Older adult preferences regarding benefits and harms of statin and aspirin therapy for cardiovascular primary prevention

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Abstract: OBJECTIVE Personalizing preventive therapies for atherosclerotic cardiovascular disease (ASCVD) is particularly important for older adults, as they tend to have multiple chronic conditions, increased risk for medication adverse effects, and may have heterogenous preferences when weighing health outcomes. However, little is known about outcome preferences related to ASCVD preventive therapies in older adults. METHODS In May 2021, using an established online panel, KnowledgePanel, we surveyed older US adults aged 65-84 years without history of ASCVD on outcome preferences related to statin therapy (benefit outcomes to be reduced by the therapy: heart attack, stroke; adverse effects: diabetes, abnormal liver test, muscle pain) or aspirin therapy (benefit outcomes: heart attack, stroke; adverse effects: brain bleed, bowel bleed, stomach ulcer). We used standardized best-worst scores (range of -1 for "least worrisome" to +1 for "most worrisome") and conditional logistic regression to examine the relative importance of the outcomes. RESULTS In this study, 607 ASCVD-free participants (median age 74, 46% male, 81% White) were included; 304 and 303 completed the statin and aspirin versions of the survey, respectively. For statin-related outcomes, stroke and heart attack were most worrisome (score 0.55; 95% CI 0.51, 0.60) and (0.53; 0.48, 0.58), followed by potential harms of diabetes (-0.07; -0.10, -0.03), abnormal liver test (-0.25; -0.29, -0.20), and muscle pain (-0.77; -0.82, -0.73). For aspirin-related outcomes, stroke and heart attack were similarly most worrisome (0.48; 0.43, 0.52) and (0.43; 0.38, 0.48), followed by brain bleed (0.30; 0.25, 0.34), bowel bleed (-0.31; -0.33, -0.28), and stomach ulcer (-0.90; -0.92, -0.87). Conditional logistic regression and subgroup analyses by age, sex, and race yielded similar results. CONCLUSIONS Older adults generally consider outcomes related to benefits of ASCVD primary preventive therapies-stroke and heart attack-more important than their adverse effects. Integrating patient preferences with risk assessment is an important next step for personalizing ASCVD preventive therapies for older adults.

DOI: https://doi.org/10.1016/j.ajpc.2023.100468

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DOI: https://doi.org/10.1016/j.ajpc.2023.100468

American Journal of Preventive Cardiology 13 (2023) 100468

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

Older adult preferences regarding benefits and harms of statin and aspirin therapy for cardiovascular primary prevention☆

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ARTICLE INFO

Keywords:
Older adult preferences
Cardiovascular primary prevention
Statin
Aspirin

ABSTRACT

Objective: Personalizing preventive therapies for atherosclerotic cardiovascular disease (ASCVD) is particularly important for older adults, as they tend to have multiple chronic conditions, increased risk for medication adverse effects, and may have heterogenous preferences when weighing health outcomes. However, little is known about outcome preferences related to ASCVD preventive therapies in older adults.

Methods: In May 2021, using an established online panel, KnowledgePanel, we surveyed older US adults aged 65-84 years without history of ASCVD on outcome preferences related to statin therapy (benefit outcomes to be reduced by the therapy: heart attack, stroke; adverse effects: diabetes, abnormal liver test, muscle pain) or aspirin therapy (benefit outcomes: heart attack, stroke; adverse effects: brain bleed, bowel bleed, stomach ulcer). We used standardized best-worst scores (range of -1 for "least worrisome" to +1 for "most worrisome") and conditional logistic regression to examine the relative importance of the outcomes.

Results: In this study, 607 ASCVD-free participants (median age 74, 46% male, 81% White) were included; 304 and 303 completed the statin and aspirin versions of the survey, respectively. For statin-related outcomes, stroke and heart attack were most worrisome (score 0.55; 95% CI 0.51, 0.60) and (0.53; 0.48, 0.58), followed by potential harms of diabetes (-0.07; -0.10, -0.03), abnormal liver test (-0.25; -0.29, -0.20), and muscle pain (-0.77; -0.82, -0.73). For aspirin-related outcomes, stroke and heart attack were similarly most worrisome (0.48; 0.43, 0.52) and (0.43; 0.38, 0.48), followed by brain bleed (0.30; 0.25, 0.34), bowel bleed (-0.31; -0.33, -0.28), and stomach ulcer (-0.90; -0.92, -0.87). Conditional logistic regression and subgroup analyses by age, sex, and race yielded similar results.

Conclusions: Older adults generally consider outcomes related to benefits of ASCVD primary preventive therapies—stroke and heart attack—more important than their adverse effects. Integrating patient preferences with risk assessment is an important next step for personalizing ASCVD preventive therapies for older adults.

1. Introduction

Preventive therapies for atherosclerotic cardiovascular disease (ASCVD) offer the potential benefits of reducing the risk of heart attacks and strokes [1]. Common ASCVD prevention strategies include promoting healthy lifestyles and treatment for those with hypertension and/or diabetes. In clinical guidelines, statin and aspirin therapies have especially attracted attention for primary ASCVD prevention. However, the evidence on the effectiveness of statins and aspirin is more limited in older adults, as many were excluded from earlier randomized controlled trials. Indeed, meta-analyses of statin therapy in older populations without established ASCVD are less conclusive than in younger groups [2–4]Older adults often have multiple chronic conditions, competing risks for mortality and morbidity, and limited life expectancy, all of

☆ The authors thank the staff and participants of the study for their important contributions.
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https://doi.org/10.1016/j.ajpc.2023.100468
Received 11 October 2022; Received in revised form 20 January 2023; Accepted 21 January 2023
Available online 30 January 2023

which may contribute to the decreased likelihood of accruing the long-term benefits of prevention [5,6].

In addition, adverse effects from treatment increase with age and number of chronic conditions. Older adults are also more likely to experience polypharmacy, which increases the risk for drug-drug interactions [7,8]. Prior research suggests that older adults may value outcomes not currently emphasized in clinical practice guidelines, including avoidance of treatment burden, risks and side effects [9]. In this context, personalized decision-making that considers older adults' preferences and priorities is critical [10]. The 2019 American College of Cardiology/American Heart Association (ACC/AHA) clinical guidelines for primary ASCVD prevention emphasize the importance of engaging in personalized decision-making for older adults age >75 [1]. However, as many adults between the ages 65-75 have multiple chronic conditions and limited life expectancy, personalized decision-making is important for this age group as well [11,12].

Despite the widespread use of preventive ASCVD therapy and recommendations to consider patient preferences in therapy decisions, little is known about older adults' preferences and priorities regarding clinical outcomes relevant to ASCVD prevention. A better understanding of older adults' preferences regarding the expected benefits and potential harms of ASCVD prevention could be valuable for informing clinical decision-making and tailored practice guidelines [13,14]. In this study, we aimed to quantify relative preferences for benefit and harm outcomes related to two major ASCVD prevention therapies, statin and aspirin, in older adults aged 65-84 years.

2. Methods

2.1. Study population

In May 2021, we conducted an online, cross-sectional preference-eliciting survey of older adults aged 65 to 84 years recruited from the KnowledgePanel, which is a probability-based online panel of over 60,000+ participants designed to be representative of adults living in households across the United States [15]. A random subset of panel members who were 1) ages 65-84 at the time of study and 2) without prevalent coronary heart disease or stroke in their participant profiles were invited to participate. We independently confirmed the above eligibility by asking a question about history of ASCVD at the beginning of the survey.

Panelists invited to participate were randomized to complete a survey related to either statin or aspirin therapy. We stratified recruitment by age (65-74 vs 75-84) within each survey version. The institutional review board of Johns Hopkins University approved this study.

3. Survey development and conduct

Each survey assessed participants' priorities regarding outcomes related to statin or aspirin therapy, including expected benefits and potential harms. Outcomes were identified based on the 2018 AHA/ACC/Multisociety Cholesterol Management Guidelines [16] and the 2019 ACC/AHA primary CVD prevention guidelines [1], and final selection was made by the study authors including primary care physicians, geriatricians, cardiologists, and epidemiologists. For the statin survey, we included benefit outcomes (i.e. outcomes expected to be reduced by the therapy) of heart attack and stroke, and harm outcomes (i.e., potential adverse effects) of diabetes, abnormal liver test, and muscle pain. For the aspirin survey, we included benefit outcomes of heart attack and stroke, and harm outcomes of brain bleed, bowel bleed, and stomach ulcer. The surveys were piloted with seven older adults who were not included in the final study sample and the surveys were iteratively revised (e.g. reworded, shortened, simplified) based on their feedback.

In the final survey (Supplement), after providing a description of each outcome, we first assessed the absolute importance of each outcome by asking the participants to rate the outcome's seriousness on a 10-point Likert scale. We then used best-worst scaling (BWS), a novel stated-preference research method, to examine the relative importance of the outcomes. BWS is a technique in which each participant is presented a list of objects (i.e. health outcomes in this study) and asked to choose the one object that they consider the best and the one object that they consider the worst [17,18]. As part of this technique, a subset of all relevant objects is presented at a given time in a single choice task and the participant is asked to complete a series of choice tasks where the objects in each choice task are systematically varied [19]. We constructed choice tasks using a balanced incomplete block design, which ensures that each outcome appeared with equal replication and co-occurrence with all other outcomes [20,21]. Each survey included five choice tasks where each choice task displayed four of the five outcomes. Within each choice task, participants were asked to choose the most and least worrisome outcomes. This method provides a ranked comparison and quantification of relative importance across outcomes, something that is not possible with traditional Likert scale surveys [22].

KnowledgePanel routinely collects data on the following sociodemographic characteristics: age, sex, race-ethnicity, education, and income. We collected additional health information on diabetes status, family history of ASCVD, and medication use.

4. Statistical methods

Participant characteristics were stratified by survey version (statin, aspirin) and age group (65-74, 75-84 years). Continuous variables were described as median and interquartile interval (IQI). Categorical variables were described as count and percentages. The characteristics of respondents and non-respondents were compared using the Kruskal-Wallis test for continuous variables and Fisher's exact test for categorical variables. The distributions of perceived seriousness for each outcome from the Likert scale rating were presented as histograms.

The relative importance of the outcomes from the BWS choice tasks was quantified using two approaches. First, we generated a best-worst score for each individual, which is the number of times each outcome was selected as "most worrisome" subtracted by the number of times it was selected as "least worrisome" across the number of choice tasks, standardized to the number of times the outcome was presented [23]. We then aggregated them for all participants. The best-worst score ranges from -1 for "least worrisome" outcome to +1 for "most worrisome". Second, we used conditional logistic regression to account for clustering by participant and by choice task [17]. An outcome was assigned a value of -1 if it was chosen as least worrisome, +1 if it was chosen as most worrisome, and 0 otherwise. The regression coefficients were transformed into odds ratios (OR), where an OR of 2 would mean that there was a two-fold higher odds of participants considering an outcome as more worrisome than the reference. We conducted pre-specified subgroup analyses by age (65-74, 75-84), sex, and race (White, non-White).

All analyses were performed using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided p-value less than 0.05 was used to determine statistical significance and 95% confidence intervals are presented.

5. Results

Out of 1,062 panel members age 65-84 invited to participate, 799 responded (75.2%). Among these, 607 confirmed that they did not have history of coronary heart disease or stroke and were included in the analysis. Responders and non-responders had similar sociodemographic characteristics, except that non-respondents age 65-74 tended to have slightly lower income (**Supplemental Table 1** and **2**). In our final analytic sample, 304 older adults (152 adults aged 75-84 years) completed the statin survey and 303 (151 adults aged 75-84 years) completed the aspirin survey. The median age was 74 years, 277 (46%) were male, and

Table 1
Participant characteristics by survey type and age group.

	Overall	Statins Age 65-74	Statins Age 75-84	Aspirin Age 65-74	Aspirin Age 75-84
n	607	152	152	152	151
Age (median [IQI])	74 [69, 78]	69 [67, 71]	78 [76, 80]	69 [67, 71]	78 [76, 80]
Male (%)	277 (45.6)	70 (46.1)	67 (44.1)	68 (44.7)	72 (47.7)
Race-Ethnicity (%)					
White, Non-Hispanic	493 (81.2)	118 (77.6)	127 (83.6)	120 (78.9)	128 (84.8)
Black, Non-Hispanic	47 (7.7)	14 (9.2)	9 (5.9)	17 (11.2)	7 (4.6)
Hispanic	40 (6.6)	11 (7.2)	9 (5.9)	9 (5.9)	11 (7.3)
Other	27 (4.4)	9 (5.9)	7 (4.6)	6 (3.9)	5 (3.3)
Education (%)					
No high school diploma or equivalent	37 (6.1)	10 (6.6)	13 (8.6)	6 (3.9)	8 (5.3)
High school	173 (28.5)	37 (24.3)	48 (31.6)	44 (28.9)	44 (29.1)
Some college/ Associate's degree	187 (30.8)	52 (34.2)	41 (27.0)	50 (32.9)	44 (29.1)
Bachelor's degree	93 (15.3)	22 (14.5)	25 (16.4)	26 (17.1)	20 (13.2)
Master's degree or higher	117 (19.3)	31 (20.4)	25 (16.4)	26 (17.1)	35 (23.2)
Household Income (%)					
Less than $10,000	6 (1.0)	2 (1.3)	1 (0.7)	2 (1.3)	1 (0.7)
$10,000 to $24,999	39 (6.4)	4 (2.6)	12 (7.9)	10 (6.6)	13 (8.6)
$25,000 to $49,999	129 (21.3)	34 (22.4)	39 (25.7)	27 (17.8)	29 (19.2)
$50,000 to $74,999	147 (24.2)	32 (21.1)	39 (25.7)	39 (25.7)	37 (24.5)
$75,000 to $99,999	89 (14.7)	21 (13.8)	24 (15.8)	24 (15.8)	20 (13.2)
$100,000 to $149,999	103 (17.0)	33 (21.7)	21 (13.8)	25 (16.4)	24 (15.9)
$150,000 or more	94 (15.5)	26 (17.1)	16 (10.5)	25 (16.4)	27 (17.9)
Region of Residence (%)					
Northeast	115 (18.9)	30 (19.7)	30 (19.7)	27 (17.8)	28 (18.5)
Midwest	122 (20.1)	36 (23.7)	23 (15.1)	32 (21.1)	31 (20.5)
South	221 (36.4)	52 (34.2)	59 (38.8)	57 (37.5)	53 (35.1)
West	149 (24.5)	34 (22.4)	40 (26.3)	36 (23.7)	39 (25.8)
Diabetes (%)	119 (19.6)	35 (23.2)	25 (16.4)	25 (16.4)	34 (22.5)
Family History of Heart Attack/Stroke before age 60 (%)	117 (19.4)	29 (19.3)	30 (19.7)	29 (19.1)	29 (19.3)
Number Prescribed Medicines/Day (%)					
<4	354 (58.6)	95 (62.9)	77 (50.7)	99 (65.6)	83 (55.3)
4-7	197 (32.6)	42 (27.8)	64 (42.1)	43 (28.5)	48 (32.0)
8-11	45 (7.5)	13 (8.6)	10 (6.6)	8 (5.3)	14 (9.3)
12-15	7 (1.2)	1 (0.7)	1 (0.7)	1 (0.7)	4 (2.7)
More than 15	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
Emergency Department Visit/ Hospitalization from Medication Adverse Effects (%)					
Yes	12 (2.0)	4 (2.6)	2 (1.3)	3 (2.0)	3 (2.0)
No	584 (96.4)	146 (96.7)	147 (96.7)	147 (96.7)	144 (95.4)
Not sure	10 (1.7)	1 (0.7)	3 (2.0)	2 (1.3)	4 (2.6)
Aspirin Daily (%)					
Current	215 (35.6)	51 (34.0)	56 (36.8)	59 (39.1)	49 (32.5)
Former	130 (21.5)	27 (18.0)	36 (23.7)	21 (13.9)	46 (30.5)
Never	259 (42.9)	72 (48.0)	60 (39.5)	71 (47.0)	56 (37.1)
Statin Use (%)					
Current	303 (50.2)	67 (44.7)	84 (55.6)	76 (50.0)	76 (50.3)
Former	53 (8.8)	12 (8.0)	16 (10.6)	10 (6.6)	15 (9.9)
Never	248 (41.1)	71 (47.3)	51 (33.8)	66 (43.4)	60 (39.7)

Table 2
Relative importance of outcomes related to use of statin and aspirin.

	Standardized Best-Worst Score (95% CI)*	Odds Ratios (95% CI)†
Statin Outcomes		
Stroke	0.553 (0.509, 0.598)	85.70 (69.46, 105.75)
Heart Attack	0.532 (0.484, 0.580)	80.96 (65.64, 99.86)
Diabetes	-0.065 (-0.101, -0.029)	9.55 (8.02, 11.39)
Abnormal Liver Test	-0.245 (-0.286, -0.204)	4.53 (3.88, 5.28)
Muscle Pain	-0.774 (-0.817, -0.730)	1 (Reference)
Aspirin Outcomes		
Stroke	0.479 (0.434, 0.523)	372.39 (263.01, 527.27)
Heart Attack	0.429 (0.383, 0.475)	321.96 (227.45, 455.73)
Brain Bleed	0.295 (0.252, 0.338)	221.37 (156.53, 313.06)
Bowel Bleed	-0.308 (-0.332, -0.283)	7.39 (6.06, 8.99)
Stomach Ulcer	-0.895 (-0.922, -0.868)	1 (Reference)

*Best-worst scores were calculated by summing the number of times each outcome was selected as "most worrisome" subtracted by the number of times it was selected as "least worrisome" for each participant, standardized to the number of times the outcome was presented, then averaged across all participants.[23] It ranges from -1 for "least worrisome" outcome to +1 for "most worrisome".

† Odds ratios, derived from conditional logistic regression, indicate the importance of outcomes relative to the reference. As an example interpretation, under statin outcomes, stroke is considered a 85.7 times more important outcome than muscle pain.

493 (81%) identified as non-Hispanic White (Table 1). Participants randomly assigned to the statin and aspirin survey had similar characteristics. Compared to those age 65-74, participants age 75-84 took more prescribed medications including aspirin and statin.

For both statin and aspirin surveys, stroke and heart attack were considered more worrisome than the harm outcomes (Table 2). For the statin-related outcomes, stroke and heart attack had best-worst scores of 0.55 (95% CI 0.51, 0.60) and 0.53 (0.48, 0.58), respectively. Diabetes was a moderately worrisome outcome (-0.07; -0.10, -0.03) out of the choices, followed by abnormal liver test (-0.25; -0.29, -0.20), and muscle pain was the least worrisome (-0.77; -0.82, -0.73). For aspirin outcomes, stroke and heart attack had scores of 0.48 (0.43, 0.52) and 0.43 (0.38, 0.48), respectively. Brain bleed was also worrisome with an average score of 0.30 (0.25, 0.34), followed by bowel bleed (-0.31; -0.33, -0.28).

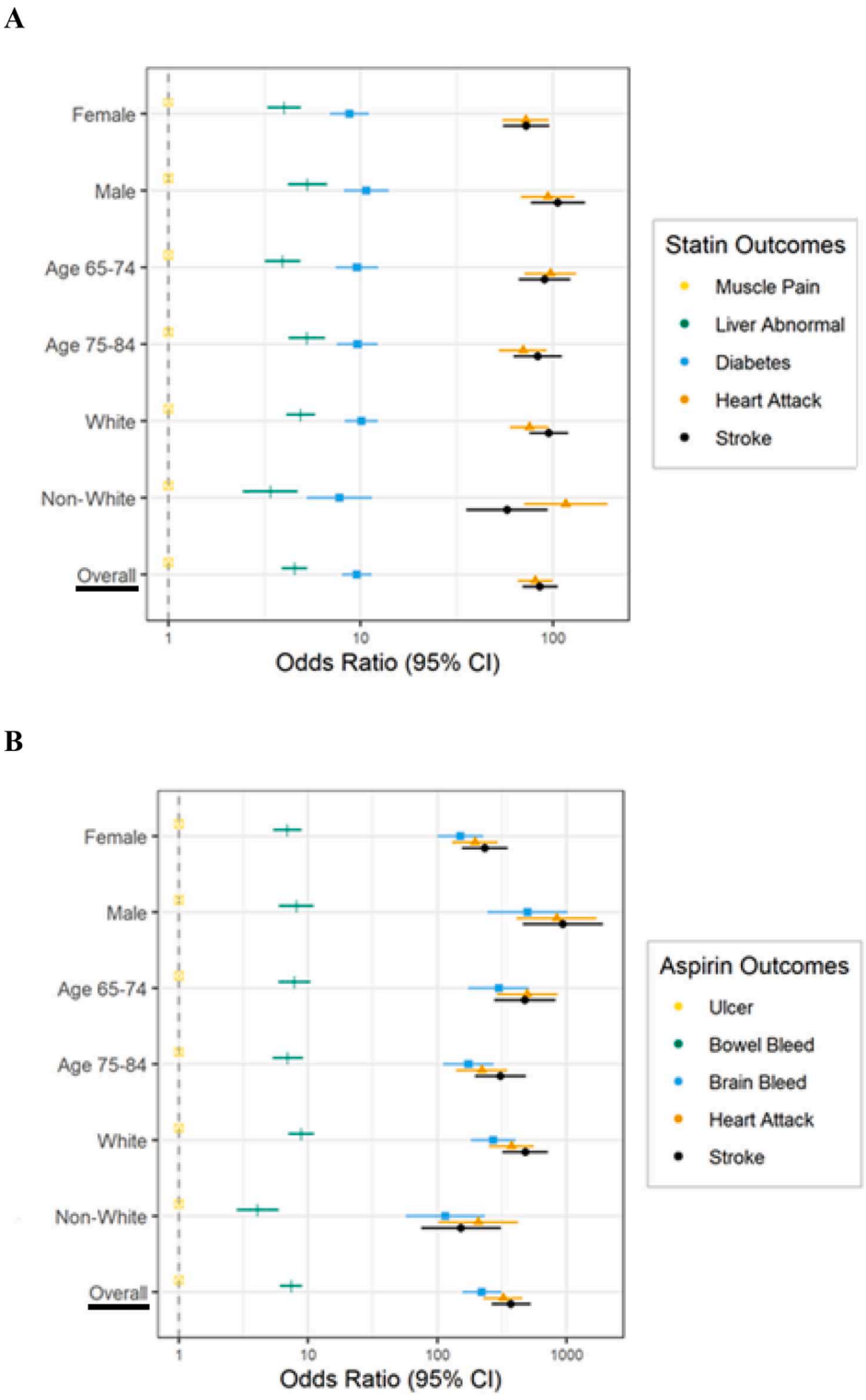

Fig. 1. Conditional logit subgroup analyses of outcome rankings by sex, age, and race for outcomes related to use of A) Statin and B) Aspirin.

Stomach ulcer was the least worrisome (-0.90; -0.92, -0.87).

Conditional logistic regression analyses demonstrated similar trends (Table 2). For statin-related outcomes, stroke (OR 85.7; 95% CI 69.5, 105.8) and heart attack (OR 81.0; 65.6, 99.9) had significantly higher odds of being perceived as more worrisome compared to muscle pain. For aspirin-related outcomes, stroke (OR 372.4; 263.0, 527.3) and heart attack (OR 322.0; 227.5, 455.7) were again considered significantly more worrisome than stomach ulcers. In subgroup analyses, the relative importance of outcomes was generally consistent across age, sex, and racial subgroups (Fig. 1).

Although stroke and heart attack were the most worrisome outcomes overall, there was heterogeneity in participants' priorities. Some individuals prioritized harm-related outcomes and chose those as the most worrisome in choice tasks (**Supplemental Fig. 1**). For example, brain bleed and diabetes were each chosen as the most worrisome outcome in ~25% and 5% of the choice sets, respectively. The distributions of the Likert-based 1-10 seriousness ratings of the individual outcomes, which do not consider relativity to other outcomes, are depicted in Fig. 2. Even

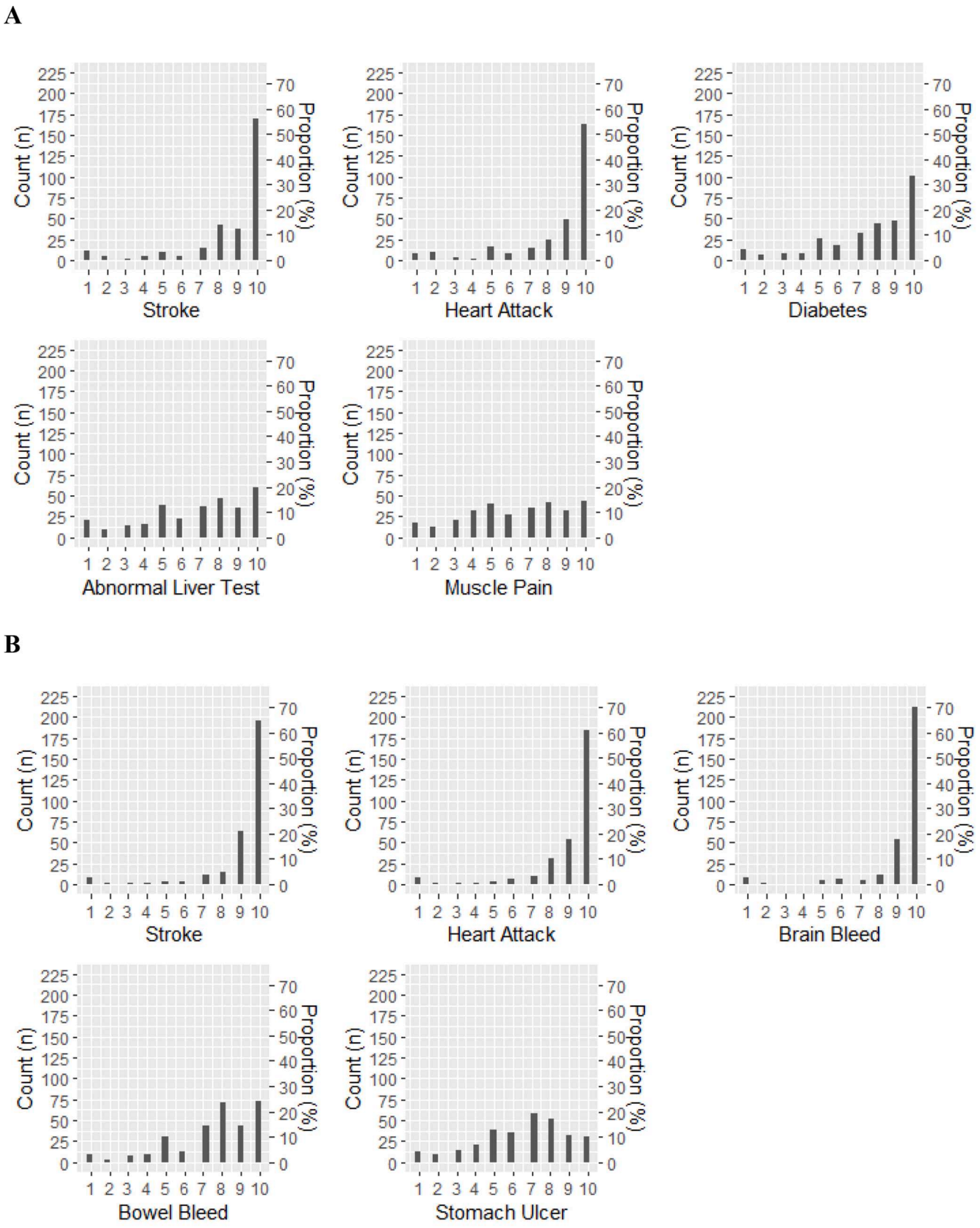

Fig. 2. Outcome seriousness rating (1-Least Serious to 10-Most Serious) for outcomes related to use of A) Statin and B) Aspirin.

the outcomes that were rated as least worrisome in BWS rankings were still rated as highly (i.e., 10/10) serious by some participants. For example, for statin-related outcomes, 20% rated abnormal liver test as 10/10 serious, and 14% rated muscle pain as 10/10 serious. For aspirin-related outcomes, 24% rated bowel bleed as 10/10 serious, 10% rated stomach ulcer as 10/10 serious.

6. Discussion

To our knowledge, this is the first national study in the US on older adults' priorities regarding ASCVD primary prevention therapy outcomes. In this online survey of older adults ages 65-84 without prevalent coronary heart disease or stroke, we found that outcomes related to expected benefits of statin and aspirin therapy—stroke and heart attack—were perceived as significantly more worrisome than outcomes related to the potential harms of these therapies, with a difference in relative importance of up to 372-fold higher odds. Among the harm outcomes, diabetes and brain bleed were the most worrisome. The patterns and magnitudes of these preferences were consistent between older adults aged 65-74 and 75-84 years and by sex and race.

Our findings are consistent with studies from other countries. In middle aged populations in Ethiopia and Switzerland, stroke and myocardial infarction were found similarly to be more worrisome relative to potential side-effects of statins including liver injury and diabetes [20]. Another pilot study of 42 participants in Canada similarly reported that aspirin-related benefits of stroke and heart attack were most worrisome outcomes, followed by the aspirin-related harm of bleeding events [24].

There is an increasing recognition of the need to generate more evidence on the benefits and harms of ASCVD prevention in the older adult population. Our results add complementary information on how older adults prioritize such benefits and harms. Benefit-harm balance is assessed using three key inputs: the relative effect estimates of therapy on benefit and harm outcomes, baseline risk of outcomes without therapy, and preference weighting for the benefit and harm outcomes from the patient perspective [13,25,26]. Our results supply the preference weighting inputs for such work and can help inform guideline recommendations at the population level.

The preferences reported by older adults in our study align with current guideline recommendations regarding risk-based use of statins—with more consideration placed on preventing ASCVD than avoiding statin side effects for those at intermediate ASCVD risk. Interestingly, the older adults' preferences were not significantly different between those ages 75-84 and those ages 65-74, even though guidelines on statin use for ASCVD prevention shift away from risk-based recommendations in older adults ages 75-and-older [27]. Studies to better evaluate the efficacy of statin therapy in older adults, such as the ongoing PREVENTABLE trial, are much needed since adults 75 years and older still place high importance over the outcomes that statins can potentially help prevent or reduce [28]. Recent guidelines have shifted against routinely recommending aspirin therapy for primary ASCVD prevention in older adults, including those age 60-and-older per the USPSTF or those older than 70 per the ACC/AHA, due to a high risk of adverse bleeding outcomes relative to ASCVD prevention value [1,12]. However, on a patient preference standpoint, our findings suggest that many older adults nonetheless prioritize the expected benefit outcomes of aspirin therapy over the potential side effects.

Our results also highlight the heterogeneity in older adults' priorities regarding the outcomes [29]. Even the outcomes that were considered the least worrisome overall, such as muscle pain and stomach ulcer, were still rated as highly serious by >10% of older adults. These results suggest that most older adults may prefer to choose therapies to avoid ASCVD whereas some may prioritize avoiding side effects. Thus, for both statin and aspirin therapy decisions, it is important for clinicians to fully discuss the benefits and harms of therapy and engage in shared decision making that considers individual older adult preferences. Also, this heterogeneity in preferences may, in turn, contribute to different behaviors related to medication adherence; thus, it would be of interest to explore whether individual preferences are linked with adherence to preventive therapies in older adults.

This study has limitations. First, our findings could be susceptible to non-response bias, although we achieved a relatively high response rate and there were no notable sociodemographic differences between respondents and non-respondents. Second, the format of BWS may be unfamiliar to participants which could lead to inaccurate responses. However, this limitation is true for all preference eliciting techniques and at the end of the choice tasks, only 1% of the participants disagreed with the statement "I answered the questions in this section in a way consistent with my preferences." Additionally, to minimize the survey burden on older adult participants, we limited the survey to five outcomes for each therapy and did not include other potentially relevant outcomes such as bruising or dyspepsia from aspirin therapy. Lastly, while this study focuses on statin and aspirin therapy, it is important to note there are other lifestyle and pharmacologic primary prevention therapies not covered in the scope of this analysis including anti-hypertensive and anti-diabetes medications.

In conclusion, older adults ages 65-84 considered outcomes related to expected benefits of statins and aspirin, i.e., prevention of stroke and heart attack, significantly more worrisome than their potential harms. These results highlight the importance older adults place on preventing ASCVD outcomes, despite ambiguity in ASCVD primary prevention guidelines for older adults beyond age 75. However, some of the harm outcomes were also considerably worrisome to some participants, particularly brain bleed and diabetes. This implies the need for tailored ASCVD primary prevention discussions based on risk profiles and patient preferences for therapy-related benefit and harm outcomes.

Disclosures

The authors declare no conflicting interests.

Declaration of Competing Interest

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

Acknowledgment

This study was supported by R01HL136592 from the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) F.W. received support from the NIH T32 institutional training grant (T32 HL007024).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2023.100468.

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