

# Walking and Dementia in Physically Capable Elderly Men

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**P**HYSICAL AND ENVIRONMENTAL factors associated with the risk of dementia remain largely undefined. Although equivocal, evidence suggests that physical activity may have a relationship with the clinical expression of dementia.<sup>1-7</sup> Whether the association includes low-intensity activity such as regular walking is not known. One study showed that a composite measure of physical activity, partially based on walking histories, is associated with a reduced risk of dementia.<sup>1</sup> In a large cohort of women, those who walked more had significantly smaller declines in a modified Mini-Mental State Examination score over a 6- to 8-year period of follow-up.<sup>2</sup> Others describe relations that are weak while also providing contrasting evidence for an important and protective effect of cognitive activities on risk of dementia.<sup>8-10</sup> While cognitive activity appears to be a predictor of future dementia, overlap with physical activity may make it difficult to detect a relation between walking and dementia.

The purpose of this report is to examine the association between walking and future risk of dementia. Findings are based on a sample of physically capable elderly men enrolled in the Honolulu-Asia Aging Study. To account for the possibility that limited amounts

See also p 1454 and Patient Page.

**Context** Evidence suggests that physical activity may be related to the clinical expression of dementia. Whether the association includes low-intensity activity such as walking is not known.

**Objective** To examine the association between walking and future risk of dementia in older men.

**Design** Prospective cohort study.

**Setting and Participants** Distance walked per day was assessed from 1991 to 1993 in 2257 physically capable men aged 71 to 93 years in the Honolulu-Asia Aging Study. Follow-up for incident dementia was based on neurological assessment at 2 repeat examinations (1994-1996 and 1997-1999).

**Main Outcome Measures** Overall dementia, Alzheimer disease, and vascular dementia.

**Results** During the course of follow-up, 158 cases of dementia were identified (15.6/1000 person-years). After adjusting for age, men who walked the least (<0.25 mile/d) experienced a 1.8-fold excess risk of dementia compared with those who walked more than 2 mile/d (17.8 vs 10.3/1000 person-years; relative hazard [RH], 1.77; 95% confidence interval [CI], 1.04-3.01). Compared with men who walked the most (>2 mile/d), an excess risk of dementia was also observed in those who walked 0.25 to 1 mile/d (17.6 vs 10.3/1000 person-years; RH, 1.71; 95% CI, 1.02-2.86). These associations persisted after accounting for other factors, including the possibility that limited amounts of walking could be the result of a decline in physical function due to preclinical dementia.

**Conclusions** Findings suggest that walking is associated with a reduced risk of dementia. Promoting active lifestyles in physically capable men could help late-life cognitive function.

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of walking in late life could be the result of a decline in physical function due to preclinical dementia, adjustments were made for genetic susceptibility to dementia, cognitive performance, and declines in physical activity since mid adulthood.

## METHODS

### Background

From 1965 to 1968, the Honolulu Heart Program began following up 8006 men

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of Japanese ancestry living on the island of Oahu, Hawaii, for development of cardiovascular disease.<sup>11</sup> Beginning with examinations given from 1991 to 1993, the Honolulu-Asia Aging Study was launched as an expansion of the Honolulu Heart Program for the study of neurodegenerative diseases and cognitive function in elderly persons.<sup>12</sup> Participants included 3734 men aged 71 to 93 years (approximately 80% of the survivors in the original Honolulu Heart

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Program cohort). Findings for this report are based on follow-up for incident dementia based on neurological assessment at 2 repeat examinations (1994-1996 and 1997-1999). Procedures were in accordance with institutional guidelines and approved by an institutional review committee. Written informed consent was obtained from the study participants.

### Study Sample

Men who died (n=377) before the scheduling of the second cycle of cognitive assessments (1994-1996) were excluded from follow-up, as were an additional 145 cases of prevalent dementia. Men with poor cognitive function (n=75) whose dementia status could not be confirmed were also excluded. To reduce the confounding effects of Parkinson disease and stroke on the capacity to walk, 39 men with prevalent Parkinson disease and 116 with prevalent stroke were excluded. Among the remaining sample, 194 men had missing data on physical activity.

To help isolate the association of walking from that of work-related activities, 143 men were excluded because of continued employment. To reduce confounding due to disability on the relation between walking and risk of dementia, only men who were physically capable were considered for follow-up. Men were considered to be physically capable if they presented for a baseline clinical examination at the Kuakini Medical Center and reported undertaking slight or moderate activities in a typical 24-hour period. Here, based on the Physical Activity Index,<sup>13,14</sup> "walking on level ground" and "gardening or carpentry" were used as references to help define slight and moderate activities, respectively. There were 124 men who failed to present for a clinic visit (122 received home visits) and 76 whose daily activities failed to meet the criteria for being slight or moderate. Because cigarette smoking reduces the health benefits of being physically active,<sup>14,15</sup> an additional 161 smokers were removed. After these exclusions, there remained 1 man who

used a walker and 26 who used a cane. These men were also excluded from follow-up. The final sample for this report includes 2257 men.

### Diagnosis of Dementia

Cases of dementia were identified through a system of screening for cognitive function following a rigid study protocol.<sup>12</sup> Initial screening considered a participant's age and cognitive performance on the Cognitive Abilities Screening Instrument (CASI). The latter is a comprehensive measure of intellectual function that has been developed and validated for use in cross-cultural studies.<sup>16</sup> Performance scores range from 0 to 100, with high scores indicating better cognitive function than low scores. Scores lower than 74 were selected a priori as an indicator of possible dementia during dementia screening.<sup>12</sup> The value of 74 corresponds closely to a score of 22 on the Mini-Mental State Examination.<sup>17</sup>

The CASI was administered twice at the baseline examination (1991-1993) as part of 3 phases of screening.<sup>12</sup> All men with an initial CASI score of lower than 74 were invited to return for a second phase of evaluation. At phase 2, if a repeat CASI score was also lower than 74 or if a score on the Informant Questionnaire on Cognitive Decline in the Elderly<sup>18</sup> was 3.6 or higher, a return visit was requested for a complete dementia assessment. Among the remaining men, recruitment for subsequent phases was based on a sampling scheme that increased the likelihood for selection in older men and in men with intermediate vs high CASI scores. Through this process of screening, 145 cases of prevalent dementia were observed. As noted, these men were excluded from this study. For these men with prevalent dementia, 96% had a CASI score lower than 74. Among men without dementia, 11% had a CASI score lower than 74. As noted, 75 men with poor cognitive function (defined as an initial CASI score <74) whose dementia status could not be confirmed were excluded from follow-up.

For the follow-up examinations used to identify incident cases of dementia reported in this study, the CASI was administered once.<sup>19</sup> For the first follow-up examination (1994-1996), participants were recruited for complete dementia assessment if 1 of the following occurred: the repeat CASI score declined at least 9 points from the initial baseline CASI score; the repeat CASI score was 77 or lower and the participant had less than 12 years of education; or the repeat CASI score was 79 or lower and the participant had 12 or more years of education. At the second follow-up examination (1997-1999), complete assessment was requested when a CASI score was lower than 70. In all instances, trained technicians administered the CASI without regard to physical function and activity.

For diagnosis of dementia, information from a variety of sources was considered, including a history given by a family member, a standardized neuropsychological evaluation, and a thorough neurological examination. Laboratory findings and computed tomography were also used for the classification of dementia. Final diagnoses were assigned by a consensus panel consisting of a neurologist and additional physicians with expertise in dementia in the absence of information on physical activity. Participants with dementia met criteria based on the *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*.<sup>20</sup> Research criteria established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association were used in the diagnosis of Alzheimer disease.<sup>21</sup> Alzheimer disease was defined to include cases of dementia in which Alzheimer disease was judged to be the sole or primary cause. Diagnoses of vascular dementia adhered to the criteria of the California Alzheimer's Disease Diagnostic and Treatment Centers.<sup>22</sup> Vascular dementia included cases in which a vascular cause was considered the sole or primary cause.

### Walking, Markers of Preclinical Dementia, and Other Characteristics

At the beginning of follow-up (1991-1993), study participants were asked about the average amount of distance walked per day. To account for the possibility that a limited amount of walking in late life could be the result of a decline in physical function due to preclinical dementia, adjustments were made for genetic susceptibility to dementia (presence of 1 or 2 apolipoprotein  $\epsilon 4$  alleles),<sup>19,23,24</sup> the baseline measure of cognitive function (CASI assessed in 1991-1993), and declines in physical activity since mid adulthood.

Presence of apolipoprotein  $\epsilon 4$  alleles was identified through genotyping performed at Duke University, Durham, NC, following conventional methods.<sup>24</sup> Physical activity was measured by the Physical Activity Index, a common measure of daily metabolic output that is inversely related to the risk of cardiovascular disease.<sup>13,14</sup> Because high levels of the Physical Activity Index are associated with more active lifestyles than low levels, a decline in physical activity since mid adulthood (as a continuous measure) was defined as the Physical Activity Index at the time of study initiation (1965-1968) minus the index when follow-up began for the current report (1991-1993).

Among the other characteristics, physical function was assessed based on performance on a battery of tests, including ability to walk 10 ft (3 m) with a normal gait, ability to walk on toes and heels, measures of balance, ability to stand from a sitting position, and other factors related to physical function. Based on a weighted average of these items, a "physical performance score" was created.<sup>25</sup> High scores indicate better physical function than low scores. Additional characteristics included age, years of education, body mass index (calculated as weight in kilograms divided by the square of height in meters), childhood years spent living in Japan, status as a skilled professional, hypertension, diabetes, prevalent coronary heart disease, and total

and high-density lipoprotein cholesterol levels. For this analysis, a diagnosis of hypertension was made when systolic or diastolic blood pressure was at least 160 or 95 mm Hg, respectively, or when a study participant was receiving medication for treatment of hypertension. Diabetes was defined on the basis of medical history or use of insulin or oral hypoglycemic therapy. Prevalent coronary heart disease included myocardial infarction, angina pectoris, and coronary insufficiency.<sup>26</sup> A timed walk was also performed at the baseline examination (1991-1993).

### Statistical Analysis

To describe the association between walking and dementia, estimates of the age-adjusted incidence of dementia are provided across ranges of distance walked based on standard analysis of covariance methods and logistic regression models.<sup>27,28</sup> Similar procedures were used to describe the association between walking and the markers of preclinical dementia and the other characteristics.

To estimate the relative hazard (RH) of dementia (and 95% confidence interval [CI]) between ranges of distance walked, proportional hazards regression models were used.<sup>29</sup> Time to dementia was defined as the time to diagnosis of dementia cases observed in the course of follow-up. Men who died without a diagnosis of dementia prior to the end of follow-up were censored at the time of death and those who remained alive were censored at the close of the second repeat examination (1999). Adjustments were made for age, the markers of preclinical dementia, and the other characteristics as separate independent variables in a single regression model. Presence of apolipoprotein  $\epsilon 4$  alleles (yes vs no), status as a skilled professional (yes vs no), hypertension, diabetes, and prevalent coronary heart disease were modeled as dichotomous variables and the other characteristics were modeled as continuous variables. All reported *P* values were based on 2-sided tests of significance and *P* values <.05 were

considered statistically significant. Statistical analyses were carried out using SAS software, version 8.02 (SAS Institute Inc, Cary, NC).

### RESULTS

TABLE 1 describes the association between walking and the markers of preclinical dementia and the other characteristics. On average, men who reported walking longer distances were younger than those who reported walking less ( $P < .001$ ). Among the markers of preclinical dementia, walking was unrelated to presence of apolipoprotein  $\epsilon 4$  alleles. Men who walked the most had the highest CASI scores and the lowest declines in physical activity since mid adulthood. The physical performance score ( $P < .001$ ) and years of education ( $P = .03$ ) tended to be higher in men who walked the most, although associations were modest. Possibly in response to the diagnosis of coronary heart disease, prevalent coronary heart disease tended to be more common in men who walked the longest distances. Prevalence of diabetes became progressively less frequent as walking distances increased. For both coronary heart disease and diabetes, however, associations with walking were not statistically significant. There were no clear relations between walking and the remaining characteristics.

During the course of follow-up, 158 cases of dementia were identified (15.6/1000 person-years). The mean time from baseline examination (1991-1993) to diagnosis was 4.7 years (range, 2.4-7.4 years) with nearly 7 years of follow-up, on average, for the study participants. The mean age at diagnosis was 84 years (range, 75-98 years). Among the cases of dementia, 101 (10.0/1000 person-years) were attributed to Alzheimer disease as the sole or primary cause and 30 (3.0/1000 person-years) were attributed to vascular dementia as the sole or primary cause. For the remaining 27 cases (2.7/1000 person-years), Alzheimer disease and vascular dementia were mixed as contributing causes with Parkinson disease or atypical parkinsonism in 7 cases, Lewy bodies in 6 cases,

and a variety of other contributing factors in 12 cases. For 2 cases, a cause could not be identified.

The proportion of men who presented for the first repeat examination (1994-1996) was 85% (1920/2257) and the proportion of survivors who presented for the second examination

(1997-1999) was 74% (1495/2025). Although efforts are ongoing to determine dementia status, 199 men who were alive at the end of follow-up had yet to receive a repeat examination. Compared with those who were examined, those without a repeat examination were 1 year older and had 1 less

year of education on average ( $P < .001$ ). Those without a repeat examination were also more likely to have a lower CASI score at baseline (85.0 vs 88.1 in those with an examination;  $P < .001$ ). Based on age, education, CASI performance, and the other study characteristics, we projected that 16 cases of dementia may have been missed in this sample. Among 666 men who received a repeat examination and met the CASI criteria for complete neurological evaluation, 76 (11%) had failed to return for follow-up assessment. Among this group, we projected that 8 cases of dementia may have been missed.

TABLE 2 describes the incidence of dementia according to ranges of distance walked. After adjusting for age, men who walked the least ( $<0.25$  mile/d [ $<0.40$  km/d]) experienced a 1.8-fold excess of total dementia compared with those who walked more than 2 mile/d ( $>3.2$  km/d) (17.8 vs 10.3/1000 person-years; RH, 1.77; 95% CI, 1.04-3.01). Compared with men who walked the most ( $>2$  mile/d), an excess of dementia was also observed in those who walked 0.25 to 1 mile/d (17.6 vs 10.3/1000 person-years; RH, 1.71; 95% CI, 1.02-2.86). The association between walking and dementia also persisted in both those who did and those who did not have apolipoprotein  $\epsilon 4$  alleles. Although the number of men with apolipoprotein  $\epsilon 4$  alleles was small ( $n = 365$ ), the age-adjusted incidence of dementia in those who walked less than 0.25 mile/d was 26.0 per 1000 person-years vs 16.1 per 1000 person-years in men who walked more than 2 mile/d (RH, 1.63; 95% CI, 0.57-4.67). Among those with no apolipoprotein  $\epsilon 4$  allele, incidence of dementia was 16.9 per 1000 person-years in those who walked the least vs 8.0 per 1000 person-years in those who walked the most (RH, 2.16; 95% CI, 1.17-4.01).

There was a 1.8-fold excess of Alzheimer disease in men who walked 2 mile/d or less vs those who walked more than 2 mile/d (10.9 vs 6.0/1000 person-years; RH, 1.81; 95% CI, 0.97-3.40). Although an association with other dementia subtypes was not statistically

**Table 1.** Baseline Characteristics According to Distance Walked per Day, Adjusted for Age\*

Characteristics	Distance Walked, mile/d			
	<0.25 (n = 600)	0.25 to 1 (n = 769)	>1 to 2 (n = 433)	>2 (n = 455)
Age, y†	77.4 (4.4)	77.3 (4.2)	76.7 (3.8)	76.0 (3.6)
Presence of apolipoprotein $\epsilon 4$ alleles, % (No.)	18.5 (109)	15.1 (113)	15.0 (65)	16.9 (78)
Cognitive Abilities Screening Instrument score	86.8 (7.8)	87.3 (7.5)	87.1 (7.0)	87.6 (7.2)
Decline in physical activity since mid adulthood	1.5 (6.5)	1.5 (5.8)	1.3 (6.0)	0.8 (5.9)
Physical performance score‡	9.6 (1.0)	9.7 (0.7)	9.8 (0.5)	9.8 (0.6)
Education, y§	10.6 (3.1)	10.9 (3.2)	10.6 (3.0)	11.1 (3.1)
Body mass index	23.8 (3.2)	23.7 (3.1)	23.8 (2.9)	23.6 (2.9)
Childhood years spent living in Japan	1.9 (4.5)	1.6 (4.0)	1.9 (4.2)	1.7 (4.3)
Skilled professional, % (No.)	65.7 (392)	65.2 (500)	63.0 (273)	63.2 (290)
Hypertension, % (No.)	54.5 (330)	53.4 (414)	53.9 (232)	59.9 (268)
Diabetes, % (No.)	15.3 (87)	14.4 (106)	12.8 (54)	12.9 (58)
Coronary heart disease, % (No.)	14.5 (87)	15.9 (122)	18.2 (79)	18.4 (84)
Total cholesterol, mg/dL	195 (33.2)	191 (30.8)	193 (31.5)	194 (31.7)
High-density lipoprotein cholesterol, mg/dL	51.3 (13.0)	50.8 (13.2)	51.5 (12.9)	50.9 (12.5)

SI conversion: To convert total and high-density lipoprotein cholesterol to mmol/L, multiply by 0.0259. To convert miles to kilometers, multiply by 1.6.

\*Data are mean (SD) unless otherwise noted.

†Significant inverse relation with distance walked ( $P < .001$ ).

‡Significant positive relation with distance walked ( $P < .001$ ).

§Significant positive relation with distance walked ( $P = .03$ ).

||Body mass index was calculated as weight in kilograms divided by the square of height in meters.

**Table 2.** Unadjusted and Age-Adjusted Incidence of Dementia According to Distance Walked per Day

Dementia	Incidence per 1000 Person-Years (No. of Cases/Men at Risk)						
	<0.25, mile/d	P Value*	0.25 to 1, mile/d	P Value*	>1 to 2, mile/d	P Value*	>2, mile/d
Total dementia							
Unadjusted	18.7 (49/600)	.006	18.6 (63/769)	.006	13.5 (27/433)	.18	9.0 (19/455)
Age-adjusted	17.8	.04	17.6	.04	14.1	.29	10.3
Alzheimer disease							
Unadjusted	11.5 (30/600)	.02	11.5 (39/769)	.02	10.5 (21/433)	.06	5.2 (11/455)
Age-adjusted	10.8	.09	10.8	.09	11.0	.11	6.0
Vascular dementia							
Unadjusted	3.8 (10/600)	.57	3.8 (13/769)	.56	0.5 (1/433)	.11	2.9 (6/455)
Age-adjusted	3.7	.76	3.7	.76	0.5	.09	3.1
Mixed and other dementia							
Unadjusted	3.4 (9/600)	.09	3.2 (11/769)	.11	2.5 (5/433)	.25	1.0 (2/455)
Age-adjusted	3.3	.14	3.1	.17	2.6	.29	1.1

SI conversion: To convert miles to kilometers, multiply by 1.6.

\*P values compare excess of dementia in each category of distance walked per day vs men who walked more than 2 mile/d.

significant, incidence of mixed and other dementia declined from 3.3 to 1.1 per 1000 person-years as walking increased from less than 0.25 to more than 2 mile/d. An association between walking and vascular dementia was less apparent (Table 2).

To help determine whether the excess in dementia in those who walked the least could be attributed to confounding by other factors, the relation between walking and dementia was further adjusted for the characteristics in Table 1. After adjustment (TABLE 3), a 1.9-fold excess risk of total dementia occurred in men who walked less than 0.25 mile/d compared with men who walked more than 2 mile/d (RH, 1.93; 95% CI, 1.11-3.34). Compared with the most active men, those who walked 0.25 to 1 mile/d experienced a 1.7-fold excess in dementia risk (RH, 1.75; 95% CI, 1.03-2.99). Risk of Alzheimer disease was 2.2-fold higher in men who walked less than 0.25 mile/d vs those who walked the most (RH, 2.21; 95% CI, 1.06-4.57).

The focus of this report is on day-to-day activity; however, a faster timed walk at the baseline examination (1991-1993) was also associated with a decreased age-adjusted incidence of dementia. For men who walked 10 ft (3 m) in more than 6 seconds, incidence was 20.2/1000 person-years compared with 13.1 per 1000 person-years for those with walking times of 3 seconds or less (RH, 1.57; 95% CI, 0.77-3.21). Among men who were able to walk 10 ft in 4 seconds or less (n=1682), incidence was 15.3 per 1000 person-years in those who walked 1 mile/d or less vs 8.0 per 1000 person-years in those who walked more than 2 mile/d (RH, 1.93; 95% CI, 1.04-3.57). In those who were slower walkers (>4 seconds to walk 10 ft), an association was also present; risk also appeared to be increased, although nonsignificantly. Based on a small sample of 568 men, incidence of dementia declined from 26.1 to 19.8 per 1000 person-years as distance walked increased from less than 0.25 mile/d to more than 2 mile/d (RH for those who walked <0.25

vs >2 mile/d, 1.31; 95% CI, 0.56-3.09).

## COMMENT

Our findings suggest that physically capable elderly men who walk more regularly are less likely to develop dementia. The capacity to walk quickly during a timed walk also appears to be associated with a reduced risk of dementia, although these results should be confirmed. There is also a need to better characterize walking behaviors and patterns that have relations with late-life cognition, including metabolic equivalents that are easily adopted by elderly individuals. Although this study did not enroll women, observations in women of an association between walking and changes in cognitive function over time suggest that the relationship between walking and dementia may apply to them as well.<sup>2</sup> Promoting active lifestyles may have important effects on late-life cognitive function.

There are no clear explanations for the relation between walking and dementia. Although associations were independent of other study characteristics that were determined at the time when walking was assessed, it may be

that men who walk frequently are more resistant to risk factor changes or transitions into adverse risk factor states. Although changes in risk factor status in the course of follow-up were not considered in the current study (nor were such data always available), it would be important to determine if men who walk regularly are less prone to development of intervening conditions that have a closer link with dementia.

It also is likely that the relationship of walking and dementia is modulated by many factors, including environmental and lifestyle exposures that could influence cognitive capacity. Walking and dementia may be related through general effects on overall vitality and biological aging. Other mechanisms may involve links between cardiovascular health and dementia,<sup>30</sup> tracking with preclinical dementia, and, possibly, direct influences on brain plasticity and structural and functional brain reserves.<sup>31,32</sup> The role of diet and its relation with physical activity also needs to be examined, as does constitutional frailty.

While our study was observational, we took several measures to avoid residual confounding. We included only

**Table 3.** Estimated Relative Hazard of Dementia Comparing Ranges of Distance Walked per Day

Dementia	Estimated Relative Hazard (95% CI)					
	<0.25 vs >2, mile/d	P Value*	0.25 to 1 vs >2, mile/d	P Value*	>1 to 2 vs >2, mile/d	P Value*
Total dementia						
Unadjusted	2.12 (1.25-3.60)	.006	2.06 (1.23-3.44)	.006	1.50 (0.83-2.69)	.18
Adjusted†	1.93 (1.11-3.34)	.02	1.75 (1.03-2.99)	.04	1.33 (0.73-2.45)	.35
Alzheimer disease						
Unadjusted	2.24 (1.12-4.48)	.02	2.21 (1.13-4.31)	.02	2.01 (0.97-4.17)	.06
Adjusted†	2.21 (1.06-4.57)	.03	1.86 (0.91-3.79)	.09	1.88 (0.87-4.04)	.11
Vascular dementia						
Unadjusted	1.34 (0.49-3.70)	.57	1.34 (0.51-3.51)	.56	0.18 (0.02-1.46)	.11
Adjusted†	1.17 (0.42-3.27)	.77	1.21 (0.45-3.22)	.70	0.16 (0.02-1.36)	.09
Mixed and other dementia						
Unadjusted	3.75 (0.81-17.35)	.09	3.43 (0.76-15.45)	.11	2.63 (0.51-13.56)	.25
Adjusted†	2.83 (0.59-13.55)	.19	2.84 (0.62-12.92)	.18	2.00 (0.36-11.01)	.43

Abbreviation: CI, confidence interval.

SI conversion: To convert miles to kilometers, multiply by 1.6.

\*P values compare excess of dementia in each category of distance walked per day vs men who walked more than 2 mile/d.

†Adjusted for age, presence of apolipoprotein ε4 alleles, baseline Cognitive Abilities Screening Instrument score, decline in physical activity since mid adulthood, physical performance score, years of education, body mass index, childhood years spent living in Japan, status as a skilled professional, hypertension, diabetes, prevalent coronary heart disease, and total and high-density lipoprotein cholesterol.

physically capable men, which diminishes the possibility that relations between walking and dementia could have been through associations with overt disability and physical impairment. Even when focusing on men who were capable of walking 0.25 to 1 mile/d, there was an excess of dementia vs men who walked more than 2 mile/d. Among the 76 men who were neither slightly nor moderately active, 6 eventually developed dementia and all reported walking less than 0.25 mile/d.

Based on the observation that cigarette smoking can reduce the benefits of being physically active for outcomes such as mortality and stroke,<sup>14,15</sup> cigarette smokers were also excluded from follow-up. The smokers who were excluded in the current study (n=161) had no association of dementia with walking. Here, the age-adjusted incidence of dementia was 9.8, 34.7, 35.5, and 12.6 per 1000 person-years as the range of distance walked increased from less than 0.25 mile/d to more than 2 mile/d. An earlier report from the Honolulu-Asia Aging Study also suggests that smoking increases the risk of dementia.<sup>33</sup>

Studying a sample of elderly men in the mild climate of Hawaii has the advantage that walking on a continuous basis may be more easily sustained throughout the year. Self-reported activity may be more consistent with actual behavior since recall is less likely to be interrupted by months of inclement weather. With a focus on retired men, the walking that occurred was also likely to be related to domestic needs or a modifiable decision to walk for leisure. We did not obtain further data on participants' purposes of walking, however.

The stable environment in Hawaii that permits year-round walking may also explain why a relation between walking and dementia has not been observed elsewhere. Identifying a relation between walking and cognition may require samples where levels of walking are continuous rather than sporadic. Intensity may also be important. Since all men in the Honolulu sample were retired and older than 70 years, however, variation in intensity

may be low. In addition, nearly 90% of the men were born in Hawaii, and outmigration has been rare (about 1 per 1000 per year), further suggesting that associations could reflect lifelong patterns of walking behaviors.

In combination with a low rate of outmigration, the continuous efforts to identify cases of dementia in the Honolulu-Asia Aging Study are likely to have resulted in case finding that is more complete than in general population-based settings, where cognitive impairment is often unrecognized.<sup>34</sup> Within the current study, the CASI criterion for neurological assessment at the second follow-up examination (score <70) was lowered from levels that were used at the first follow-up examination (1994-1996). Although more cases were identified at the second follow-up examination (82/158), we may have identified fewer cases because we reduced the sensitivity of the screening test. Had the CASI criterion for the second follow-up examination been used at the first follow-up examination, 20 cases would have been missed. Here, dementia incidence would become 14.8, 16.0, 12.0, and 8.6 per 1000 person-years as distance walked increases from less than 0.25 to more than 2 mile/d. The consequence of this loss is minimal, however, since the excess of dementia in men who walked 1 mile/d or less remains significantly higher than in men who walked more than 2 miles/day (RH after age and risk factor adjustment, 1.80; 95% CI, 1.05-3.07). In addition, the 20 dementia cases that would have been missed tended to walk less than the overall cohort (8/20 walked <0.25 mile/d while 3/20 walked >2 mile/d), suggesting that the observed association between walking and dementia could have been even stronger had dementia case finding been more complete at the second follow-up examination.

Consistent with previous reports,<sup>8-10</sup> cognitive performance in the Honolulu sample (as measured by the CASI) was a markedly stronger predictor of incident dementia than was walking. Nevertheless, walking continued to

be associated with reduced risk of dementia independent of cognitive function, suggesting that the risk of dementia could include important factors other than cognition. Other studies have suggested an association between physical activity and cognition.<sup>1-7</sup> Even in the Bronx Aging Study, in which the associations between walking and dementia were weak, participants who rarely walked had a 1.5-fold excess risk of dementia compared with those who walked frequently.<sup>8</sup> Although the latter was not significant, findings were based on a small sample of 469 men and women, limiting the power to detect a difference. Walking in the cohort of elderly men in Hawaii has also been associated with a lower risk of coronary heart disease, total mortality, and death due to cancer.<sup>26,35</sup> Although complex, this study and past evidence suggest that walking and active lifestyles in general are associated with a reduced risk of dementia.

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