

SUPPLEMENTAL DATA

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eTable 1. Association of depressive symptoms (at ages 50 & 70y) and incidence of dementia.

	Depressive symptoms at mean age 50 (45-55) years N dementia/N total = 276/9004 Mean FU 21.2 (SD=6.0) years		Depressive symptoms at mean age 70 (65-75) years N dementia/N total = 193/5552 Mean FU 5.7 (SD=3.7) years	
	HR (95% CI)	P	HR (95% CI)	P
Model 1: Analysis adjusted for age, sex, marital status, ethnicity, education, occupation				
GHQ-30	Ref.		Ref.	
caseness	1.21 (0.93, 1.57)	0.16	2.65 (1.94, 3.61)	<0.001
CES-D				
≥16 caseness			2.11 (1.37, 3.25)	0.001
Model 2: Model 1 + health behaviors ^a				
GHQ-30	Ref.		Ref.	
caseness	1.17 (0.89, 1.52)	0.26	2.54 (1.86, 3.46)	<0.001
CES-D				
≥16 caseness			2.09 (1.35, 3.23)	0.001
Model 3: Model 2 + chronic conditions ^b				
GHQ-30	Ref.		Ref.	
caseness	1.15 (0.88, 1.50)	0.31	2.47 (1.80, 3.40)	<0.001
CES-D				
≥16 caseness			2.04 (1.30, 3.20)	0.002

^aSmoking, alcohol consumption, physical activity, fruit and vegetable consumption.

^bDiabetes, coronary heart disease, stroke, use of medication for cardiovascular disease, antidepressants.

FU: Follow-up

GHQ-30 caseness: 26.3% at age 45-55 years, 16.0% at age 65-75 years.

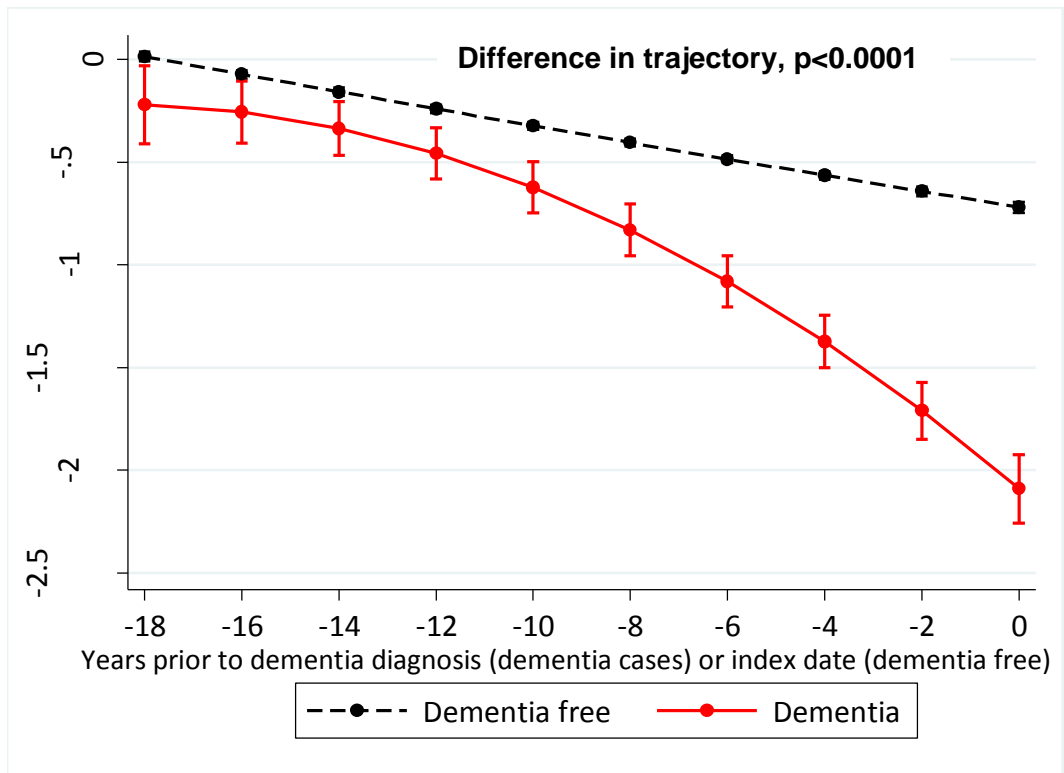
CES-D≥16 caseness: 12.5% at age 70y.

eTable 2. Difference GHQ-30 and CES-D scores in the years preceding dementia between dementia cases and others.

Year	GHQ-30 score Range: 0-30		CES-D score Range: 0-60	
	Difference in score (95% CI)	<i>p</i>	Difference in score (95% CI)	<i>p</i>
-28	0.81 (-0.07, 1.68)	0.07		
-27	0.77 (0.05, 1.48)	0.04		
-26	0.71 (0.10, 1.32)	0.02		
-25	0.65 (0.10, 1.19)	0.02		
-24	0.57 (0.06, 1.09)	0.03		
-23	0.50 (-0.01, 1.01)	0.06		
-22	0.43 (-0.09, 0.94)	0.11		
-21	0.36 (-0.16, 0.88)	0.18		
-20	0.29 (-0.23, 0.81)	0.27		
-19	0.24 (-0.28, 0.76)	0.37		
-18	0.20 (-0.32, 0.72)	0.45		
-17	0.18 (-0.33, 0.69)	0.49		
-16	0.18 (-0.33, 0.68)	0.49		
-15	0.20 (-0.30, 0.70)	0.43		
-14	0.25 (-0.24, 0.75)	0.32		
-13	0.34 (-0.17, 0.84)	0.19		
-12	0.45 (-0.06, 0.96)	0.08	3.69 (1.15, 6.22)	0.006
-11	0.61 (0.09, 1.13)	0.02	2.39 (0.70, 4.09)	0.02
-10	0.81 (0.27, 1.34)	0.003	1.64 (0.29, 3.00)	0.04
-9	1.05 (0.50, 1.59)	<0.001	1.36 (0.06, 2.66)	0.03
-8	1.34 (0.78, 1.89)	<0.001	1.44 (0.15, 2.74)	0.005
-7	1.68 (1.11, 2.24)	<0.001	1.81 (0.55, 3.08)	<0.001
-6	2.08 (1.50, 2.65)	<0.001	2.38 (1.17, 3.60)	<0.001
-5	2.53 (1.94, 3.12)	<0.001	3.07 (1.87, 4.27)	<0.001
-4	3.05 (2.43, 3.67)	<0.001	3.78 (2.57, 5.00)	<0.001
-3	3.63 (2.97, 4.29)	<0.001	4.44 (3.17, 5.71)	<0.001
-2	4.28 (3.55, 5.02)	<0.001	4.95 (3.60, 6.30)	<0.001
-1	5.01 (4.16, 5.85)	<0.001	5.23 (3.71, 6.74)	<0.001
0	5.81 (4.81, 6.81)	<0.001	5.18 (3.28, 7.09)	<0.001
Difference in trajectories	Wald chi-squared test with 3 degrees of freedom = 126.85; <i>p</i> <0.001		Wald chi-squared test with 3 degrees of freedom = 21.52; <i>p</i> <0.001	

Model adjusted for age at year 0, sex, ethnicity, education, 5-year birth cohort, and time-dependent occupational position, and marital status.

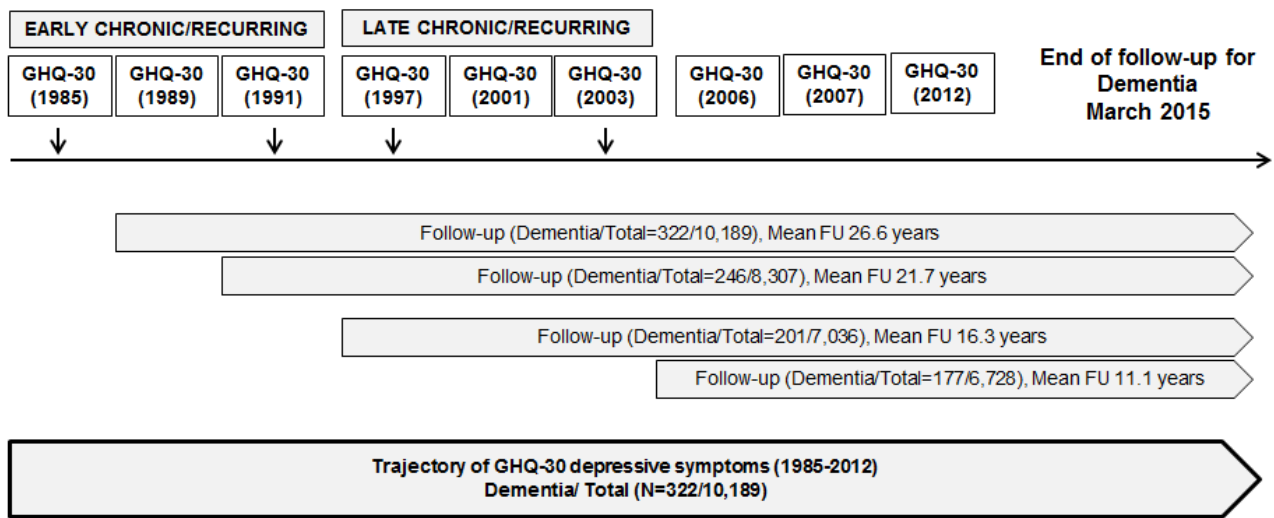
eFigure 1. Trajectory of global cognitive score in dementia cases and other participants in the years leading to dementia diagnosis.



Number of observations in the analysis

Years	-18 to -16	-16 to -12	-12 to -8	-8 to -4	-4 to 0
Dementia free (N=7311)	5192	2489	3714	5938	4777
Dementia cases (N=195)	31	81	119	110	89

eFigure 2. Study design to assess association of dementia risk with GHQ caseness* and GHQ-30 trajectories.

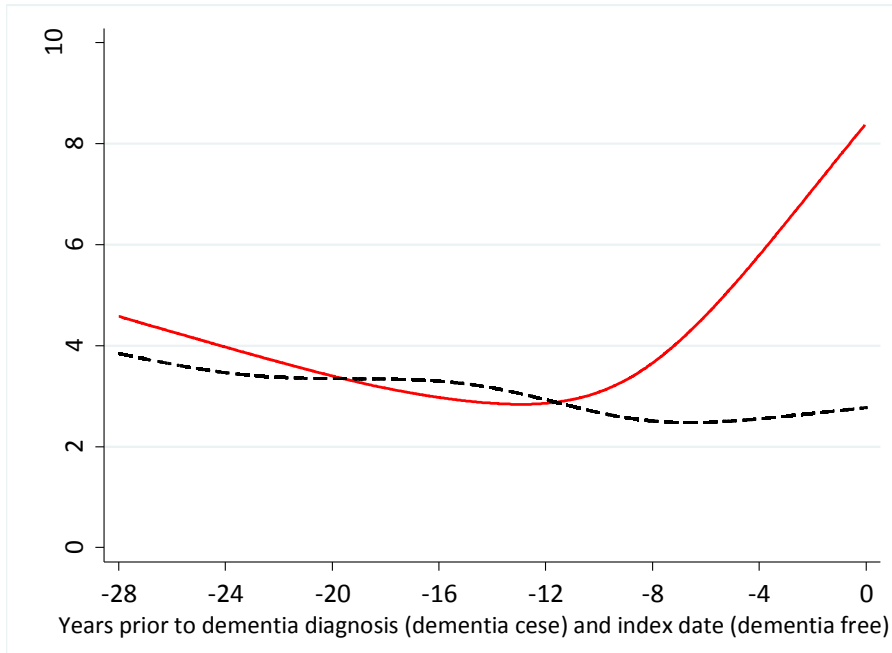


FU: Follow-up

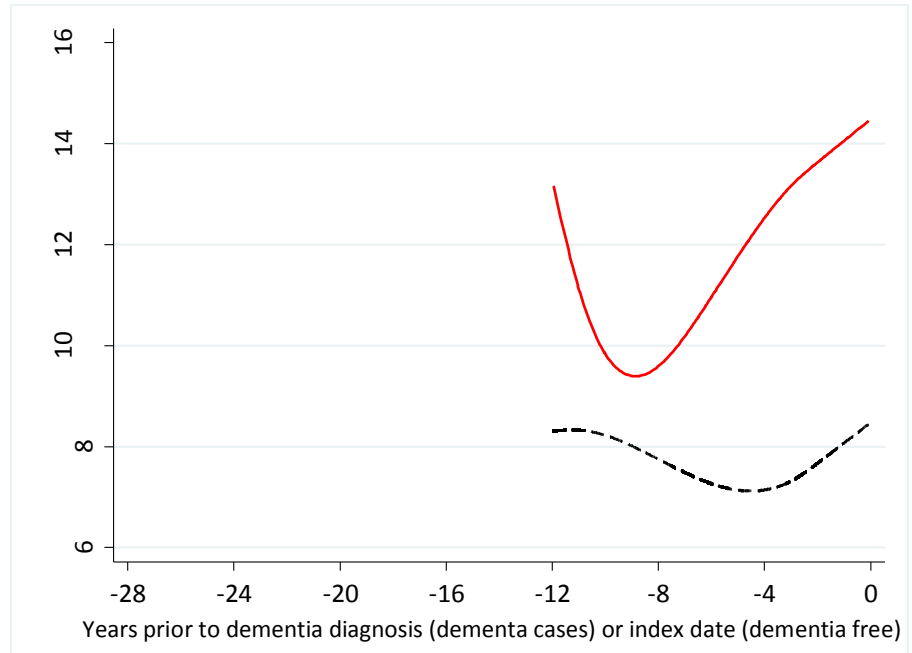
*Early and late chronic GHQ-30 caseness requires at least 2 out of the 3 corresponding measures.

eFigure 3. Trajectories of depressive symptoms preceding dementia using cubic regression splines.

A. GHQ-30 score



B. CES-D score



Legend — Dementia cases - - - Dementia free