals aged 40–59 years without a self-reported history of ASCVD were included. 10-year estimated ASCVD risk ≥10 % as calculated by the Pooled Cohort Equations (PCE) and **increased** bleeding risk determined using variables adapted from USPSTF guidelines were further applied as inclusion and exclusion criteria, respectively. The weighted frequencies of US adults aged 40–59 years qualifying for primary prevention aspirin, subgrouped by gender, age, and race/ethnicity, were calculated.

Results: Among 72,840,734 US individuals aged 40–59 years, 7.2 million (10 %) are eligible for consideration of primary prevention aspirin by PCE criteria. Of these, approximately 30 % would be potentially excluded based on increased bleeding risks, resulting in a net eligible cohort of 5 million. This represents 7 % of US adults aged 40–59 years and only 2.6 % of adults ≥18 years. Men, age 50–59 years, and Black race have higher proportions meeting aspirin use eligibility.

Conclusions: The overall prevalence of US individuals who qualify for aspirin for primary prevention under the 2022 USPSTF guidelines is modest, with larger proportional eligibility among men, older age, and Black individuals.

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1. Introduction

The role of aspirin for primary prevention of atherosclerotic cardiovascular disease (ASCVD) has become more limited based on recent trial evidence [1,2]. This shift can be attributed to three landmark primary prevention trials demonstrating a neutral or small treatment benefit of aspirin but significantly increased risk of bleeding [3–5]. The latest guideline comes from the US Preventive Services Task Force (USPSTF), which gives a grade C recommendation (at least moderate certainty that the net benefit is small) to consider aspirin for primary prevention in adults aged 40–59 years with an estimated 10-year ASCVD risk ≥10 % and not at increased risk of bleeding [1]. We sought to determine the prevalence and demographics of the US population eligible for aspirin use for ASCVD primary prevention under the new USPSTF guidelines.

2. Methods

The National Health and Nutrition Examination Survey (NHANES) is a series of cross-sectional surveys conducted by the National Center for Health Statistics to gather the health information of US civilian, non-institutionalized individuals. Detailed information on survey participants and data collection can be found on the NHANES website [6]. The present study combines data from the 2011-March 2020 survey cycles. Data beyond March 2020 were not included due to suspension of data collection as a result of the COVID-19 pandemic. Adults 40–59 years without a history of ASCVD were included in the primary analyses, with additional analyses including all adults ≥18 years without a history of ASCVD, so as not to restrict the population denominator by already using one of the criteria stipulated by USPSTF. Local institutional board review is not required for use of publicly available, de-identified NHANES data.

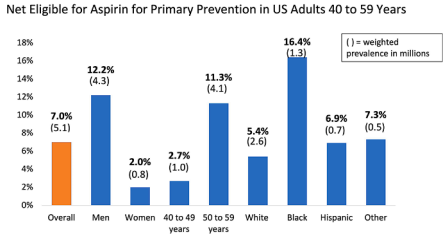
NHANES variables were selected and defined to replicate with as much fidelity as possible the corollary variables used by USPSTF. History of ASCVD was defined as an affirmative response to "ever told you had coronary heart disease," "ever told you had a heart attack," or "ever told you had a stroke." 10-year estimated ASCVD risk was derived using the Pooled Cohort Equations (PCE), which includes age, sex, race, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, diabetes status ("ever told you have diabetes" or A1c ≥6.5 %), treatment for hypertension ("taking prescribed medicine for high blood pressure"), and smoking status ("now smoke cigarettes") [7].

Increased bleeding risk was defined using criteria applied by USPSTF to exclude those with such risk. Specifically, the USPSTF Decision Analysis involved excluding those meeting any elevated bleeding risk criteria [8], which were derived from an analysis by Selak et al. [9]. Presence of any of these variables led to exclusion due to increased bleeding risk: congestive heart failure, atrial fibrillation, stage 4 or 5 chronic kidney disease, diabetic kidney disease, peptic ulcer disease, chronic liver disease, chronic pancreatitis, or alcohol-related disease; prior intracranial hemorrhage, gastrointestinal bleeding, or other bleeding; thrombocytopenia; and use of aspirin, other antiplatelet, anticoagulation, corticosteroid, non-steroidal anti-inflammatory drugs (NSAID), or selective serotonin reuptake inhibitors (SSRI) in the preceding six months (**Supplementary Table 1**). Current medication use at the time of the NHANES survey was applied for analyses since NHANES does not account for timing of medication use. Chronic liver disease was excluded due to lack of specificity in the NHANES variable (i.e., "ever told you have any kind of liver condition"). Chronic pancreatitis and alcohol-related disease were excluded due to lack of appropriate representative NHANES variables. Aspirin use did not comprise an exclusion criterion for increased bleeding risk, since its self-initiated use does not preclude an individual from meeting aspirin eligibility criteria in the current modeling study. NHANES does not inquire about prior bleeding. An affirmative response to "during the past three months, have you received treatment for anemia" was used as a surrogate for bleeding history.

Among those 40–59 years without a history of ASCVD, we determined the prevalence of individuals with an estimated 10-year ASCVD risk ≥10 % and not at increased bleeding risk (net eligible cohort) within NHANES and extrapolated these results to the US population, with subsequent subgroup analyses by gender, age, and race/ethnicity. Those missing PCE data (8.3 % of the sample weighted US population) were excluded from analysis (**Supplementary Table 2**). Sensitivity analysis was performed removing NSAID and SSRI use as bleeding variables due to their high prevalence of use. Sample prevalence estimates were weighted using NHANES-supplied sample weights to obtain nationally representative prevalence estimates (**Supplement**). Comparisons among aspirin-eligible versus ineligible cohorts were performed using a first-order Rao-Scott chi-square test that accommodates the NHANES sampling methodology.

3. Results

The study cohort comprised 6957 individuals corresponding to 72,840,734 US adults (Fig. 1). An estimated 7.2 million individuals (10 % of the US population aged 40–59 years) qualify by PCE criteria for consideration of primary prevention aspirin (Table 1). Of these, 30 % meet treatment exclusion criteria due to increased bleeding risk, resulting in an overall net eligible cohort of 5 million (7 % of the US population aged 40–59 years). Net eligibility is higher among men (12.2 %), age 50–59 years (11.3 %), and Black individuals (16.4 %) (Central Illustration). Increased bleeding risk is more common among women and older (aged 50–59) individuals (Table 1). Those aspirin-ineligible due to lower ASCVD risk have a more favorable risk profile compared to those net eligible, while those aspirin-ineligible due to increased bleeding risk have increased ASCVD risk factors (more statin use, hypertension treatment, and diabetes) (Table 2). Removing NSAID and SSRI use as bleeding criteria, an estimated 5.9 million individuals (8.1 % of the US population aged 40–59 years) are net eligible (**Supplementary Table 3**). Among the entire US adult primary prevention population ≥18 years, only 2.6 % are net eligible.



Central Illustration. Net Eligible for Aspirin for Primary Prevention in US Adults 40–59 Years

The net eligible proportion of US adults aged 40–59 overall and by demographic subgroup for primary prevention aspirin under the 2022 USPSTF recommendations. The data are derived from NHANES 2011-March 2020 cohorts, applying sample weights to obtain nationally representative prevalence estimates.

4. Discussion

Using NHANES, we found that the prevalence of the US population who qualify for aspirin for primary prevention under the 2022 USPSTF guidelines is modest, representing 7 % of individuals aged 40–59 years and only 2.6 % of those ≥18 years. This finding suggests that from a population level, aspirin is anticipated to have a small impact on overall ASCVD prevention when applying the USPSTF recommendations. By way of reference, nearly 35 million individuals are statin eligible in the US population by USPSTF recommmendations [10]. The 2016 USPSTF guidelines give a grade B recommendation to initiate low-dose aspirin for primary ASCVD prevention in adults 50–59 years who have a 10-year ASCVD risk ≥10 % and not at increased risk of bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin

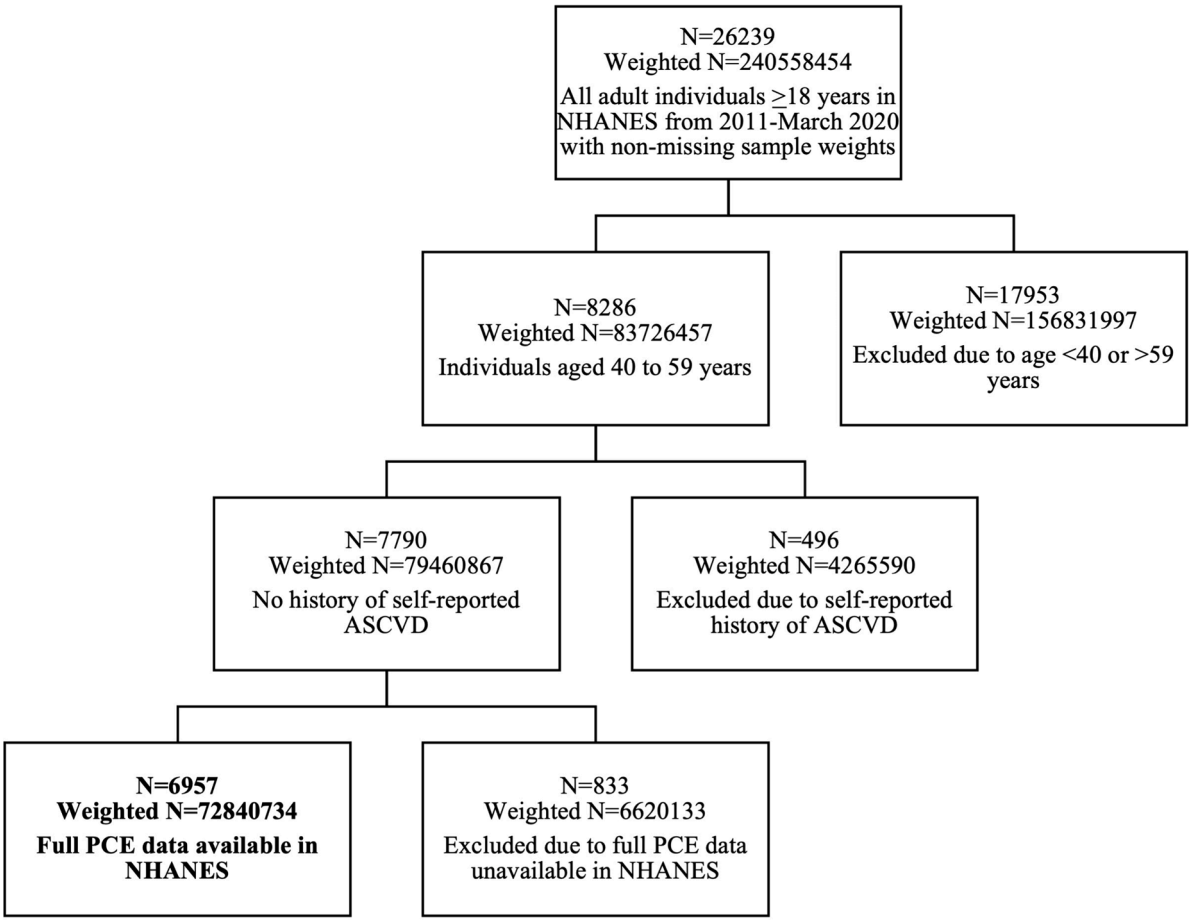


Fig. 1. NHANES study cohort diagram.
This flow diagram depicts how the initial study cohort group was derived within NHANES. The entire adult NHANES cohort from 2011-March 2020 with non-missing sample weights was narrowed based on age, no self-reported history of ASCVD, and full PCE data available within NHANES.

Table 1
Aspirin eligible cohorts among US adults 40–59 years.

Subgroup	Meeting Eligibility Criteria in NHANES N / total	Weighted Population N (% of weighted total)	Meeting Bleeding Risk Criteria among Eligible in NHANES N / total	Weighted Population N (% of weighted total)
Overall	896 / 6957	7,248,093 (10.0 %)	268 / 896	2,174,191 (30.0 %)
Men	701 / 3285	5,971,405 (16.8 %)	196 / 701	1,649,883 (27.6 %)
Women	195 / 3672	1,276,689 (3.4 %)	72 / 195	524,310 (41.1 %)
40–49 Years	170 / 3574	1,335,622 (3.7 %)	51 / 170	358,030 (26.8 %)
50–59 Years	726 / 3383	5,912,471 (16.2 %)	217 / 726	1,816,161 (30.7 %)
White	215 / 2377	3,812,314 (8.0 %)	76 / 215	1,236,778 (32.4 %)
Black	409 / 1642	1,901,817 (24.0 %)	129 / 409	600,597 (31.6 %)
Hispanic	162 / 1696	948,507 (8.9 %)	36 / 162	209,719 (22.1 %)
Other	110 / 1242	585,455 (9.3 %)	27 / 110	127,098 (21.7 %)

for at least 10 years. For comparison of the net eligibility with the current 2022 USPSTF guidelines, the estimated prevalence of net aspirin-eligible individuals using the 2016 criteria is 4.1 million individuals (11.3 % of adults aged 50–59 years). This estimation, however, does not account for the life expectancy criterion, as this is not able to be captured using NHANES.

The limited eligibility of aspirin in these recommendations derives from the higher 10-year ASCVD risk threshold required for aspirin consideration (≥10 %). In contrast with the USPSTF guidelines, the 2019 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend consideration of primary prevention aspirin among adults 40–70 years at higher ASCVD risk and not at increased bleeding risk [2]. Those guidelines were not proscriptive on what characterizes higher ASCVD or bleeding risk, but rather provided a general framework.

Our results support findings from a previous study reporting a similarly small proportion (5 %) of aspirin eligibility among US adults from the Multi-Ethnic Study of Atherosclerosis database applying the 2019 ACC/AHA guidelines [11]. The differences in eligibility by gender/age in the present study are likely attributable to higher ASCVD risk in the men/older age subgroups, as has been shown in another NHANES-based study [12]. Notably, 12.2 % of men versus only 2.0 % of women are net eligible. Interestingly, in the Women's Health Study, aspirin for primary prevention was only effective in women ≥65 years, a

Table 2
Characteristics of aspirin ineligible versus aspirin eligible cohorts among US adults 40–59 years.

Characteristic	Ineligible due to Lower ASCVD Risk $n = 6061$ Weighted $n = 65,592,641$	Ineligible due to Bleeding Risk $n = 268$ Weighted $n = 2,174,192$	Net Eligible $n = 628$ Weighted $n = 5,073,902$
Age, years (mean, 95 % CI)	49.1 (48.8–49.3)*	54.1 (53.4–54.9)	53.6 (53.1–54.0)
Men (%)	45.1 %*	75.9 %*	85.2 %
Race (%)			
White	67.3 %*	56.9 %	50.8 %
Black	9.2 %	27.6 %	25.6 %
Hispanic	14.9 %	9.6 %	14.6 %
Other	8.7 %	5.8 %	9.0 %
Total cholesterol, mg/dL (mean, 95 % CI)	200 (198–202)*	209 (195–223)	218 (210–226)
LDL-C, mg/dL (mean, 95 % CI)	115 (114–116) $n = 6036$	105 (94–116)* $n = 267$	121 (115–128) $n = 622$
HDL-C, mg/dL (mean, 95 % CI)	55 (54–56)*	43 (41–45)	44 (42–45)
Statin use (%)	12.8 %*	45.4 %*	19.0 %
BMI, kg/m^2 (mean, 95 % CI)	29.7 (29.4–30.0)* $n = 6026$	32.6 (31.3–33.9) $n = 267$	31.2 (30.4–31.9) $n = 621$
Hypertension treatment (%)	18.2 %*	61.9 %*	42.1 %
SBP, mmHg (mean, 95 % CI)	120.5 (120.0–121.1)*	139.0 (135.9–142.1)	136.7 (134.2–139.3)
Diabetes mellitus (%)	9.3 %*	61.8 %*	42.7 %
Current smoking (%)	16.1 %*	51.9 %	54.1 %
eGFR ≤45 mL/min/1.73m^2 (%)	0.4 % $n = 6037$	6.9 %* $n = 267$	0.2 % $n = 623$

Lower ASCVD risk is defined as 10-year estimated atherosclerotic cardiovascular disease risk <10 %.
BMI = body mass index.
eGFR = estimated glomerular filtration rate, calculated using the CKD-EPI equation.
HDL-C = high-density lipoprotein cholesterol.
LDL-C = low-density lipoprotein cholesterol.
SBP = systolic blood pressure.
* Indicates $p < 0.05$ compared to net eligible group.

group excluded from the USPSTF recommendations [13]. Our study also demonstrates differences in aspirin eligibility across race, with 1 in 4 Black individuals versus 1 in 12 White individuals meeting PCE criteria, which may reflect the greater weight placed on Black race within the PCE. Yet studies have shown that actual aspirin use for primary prevention among Black individuals is lower than that of White individuals, even after adjusting for socioeconomic status and ASCVD risk [14,15]. The reasons behind these differences are not completely elucidated.

We also found that 30 % of the aspirin-eligible cohort meet criteria for increased bleeding risk. Diabetic kidney disease, NSAID use, SSRI use, and thrombocytopenia comprised the highest frequency bleeding risk variables (**Supplementary Table 3**). Older age, statin users, those on hypertension treatment, and diabetic individuals meet bleeding risk criteria by USPSTF in higher proportions and therefore are ineligible for aspirin, despite their more adverse ASCVD risk profile. Interestingly, women also more commonly meet increased bleeding risk compared with men, although this may be driven by the proportionally higher rates of SSRI use among women. Overall, these results must be interpreted with the caveat that bleeding risk itself is not clearly defined in the USPSTF guidelines, allowing room for clinical interpretation, and that definitions of bleeding risk variables were delineated within the limits of ascertained NHANES variables.

Despite the extensive data captured in NHANES, some bleeding variables were unavailable for analysis. However, increased bleeding risk is not consistently defined by USPSTF or in clinical practice, and sensitivity analyses of select bleeding parameters did not meaningfully change results. 8.3 % of the cohort was missing data for PCE variables and excluded from analysis, but aside from race/ethnicity, other key risk variables were comparable to the study cohort, suggesting a similar proportion of aspirin eligibility in these excluded individuals. Furthermore, the cross-sectional nature of NHANES implies that the estimated prevalence represents a snapshot of aspirin eligibility that may change over time. The survey design of NHANES also renders the data subject to participant recall and self-report, although this is less applicable to objective PCE variables. Additionally, the current study only models the US population deemed appropriate for aspirin use by USPSTF and is not intended to evaluate clinical events to validate subgroups that would derive net benefit from aspirin. Subgroups with certain risk indicators, such as higher coronary artery calcification [11,16] and lipoprotein(a) [17], may have net benefit from aspirin use, but these parameters were not part of the USPSTF criteria.

5. Conclusions

The prevalence of US adults who qualify for aspirin for primary prevention under the 2022 USPSTF guidelines is limited (7 % of those aged 40–59 years and only 2.6 % of those ≥18 years). The eligibility proportions were slightly higher for men, those of older age (50–59 years), and Black individuals compared with other demographics. The clinical role of aspirin for primary prevention in the modern era under USPSTF guidelines remains limited, although discussions for its use should remain guided by shared decision-making.

CRediT authorship contribution statement

Athena L. Huang: Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Ann Marie Navar:** Writing – review & editing, Methodology. **Colby Ayers:** Resources, Methodology, Formal analysis. **Anand Rohatgi:** Writing – review & editing. **Erin D. Michos:** Writing – review & editing. **Salim S. Virani:** Writing – review & editing. **Parag Joshi:** Writing – review & editing. **Eric D. Peterson:** Writing – review & editing. **Amit Khera:** Writing – review & editing, Visualization, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

-advisor or consultant to Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Edwards Lifescience, Esperion, Medtronic, Novartis, Novo Nordisk, and Pfizer; received grant funding (paid to her institution) from Merck; co-Editor-in Chief of AJPC - E.M. -received fees for consulting from Amgen, Astra Zeneca, Bayer, BMS, Boehringer Ingelheim, Eli Lilly, Esperion, Janssen, Merck, New Amsterdam, Novo Nordisk, Novartis, Silence Therapeutics, and Pfizer; research funding to her institution from Janssen, Amgen, and Esperion; serves as the Deputy Editor for Equity, Diversity, and Inclusion at JAMA Cardiology - A.M.N. -received grant funding from the Department of Veterans Affairs, NIH, Tahir and Jooma Family, and UK NIHR; received honorarium from the American College of Cardiology for his role as an Associate Editor for Innovations, acc.org - S.V. -Associate Editor of AJPC - A.K. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100669.

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