

Lower Mental Health Related Quality of Life Precedes Dementia Diagnosis: findings from the EPIC-Norfolk prospective population-based study.

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Supplementary Methods

Calculating a composite cognitive score:

For each of the individual cognition tests, a score of '0' or '1' was assigned based on whether the individual was in the 'poor performance' or 'good performance or reference' group for each of the eight cognitive outcome measures individually. The composite cognitive score was calculated as a sum of the score based on the performance group for all eight cognition test outcomes (range=0- 8). Participants were classified into two groups based on this score – those in the bottom decile (defined as having poor cognition) and those achieving a score above this cut-off (defined as having good cognition). The rationale for using percentile cut-offs in this population is that the prevalence of cognitive impairment using accepted standard diagnostic criteria is low and the cognitive scores were not normally distributed.

Covariates:

Education (the highest level attained) and social class were obtained from the baseline (1993- 1997) questionnaire. Education was categorized into three groups: 1) No qualification (not completing school up to the age of 16), 2) Completion of school up to the age of 16 or up to the age of 18; and finally 3) those obtaining an education to graduate level (those who obtained a degree or equivalent) or above. Social class was dichotomized, into 'non manual' and 'manual' class. The following variables were measured at the clinic appointment in the third phase of the study (3HC): Weight was measured to the nearest 0.1 kg (using digital scales, Tanita) and height was measured with a stadiometer (Chasmores, UK) to the nearest 0.1 cm to calculate body mass index (BMI: weight (in kilograms) divided by height (in meters squared)). Waist and hip circumference were measured to the nearest 0.1cm to calculate the waist-hip ratio. Physical activity levels were determined using the RUPE index^{42,43}. Systolic blood pressure was also measured at this time. Self-report of smoking status (current, former or never smoker) and alcohol intake (Units/Week) were obtained from health and lifestyle questionnaire administered at the time of the clinic appointment. Medical history of heart-attack, stroke, cancer, diabetes, hypertension, chronic obstructive pulmonary disease (COPD), depression; and memory and hearing problems, were established using self-report of a range of conditions from health and lifestyle follow up questionnaire.

Education, social class and smoking were all treated as categorical variables in the analysis, as was comorbidity (as present or not). BMI, waist-hip ratio, systolic blood pressure and alcohol consumption were entered as continuous variables. SF-36 scores were entered in terms of standard deviation changes, while the composite cognitive score was entered as a dichotomized variable based on the description above (poor performance or not).

Missing data: Missingness at the 3HC has previously been characterised by Hayat and colleagues^{24,25}

Supplementary Tables and Figures

Table S1. International Classification of Disease (ICD) – 10th revision.

ICD Code	ICD Description
F00	Dementia in Alzheimer's disease
G30	Alzheimer's disease
F00.0	Dementia in Alzheimer's disease with early onset
G30.0	
F00.1	Dementia in Alzheimer's disease with late onset
G30.1	
F00.2	Dementia in Alzheimer's disease, atypical or mixed type
G30.8	Other Alzheimer's disease
F00.9	Dementia in Alzheimer's disease, unspecified
G30.9	
F01	Vascular dementia
F01.0	Vascular dementia of acute onset
F01.1	Multi-infarct dementia
F01.2	Subcortical vascular dementia
F01.8	Other vascular dementia
F01.9	Vascular dementia, unspecified
F02	Dementia in other diseases, classified elsewhere
F02.0	Dementia in Pick's disease
F02.1	Dementia in Creutzfeldt-Jakob disease
F02.2	Dementia in Huntington's disease
F02.3	Dementia in Parkinson's disease
F02.8	Dementia in other specified diseases classified elsewhere
G31.0	Frontotemporal dementia
G31.8	Other specified degenerative diseases of nervous system. Grey-matter degeneration [Alpers] Lewy body(ies)(dementia)(disease). Subacute necrotising encephalopathy [Leigh]
F03	Unspecified dementia
F05.1	Dementia superimposed on delirium
F10.7	Residual and late-onset psychotic disorder: Includes Alcoholic dementia NOS Chronic alcoholic brain syndrome Dementia and other milder forms of persisting impairment of cognitive functions

Table S2. List of the individual cognitive tests used in the EPIC-Norfolk 3HC. Reproduced from Hayat et al, 2021¹⁵

Name of test	Predominant ability measured by test (Description of score)
1. A shortened version of the Extended Mental Status Exam (SF-EMSE)	Global function (continuous score)
2. Hopkins Verbal Learning Test (HVLТ)	Verbal episode memory (continuous score)
3. Cambridge Neuropsychological Test Automated Battery Paired Associates Learning Test. First trial Memory Score (CANTAB-PAL FTMS)	Non-verbal episodic memory (continuous score)
4. PW Letter Cancellation Task (PW-Accuracy Score)	Attention (continuous score)
5. Event and Time Based Task (prospective memory)	Prospective memory (dichotomous outcome, success or fail)
6. Visual Sensitivity Test (VST)-Simple	Simple and complex visual processing speed measured in milliseconds (continuous score)
7. Visual Sensitivity Test (VST)-Complex	
8. Shortened version of the National Adult Reading Test (short-NART)	Reading ability and crystallised intelligence (continuous score)

Table S3. Baseline characteristics by SF-36 MCS component score tertile

Variable	Total (n = 7452)	Tertile 1 0.0 – 53.8 (n=2552)	Tertile 2 53.9– 58.5 (n= 2482)	Tertile 3 58.6 – 74.0 (n=2424)	p-value
Age (years)	69.3 (8.3)	68.6 (8.6)	68.4 (8.0)	70.9 (8.0)	<0.001
Sex					
Men	3202 (43.0)	997 (39.1)	1083 (43.6)	1124 (46.4)	
Women	4250 (57.0)	1555 (60.9)	1399 (56.4)	1300 (53.6)	<0.001
BMI (kg/m²)	26.7 (4.2)	26.4 (4.5)	26.4 (4.0)	27.0 (4.2)	<0.001
Waist-hip ratio	0.89 (0.1)	0.89 (0.1)	0.89 (0.1)	0.90 (0.1)	<0.001
Education level					
No formal qualifications	1954 (26.2)	687 (26.9)	601 (24.2)	666 (27.5)	
Formal qualifications	5498 (73.8)	1865 (73.1)	1881 (75.8)	1752 (72.2)	0.02
Socioeconomic status					
Non-manual	4917 (66.6)	1685 (66.0)	1651 (66.5)	1581 (65.2)	
Manual	2462 (33.4)	842 (33.0)	806 (32.5)	814 (33.6)	0.66
Physical activity					
Inactive	2916 (39.1)	1037 (40.6)	880 (35.5)	1000 (41.3)	
Moderately inactive	2103 (28.2)	688 (27.0)	735 (29.6)	680 (28.1)	
Moderately active	1277 (17.1)	447 (17.5)	459 (18.5)	371 (15.3)	
Active	1155 (15.5)	380 (14.9)	407 (16.4)	368 (15.2)	<0.001
Smoking status					
Current or former	3716 (49.9)	1313 (51.4)	1224 (49.3)	1179 (48.7)	
Never	3736 (50.1)	1239 (48.6)	1258 (50.7)	1239 (51.1)	0.13
Alcohol Units (median)	3.0 (8.0)	2.0 (7.0)	4.0 (9.0)	3.0 (8.0)	<0.001
Self-reported comorbidity					
Cancer					
Yes	616 (8.3)	219 (8.6)	180 (7.3)	217 (9.0)	0.09
Myocardial infarction					
Yes	193 (2.6)	60 (2.4)	60 (2.4)	73 (3.0)	0.42
Stroke					

Yes	97 (1.3)	37 (1.4)	27 (1.1)	33 (1.4)	0.46
Bronchitis					
Yes	634 (8.5)	242 (9.5)	201 (8.1)	191 (8.1)	0.03
Asthma					
Yes	695 (9.3)	271 (10.6)	218 (8.8)	206 (8.5)	0.006
Arthritis					
Yes	2099 (28.2)	726 (28.4)	618 (24.9)	755 (31.1)	<0.001
Depression					
Yes	1041 (14.0)	588 (23.0)	270 (10.9)	183 (7.5)	<0.001
Hearing problems					
Yes	2385 (32.0)	839 (32.9)	757 (30.5)	789 (32.5)	0.11
Systolic blood pressure (mmHg)	136.0 (16.8)	135.1 (17.9)	136.1 (16.6)	137.2 (15.6)	<0.001
Mean follow-up time (years)	9.6 (2.7)	6.8 (3.0)	7.7 (2.6)	8.0 (2.8)	<0.001
Incident Dementia	511 (6.9)	213 (8.3)	148 (6.0)	156 (6.4)	0.002

Table S4. Baseline characteristics by SF-36 PCS component score tertile

Variable	Total (n = 7452)	Tertile 1 0.0 – 45.3 (n=2460)	Tertile 2 45.4-53.7 (n=2535)	Tertile 3 53.8 -69.0 (n=2457)	p- value
Age (years)	69.3 (8.3)	73.0 (8.3)	68.8 (7.7)	66.1 (7.3)	<0.001
Sex					
Men	3202 (43.0)	1004 (40.8)	1114 (43.9)	1084 (44.1)	
Women	4250 (57.0)	1456 (59.2)	1421 (56.1)	1373 (55.9)	0.03
BMI (kg/m²)	26.7 (4.2)	28.0 (4.9)	26.6 (4.0)	25.5 (3.5)	<0.001
Waist-hip ratio	0.89 (0.1)	0.91 (0.1)	0.89 (0.1)	0.88 (0.1)	<0.001
Education level					
No formal qualifications	1954 (26.2)	744 (30.2)	668 (26.3)	542 (22.1)	
Formal qualifications	5498 (73.8)	1716 (69.8)	1867 (73.6)	1915 (77.9)	<0.001
Socioeconomic status					
Non-manual	4917 (66.6)	1579 (64.2)	1660 (65.5)	1678 (68.3)	
Manual	2462 (33.4)	856 (34.8)	853 (33.6)	753 (30.6)	0.007
Physical activity					
Inactive	2916 (39.1)	1347 (54.8)	912 (36.0)	656 (26.7)	
Moderately inactive	2103 (28.2)	597 (24.3)	737 (29.1)	769 (31.3)	
Moderately active	1277 (17.1)	308 (12.5)	473 (18.7)	496 (20.2)	
Active	1155 (15.5)	208 (8.5)	413 (16.3)	534 (21.7)	<0.001
Smoking status					
Current or former	3716 (49.9)	1339 (54.4)	1267 (50.0)	1110 (45.2)	
Never	3736 (50.1)	1121 (45.6)	1268 (50.0)	1347 (54.8)	<0.001
Alcohol Units (median)	3.0 (8.0)	2.0 (7.0)	3.0 (8.0)	4.0 (9.0)	<0.001
Self-reported comorbidity					
Cancer					
Yes	616 (8.3)	273 (11.1)	190 (7.5)	153 (6.2)	<0.001
Myocardial infarction					
Yes	193 (2.6)	124 (5.0)	37 (1.5)	32 (1.3)	<0.001
Stroke					

Yes	97 (1.3)	62 (2.5)	20 (0.8)	15 (0.6)	<0.001
Bronchitis					
Yes	634 (8.5)	297 (12.1)	178 (7.0)	159 (6.5)	<0.001
Asthma					
Yes	695 (9.3)	303 (12.3)	224 (8.8)	168 (6.8)	<0.001
Arthritis					
Yes	2099 (28.2)	1107 (45.0)	672 (26.5)	319 (13.0)	<0.001
Depression					
Yes	1041 (14.0)	405 (16.4)	339 (13.4)	297 (12.1)	<0.001
Hearing problems					
Yes	2385 (32.0)	957 (38.9)	791 (31.2)	636 (25.9)	<0.001
Systolic blood pressure (mmHg)	136.0 (16.8)	136.6 (16.5)	136.4 (16.0)	135.5 (17.7)	0.07
Mean follow-up time (years)	9.6 (2.7)	8.6 (3.3)	9.4 (2.8)	9.8 (2.5)	<0.001
Incident Dementia	511 (6.9)	257 (10.4)	149 (5.9)	105 (4.3)	<0.001

Table S5. Demographic variables in the entire sample at the 3HC, and comparison of participants based on dementia status at 31 March 2019.

Variable	N (including = 7452)	Total (n = 7452)	Incident dementia (n = 511)	No incident dementia (n = 6941)	p-value
Age (years)	7452	69.3 (8.3)	76.5 (6.3)	68.8 (8.2)	<0.001
Sex	7452				
Men		3202 (43.0)	222 (43.4)	2980 (42.9)	
Women		4250 (57.0)	289 (56.6)	3961 (57.1)	0.91#
BMI (kg/m²)	6191	26.7 (4.2)	26.4 (4.2)	26.7 (4.2)	0.99
Waist-hip ratio	6185	0.89 (0.1)	0.90 (0.1)	0.89 (0.1)	0.02
Education level	7452				
No formal qualifications		1954 (26.2)	168 (32.9)	1786 (25.7)	
Formal qualifications		5498 (73.8)	343 (67.1)	5155 (74.3)	<0.001^
Socioeconomic status	7385				
Non-manual		4917 (66.6)	342 (67.5)	4575 (66.6)	
Manual		2462 (33.4)	165 (32.5)	2297 (33.4)	<0.001#
Physical activity	7451				
Inactive		2916 (39.1)	237 (46.4)	2679 (38.6)	
Moderately inactive		2103 (28.2)	125 (24.5)	1978 (28.5)	
Moderately active		1277 (17.1)	81 (15.9)	1196 (17.2)	
Active		1155 (15.5)	68 (13.3)	1087 (15.7)	<0.001^
Smoking status	7442				
Current or former		3716 (49.9)	282 (55.2)	3434 (49.5)	
Never		3736 (50.1)	229 (44.8)	3507 (50.5)	<0.001#
Alcohol Units (median)	7298	3.0 (8.0)	2.0 (7.0)	3.0 (8.0)	<0.001^
Self-reported comorbidity					
Cancer	7452				
Yes		616 (8.3)	43 (9.8)	573 (9.5)	0.20#
Myocardial infarction	7452				
Yes		193 (2.6)	11 (2.5)	182 (3.0)	0.68#
Stroke	7452				
Yes		97 (1.3)	9 (2.0)	88 (1.4)	0.54#
Bronchitis	7452				
Yes		634 (8.5)	43 (9.6)	591 (9.6)	0.96#

Asthma	7452				
Yes		695 (9.3)	36 (8.1)	659 (10.5)	0.23#
Arthritis	7452				
Yes		2099 (28.2)	176 (39.5)	1923 (31.1)	<0.001#
Depression	7452				
Yes		956 (12.8)	64 (14.1)	892 (15.5)	0.44#
Hearing problems	7452				
Yes		2385 (32.0)	213 (42.9)	2172 (32.4)	<0.001#
Systolic blood pressure (mmHg)	6201	136.0 (16.8)	138.0 (17.6)	136.0 (16.7)	0.02
Mean follow-up time (years)	7452	9.6 (2.7)	7.4 (2.9)	9.7 (2.6)	<0.001^
SF-36 summary scores	7452				
PCS		47.0 (10.7)	43.7 (11.0)	47.3 (10.6)	<0.001
MCS		54.3 (8.0)	52.9 (9.1)	54.4 (7.9)	<0.001
SF-36 subscale scores					
Physical functioning	7452	75.1 (24.7)	64.5 (27.3)	76.0 (24.2)	<0.001
Role-physical functioning	7452	72.0 (39.6)	55.6 (43.7)	73.2 (38.9)	<0.001
Bodily pain	7452	76.4 (21.7)	72.9 (22.8)	76.7 (21.6)	<0.001
General health	7452	72.0 (20.6)	67.8 (21.1)	72.3 (20.5)	<0.001
Social functioning	7452	88.4 (20.3)	82.2 (23.7)	88.9 (20.0)	<0.001
Role-emotional functioning	7452	88.0 (28.2)	76.8 (37.7)	88.9 (27.2)	<0.001
Vitality	7452	62.7 (19.2)	58.0 (19.7)	63.1 (19.1)	<0.001
Mental health	7452	79.2 (14.9)	76.5 (16.0)	79.4 (14.8)	<0.001

Those who were missing comorbidity information were classed as not being diagnosed with the respective comorbidity. Values in brackets are SDs, interquartile range values or proportions, as appropriate. #Chi-squared test. ^Mann-Whitney U-test. Abbreviations: BMI = body mass index, PCS = physical component summary, MCS = mental component summary.

Table S6. Association between SF-36 subscale measures and incident all-cause dementia.

SF-36 subscale	Model 1		Model 2		Model 3		Model 4		Model 5	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
N (no. incident dementia cases)		7452 (511)		7452		7221		7452		5995 (366)
Physical functioning	0.90	(0.83, 0.98)	0.90	(0.83, 98)	0.91	(0.84, 1.00)	0.89	(0.82, 0.97)	0.95	(0.84, 1.06)
Role-physical functioning	0.90	(0.83, 0.98)	0.90	(0.83, 0.98)	0.92	(0.85, 1.01)	0.90	(0.82, 0.97)	0.92	(0.83, 1.01)
Bodily pain	0.99	(0.91, 1.08)	0.99	(0.91, 1.08)	1.00	(0.92, 1.00)	0.99	(0.90, 1.07)	1.06	(0.95, 1.18)
General health	0.93	(0.85, 1.02)	0.93	(0.85, 1.02)	0.94	(0.85, 1.03)	0.92	(0.84, 1.01)	0.93	(0.82, 1.04)
Social functioning	0.77	(0.70, 0.83)	0.76	(0.70, 0.83)	0.85	(0.69, 0.82)	0.76	(0.70, 0.83)	0.77	(0.69, 0.86)
Role-emotional functioning	0.78	(0.73, 0.84)	0.79	(0.73, 0.84)	0.79	(0.74, 0.85)	0.78	(0.73, 0.84)	0.78	(0.72, 0.85)
Vitality	0.85	(0.76, 0.94)	0.85	(0.76, 0.94)	0.82	(0.68, 0.99)	0.84	(0.76, 0.94)	0.84	(0.74, 0.96)
Mental health	0.80	(0.74, 0.87)	0.80	(0.74, 0.87)	0.80	(0.73, 0.86)	0.80	(0.73, 0.87)	0.77	(0.70, 0.85)

Model 1: Age and sex. Model 2: Age, sex, education level. Model 3: Age, sex, socioeconomic status (manual vs non-manual labour), smoking status (current/former vs never), alcohol consumption (units). Model 4: Age, sex, self-reported comorbidity (cancer, myocardial infarction, stroke, bronchitis, asthma, arthritis, depression) and hearing problems. Model 5: Age, sex, socioeconomic status, smoking status, alcohol consumption, self-reported comorbidity, hearing problems, waist-hip ratio and systolic blood pressure. Each unit change in HR represents one SD change in the respective measure; physical health subscales additionally adjusted for Mental Component Summary score & mental health subscales for Physical Component Summary score.

Table S7. Sensitivity analysis for the association between SF-36 summary scores and incident all-cause dementia (excluding those with dementia diagnosis in first five years after 3HC).

SF-36 summary measure	Model 1				Model 5			
	N	HR	95% CI	p	N	HR	95% CI	P
PCS	7351	0.91	(0.83, 1.00)	0.06	5936	0.92	(0.82, 1.04)	0.19
MCS		0.83	(0.76, 0.91)	<0.001		0.80	(0.82, 0.89)	<0.001

Model 1: Age and sex. Model 5: Age, sex, socioeconomic status (manual vs non-manual labour), smoking status (current/former vs never), alcohol consumption (units), self-reported comorbidity (cancer, myocardial infarction, stroke, bronchitis, asthma, arthritis, depression), hearing problems, waist-hip ratio and systolic blood pressure. HRs represent the risk of incident dementia associated per SD change in the respective measure. N = Number of participants included in each respective model. PCS = Physical component summary, MCS = Mental component summary.

Table S8. Sensitivity analysis for the association between SF-36 subscale scores and incident all-cause dementia (excluding those with dementia diagnosis in first five years after 3HC).

SF-36 subscale	Model 1			Model 5		
	N	HR	95% CI	N	HR	95% CI
Physical functioning	7028	0.90	(0.75, 1.07)	5675	1.15	(0.89, 1.49)
Role-physical functioning		0.87	(0.72, 1.05)		0.90	(0.71, 1.14)
Bodily pain		1.00	(0.99, 1.01)		1.01	(1.00, 1.02)
General health		0.96	(0.80, 1.17)		1.02	(0.78, 1.33)
Social functioning		0.98	(0.98, 0.99)		0.98	(0.97, 0.99)
Role-emotional functioning		0.61	(0.54, 0.69)		0.62	(0.53, 0.74)
Vitality		0.98	(0.97, 0.99)		0.98	(0.97, 0.99)
Mental health		0.64	(0.55, 0.74)		0.59	(0.49, 0.73)

Model 1: Age and sex. Model 5: Age, sex, socioeconomic status (manual vs non-manual labour), smoking status (current/former vs never), alcohol consumption (units), self-reported comorbidity (cancer, myocardial infarction, stroke, bronchitis, asthma, arthritis, depression), hearing problems, waist-hip ratio and systolic blood pressure. HRs represent the risk of incident dementia associated per SD change in the respective measure. N = Number of participants included in each respective model.

Table S9. Association between deciles of SF-36 summary scores and incident all-cause dementia.

SF-36 summary measure	Model 1				Model 5			
	N	HR	95% CI	p	N	HR	95% CI	p
PCS	7452				5995			
Decile 1		1.13	(0.89, 1.43)	0.32		1.09	(0.79, 1.50)	0.61
Deciles 2-9		1.00				1.00		
Decile 10		0.89	(0.60, 1.31)	0.54		0.88	(0.56, 1.37)	0.58
MCS								
Decile 1		1.98	(1.55, 2.52)	<0.001		2.12	(1.57, 2.86)	<0.001
Deciles 2-9		1.00				1.00		
Decile 10		0.66	(0.49, 0.89)	0.007		0.65	(0.46, 0.93)	0.02

Model 1: Age and sex. Model 5: Age, sex, socioeconomic status, smoking status, alcohol consumption, self-reported comorbidity, hearing problems, waist-hip ratio and systolic blood pressure. Each unit change in HR represents one SD change in the respective measure. N = Number of participants included in each respective model. PCS = Physical component summary, MCS = Mental component summary.

Table S10. Association between quintiles of SF-36 summary scores and incident all-cause dementia.

SF-36 summary measure	Model 1				Model 5			
	N	HR	95% CI	p	N	HR	95% CI	p
PCS	7452				5995			
Quintile 1		1.30	(0.98, 1.71)	0.06		1.29	(0.93, 1.79)	0.13
Quintile 2		1.23	(0.93, 1.63)	0.15		1.17	(0.84, 1.62)	0.35
Quintile 3		1.00				1.00		
Quintile 4		1.03	(0.75, 1.42)	0.85		1.07	(0.75, 1.54)	0.70
Quintile 5		1.03	(0.73, 1.44)	0.86		1.03	(0.70, 1.50)	0.90
MCS								
Quintile 1		1.51	(1.15, 1.98)	0.003		1.69	(1.20, 2.36)	0.002
Quintile 2		1.10	(0.82, 1.46)	0.54		1.39	(0.99, 1.95)	0.06
Quintile 3		1.00				1.00		
Quintile 4		0.85	(0.63, 1.16)	0.31		1.01	(0.71, 1.44)	0.96
Quintile 5		0.74	(0.55, 0.99)	0.04		0.83	(0.58, 1.19)	0.32

Model 1: Age and sex. Model 5: Age, sex, socioeconomic status, smoking status, alcohol consumption, self-reported comorbidity, hearing problems, waist-hip ratio and systolic blood pressure. Each unit change in HR represents one SD change in the respective measure. N = Number of participants included in each respective model. PCS = Physical component summary, MCS = Mental component summary.

Figure S1. Crude Cumulative Incidence of dementia according to the mental component score (MCS) deciles. MCS = Mental component summary score. Decile 1 = Lowest; Decile 10 = Highest.

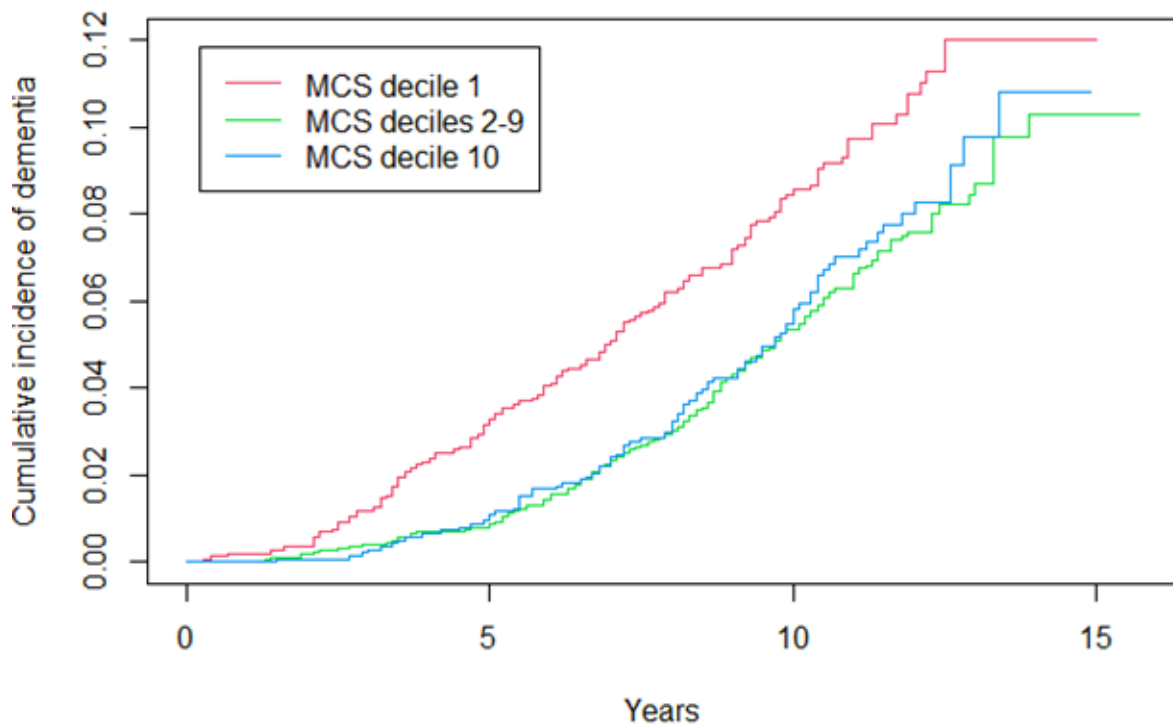


Figure S2. Crude Cumulative Incidence of dementia according to the physical component score (PCS) deciles. PCS = Physical component summary score. Decile 1 = Lowest; Decile 10 = Highest.

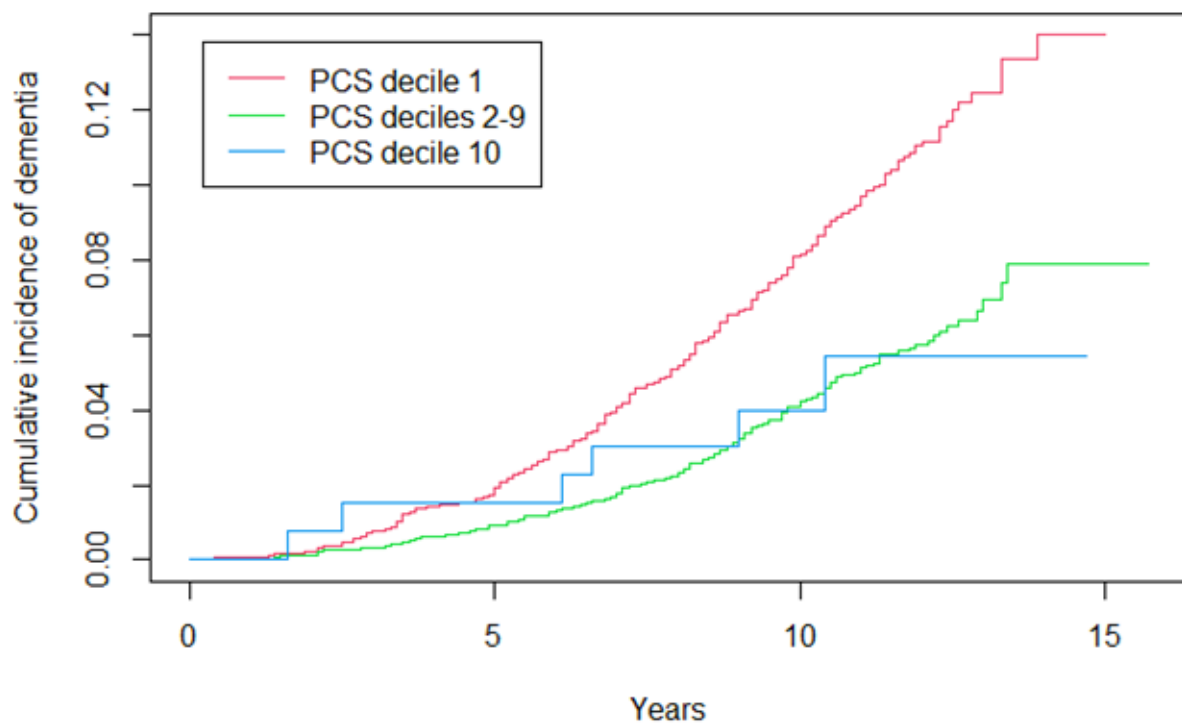


Figure S3. Crude Cumulative Incidence of dementia according to the mental component score (MCS) quintiles. MCS = Mental component summary score. Quintile 1 = Lowest; Quintile 5 = Highest.

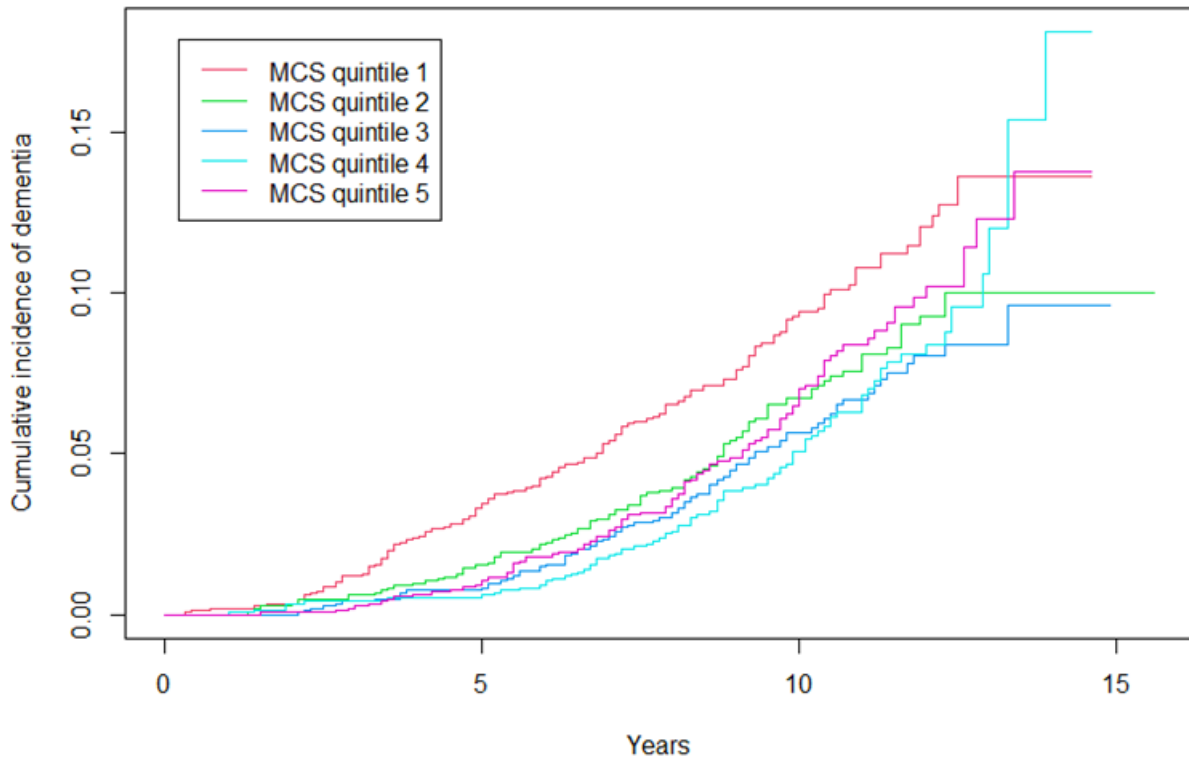


Figure S4. Crude Cumulative Incidence of dementia according to the physical component score (PCS) quintiles. PCS = Physical component summary score. Quintile 1 = Lowest; Quintile 5 = Highest.

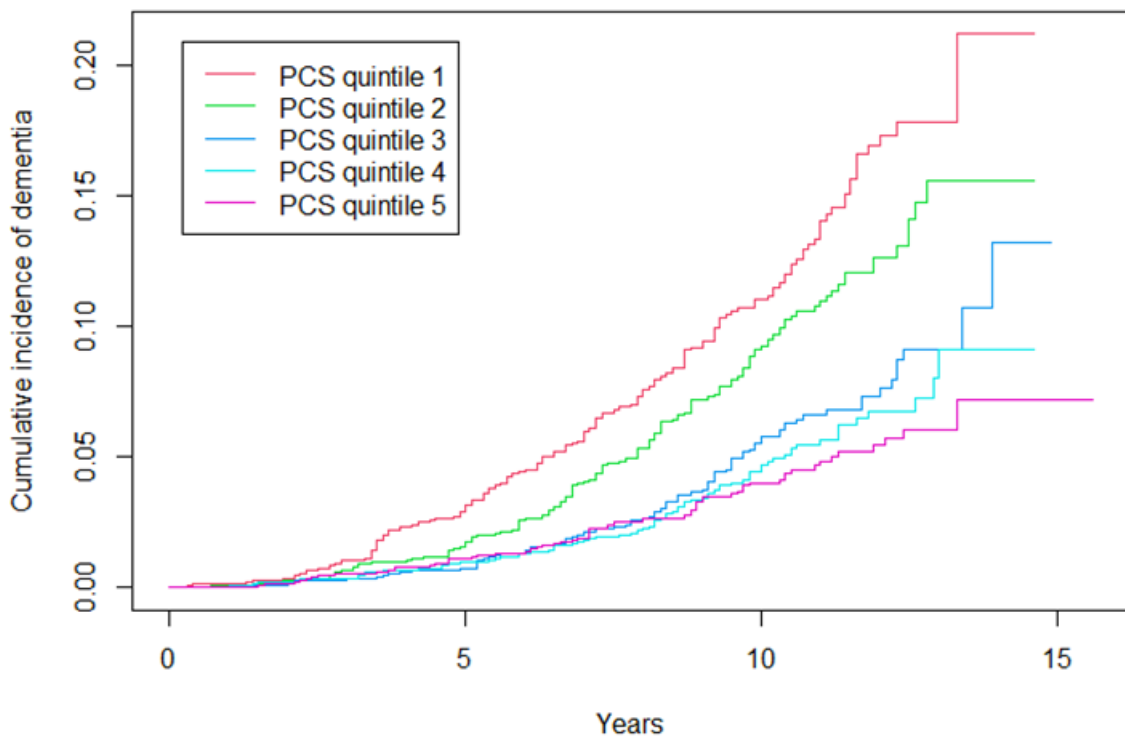


Table S11. Association between SF-36 summary scores and incident all-cause dementia, stratified by age.

Exposure	Model 1			Model 2**			Model 5**		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
50-69 years									
N (n)		3946 (77)			3946 (77)			3366 (61)	
Average MCS*	0.78	(0.65, 0.94)	0.01	0.79	(0.65, 0.95)	0.01	0.76	(0.62, 0.94)	0.01
Average PCS*	0.82	(0.68, 0.98)	0.03	0.82	(0.68, 0.99)	0.04	0.88	(0.69, 1.12)	0.31
Change in MCS									
Increase	0.81	(0.63-1.05)	0.11	0.88	(0.47-1.65)	0.68	1.07	(0.53-2.17)	0.85
Stable (Ref)	1.00			1.00			1.00		
Decrease	1.44	(1.14-1.82)	0.002	1.66	(0.92-2.99)	0.09	1.70	(0.85-3.36)	0.13
Change in PCS									
Increase	1.04	(0.77-1.41)	0.80	1.26	(0.66-2.40)	0.48	1.24	(0.59-2.60)	0.57
Stable (Ref)	1.00			1.00			1.00		
Decrease	1.21	(0.98-1.49)	0.08	1.53	(0.90-2.61)	0.12	1.38	(0.75-2.56)	0.30
≥70 years									
N (n)		3266 (417)			3266 (417)			2449 (295)	
Average MCS*	0.81	(0.75, 0.89)	<0.001	0.81	(0.75, 0.89)	<0.001	0.81	(0.73, 0.89)	<0.001
Average PCS*	0.95	(0.86, 1.04)	0.27	0.95	(0.86, 1.04)	0.27	0.96	(0.85, 1.10)	0.57
Change in MCS									
Increase	0.82	(0.63-1.05)	0.11	0.60	(0.44-0.82)	0.001	0.52	(0.36-0.75)	<0.001
Stable (Ref)	1.00			1.00			1.00		
Decrease	1.44	(1.14-1.82)	0.002	1.44	(1.14-1.83)	0.002	1.49	(1.11-1.98)	0.007
Change in PCS									
Increase	1.04	(0.77-1.41)	0.80	0.99	(0.71-1.37)	0.95	0.92	(0.62-1.35)	0.66
Stable (Ref)	1.00			1.00			1.00		
Decrease	1.21	(0.98-1.49)	0.08	1.19	(0.96-1.47)	0.11	1.04	(0.81-1.34)	0.77

Model 1: Age and sex. Model 2: Age, sex, education level. Model 3: Age, sex, socioeconomic status (manual vs non-manual labour), smoking status (current/former vs never), alcohol consumption (units). Model 4: Age, sex, self-reported comorbidity (cancer, myocardial infarction, stroke, bronchitis, asthma, arthritis, depression) and hearing problems. Model 5: Age, sex, socioeconomic status, smoking status, alcohol consumption, self-reported comorbidity, hearing problems, waist-hip ratio and systolic blood pressure. N = Number of participants included in each respective model, n=number of incident cases of dementia. PCS = Physical component summary, MCS = Mental component summary. *Each unit change in HR represents one SD change in the respective measure; all co-variables measured at 3HC; **for change analyses: Models 2 and 5 are additionally adjusted for MCS/PCS scores at HLEQ1.

