Journal of the American Geriatrics Society

Journal of the
American Geriatrics Society

CLINICAL INVESTIGATION OPEN ACCESS

The Bright Side of Life: Optimism and Risk of Dementia

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Received: 29 October 2025 | **Revised:** 24 February 2026 | **Accepted:** 4 March 2026

Keywords: cognitive aging | dementia | optimism | psychosocial factors

ABSTRACT

Background: Previous studies suggest that higher optimism is associated with better cognitive function and slower cognitive decline in aging. Using data from the Health and Retirement Study, a nationally representative sample of older U.S. adults, we examined whether optimism was associated with lower risk of developing dementia in different population groups and if associations were maintained after accounting for initial health status and other potential confounders and across multiple sensitivity analyses.

Methods: Optimism was measured using the validated Life Orientation Test-Revised in 9071 cognitively healthy individuals within 2 years of obtaining each person's first measure of cognitive function. Dementia was identified by an algorithm developed to perform well across major racial and ethnic groups, obtained at each of eight waves of data collection from 2006 to 2020. Cox proportional hazard models were used, and sensitivity analyses addressed major concerns such as reverse causation.

Results: We observed that a 1-standard deviation increase in optimism was associated with a lower hazard of developing dementia (hazard ratio = 0.85, 95% confidence interval 0.82–0.88), after adjusting for age, sex, race and ethnicity, education, depression, and major health conditions over follow-up ranging up to 14 years. When stratifying by race and ethnicity, we observed similar associations in the Non-Hispanic White and Black sub-populations. Associations did not substantially change when health behaviors were included in the models, when we removed the first 2 years of follow-up to mitigate concerns about potential reverse causation, or when we excluded individuals with the poorest mental health.

Conclusion: Higher optimism was associated with a lower incidence of dementia. These findings suggest a potential value of optimism in supporting healthy aging, which could be considered in future research on dementia prevention initiatives.

1 | Introduction

Approximately 57 million people in the world live with dementia [1]. Given its high prevalence and limited options for curative treatment, identifying strategies for prevention is critical. Emerging epidemiological evidence suggests that psychosocial factors are related to the risk of developing dementia, providing possible novel upstream targets for prevention [2, 3]. Recent studies have linked optimism with exceptional longevity and healthy aging more generally [4–7], suggesting it may also contribute to protecting cognitive health in aging [4, 7–9]. While optimism has been estimated to be about 25% heritable [10], numerous studies show it can be modified with interventions specifically designed to alter levels of optimism [11–13]. Therefore,

The results have been submitted and accepted as a poster at GSA Annual Scientific Meeting.

Summary

- Key points
  - Higher optimism was associated with a lower risk of developing dementia over up to 14 years of follow-up in a large, nationally representative cohort.
  - Sensitivity analyses suggested that this association was robust and not due to reverse causality, confounding, or poor baseline mental health.
  - The protective association of optimism with dementia risk was consistent in both Non-Hispanic White and Black sub-populations.
- Why does this paper matter?
  - Identifying optimism as a protective psychosocial factor highlights the potential value of optimism in supporting healthy aging. Although optimism is a complex construct, and it is not clear exactly how it might translate in terms of future dementia prevention initiatives, this is an area which merits future research. This is important given the rising prevalence of dementia and the current lack of effective treatments.

studies on optimism and dementia could provide important evidence for future dementia prevention initiatives. Findings thus far are promising, but concerns remain regarding potential reverse causation. Furthermore, studies with lengthy follow-up periods (i.e., > 10 years) that include both men and women are not yet available but would facilitate greater understanding of these associations and their strength in different populations.

Associations between optimism and cognitive health have been observed in several studies to date [3, 14–16]. Of note, most were longitudinal, but follow-up varied from 4 to 17 years, with a median follow-up of 9 years in the longest study including only women. The longest study used data from the Women's Health Initiative, a longitudinal study on postmenopausal women aged 65–79 at baseline, and showed that women with higher optimism were less likely to develop dementia [3]. In addition, two studies were conducted among participants in the Health and Retirement Study (HRS). One included 4624 adults older than 65 years and found reduced odds of becoming cognitively impaired with higher optimism levels over the relatively short follow-up of 4 years [14]; the second included a subsample of Black participants in HRS (mean age of 61 years) who lived during the Jim Crow era and Civil Rights Movement followed across 8 years and found an association of higher optimism with better cognitive status at baseline but not over time [16]. Given the limited set of longitudinal studies, some with relatively shorter follow-up periods, concerns remain regarding the potential for reverse causality whereby declining cognitive health may influence optimism rather than vice versa. Relatedly, questions remain regarding the durability of the association over time. Additional longitudinal data is now available in the HRS as well as a new dementia algorithm which has been validated in major racial and ethnic groups [17]. The more extended follow-up permits additional analyses that can further address concerns about reverse causation that were not feasible in the original studies.

Compared to prior work in the same HRS cohort, a diverse, nationally representative sample of U.S. men and women, the present study extends the follow-up to 14 years (2006–2020), captures a larger number of dementia cases, and includes sensitivity analyses to examine the relationship between dispositional optimism and the risk of developing dementia. We hypothesized higher levels of optimism at baseline among dementia-free adults would be associated with lower risk of developing dementia in different populations including men and women, Non-Hispanic White and Black participants.

2 | Methods

2.1 | Study Population

The HRS is an ongoing, nationally representative cohort study in the U.S. that began in 1992 and has followed men and women aged 50 years and older through biennial in-person interviews, telephone, and mailed questionnaires. The HRS is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan. Further details of the HRS are described elsewhere [18]. We included participants who had cognitive assessments and the other required measures for the dementia algorithm from in-person or telephone interviews at the age of 70 and thereafter, because our dementia algorithm was developed for that age group. Cognitive assessments have been conducted at each wave starting in 1996 through 2020. The analytic baseline for each participant was ascertained once they reached age 70, set as the earliest time at which a dementia algorithm measure could be derived, and an optimism measure was completed (at the same time or 2 years prior). Optimism was first assessed in 2006 when half of the HRS participants, randomly selected, received a self-administered psychosocial survey that included a measure of dispositional optimism. The remaining participants received the same survey in 2008, and, subsequently, the questionnaire has been administered every 4 years. Thus, the earliest start of follow-up in the present study was 2006 or 2008.

Participants were excluded if they lacked complete data for the dementia algorithm from at least two waves once they reached the age of 70 or had not completed an optimism measure within 2 years of a dementia assessment. Participants were also excluded if they had probable dementia at or before their analytic baseline. Because the algorithm was not optimized to estimate dementia status for participants who were not Non-Hispanic White, Non-Hispanic Black, or Hispanic/Latino, these participants were excluded ($n = 332$). Further details on sample selection are included in Figure S1. This study used de-identified, publicly available data [19], resulting in a non-human subjects research determination from the Institutional Review Board at the Harvard T.H. Chan School of Public Health.

2.2 | Measures

Optimism was measured through self-report via the Life Orientation Test-Revised (LOT-R), which has good discriminant and convergent validity and reliability [20]. Participants rated six statements on a 6-point Likert scale, ranging from 1

("strongly disagree") to 6 ("strongly agree"). See Methods S1 for specific items. The scale was developed to provide a sum score that combines both positively and negatively worded items [21]. Therefore, three negatively worded items were reverse-coded, and all items were summed (score range: 6–36), with higher scores reflecting higher optimism. To make findings more easily comparable with other studies, we standardized the scores. Following similar work with psychological measures, if participants were missing > 50% of the optimism items, they were excluded; otherwise, missing items were replaced using mean imputation ($N = 412$, 4.5%) [22]. We also created distributional quartiles of raw optimism scores in the sample, to assess if the association appears monotonic across quartiles.

Dementia status (yes/no) was derived using the Expert algorithm that was trained with data from gold-standard neuropsychological testing. The algorithm was specifically developed in HRS to account for racial and ethnic differences in probable dementia more accurately compared to other algorithms used for dementia classification [17]. The Expert algorithm uses logistic regression models to predict probable dementia using 17 indicators across the following domains: demographic factors, seven cognitive tests, proxy-rated cognition (when necessary), physical functioning, physical health, and social engagement. The cognitive scale includes: immediate and delayed 10-noun free recall tests to measure memory; a serial sevens subtraction test to measure working memory; a counting backwards test to measure speed of mental processing. There are three additional mental status questions that include: date naming; object naming; and naming the president and the vice president of the United States. Further details of the algorithm have been described previously [17]. For sensitivity analyses, we also obtained a measure of dementia status via the Langa-Weir algorithm, the most frequently used dementia algorithm in HRS [23].

2.3 | Covariates

All covariates were self-reported and derived from each participant's analytic baseline unless otherwise indicated. Demographic variables included age, sex (male, female), and race and ethnicity (Non-Hispanic White, Non-Hispanic Black, and Hispanic/Latino). Educational attainment was categorized as less than high school; general education diploma (GED) or high school diploma; some college; or college or higher education. Depression was assessed using the validated 8-item Center for Epidemiologic Studies Depression Scale (CES-D8) [24]. The scale yields a sum score of participants' ratings (no/yes) of whether they felt each of the eight depressive symptoms much of the time during the past week, with participants categorized as having probable depression if they had a score of ≥ 4, a previously established cut point [25]. Participants also reported whether a doctor ever told them (no/yes) that they have diabetes, heart disease, stroke, or cancer. We computed a sum score of the number of major health conditions reported (range 0–4) to reflect physical health status. Health behaviors linked to dementia risk were also considered, including smoking (current smoker, past smoker, never smoker) and physical activity. For physical activity, participants reported on separate questions how often they engage in vigorous (e.g., running, tennis), and moderate (e.g., gardening, walking at a moderate pace) physical activity, and were then categorized according to level of engagement in each type of physical activity as follows: never; less than once a month; 1–3 times per month; once a week; more than once a week; or every day.

2.4 | Statistical Analysis

Participants were followed from their analytic baseline until they were characterized as having probable dementia for the first time, the time of their last cognitive measure, or the administrative end of follow-up (2020). Death was treated as non-informative censoring, and thus participants who died during the follow-up were censored at their last cognitive assessment.

We first examined the distribution of covariates across optimism quartiles. Next, we plotted Kaplan–Meier curves to visualize the association between optimism quartiles and risk of probable dementia. Third, we used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing probable dementia associated with optimism as a continuous measure. Models sequentially adjusted for the following covariate sets: Model 1: age, sex, race and ethnicity, and education; Model 2 further added probable depression status and the number of major health conditions; Model 3 further added smoking and physical activity, behaviors that could be either confounders or intermediate variables. All models were also conducted using optimism quartiles to assess potential threshold effects.

We excluded participants who were missing data on factors included in the dementia algorithm, that is, race and ethnicity, physical activity, and health conditions ($n = 631$, Figure S1). Missingness on other covariates was handled via multiple imputation using the R package mice [26]. Analyses were performed using 10 imputed datasets, and estimates were combined using Rubin's rules [27].

Associations of optimism and dementia risk were also evaluated separately in the Non-Hispanic White and Black subgroups, as these groups included more dementia cases across optimism quartiles; however, no subgroup analyses were conducted for the Hispanic subpopulation due to smaller dementia case numbers. When considering subgroup associations with categorical optimism, the optimism quartiles were derived within each subgroup. Additional sensitivity analyses were conducted, all using the covariates included in our core model (Model 2). First, we evaluated possible reverse causation by excluding participants who developed dementia within 2 years after their analytic baseline (follow-up time for remaining participants was shortened by 2 years). Second, given the strength of associations of depression with optimism [10] and dementia [28], we further evaluated potential confounding by excluding participants with the worst 10% of depression scores (> 4 points on the CES-D8), representing individuals with the highest depressive symptom levels. Further, we assessed sensitivity to the selection of the algorithm used to classify dementia status by replicating analyses using the Langa–Weir algorithm for dementia classification. We also examined the effect of additionally adjusting for the time between the optimism measure and baseline cognition as, for a portion of participants ($n = 2065$), optimism was assessed 2 years

prior to their cognitive baseline. Lastly, we examined whether estimates changed when we excluded participants for whom any optimism items were imputed by mean-imputation. We also tested for effect modification by sex by examining an interaction term between optimism and sex in Model 2. The interaction was not significant and is not, therefore, presented in the results section. We also computed an *E*-value to estimate the possible effect of unmeasured confounding, adjusting for the variables used in our core models including age, sex, education, race and ethnicity, probable depression, and health conditions [29].

All hypothesis tests were 2-sided and performed at the $\alpha = 0.05$ level. The proportional hazard assumption was assessed by Schoenfeld residuals and the interaction between time and optimism, which did not indicate evidence that the assumption was violated. Complete-case analyses (Table S1) were consistent with our main results.

3 | Results

3.1 | Sample Characteristics

Our study population consisted of 9071 individuals who were dementia-free and, on average, 74 years (SD = 4.6) at their personal analytic baseline and had an average follow-up of 6.7 years (SD = 3.6, range 2–14). Slightly more than half of the sample were women (57%). The sample included Non-Hispanic White (79%), Non-Hispanic Black (12%), and Hispanic/Latino participants (8%). Table 1 shows the distribution of covariates across quartiles of optimism. Participants with higher optimism had higher education, (e.g., at least a college degree for 32% versus 11% in the highest versus lowest optimism quartile). Participants in the highest optimism quartile (vs. lowest) were less likely to smoke currently (5.6% vs. 11%) and more likely to engage in moderate or vigorous physical activity more than once a week (28% vs. 12%). They also had on average fewer health conditions (mean 0.66 vs. 0.88) and were substantially less likely to have probable depression (3.4% vs. 20%). Among participants who were or who turned 70 in the HRS data during our follow-up window, participants were most likely excluded due to missing optimism data ($n = 2756$) and for having dementia at their analytic baseline ($n = 1304$). For complete details of exclusions, see Figure S1. Compared to those excluded ($n = 6195$), included participants were slightly younger, more often Non-Hispanic White, had somewhat higher education, and were generally healthier (Table S1).

3.2 | Optimism and Dementia Incidence

Over the follow-up, 3027 participants developed dementia. In unadjusted analyses, individuals with scores in higher versus lower optimism quartiles demonstrated lower risk of developing dementia over the follow-up period (Figure 1). Associations were maintained in each sequentially adjusted model with the continuous optimism measure (Table 2). For example, with each one standard deviation (SD) increment in optimism scores (corresponding to 6 points on the optimism scale), we observed a 15% reduced hazard (HR = 0.85, 95% CI = 0.82–0.88) after adjusting for age, sex, race and ethnicity, education, chronic health conditions, and probable depression (see Table S3 for HR estimates and 95% CIs for covariates). Adding health behaviors also did not qualitatively change the findings. In adjusted models comparing the highest versus each lower quartile of optimism, the magnitude of the association with probable dementia increased across quartiles, suggesting a monotonic relationship (Table 2).

3.3 | Subgroup and Sensitivity Analyses

Associations were similar among participants who were Non-Hispanic White ($n = 7216$, e.g., HR = 0.84, 95% CI = 0.81–0.88, Model 2) and Non-Hispanic Black ($n = 1105$, HR = 0.81, 95% CI = 0.74–0.88, Model 2). However, the case numbers were smaller for the Non-Hispanic Black subpopulation ($n = 444$), and thus estimates were less precise with wider CIs. See also Figure 2 and Table S4.

In sensitivity analyses (Table S5), excluding individuals who developed dementia within 2 years from their baseline, we observed results similar to the main analysis ($n = 7302$, HR = 0.86, 95% CI = 0.82–0.89, Model 2). Next, removing participants with the highest 10% of depression scores also produced estimates similar to those from the main analyses ($n = 8274$, HR = 0.83, 95% CI = 0.80–0.86, Model 2). Using the Langa-Weir algorithm to identify probable dementia cases, we again found estimates similar to those derived from our primary models ($n = 8846$, HR = 0.85, 95% CI = 0.80–0.89). Furthermore, the estimates remained essentially unchanged when further adjusting for the years between baseline cognition and optimism, or when excluding participants for whom optimism items were imputed (Table S5). Finally, analyses quantifying the robustness of our findings produced an *E*-value of 1.48 (lower 95% CI 1.41), suggesting that an unmeasured confounder(s) would need to have an association with both optimism and dementia incidence comparable to a HR of 1.48 (above and beyond the measured covariates) to fully explain away the observed association [30]. The magnitude of the E-value was close to that of probable depression in our models, a key confounder of concern ($HR_{depression} = 1.45$, 95% CI = 1.30–1.60). For complete results with this model, see Table S3.

4 | Discussion

This study in a nationally representative sample of older U.S. adults demonstrated strong associations between higher levels of dispositional optimism and reduced risk of developing dementia across up to 14 years of follow-up, even after considering a wide array of covariates and potential confounders. Specifically, each one standard deviation increase in optimism was associated with a 15% lower risk of developing dementia during the follow-up period. Importantly, associations were robust to multiple sensitivity analyses, from excluding initial years of follow-up to excluding those with the highest level of depressive symptoms. Estimates from the primary models were not materially changed with any sensitivity analyses. Further, in stratified analyses, we found optimism was related to lower risk of developing dementia similarly in Non-Hispanic Black and White participants. This study provides consistent evidence

TABLE 1 | Distribution of baseline characteristics of the study population by optimism level ($N = 9071$)[a].

	Optimism quartiles			
	Quartile 1 $n = 2554$	**Quartile 2 $n = 2103$**	**Quartile 3 $n = 2541$**	**Quartile 4 $n = 1873$**
Age, mean (SD)	74.2 (5.0)	74.3 (5.1)	74.0 (4.8)	73.9 (4.8)
Sex				
Female	1423 (56)	1171 (56)	1428 (56)	1178 (63)
Male	1131 (44)	932 (44)	1113 (44)	695 (37)
Race and ethnicity				
Non-Hispanic White	1917 (75)	1615 (77)	2097 (83)	1587 (85)
Non-Hispanic Black	342 (13)	294 (14)	277 (11)	192 (10)
Hispanic/Latino	295 (12)	194 (9.2)	167 (6.6)	94 (5.0)
Education				
< High school	804 (31)	428 (20)	355 (14)	177 (9.5)
High school or GED	1406 (55)	1228 (58)	1443 (57)	1000 (53)
Some college	64 (2.5)	89 (4.2)	108 (4.3)	89 (4.8)
College and above	279 (11)	358 (17)	635 (25)	607 (32)
Missing	1	0	0	0
Probable depression	508 (20)	239 (12)	149 (6.0%)	63 (3.4)
Missing	58	36	38	26
Number of health conditions mean (SD)[b]	0.88 (0.89)	0.77 (0.82)	0.74 (0.82)	0.66 (0.78)
Moderate or vigorous physical activity				
Never	1809 (71)	1339 (64)	1459 (57)	992 (53)
1–3× per month	204 (8.0)	191 (9.1)	223 (8.8)	163 (8.7)
1× per week	237 (9.3)	219 (10)	282 (11)	200 (11)
> 1× per week	273 (11)	336 (16)	541 (21)	475 (25)
Every day	31 (1.2)	18 (0.9)	36 (1.4)	43 (2.3)
Smoking				
Never smoker	999 (39)	873 (42)	1121 (44)	874 (47)
Past smoker	1255 (50)	1013 (49)	1227 (49)	884 (47)
Current smoker	281 (11)	191 (9.2)	179 (7.1)	104 (5.6)
Missing	19	26	14	11

[a]Data are presented as counts (percentages) unless otherwise stated.
[b]The score on chronic health conditions ranged 0–4.

for a protective association between higher optimism and risk of developing dementia in older adults.

Our results demonstrating a protective association between higher optimism and lower risk of developing dementia are fairly consistent with previous studies in HRS with shorter follow-up times and in specific subpopulations, and also in other cohorts comprised of only women [3, 14, 16]. The longest follow-up study demonstrated a 3% reduced risk of dementia per one point increment on the optimism scale [3]. One standard deviation in our study corresponded to 6 points on the optimism scale and an observed 15% risk reduction. Another prior study with HRS participants reported that each one standard deviation increment in optimism was associated with a 28% decrease in the risk of cognitive impairment in a follow-up of 4 years [14]. A third study comprised of only HRS non-Hispanic Black participants reported a cross-sectional but not longitudinal association with cognitive impairment over the 8 years of follow-up [13].

Our study is the first to directly address concerns about reverse causation, a significant issue as psychological symptoms, such as low mood, have been observed to represent early symptoms

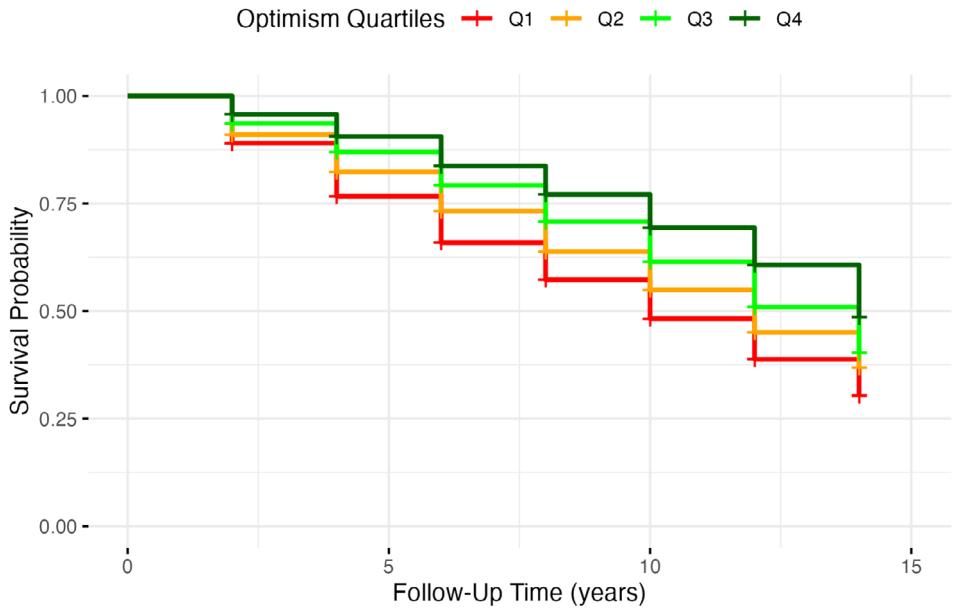

FIGURE 1 | Unadjusted Kaplan–Meier curves presenting the probability of being dementia-free (classified using the Expert algorithm) by quartiles of optimism among participants aged 70 or above in the Health and Retirement Study ($N = 9071$). Higher optimism score and quartile indicated more optimism: Q1, 6–23; Q2, 24–27; Q3, 28–32; Q4, 33–36.

TABLE 2 | Hazard ratios (95% confidence intervals) from models assessing the relationship between baseline optimism[a] and the risk of developing dementia[b] in participants aged 70 and older in the Health and Retirement Study ($N = 9071$).

		Cases/person years	Model 1	Model 2	Model 3
Optimism as a continuous score		3027/60,374	0.82 (0.79–0.85)	0.85 (0.82–0.88)	0.86 (0.83–0.89)
Optimism quartiles[c]	Q1	1041/15,644	Ref.	Ref.	Ref.
	Q2	744/13,658	0.85 (0.77–0.93)	0.88 (0.80–0.97)	0.89 (0.81–0.97)
	Q3	783/17,578	0.73 (0.67–0.80)	0.78 (0.71–0.85)	0.79 (0.73–0.87)
	Q4	459/13,494	0.57 (0.51–0.63)	0.62 (0.55–0.69)	0.64 (0.57–0.71)

Note: Model 1 adjusted for age, sex, education, and race and ethnicity. Model 2 adjusted additionally for probable depression and health conditions. Model 3 adjusted additionally for smoking and physical activity.
[a]Higher optimism score indicates more optimism.
[b]Probable dementia was classified using the Expert algorithm.
[c]Optimism quartile ranges: Q1, 6–23; Q2, 24–27; Q3, 28–32; Q4, 33–36.

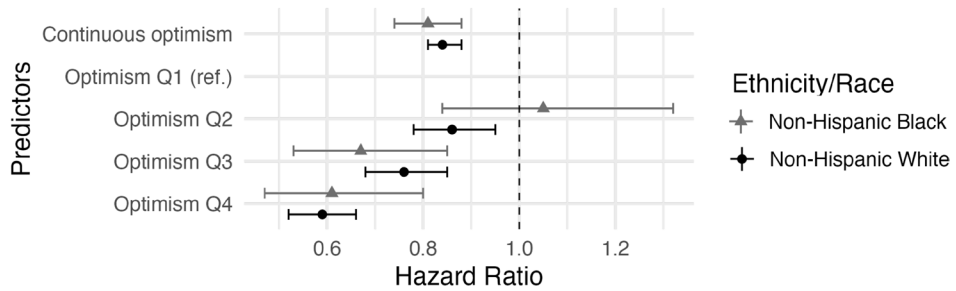

FIGURE 2 | Hazard ratios (95% confidence intervals) from models assessing the relationship between baseline optimism and risk of developing dementia in Non-Hispanic White and Black participants aged 70 and older in the Health and Retirement Study (N–H White, $n = 7216$; N–H Black, $n = 1105$). These models are adjusted for age, sex, education, probable depression, and health conditions. A higher optimism score indicates more optimism and in these analyses, optimism quartiles were determined within each subgroup (N–H White: Q1 6–23, Q2 24–28, Q3 29–32, Q4 33–36. N–H Black: Q1 6–23, Q2 24–26, Q3 27–31, Q4 32–36).

of dementia [31]. Therefore, an observed association could be driven by decreased optimism being caused by early stages of dementia. However, after excluding individuals who developed dementia within the first 2 years of follow-up, the estimates for the optimism-dementia association did not change. The robustness of the results is further ensured through the extended follow-up and sensitivity analyses additionally demonstrating robust associations in Non-Hispanic White and Non-Hispanic Black subgroups, the use of an alternative algorithm, and consideration of the E-value and the extent of possible residual confounding.

Together with previous studies, our findings provide support for the possibility that optimism causally contributes to cognitive health and may be considered an asset for brain health. Prior work demonstrates that optimism can be enhanced through interventions, including evidence from a meta-analysis [12]. Furthermore, in a randomized trial of an intervention designed to increase optimism, the intervention group showed improvements in risk-related biomarkers of coronary artery disease [13]. Thus, there are interventions that successfully shift individuals' views and beliefs about the future, a shift that could potentially improve an individual's quality of life, long-term health, and possibly the risk of dementia, as suggested by our study. However, given optimism and its relationship with health might differ depending on contexts and culture [32, 33], any consideration of interventions to target optimism should carefully assess its role in the target population.

Several processes may help to explain how optimism could influence dementia risk. Direct biological mechanisms are possible. For example, prior work has found optimism is associated with healthier immune responses [34] and higher levels of plasma antioxidants [35]. Such health-promoting processes could buffer against immune dysregulation, which can contribute to the emergence of Alzheimer-related dementia [36]. For example, prior work suggests that immune dysregulation may lead to immune cell infiltration to the central nervous system and to neuroinflammation [36]. More indirect mechanisms may play a role. For example, studies suggest optimism contributes to having more psychosocial resources such as stronger social networks [37], and lower levels of stress [38], factors also associated with healthier trajectories of cognitive aging [39–41]. Behavioral mediators are also plausible, given prior work showing higher optimism is associated with higher levels of physical activity [42, 43] and lower rates of smoking [44]. These behaviors have also been identified as modifiable risk factors for dementia [45], although associations with cognitive health have been somewhat inconsistent [46, 47]. Also important to note is that after adjusting for both smoking and physical activity in the current study, we observed no substantial change in estimates, suggesting other factors may matter more at least in older adulthood. Overall, multiple mechanisms are likely at play simultaneously, and future research should evaluate these pathways and their mutual relationships in more detail.

The present study has several strengths, including follow-up of almost a decade and a half in a richly characterized cohort of racially and ethnically diverse men and women above the age of 70 who are at the greatest risk for developing dementia. The algorithm used to classify probable dementia cases included information beyond cognitive testing and was specifically designed to perform well across major racial and ethnic subgroups [17]. However, several limitations should be considered. As with any observational study, the possibility of residual or unmeasured confounding remains. Residual confounding could occur due to the use of relatively crude categorizations on key covariates. For example, a more nuanced classification of education might permit greater differentiation regarding when and how more educated individuals remain socially and cognitively active in older age. However, we did control for a range of known confounders, including probable depression and educational attainment, and the calculated *E*-values suggested that observed associations were at least somewhat robust to unmeasured confounding. Although we tried to address the possibility of reverse causation by analyses in which we removed participants who developed dementia within 2 years after their personal baseline, it is not possible to rule out reverse causation; we acknowledge that our results may be explained, in part, by reverse causation. Finally, a number of potentially eligible participants were excluded due to missing data. The included participants were slightly younger, more often Non-Hispanic White, had somewhat higher education, and generally healthier. This composition could affect generalizability of findings, although we note that we observed similar results in the subpopulation of Black adults. Furthermore, adjusting for age, education, and chronic conditions did not substantially alter the association.

Our study demonstrated a robust association between dispositional optimism and the incidence of dementia over up to 14 years of follow-up in a diverse cohort of U.S. men and women. Although optimism is a complex construct, future research is needed to better understand whether optimism might be part of dementia prevention initiatives, including among Non-Hispanic Black adults who generally demonstrate higher rates of dementia [48]. Identifying mediating pathways may provide insight into both causal mechanisms and key targets for optimism interventions. Randomized trials designed to increase optimism among older adults may also be informative and further inform whether optimism learned or increased later in life also contributes to maintaining healthy cognitive function. Should findings be maintained across mechanistic and experimental studies, evaluating optimism levels among older adults may be a way to identify resources for health in aging.

Author Contributions

L.D.K. and F.G. conceived the idea and obtained funding; S.S., H.K.K., P.J., J.F., C.B.M., F.G., L.D.K., designed the study, S.S. completed the formal analysis, drafted and revised the manuscript; S.S., H.K.K., P.J., J.F., C.B.M., F.G., L.D.K., provided revisions to the manuscript; F.G. and L.D.K. supervised the analysis and writing process.

Acknowledgments

We thank Ken Langa for providing valuable guidance regarding the cognitive assessment in the Health and Retirement Study. Open access publishing facilitated by Turun yliopisto, as part of the Wiley - FinELib agreement.

Funding

This work and S.S. were supported by an NIH grant (R01AG085375).

Disclosure

NIH did not affect the design of this study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data are publicly available on the Health and Retirement Study website https://hrsdata.isr.umich.edu/data-products [19].

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Flowchart of participant selection. **Table S1:** Hazard ratios (95% confidence intervals) from models assessing the relationship between baseline optimism[1] and risk of developing dementia[23], for participants with complete data for covariates in the Health and Retirement Study ($N = 8849$). **Table S2:** Comparison of characteristics in 2006 of the participants who were or turned 70 during our follow-up but were excluded due to missingness of data or having dementia at baseline and the participants included in the final analytic sample[1]. **Table S3:** Hazard ratios (95% confidence intervals) across all variables from primary models used to calculate and compare E-Values[1] assessing the relationship between baseline optimism[2] and the risk of developing dementia[34] in participants aged 70 and older in the health and retirement study ($^{N} = 9071$). **Table S4:** Hazard ratios (95% confidence intervals) from models assessing the relationship between baseline optimism[1] and risk of developing dementia[2] in the Non-Hispanic White and Black subgroups in participants aged 70 and older in the Health and Retirement Study (N-H White, $n = 7216$; Black, $n = 1105$)3. **Table S5:** Hazard ratios (95% confidence intervals) derived from sensitivity analyses for models[1] assessing the relationship between baseline optimism[2] and risk of developing dementia[3] in participants aged 70 and older in the Health and Retirement Study.