Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Variable Definitions

The Health and Retirement Study (HRS) has been a source of considerable prior research on dementia risk factors in the U.S.[1] Below are the variable definitions that were used to calculate risk factor prevalence and communality of risk factors using the HRS. When possible, we sought to replicate the approach used by *The Lancet* Commission on dementia, though the variable definitions used in the Commission's principal-components analysis were not specified for all risk factors (e.g., hearing loss).[2,3]

Vision impairment

To calculate communality, a measure of visual difficulty in HRS was derived from the question: "Is your eyesight excellent, very good, good, fair, or poor using glasses or corrective lenses as usual?" Respondents who indicated "fair" or "poor" in the 2018 HRS were categorized as having poor vision, consistent with prior analyses using data from the HRS.[4] To determine the prevalence of vision impairment (VI), we used the results of a recent Bayesian meta-analysis that estimated the prevalence of better-eye visual acuity ≤logMAR 0.3 (e.g., 20/40 or 6/12).[5] The results of this study are available through the Center for Disease Control and Prevention Vision and Eye Health Surveillance System (ddt-vehss.cdc.gov). In sensitivity analyses, we also considered the prevalence of self-reported visual difficulty in HRS, as described above. For the primary analysis in this study, the effect size was derived from a meta-analysis reporting the relative risk of dementia due to VI from longitudinal studies.[6] Effect sizes from other meta-analyses[7,8] were used in sensitivity analyses. Accordingly, in eTable 3 we provide a range of possible values for the population attributable fractions (PAF) for dementia due to VI based on the varied estimates of prevalence and effect size.

Less education

Less education was defined as having completed no formal education or less than a high school degree.

Hearing loss

Hearing loss was indicated by responses to the question, "Is your hearing excellent, very good, good, fair, or poor?" Those who had indicated in the 2018 interview or any prior HRS interview were asked to rate their hearing "using a hearing aid as usual." Respondents who indicated "fair" or "poor" in the 2018 HRS were categorized as having hearing loss, consistent with prior research using data from HRS.[9]

Traumatic brain injury

In 2014, a sub-set of HRS participants were randomly assigned to participate in a traumatic brain injury (TBI) module. An indicator of a history of TBI was derived from six items assessing lifetime head or neck injuries that included the following: vehicle accident, fall or being hit, playing sports or on a playground, being hit by someone or from being shaken violently, shot, or exposed to an explosion. If respondents indicated that they sustained a head or neck injury and lost consciousness for any of these six items, they were flagged as having sustained a TBI.

Hypertension

An indicator of hypertension was derived from the question "Has a doctor ever told you that you have high blood pressure or hypertension?" Respondents were flagged who indicated in the 2018 HRS ever having hypertension.

Alcohol

Heavy alcohol consumption was defined as consuming 21 or more alcoholic drinks per week (as in the Commission report). The measured using three items from the 2018 HRS: (1) "Do you ever drink any alcoholic beverages such as beer, wine, or liquor?"; (2) "In the last three months, on average, how many days per week have you had any alcohol to drink? (For example, beer, wine, or any drink containing liquor)"; (3) "In the last three months, on the days you drink, about how many drinks do you have?"

Obesity

This measure was derived from two questions asking about height and weight in the 2016 and 2018 HRS. Body mass index (BMI) was calculated and respondents with a BMI of 30 or greater were flagged as obese (as in the Commission report). Data from 2016 was used to calculate BMI only if respondents had missing or incomplete data for these measures in 2018.

Smoking

An indicator of current smoking was derived from two survey items in the 2018 HRS: (1) "Have you ever smoked cigarettes?" and (2) "Do you smoke cigarettes now?" These measures were combined to flag respondents who were current smokers.

Depression

This variable was indicated by responses in the 2018 HRS to the question, "Has a doctor ever told you that you have had problems with depression?" Those who indicated any depression during their lifetime were flagged as having this risk factor.

Social isolation

This variable was defined based on Cudjoe et al's typology of social isolation.[10] In a 2018 HRS leave behind questionnaire, a subset of respondents were asked about the following: (1) co-habitation; (2) talking to 2 or more people about important things; (3) attending religious services; and (4) participation in a club, class, or organized activity. Those who did not indicate taking part in any of the aforementioned social activities were flagged as socially isolated.

Physical inactivity

A measure of physical inactivity was derived from two items in the 2018 HRS: (1) "How often do you take part in sports or activities that are vigorous, such as running or jogging, swimming, cycling, aerobics or gym workout, tennis, or digging with a spade or shovel?" and (2) "How often do you take part in sports or activities that are moderately energetic such as, gardening, cleaning the car, walking at a moderate pace, dancing, floor or stretching exercises?" Response options for both items included: more than once a week, once a week, one to three times a month, or hardly ever or never. Those who indicated either "never" or "hardly ever"' for both items were flagged as physically inactive.

Diabetes

An indicator of diabetes was derived from the 2018 HRS question "Has a doctor ever told you that you have diabetes or high blood sugar?" A positive response was considered an indicator of diabetes.

PAF Calculation

The PAF is calculated as: $PAF = \frac{Pe\,(RRe-1)}{1+Pe\,(RRe-1)}$ where Pe is the prevalence of and RRe is the relative risk (RR) of dementia due to that risk factor. The RR for each risk factor was derived from published meta-analyses. For risk factors in the *Lancet* Commission report we used the same RR estimates. For vision impairment we used the results of a recently published meta-analysis.[5]

The next step in the PAF calculation was to weight estimates for communality (clustering of risk factors).[13,14] To do so, we conducted a principal-component analysis. Components with eigenvalues>1 were retained (**eTable 1**) and communality was set equal to the sum of the square of factor loadings. Each risk factor PAF was weighted: $Weight\ (w) = 1 - communality$. Then, an overall weighted PAF was calculated: $PAFw = 1 - [(1 - w * PAF_1)(1 - w * PAF_2)(1 - w * PAF_3)\ \ldots]$ from which individual risk factor PAFs were derived: $PAFe_w = \frac{individual\ PAF}{\sum(individual\ PAF)(overall\ PAFw)}$.

eTable 1. Principal-component analysis of potentially modifiable risk factors for dementia in the Health and Retirement Study.

Factor	Eigenvalue	Factor loading (rotated)	Variable[a]
1	2.702		
		.252	Less education
		.201	Hearing loss
		-.064	TBI[b]
		.640	**Hypertension**
		-.093	Alcohol
		.510	**Obesity**
		-.093	Smoking
		.223	Depression
		.219	Social Isolation[b]
		.402	**Physical Inactivity**
		.674	**Diabetes**
		.196	Poor vision
2	1.761		
		.534	**Less education**
		.473	**Hearing loss**
		.187	TBI[b]
		.263	Hypertension
		.167	Alcohol
		-.001	Obesity
		.384	Smoking
		.377	Depression
		.394	Social Isolation[b]
		.508	**Physical Inactivity**
		.221	Diabetes
		.644	**Poor vision**
Confirmatory Factor Analysis comparing a 2 factor and 1 factor solution			
2 Factor	$X^2 = 195.579$	df = 43	p<.001
1 Factor	$X^2 = 1035.95$	df = 54	p<.001
	$\Delta X^2 = 930.78$	Δ df = 1	p<.001

X^2 :Chi-square, ΔX^2 :change in Chi-square, df: degrees of freedom, TBI: traumatic brain injury.

[a] Bolded text indicates that variables load with the corresponding factor

[b] Missing data were treated using full information maximum likelihood estimation (FIML). Note that FIML was necessary given that measures of TBI and social isolation were only asked to a subset of respondents in the HRS.

eTable 2. Potentially modifiable dementia risk factors by race and ethnicity.

Risk factor	RR (95% CI) for dementia	Risk factor prevalence	Unweighted PAF	Weighted PAF
Black, non-Hispanic				
Vision impairment[a]	1.5 (1.4-1.6)	9.9%	4.7%	2.1%
Less education	1.6 (1.3-2.0)	21.1%	11.2%	4.9%
Hearing loss	1.9 (1.4-2.7)	17.0%	13.2%	5.8%
TBI	1.8 (1.5-2.2)	21.8%	14.8%	6.5%
Hypertension	1.6 (1.2-2.2)	76.3%	31.4%	13.7%
Alcohol	1.2 (1.1-1.3)	1.5%	0.29%	0.1%
Obesity	1.6 (1.3-1.9)	50.0%	23.1%	10.1%
Smoking	1.6 (1.2-2.2)	18.6%	10.0%	4.4%
Depression	1.9 (1.6-2.3)	24.8%	18.2%	7.9%
Social isolation	1.6 (1.3-1.9)	13.1%	7.3%	3.2%
Physical inactivity	1.4 (1.2-1.7)	23.4%	8.6%	3.7%
Diabetes	1.5 (1.3-1.8)	33.5%	14.3%	6.2%
Overall				68.6%
Hispanic, any race				
Vision impairment[a]	1.5 (1.4-1.6)	11.0%	5.2%	2.2%
Less education	1.6 (1.3-2.0)	44.6%	21.1%	9.0%
Hearing loss	1.9 (1.4-2.7)	26.2%	19.1%	8.2%
TBI	1.8 (1.5-2.2)	12.1%	8.8%	3.8%
Hypertension	1.6 (1.2-2.2)	59.3%	26.2%	11.2%
Alcohol	1.2 (1.1-1.3)	2.1%	0.42%	0.2%
Obesity	1.6 (1.3-1.9)	45.3%	21.4%	9.1%
Smoking	1.6 (1.2-2.2)	13.0%	7.2%	3.1%
Depression	1.9 (1.6-2.3)	30.3%	21.4%	9.2%
Social isolation	1.6 (1.3-1.9)	13.3%	7.4%	3.2%
Physical inactivity	1.4 (1.2-1.7)	19.9%	7.4%	3.2%
Diabetes	1.5 (1.3-1.8)	39.3%	16.4%	7.0%
Overall				69.3%
White, non-Hispanic				
Vision impairment[a]	1.5 (1.4-1.6)	7.7%	3.7%	1.8%
Less education	1.6 (1.3-2.0)	8.8%	5.0%	2.4%
Hearing loss	1.9 (1.4-2.7)	19.4%	14.9%	7.2%
TBI	1.8 (1.5-2.2)	17.8%	12.5%	6.0%
Hypertension	1.6 (1.2-2.2)	54.7%	24.7%	11.9%
Alcohol	1.2 (1.1-1.3)	3.1%	0.61%	0.3%
Obesity	1.6 (1.3-1.9)	39.2%	19.0%	9.2%
Smoking	1.6 (1.2-2.2)	10.9%	6.1%	3.0%
Depression	1.9 (1.6-2.3)	26.8%	19.4%	9.4%
Social isolation	1.6 (1.3-1.9)	6.1%	3.5%	1.7%
Physical inactivity	1.4 (1.2-1.7)	16.8%	6.3%	3.0%
Diabetes	1.5 (1.3-1.8)	22.2%	9.9%	4.8%
Overall				60.6%

CI: confidence interval, PAF: population attributable fraction, RR: relative risk, TBI: traumatic brain injury

[a] Prevalence estimates were derived from a Bayesian meta-analysis published by Flaxman et al[12] with results made available through the Vision and Eye Health Surveillance System (ddt-vehss.cdc.gov).

eTable 3. Sensitivity analyses for population attributable fraction of dementia due to vision impairment.

	Effect sizes from different meta-analyses		
Prevalence	RR=1.38 (1.19-1.59)[7]	RR=1.47 (1.36-1.60)[6]	OR=2.1 (1.4-3.2)[8]
VEHSS meta-analysis[a] (8.3%)	PAF=3.1%/wPAF=1.4%	PAF=3.8%/wPAF=1.8%	PAF=8.3%/wPAF=3.8%
HRS Poor[a] (9.2%)	PAF=3.4%/wPAF=1.6%	PAF=4.1%/wPAF=1.9%	PAF=9.1%/wPAF=4.2%
HRS Poor/Fair[b] (21.4%)	PAF=7.5%/wPAF=3.5%	PAF=9.1%/wPAF=4.2%	PAF=19.1%/wPAF=8.5%

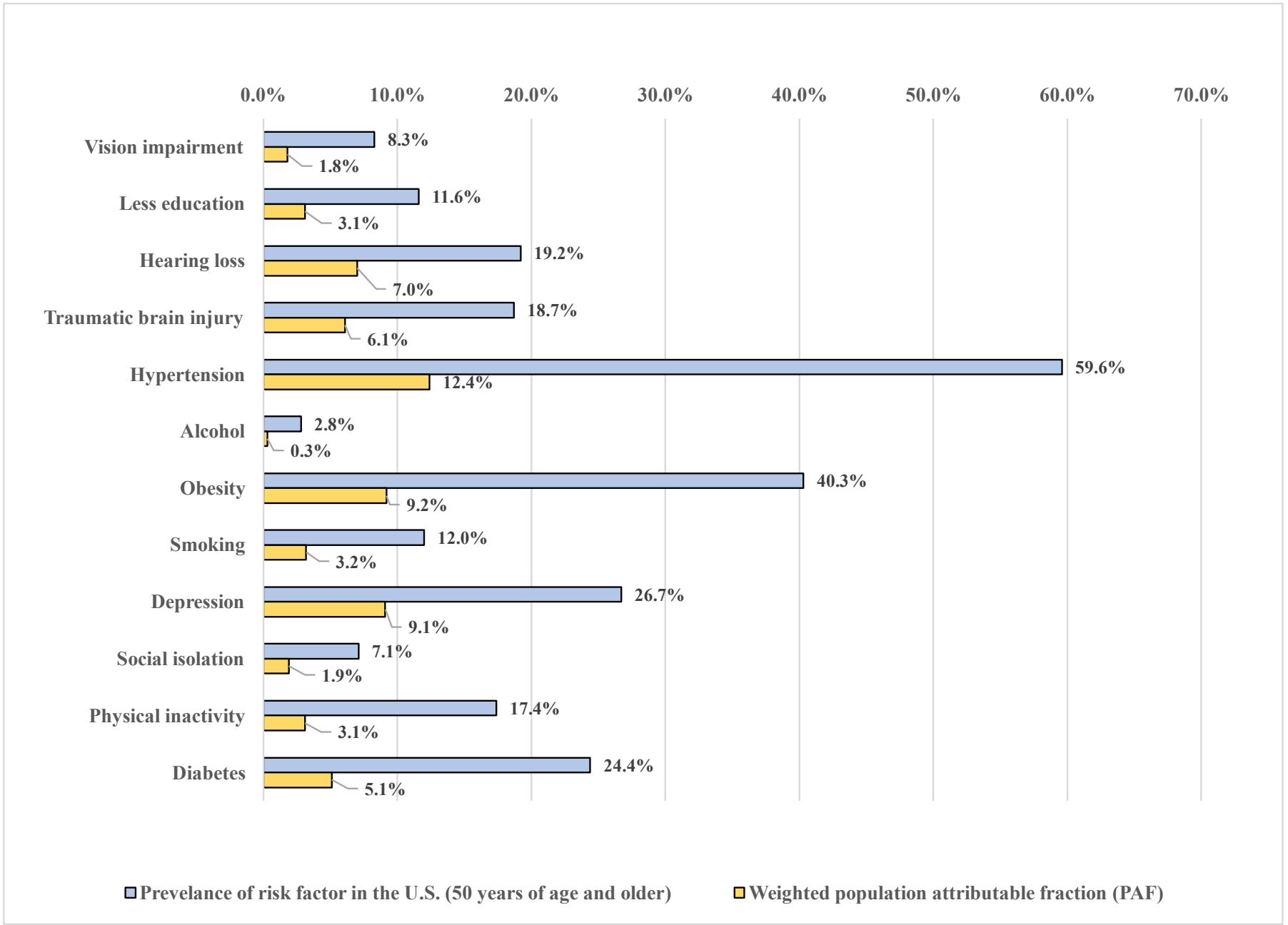
HRS: Health and Retirement Study, OR: odds ratio, PAF: population attributable fraction, RR: relative risk, wPAf: weighted population attributable fraction, VEHSS: Vision and Eye Health Surveillance System

[a] Prevalence was derived from a Bayesian meta-analysis published by Flaxman et al[5] with results made available through the Vision and Eye Health Surveillance System (ddt-vehss.cdc.gov)

[b] This measure was derived from the HRS question, "Is your eyesight excellent, very good, good, fair, or poor using glasses or corrective lenses as usual?" A response of poor was used to calculate prevalence.

[c] This measure was derived from the HRS question, "Is your eyesight excellent, very good, good, fair, or poor using glasses or corrective lenses as usual?" A response of poor or fair was used to calculate prevalence.

eFigure. Population attributable fraction of potentially modifiable dementia risk factors



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