



Do Patient Concerns About Antihypertensive Use For Dementia Prevention Vary By Current Use Of Antihypertensive?

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Purpose: Antihypertensives may have effects on the brain beyond blood pressure lowering. Ongoing clinical trials aim to evaluate the effectiveness of approved antihypertensives in preventing dementia, including patients with and without hypertension. In order for a dementia prevention strategy using antihypertensives to be effective, it is critical to understand patient concerns about this strategy in both users and non-users of antihypertensives. Thus, this study examined the association between current use of antihypertensive and having concerns about using an antihypertensive as a dementia prevention strategy, as well as sociodemographic factors associated with concerns.

Patients and methods: Cross-sectional, self-administered, web-based survey was conducted among 1661 patients in a large health system in January 2018. Participants reported whether they were currently taking an antihypertensive (yes/no), and what types of hypothetical concerns they have about the idea of taking an antihypertensive to prevent dementia (yes/no, for each of 7 concerns). Associations between the two variables were assessed via logistic regression, and odds ratios with 95% confidence intervals were calculated.

Results: Most respondents were female (77%), 51–70 years of age (64%), and white (89%), with 30% reporting current antihypertensive use. Compared to current users, non-users were more likely to report the five following concerns: side effects from the medication, hassle to take medications, lack of evidence, not wanting to use medications, and already having normal/low blood pressure. Non-users were also less likely to report having no concerns (adjusted OR = 0.3; 95% CI = 0.2–0.4) compared to current users. Younger age and lower income were associated with having more concerns.

Conclusion: Patients not currently using an antihypertensive are more likely to have concerns about using an antihypertensive for dementia prevention, compared to current antihypertensive users. Patient perspectives are important to consider for the implementation of dementia prevention strategies.

Keywords: dementia, antihypertensives, primary prevention, patient concerns, patient perspectives

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Introduction

Ongoing clinical trials, such as the Mechanistic Potential of Antihypertensives in Preclinical Alzheimer's Trial (HEART), aim to evaluate whether approved antihypertensives can be repurposed as a dementia prevention strategy.^{1–4} Such trials are supported by a large body of literature from both animals and humans on the role of the renin-angiotensin system in dementia development.^{4–14} Of note, some

antihypertensives are thought to have brain protectant effects beyond their role in decreasing blood pressure.^{1,2} Given this, individuals with and without hypertension could possibly benefit from antihypertensive use to reduce the risk of dementia.

Despite these potential benefits, little is known about people's specific concerns (e.g., side effects such as hypotension) regarding the use of antihypertensives as a dementia prevention strategy. We previously published results from a mixed-method study showing that the vast majority of respondents currently taking an antihypertensive reported that they would be willing to take that specific antihypertensive starting as early as mid-life if it were shown to prevent or delay dementia.¹⁵ Moreover, those currently taking an antihypertensive were more likely to report no concerns compared to those not taking an antihypertensive. This finding suggests differential beliefs toward this emerging dementia prevention strategy based on current antihypertensive use; however, this association may be confounded by individual characteristics.¹⁵ Thus, the current analysis aims to examine the association between current use of an antihypertensive and having concerns about using an antihypertensive as a dementia prevention strategy, adjusting for potential confounders. In addition, we examine if those concerns vary by sociodemographic characteristics.

Materials And Methods

Study Design

This cross-sectional study used data obtained from a web-based survey. The survey includes sociodemographic characteristics of members of Kaiser Permanente Washington, an integrated healthcare delivery system in Washington State, as well as responses from the following three domains: (1) brain health and dementia prevention; (2) medications as risk or protective factors for dementia; and (3) antihypertensive use as a potential dementia prevention strategy. Development of the survey has been previously described.¹⁶

Participants

Study participants were sampled in January 2018 through Northwest Health News, a monthly electronic newsletter emailed to Kaiser Permanente Washington members. The newsletter included information on the study and a link to direct interested participants to the web-based survey via the newsletter. Eligible participants were those aged 18 or

older, were Kaiser Permanente Washington members, and could read and write English. A total of 1661 people completed the survey and were included in the analysis. The Institutional Review Board at the Kaiser Permanente Washington Health Research Institute approved all study materials and procedures.

Measures

For this analysis, the primary independent variable was self-reported current use of an antihypertensive. To operationalize this variable, we used an item from the third survey domain that asks all participants "Are you currently taking a medication for your blood pressure?" Participants responded either yes or no.

Our outcome variables of interest – concerns about taking antihypertensives as a dementia prevention strategy – were also collected from the third survey domain. All participants were asked, "What main concerns do you have about the idea of taking a blood pressure medication for the rest of your life in order to possibly prevent Alzheimer's disease or other forms of Dementia?" Participants were then asked to select all that apply from eight different options as follows: (1) side effects from the medication; (2) hassle to take medication every day; (3) expense/cost of the medication; (4) inability to remember to take medication when I should; (5) lack of evidence showing that this will reduce my risk; (6) do not want to use a medication; (7) my blood pressure is already normal or low; and (8) I have no concerns. Participants responded either yes or no.

Sociodemographic factors – sex, age, race, ethnicity, education, and annual household income – were included to adjust for potential confounding and to be investigated for association with the outcome variables.

Data Analysis

Frequency distributions were used to describe respondent characteristics. Statistical differences in participants' demographic factors between those who reported currently taking antihypertensives versus those who did not were compared using a z-test.¹⁷ To examine whether current use of antihypertensives was associated with reporting each individual concern, eight separate logistic regression models were fitted for each outcome, adjusted for sex, age, race, ethnicity, education, and annual household income. For each of these concerns (models), an odds ratio and a 95% confidence interval were calculated, contrasting non-users (of antihypertensives) relative to current users. To

examine the association between sociodemographic covariates and the outcome variables, joint significance of each covariate was tested using a Wald test, with p-value reported. Odds ratios comparing each subgroup with the corresponding reference group were estimated using partial F-tests. Significance level was set at 0.05. All analyses were conducted using STATA/MP software, version 14.2.

Results

Respondent Characteristics

Of the 1661 participants, 76.7% identified as female and 63.5% were aged 51–70 years. The majority were white (86.2%) and non-Hispanic (91.0%) (Table 1). Approximately one-third of respondents reported current use of antihypertensives (n=505; 30.4%). When compared to current users of antihypertensive medication (n=505), a higher proportion of non-users were male, younger, more educated, and had higher annual income (Supplemental Table A1).

Concerns By Antihypertensive Use

Logistic regression models adjusting for sociodemographic factors showed that non-users were significantly more likely to report five types of concerns: side effects from medications (OR = 2.1, 95% CI: 1.6, 2.8), hassle of taking medications every day (OR = 2.9, 95% CI: 1.7, 4.9), lack of evidence (OR = 2.3, 95% CI: 1.8, 3.0), do not want to use a medication (OR = 7.6, 95% CI: 3.3, 17.5), and normal/low blood pressure (OR = 40.3, 95% CI: 24.8, 65.5) (Table 2). An adjusted logistic regression model also demonstrated that the likelihood of “having no concerns” was significantly lower among non-users of antihypertensives (OR = 0.3, 95% CI: 0.2, 0.4) compared to current users.

Sociodemographic Characteristics Associated With Concerns

Among all sociodemographic characteristics, age, income, sex, and race were associated with having certain concerns, with other sociodemographic variables and current use of an antihypertensive controlled for (Table 3). Older respondents were less likely to have concerns about side effects from medications ($p = 0.009$), hassle of taking medications ($p < 0.001$), and costs of medications ($p < 0.001$). Higher income was associated with having fewer concerns about side effects from medications ($p = 0.012$), costs of medications ($p < 0.001$), and inability to remember to take medications when they should ($p = 0.023$). Lastly, females reported fewer concerns about lack of evidence ($p = 0.049$) and not wanting to

Table 1 Survey Respondent Characteristics (N=1661)

	Respondents No. (%)
Sex	
Female	1274 (76.7)
Male	317 (19.1)
Non-binary	3 (0.2)
Prefer not to answer/skipped	67 (4.0)
Age, y	
21–40	94 (5.7)
41–50	149 (9.0)
51–60	392 (23.6)
61–70	662 (39.9)
71–80	300 (18.1)
≥81	59 (3.6)
Skipped	5 (0.3)
Race	
White	1432 (86.2)
Asian	35 (2.1)
Black or African American	17 (1.0)
Other	69 (4.2)
Prefer not to answer/skipped	108 (6.5)
Ethnicity	
Non-Hispanic	1512 (91.0)
Hispanic	42 (2.5)
Don't know/prefer not to answer/skipped	107 (6.5)
Education	
High school graduate or lower	73 (4.4)
Some college	407 (24.5)
College graduate	412 (24.8)
Some post-graduate	178 (10.7)
Post-graduate	530 (31.9)
Prefer not to answer/skipped	61 (3.7)
Annual household income, \$	
<35,000	151 (9.1)
35,000–49,999	188 (11.3)
50,000–74,999	314 (18.9)
75,000–99,999	291 (17.5)
≥100,000	404 (24.3)
Don't know/prefer not to answer/skipped	313 (18.9)
Current use of antihypertensives	
Current use	505 (30.4)
Non-use	1151 (69.3)
Prefer not to answer	5 (0.3)

use a medication ($p = 0.019$), but were more likely to be worried about their blood pressure already being normal or low ($p = 0.001$) compared to males. Asian respondents appeared to have more concerns compared to Whites for certain concerns: hassle to take medications ($p = 0.027$),

Table 2 Association Between Antihypertensive Use And Concerns About Antihypertensive Use As A Dementia Prevention Strategy (Non-Current Users Vs Current Users; N=1661)

Concerns (Dependent Variables)	Number Of People With Concerns (%)	Adjusted Odds Ratio (OR) ^a	95% Confidence Interval Of OR	p-Value
Side effects from the medication	1,253 (75.4)	2.1	(1.6, 2.8)	<0.001
Hassle to take medication every day	195 (11.7)	2.9	(1.7, 4.9)	<0.001
Expense/cost of the medication	727 (43.8)	1.1	(0.8, 1.4)	0.63
Inability to remember to take medication when I should	78 (4.7)	1.5	(0.8, 2.9)	0.23
Lack of evidence showing that this will reduce my risk	964 (58.0)	2.3	(1.8, 3.0)	<0.001
Do not want to use a medication	123 (7.4)	7.6	(3.3, 17.5)	<0.001
My blood pressure is already normal or low	775 (46.7)	40.3	(24.8, 65.5)	<0.001
I have no concerns	175 (10.5)	0.3	(0.2, 0.4)	<0.001

Notes: ^aOdds ratios and 95% confidence intervals calculated using separate logistic regression models adjusted for sex, age, race, ethnicity, education, and annual household income.

inability to remember ($p = 0.020$), and not wanting to use medications ($p = 0.029$). However, these results should be interpreted with caution because of the small number of Asian respondents ($n = 35$).

Discussion

This cross-sectional study of a web-based survey demonstrated that those who are not currently taking antihypertensives are more likely to have concerns about the idea of using antihypertensives as a dementia prevention strategy than current antihypertensive users, after adjusting for sociodemographic variables. In addition, we found that age, income, and sex were associated with the likelihood of having certain concerns regardless of current use of antihypertensives. We extend our prior work and determine that patients' concerns about this emerging dementia prevention strategy differ significantly by current antihypertensive use and sociodemographics.

For concerns about potential side effects, hassle of taking medications, and lack of efficacy evidence, the likelihood of having these concerns was about two to three times greater in non-users of antihypertensives compared to current users. The gap between current users and non-users was much greater, however, for the concern of not wanting to use a medication and the concern about blood pressure being already normal or low. Specifically, people not currently using an antihypertensive had greater likelihood of expressing these concerns compared to current users. This result indicates that people with normal

blood pressure (i.e., not taking antihypertensives) call for strong justification of the need to take antihypertensives for dementia prevention in addition to the evidence for efficacy and safety of this strategy. This is a valid concern due to the risk of hypotension from antihypertensive use.¹⁸ Thus, clinical trials that aim to test this potential dementia prevention strategy might require additional recruitment efforts for enrolling individuals without hypertension.

It should be noted that sociodemographic characteristics such as age, annual household income, and sex were associated with different concerns about this strategy. Younger respondents appeared to have more reservations than older respondents about potential side effects, the hassle of taking a medication every day, and costs of the medication. This finding is likely explained by younger adults having more skepticism about dependence on medications to prevent diseases that may or may not develop in the distant future, which makes them less willing to accept the hassle and expense.^{19,20} In addition, we found that concerns regarding side effects, costs of medications, and inability to remember to take medications tended to be more common among people with lower income. Personal and contextual factors such as fear of harm from medication, complicated instructions, and less access to medications have shown to be major barriers to medication adherence in those with low income.²¹ Patient-centered discussions between patients, their family members, and health care providers on these potential concerns may improve patient engagement in this strategy.

Table 3 Sociodemographic Characteristics Associated With Concerns About Antihypertensive Use As A Dementia Prevention Strategy (Values Reported: Odds Ratios; N=1661)

Independent Variables ^e	Concerns ^d							
	a	b	c	d	e	f	g	h
	Side Effects	Hassle	Expense	Inability To Remember	Lack Of evidence	Not Wanting To Use Med	Normal Or Low Blood Pressure	No Concern
Sex ^f	–	–	–	–	–	–	–	–
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.93	0.66	1.10	0.69	0.75 ^a	0.53 ^a	1.77 ^b	1.01
p-value ^g	0.68	0.06	0.51	0.24	0.05	0.02	0.001	0.97
Age (year) ^h	–	–	–	–	–	–	–	–
≤50	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
51–60	0.75	0.59 ^a	0.65 ^a	0.38 ^a	0.94	0.77	1.19	1.24
61–70	0.58 ^a	0.41 ^b	0.38 ^c	0.45 ^a	0.93	0.80	1.15	2.04 ^a
71–80	0.51 ^b	0.32 ^b	0.16 ^c	0.54	1.02	0.82	1.53	1.85
≥81	0.29 ^b	Omitted ⁱ	0.13 ^c	0.50	0.94	0.58	0.67	3.55 ^b
p-value ^g	0.01	<0.001	<0.001	0.11	0.98	0.92	0.36	0.06
Race	–	–	–	–	–	–	–	–
White	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Black	0.62	0.76	1.55	Omitted ⁱ	1.54	Omitted ⁱ	0.87	1.39
Asian	0.50	2.65 ^a	0.86	3.57 ^a	0.94	2.87 ^a	2.48	0.38
Other	1.19	1.53	1.38	1.15	1.02	1.20	1.14	0.63
p-value ^g	0.34	0.11	0.62	0.06	0.93	0.11	0.41	0.64
Ethnicity	–	–	–	–	–	–	–	–
Non-hispanic	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Hispanic	1.39	0.94	1.16	0.42	1.18	2.14	0.46	1.27
p-value ^g	0.47	0.90	0.72	0.43	0.66	0.17	0.05	0.67
Education	–	–	–	–	–	–	–	–
≤High school graduate	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Some college	1.12	0.76	1.44	1.13	1.15	0.71	0.67	0.88
College graduate	1.48	0.88	1.19	1.00	1.34	1.15	0.99	0.51
Some post-graduate	1.69	1.27	1.57	1.03	1.25	2.04	0.99	0.79
Post graduate degree	1.77	1.09	1.22	0.81	1.43	1.10	0.96	0.56
p-value ^g	0.09	0.55	0.46	0.90	0.57	0.11	0.26	0.13
Income (\$)	–	–	–	–	–	–	–	–
<35,000	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
35,000–49,999	0.78	0.57	0.98	0.54	1.07	0.63	1.80 ^a	1.31
50,000–74,999	0.75	0.67	0.67	0.60	0.86	0.52	1.14	1.40
75,000–99,999	0.89	0.80	0.47 ^b	0.37 ^a	1.09	0.57	1.37	1.10
≥100,000	0.50 ^b	0.62	0.34 ^c	0.28 ^b	0.81	0.38 ^a	1.54	2.04 ^a
p-value ^g	0.01	0.50	<0.001	0.02	0.33	0.16	0.17	0.10

Notes: ^ap<0.05, ^bp<0.01, ^cp<0.001; ^d(a) Side effects from the medication, (b) Hassle to take medication every day, (c) Expense/cost of the medication, (d) Inability to remember to take medication when I should, (e) Lack of evidence showing that this will reduce my risk, (f) Do not want to use a medication, (g) My blood pressure is already normal or low, and (h) I have no concerns; ^eCurrent use of antihypertensives was included in each model as an independent variable; ^fThose who identified themselves as non-binary were omitted due to a very small sample size; ^gp-value from Wald test, adjusted for all other covariates; ^hAge categories below 40 and 41–50 were combined; ⁱDummy variables were omitted due to a perfect correlation with the outcome variable.

This study is not without limitations. Our study results may not generalize to other populations, given that this survey was implemented in a convenience sample of

adults from a single region in the US. Since older non-Hispanic white females were overrepresented in this study sample, care should be taken when applying these results

to a population with different sociodemographic distributions. There could be a potential selection bias if the respondents of survey were systematically different from non-respondents. Future surveys should examine people's concerns about this strategy in more generalizable groups that include more diverse sociodemographic characteristics. Furthermore, past medication history, which can possibly affect perspectives of medication use, was not collected and thus not adjusted for in our analysis. There is a possibility that non-users of antihypertensives have taken them in the past, which our survey did not capture. In addition, people with different diseases or past medication experience might have dissimilar concerns of this strategy. There is also a potential of residual bias since duration of antihypertensive use may influence concerns. Future studies should explore varying concerns among people, considering their disease and medication history, including duration of medication use. We were also unable to calculate a survey response rate since we could not measure how many people opened the electronic newsletter. However, we viewed results as hypothesis-generating for future research efforts.

Conclusion

In conclusion, patients not currently using an antihypertensive are more likely to have concerns about using an antihypertensive for dementia prevention, compared to current users. Specifically, non-users of antihypertensives expressed concerns about already having normal or low blood pressure as well as potential efficacy and safety issues. While not surprising, these patient perspectives can help inform the implementation of this evolving dementia prevention strategy.

Ethics Approval And Informed Consent

The Institutional Review Board at the Kaiser Permanente Washington Health Research Institute approved all study materials and procedures. Participants provided consent upon completing the survey.

Data Availability

Data are available from the corresponding author upon request.

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Author Contributions

All authors listed meet the IMCJE guidelines for authorship. All authors contributed to data analysis, drafting, or revising the article, gave final approved of the version to be published and agree to be accountable for all aspects of the work.

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