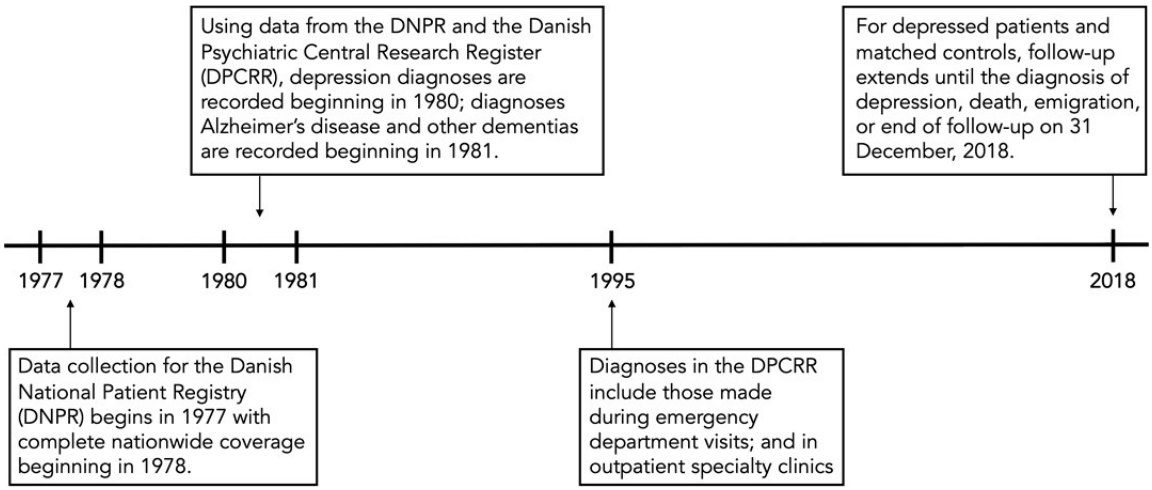
Supplementary Online Content

Elser H, Horváth-Puhó E, Gradus JL, et al. Association of early-, middle-, and late-life depression with incident dementia in a Danish cohort. *JAMA Neurol*. Published online July 24, 2023. doi:10.1001/jamaneurol.2023.2309

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



eFigure 1. Study timeline and length of follow-up for study subjects and data sources, 1977–2018

eTable 1. Diagnostic codes from the *International Classification of Diseases* (ICD)

Diagnosis	Revision	ICD Code
Depression	ICD-8	296.0
	ICD-8	296.2
	ICD-8	296.8
	ICD-8	296.9
	ICD-8	296.8
	ICD-8	296.9
	ICD-8	300.4
	ICD-8	301.1
	ICD-10	F32.0
	ICD-10	F32.1
	ICD-10	F32.2
	ICD-10	F32.3
	ICD-10	F32.4
	ICD-10	F32.5
	ICD-10	F32.8
	ICD-10	F32.81
	ICD-10	F32.9
	ICD-10	F33*
	ICD-10	F34
	ICD-10	F39
Alzheimer's Disease	ICD-8	290.09
	ICD-8	290.10
	ICD-10	F00
	ICD-10	G30
Vascular Dementia	ICD-8	293.09
	ICD-8	293.19
	ICD-10	F01
Other Dementia	ICD-8	094.19
	ICD-8	292.09
	ICD-8	290.11
	ICD-8	290.18
	ICD-8	290.19
	ICD-10	F02
	ICD-10	F03
	ICD-10	F10.73
	ICD-10	F11.73
	ICD-10	F12.73
	ICD-10	F13.73
	ICD-10	F14.73
	ICD-10	F15.73
	ICD-10	F16.73
	ICD-10	F17.73
	ICD-10	F18.73
	ICD-10	F19.73
	ICD-10	G23.1
	ICD-10	G31.0

Other Dementia	ICD-10	G31.1
	ICD-10	G31.8B
	ICD-10	G31.8E
	ICD-10	G31.85
Cardiovascular Disease (CVD)	ICD-8	400
	ICD-8	401
	ICD-8	402
	ICD-8	403
	ICD-8	404
	ICD-8	410
	ICD-8	411
	ICD-8	413
	ICD-8	421
	ICD-8	394
	ICD-8	395
	ICD-8	427.93
	ICD-8	427.94
	ICD-8	427.20
	ICD-8	427.21
	ICD-8	427.22
	ICD-8	427.23
	ICD-8	427.97
	ICD-8	427.91
	ICD-8	427.09
	ICD-8	427.10
	ICD-8	427.11
	ICD-8	427.19
	ICD-8	428.99
	ICD-8	728.49
	ICD-8	272.00
	ICD-10	I05
	ICD-10	I06
	ICD-10	I07
	ICD-10	I08
	ICD-10	I09
	ICD-10	I10
	ICD-10	I11
	ICD-10	I12
	ICD-10	I13
	ICD-10	I20
	ICD-10	I21
	ICD-10	I22
	ICD-10	I23
	ICD-10	I24
	ICD-10	I25
	ICD-10	I33
	ICD-10	I34
	ICD-10	I35
	ICD-10	I36

Cardiovascular Disease (CVD)	ICD-10	I37
	ICD-10	I39
	ICD-10	I42
	ICD-q0	I47
	ICD-10	I48
	ICD-10	I44
	ICD-10	I45
	ICD-10	I49
	ICD-10	I50
	ICD-10	E78.0
Chronic Obstructive Pulmonary Disease (COPD)	ICD-8	490
	ICD-8	491
	ICD-8	492
	ICD-10	J40
	ICD-10	J41
	ICD-10	J42
	ICD-10	J43
	ICD-10	J44
Diabetes	ICD-8	250
	ICD-8	251
	ICD-10	E08
	ICD-10	E09
	ICD-10	E10
	ICD-10	E11
	ICD-10	E13
Stroke	ICD-8	430
	ICD-8	431
	ICD-8	433
	ICD-8	434
	ICD-8	435
	ICD-10	I60
	ICD-10	I61
	ICD-10	I63
	ICD-10	I64
	ICD-10	G45.9
Head Injuries	ICD-8	N800
	ICD-8	N801
	ICD-8	N803
	ICD-8	N804
	ICD-8	N850
	ICD-8	N851
	ICD-8	N852
	ICD-8	N853
	ICD-8	N854
	ICD-10	S02.0
	ICD-10	S02.1X
	ICD-10	S02.8
	ICD-10	S02.91
	ICD-10	S04.02

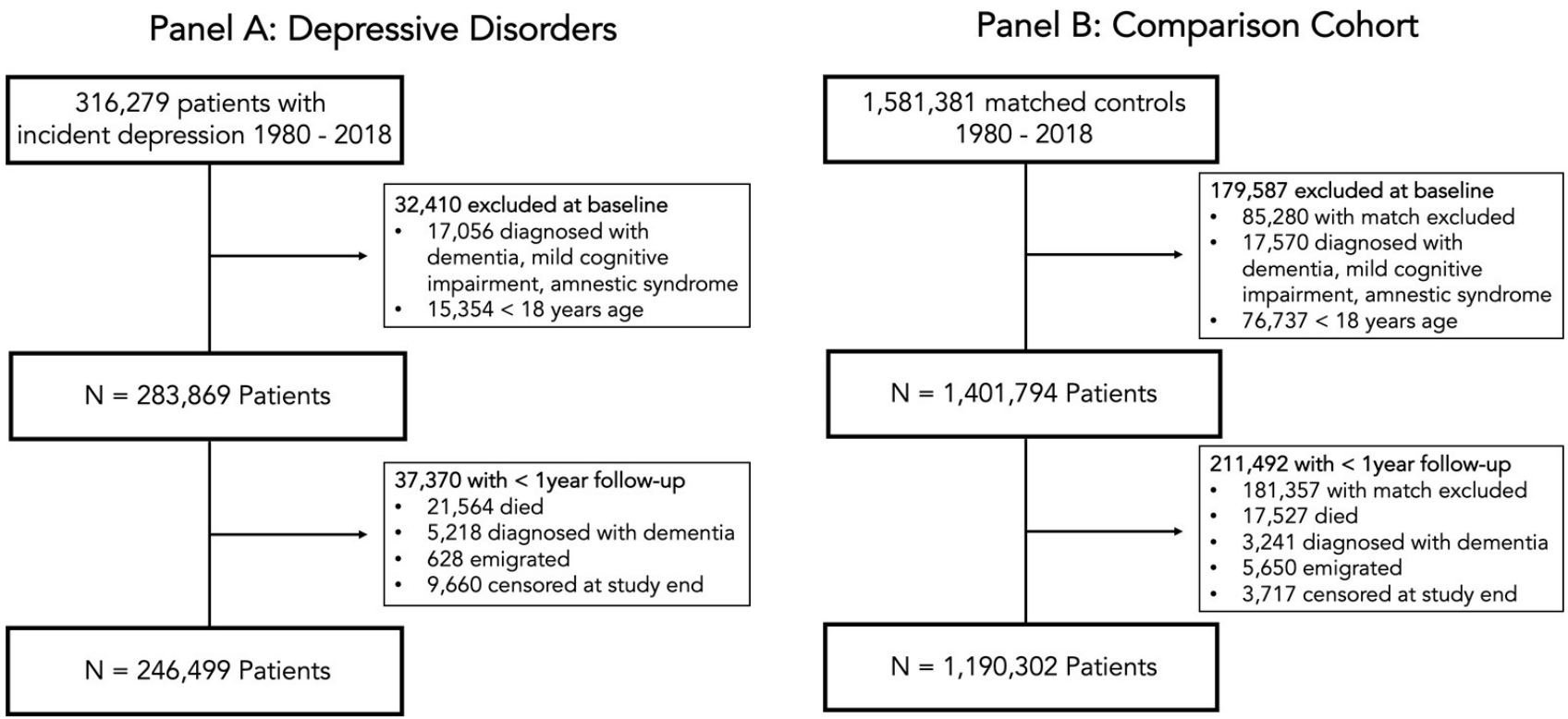
Head Injuries	ICD-10	S04.03X
	ICD-10	S04.04X
	ICD-10	S06.X
	ICD-10	S07.1
Anxiety Disorders	ICD-8	300
	ICD-8	305.9
	ICD-8	305.68
	ICD-8	307.99
	ICD-10	F40
	ICD-10	F41
	ICD-10	F42
	ICD-10	F44
	ICD-10	F45
Stress Disorders	ICD-8	308
	ICD-10	F43
Bipolar Disorder	ICD-8	296.1
	ICD-8	296.3
	ICD-10	F31
Substance Use Disorders	ICD-8	291
	ICD-8	303
	ICD-8	304
	ICD-10	F10
	ICD-10	F11
	ICD-10	F12
	ICD-10	F13
	ICD-10	F14
	ICD-10	F15
	ICD-10	F16
	ICD-10	F17
	ICD-10	F18
	ICD-10	F19
Personality Disorders	ICD-8	301
	ICD-10	F60
	ICD-10	F69
Suicide Attempt	ICD-8	E950
	ICD-8	E951
	ICD-8	E952
	ICD-8	E953
	ICD-8	E954
	ICD-8	E955
	ICD-8	E956
	ICD-8	E957
	ICD-8	E958
	ICD-8	E959
	ICD-10	X60
	ICD-10	X61
	ICD-10	X62
	ICD-10	X63
	ICD-10	X64

Suicide Attempt	ICD-10	X65
	ICD-10	X66
	ICD-10	X67
	ICD-10	X68
	ICD-10	X69
	ICD-10	X70
	ICD-10	X71
	ICD-10	X72
	ICD-10	X73
	ICD-10	X74
	ICD-10	X75
	ICD-10	X76
	ICD-10	X77
	ICD-10	X78
	ICD-10	X79
	ICD-10	X80
	ICD-10	X81
	ICD-10	X82
	ICD-10	X83
	ICD-10	X84

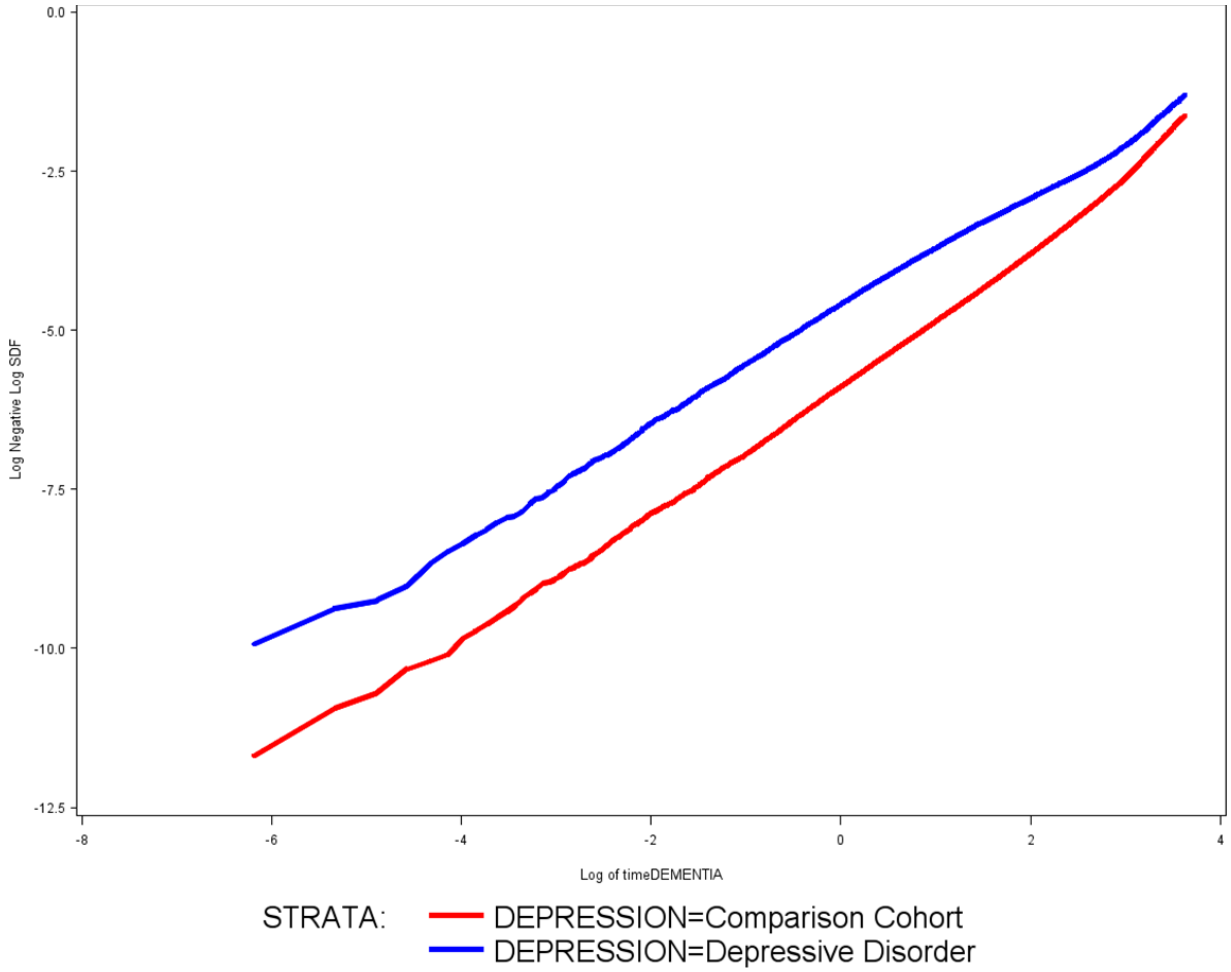
eTable 2. Anatomical Therapeutic Chemical (ATC) codes for prescribed antidepressants

ATC Code	Generic Name
N06AA01	Despiramine
N06AA02	Imipramine
N06AA03	Imipramine oxide
N06AA04	Clomipramine
N06AA05	Opipramol
N06AA06	Trimipramine
N06AA07	Lofepramine
N06AA08	Dibenzapin
N06AA09	Amitriptyline
N06AA10	Nortriptyline
N06AA11	Protryptyline
N06AA12	Doxepin
N06AA13	Iprindole
N06AA14	Melitracen
N06AA15	Butriptyline
N06AA16	Dosulepin
N06AA17	Amoxapine
N06AA18	Dimetracine
N06AA19	Amineptine
N06AA21	Maprotiline
N06AA23	Quinupramine
N06AB02	Zimeldine
N06AB03	Fluoxetine
N06AB04	Citalopram
N06AB05	Paroxetine
N06AB06	Sertraline
N06AB07	Alaproclate
N06AB08	Fluvoxamine
N06AB09	Eteperidone
N06AB10	Escitalopram
N06AF01	Isocarboxazid
N06AF02	Nialamide
N06AF03	Phenelzine
N06AF04	Tranylcypromine
N06AF05	Iproniazide
N06AF06	Iproclozide
N06AG02	Moclobemide
N06AG03	Toloxatone
N06AX01	Oxitriptan
N06AX02	Tryptophan
N06AX03	Mianserin
N06AX04	Nomifensine
N06AX05	Trazodone
N06AX07	Nefazodone
N06AX08	Bifemalane
N06AX09	Viloxazine

N06AX10	Oxaflozane
N06AX11	Mirtazapine
N06AX12	Bupropion
N06AX13	Medifoxamine
N06AX14	Tianeptine
N06AX15	Pivagabine
N06AX16	Venlafaxine
N06AX17	Milnacipran
N06AX18	Reboxetine
N06AX19	Gepirone
N06AX21	Duloxetine
N06AX22	Agomelatine
N06AX23	Desvenlafaxine
N06AX24	Vilazodone
N06AX25	Hyperici Herba
N06AX26	Vortioxetine
N06AX27	Esketamine
N06AX28	Levomilnacipran
N06AX29	Brexanolone



eFigure 2. Flow chart depicting exclusion criteria for patients diagnosed with depressive disorders (Panel A) and members of the comparison cohort (Panel B), 1977 – 2018.



eFigure 3. Complementary log-log plot for proportional hazards assumption. The logarithm of the negative logarithm of the estimated survivor function is plotted against the logarithm of survival time. If the assumption of proportional hazards is satisfied, this plot will yield curves that do not cross.

eTable 3. Adjusted HR for depression and dementia by treatment with a prescribed antidepressant

	Depression Diagnosis			Comparison Cohort				
	Events	No. at Risk	Risk (95% CI) [1]	Events	No. at Risk	Risk (95% CI) [1]	**HR (95% CI)** [2]	p-value
Treatment [3]								
1 – 10 years	9,075	194,353	5.70 (5.59,5.82)	19,996	935,663	2.81 (2.77,2.84)	2.54 (2.47,2.62)	<0.001
> 10 – 20 years	1,762	71,427	4.44 (4.22,4.67)	7,665	396,688	3.42 (3.34,3.50)	1.86 (1.73,1.99)	<0.001
> 20 – 39 years	114	9,846	2.56 (2.01,3.21)	503	60,264	1.72 (1.49,1.96)	2.20 (1.63,2.96)	<0.001
1 – 39 years	10,951	194,353	10.21 (9.85,10.59)	28,164	935,663	6.81 (6.64,6.99)	2.42 (2.35,2.49)	<0.001
No Treatment [3]								
1 – 10 years	1,699	52,146	3.95 (3.76,4.14)	3,424	254,639	1.72 (1.66,1.78)	2.83 (2.63,3.05)	<0.001
> 10 – 20 years	875	23,869	4.70 (4.40,5.01)	4,032	137,656	3.71 (3.59,3.82)	1.93 (1.74,2.15)	<0.001
> 20 – 39 years	475	9,360	9.76 (8.68,10.9)	3,032	63,306	9.26 (8.85,9.69)	1.71 (1.49,1.97)	<0.001
1 – 39 years	3,049	52,146	12.1 (11.5, 12.7)	10,488	254,639	10.8 (10.5,11.1)	2.35 (2.22,2.48)	<0.001

1. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.
2. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.
3. Treatment was defined based on prescription for an antidepressant in the six months before or the six months after the date of depression diagnosis. Antidepressants were identified from the Danish National Prescription Registry using anatomic therapeutic chemical (ATC) codes.

eTable 4. Adjusted HR for the frequency of inpatient hospitalizations and dementia among those with a baseline depression diagnosis[1]

Inpatient Visits	**Number**[2]	**HR (95% CI)**[3]	p-value
One	113,629	1 (Ref)	--
Two	45,707	1.33 (1.21,1.46)	<0.001
Three	23,949	1.62 (1.43,1.83)	<0.001
Four or more	14,399	1.49 (1.39,1.60)	<0.001

1. Analysis was restricted to individuals with at least one inpatient depression diagnosis (N=113,629). The number of inpatient visits was treated as a time-varying exposure.
2. Reflects the number of individuals with one, two, three, or four or more inpatient depression diagnoses over the course of the study period.
3. We used Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including age, sex, calendar year, education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 5. Adjusted HR for depression and dementia by baseline health characteristics[1]

	Depression Diagnosis Risk (95% CI)	**Comparison Cohort** Risk (95% CI)	**HR (95% CI)**	p-value
Cardiovascular Disease (CVD)				
No	13.0 (12.4,13.8)	11.3 (11.1,11.6)	2.51 (2.43,2.59)	<0.001
Yes	16.1 (15.2,17.0)	13.6 (12.9,14.4)	2.18 (2.06,2.31)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)				
No	13.7 (13.1,14.3)	11.6 (11.3,11.8)	2.41 (2.35,2.47)	<0.001
Yes	11.0 (10.0,12.1)	9.67 (8.50,10.9)	1.99 (1.46,2.73)	<0.001
Stroke				
No	13.4 (12.8,14.1)	11.5 (11.2,11.7)	2.47 (2.40,2.53)	<0.001
Yes	16.5 (15.2,18.0)	14.4 (13.3,15.6)	1.82 (1.52,2.19)	<0.001
Anxiety Disorder				
No	13.6 (13.0,14.2)	11.5 (11.2,11.8)	2.42 (2.36,2.48)	<0.001
Yes	13.8 (11.4,16.4)	11.8 (8.65,15.4)	1.83 (0.63,5.27)	0.26
Substance Use Disorder				
No	14.0 (13.4,14.7)	11.6 (11.3,11.8)	2.42 (2.36,2.48)	<0.001
Yes	9.39 (8.27,10.6)	8.94 (6.77,11.5)	1.55 (1.01,2.37)	0.04
Head Injuries				
No	13.7 (13.1,14.3)	11.5 (12.3,11.8)	2.40 (2.34,2.56)	<0.001
Yes	14.0 (9.98,18.7)	9.80 (7.21,12.9)	3.76 (2.30,6.13)	<0.001

1. Baseline sociodemographic and health characteristics were measured two years prior to the onset of depression beginning beginning in January 1, 1978.
2. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.
3. We used Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including age, sex, calendar year, education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 6. Semi-Bayes adjustment for multiple estimation

	All Participants		Women		Men	
	Original	**Semi-Bayes**	**Original**	**Semi-Bayes**	**Original**	**Semi-Bayes**
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
18 – 44 Years						
1 – 10 years	4.45 (2.42,5.79)	4.09 (2.12,5.36)	4.50 (3.09,6.55)	3.88 (2.75,5.46)	4.59 (3.11,6.75)	3.91 (2.76,5.54)
> 10 – 20 years	2.94 (2.27,3.82)	2.89 (2.21,3.78)	3.29 (2.28,4.75)	3.10 (2.21,4.34)	2.50 (1.70,3.68)	2.54 (1.79,3.59)
> 20 – 39 years	2.15 (1.62,2.86)	2.23 (1.68,2.96)	1.92 (1.34,2.76)	2.08 (1.49,2.91)	2.91 (1.77,4.78)	2.79 (1.87,4.18)
1 – 39 years	3.08 (2.64,3.58)	3.05 (2.52,3.69)	2.94 (2.40,3.61)	2.91 (2.31,3.66)	3.30 (2.62,4.17)	3.21 (2.50,4.11)
45 – 59 Years						
1 – 10 years	4.72 (4.22,5.72)	4.63 (2.93,5.45)	4.26 (3.62,5.00)	4.13 (3.39,5.02)	5.21 (4.46,6.09)	5.00 (4.12,6.06)
> 10 – 20 years	2.37 (2.12,2.66)	2.38 (2.02,2.80)	2.45 (2.12,2.84)	2.46 (2.05,2.96)	2.25 (1.87,2.71)	2.28 (1.84,2.82)
> 20 – 29 years	1.73 (1.46,2.05)	1.78 (1.46,2.18)	1.65 (1.36,2.01)	1.72 (1.38,2.15)	2.18 (1.52,3.11)	2.28 (1.64,3.17)
1 – 29 years	2.95 (2.75,3.17)	2.95 (2.56,3.39)	2.66 (2.42,2.92)	2.66 (2.29,3.10)	3.45 (3.08,3.85)	3.42 (2.90,4.02)
60+ Years						
1 – 10 years	2.46 (2.39,2.53)	2.46 (2.17,2.78)	2.28 (2.21,2.36)	2.28 (2.01,2.59)	3.00 (2.84,3.16)	2.99 (2.62,3.42)
> 10 – 20 years	1.65 (1.53,1.77)	1.66 (1.44,1.91)	1.54 (1.42,1.67)	1.56 (1.35,1.80)	2.09 (1.79,2.44)	2.12 (1.75,2.57)
> 20 – 39 years	1.73 (1.31,2.28)	1.85 (1.40,2.45)	1.86 (1.38,2.51)	1.99 (1.48,2.67)	1.26 (0.58,2.73)	1.98 (1.21,3.24)
1 – 39 years	2.31 (2.25,2.38)	2.31 (2.05,2.62)	2.14 (2.08,2.21)	2.15 (1.90,2.43)	2.86 (2.72,3.01)	2.86 (2.51,3.26)

1. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.
2. Semi-Bayes shrinkage narrows the distribution of observed (conventional) hazard ratios and improves their precision by applying a shrinkage estimator derived from regression methods. Imprecisely measured estimates that are substantially above or below the null value (HR=1.00), are attenuated.

eTable 7. Adjusted HR for depression and dementia within alternative age strata

	Depressive Disorders			Comparison Cohort			HR (95% CI) [2]	p-value
	Events	No. at Risk	Risk (95% CI) [1]	Events	No. at Risk	Risk (95% CI) [1]		
18 – 29 Years								
1 – 10 years	16	47,079	0.05 (0.03,0.08)	14	230,903	0.01 (0.01,0.02)	5.21 (2.05,13.2)	<0.001
> 10 – 20 years	8	20,051	0.07 (0.03,0.14)	12	96,023	0.02 (0.01,0.04)	3.57 (0.93,13.7)	0.06
> 20 – 39 years	10	3,546	1.73 (0.87,3.10)	15	17,925	0.56 (0.29,0.99)	4.52 (1.31,15.6)	0.02
1 – 39 years	34	47,079	1.75 (0.93,3.03)	41	230,903	0.58 (0.31,1.00)	4.85 (2.73,8.60)	<0.001
30 – 39 Years								
1 – 10 years	82	41,161	0.25 (0.20,0.31)	49	203,965	0.03 (0.02,0.04)	5.41 (3.44,8.51)	<0.001
> 10 – 20 years	70	20,980	0.60 (0.47,0.77)	90	106,139	0.16 (0.12,0.19)	3.02 (2.04,4.46)	<0.001
> 20 – 29 years	47	4,928	4.52 (3.13,6.27)	120	27,365	2.49 (1.94,3.14)	2.19 (1.44,3.35)	<0.001
1 – 29 years	199	41,161	4.77 (3.53,6.28)	259	203,965	2.58 (2.05,3.21)	3.10 (2.45,3.90)	<0.001
40 – 49 Years								
1 – 10 years	258	42,074	0.78 (0.69,0.88)	239	208,861	0.16 (0.14,0.18)	4.20 (3.40,5.18)	<0.001
> 10 – 20 years	187	20,664	1.58 (1.36,1.83)	296	110,188	0.48 (0.42,0.54)	2.95 (2.35,3.71)	<0.001
> 20 – 39 years	141	5,273	12.2 (9.18,15.7)	508	32,715	8.55 (7.47,9.72)	2.12 (1.64,2.74)	<0.001
1 – 39 years	586	42,074	11.2 (8.94,13.8)	1,043	208,861	8.31 (7.34,9.36)	3.02 (2.65,3.44)	<0.001
50 – 59 Years								
1 – 10 years	750	36,660	2.56 (2.38,2.75)	634	181,059	0.46 (0.43,0.50)	4.87 (4.30,5.52)	<0.001
> 10 – 20 years	554	16,656	5.52 (5.06,6.01)	1,257	96,060	2.25 (2.13,2.39)	2.27 (2.01,2.58)	<0.001
> 20 – 39 years	221	3,748	17.3 (14.8,20.0)	1,290	26,834	17.3 (16.1,18.5)	1.61 (1.32,1.97)	<0.001
1 – 39 years	1,525	36,660	16.3 (14.8,17.7)	3,181	181,059	15.8 (14.9,16.7)	2.92 (2.70,3.16)	<0.001
60+ Years								
1 – 10 years	9,668	79,525	14.0 (13.7,14.2)	22,484	365,514	7.54 (7.45,7.64)	2.46 (2.39,2.53)	<0.001
> 10 – 20 years	1,818	16,945	14.6 (14.0,15.3)	10,042	125,934	11.4 (11.2,11.6)	1.65 (1.53,1.77)	<0.001
> 20 – 39 years	170	1,711	16.4 (14.0,18.9)	1,602	18,731	15.5 (14.7,16.3)	1.73 (1.31,2.28)	<0.001
1 – 39 years	11,656	79,525	20.1 (19.8,20.5)	34,128	365,514	17.3 (17.1,17.5)	2.31 (2.25,2.38)	<0.001

Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.

We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 8. Adjusted HR for depression and dementia for inpatient and outpatient depression diagnoses

	Depressive Disorders			Comparison Cohort			HR (95% CI) [2]	p-value
	Events	No. at Risk	Risk (95% CI) [1]	Events	No. at Risk	Risk (95% CI) [1]		
Inpatient								
1 – 10 years	5,797	113,629	5.82 (5.67,5.97)	13,776	546,296	3.02 (2.97,3.07)	2.34 (2.25,2.43)	<0.001
> 10 – 20 years	1,704	46,843	5.28 (5.03,5.54)	7,736	278,952	4.07 (3.98,4.16)	1.95 (1.81,2.10)	<0.001
> 20 – 39 years	503	11,717	9.81 (8.73,11.0)	3,165	81,080	9.23 (8.81,9.65)	1.77 (1.54,2.03)	<0.001
1 – 39 years	8,004	113,629	13.3 (12.8,13.8)	24,677	546,296	11.9 (11.6,12.1)	2.22 (2.15,2.29)	<0.001
Outpatient								
1 – 10 years	4,977	132,870	4.81 (4.68,4.94)	9,644	644,006	2.11 (2.06–2.15)	2.91 (2.80,3.03)	<0.001
> 10 – 20 years	933	48,453	3.66 (3.41,3.93)	3,961	255,392	2.82 (2.72–2.91)	1.77 (1.61,1.95)	<0.001
> 20 – 39 years	86	7,489	11.1 (4.39,21.5)	370	42,490	13.6 (2.11–35.6)	1.98 (1.38,2.84)	<0.001
1 – 39 years	5,996	132,870	14.7 (9.76,20.5)	13,975	644,006	14.4 (4.6–29.6)	2.68 (2.58,2.78)	<0.001

1. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.

2. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 9. Adjusted HR for depression and dementia by year at depression diagnosis

	Depressive Disorders			Comparison Cohort			HR (95% CI) [2]	p-value
	Events	No. at Risk	Risk (95% CI) [1]	Events	No. at Risk	Risk (95% CI) [1]		
1980–1989	1,193	12,213	10.4 (9.79,11.0)	5,240	60,096	10.1 (9.76,10.4)	2.10 (1.92,2.29)	<0.001
1990–1999	4,673	42,372	13.0 (12.3,13.8)	13,972	204,132	8.97 (8.67,9.27)	2.38 (2.28,2.49)	<0.001
2000 –2009	6,110	97,751	7.21 (7.01,7.42)	15,810	471,066	4.58 (4.45,4.70)	2.37 (2.28,2.45)	<0.001
2010–2018	2,024	94,163	3.23 (3.07,3.40)	3,630	455,008	1.42 (1.36,1.48)	2.79 (2.62,2.97)	<0.001

4. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.

5. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 10. Adjusted HR for depression and dementia by dementia subtypes

	Depressive Disorders			Comparison Cohort			HR (95% CI) [2]	p-value
	Events	No. at Risk	Risk (95% CI) [1]	Events	No. at Risk	Risk (95% CI) [1]		
Alzheimer's								
1 – 10 years	2,745	246,499	1.36 (1.31,1.41)	8,825	1,190,302	0.97 (0.95,0.99)	1.90 (1.81,1.99)	<0.001
> 10 – 20 years	669	95,296	1.18 (1.09,1.28)	4,720	534,344	1.45 (1.41,1.49)	1.27 (1.14,1.40)	<0.001
> 20 – 39 years	163	19,206	3.16 (2.41,4.07)	1,457	123,570	3.99 (3.72,4.27)	1.33 (1.06,1.66)	0.01
1 – 39 years	3,577	246,499	3.86 (3.43,4.32)	15,002	1,190,302	4.84 (4.65,5.03)	1.73 (1.65,1.80)	<0.001
Vascular								
1 – 10 years	1,809	246,499	0.89 (0.85,0.93)	2,764	1,190,302	0.30 (0.29,0.31)	3.54 (3.29,3.81)	<0.001
> 10 – 20 years	402	95,296	0.69 (0.62,0.77)	1,253	534,344	0.38 (0.36,0.40)	2.61 (2.21,3.07)	<0.001
> 20 – 39 years	84	19,206	1.19 (0.91,1.55)	398	123,570	1.09 (0.91,1.29)	1.77 (1.24,2.51)	0.002
1 – 39 years	2,295	246,499	2.01 (1.84,2.20)	4,415	1,190,302	1.35 (1.23,1.48)	3.28 (3.07,3.50)	<0.001
Other dementia								
1 – 10 years	6,220	246,499	3.10 (2.03,3.18)	11,831	1,190,302	1.30 (1.27,1.32)	2.87 (2.76,2.98)	<0.001
> 10 – 20 years	1,566	95,296	2.70 (2.56,2.85)	5,724	534,344	1.74 (1.69,1.79)	2.23 (2.05,2.42)	<0.001
> 20 – 39 years	342	19,206	5.61 (4.88,6.40)	1,680	123,570	4.14 (3.86,4.42)	2.19 (1.83,2.61)	<0.001
1 – 39 years	8,128	246,499	7.96 (7.55,8.38)	19,235	1,190,302	5.51 (5.32,5.71)	2.72 (2.63,2.81)	<0.001

Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.

We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 11. Adjusted HR for depression and dementia restricted to those age >45 at baseline

	Depression Diagnosis Risk (95% CI)	**Comparison Cohort** Risk (95% CI)	**HR (95% CI)**	p-value
1 – 10 years	9.10 (8.94,9.27)	4.48 (4.42,4.54)	2.56 (2.49,2.64)	<0.001
> 10 – 20 years	8.50 (8.16,8.84)	6.23 (6.12,6.35)	1.83 (1.72,1.94)	<0.001
> 20 – 39 years	16.6 (14.6,18.8)	15.3 (14.6,16.1)	1.70 (1.48,1.96)	<0.001
1 – 39 years	18.3 (17.6,18.9)	16.0 (15.7,16.4)	2.39 (2.33,2.45)	<0.001

1. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.
2. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder.

eTable 12. Adjusted HR for depression and dementia including the first year of follow-up

	Depression Diagnosis Risk (95% CI)	**Comparison Cohort** Risk (95% CI)	**HR (95% CI)**	p-value
0 – 10 years	6.68 (6.58,6.78)	3.31 (3.28,3.35)	3.28 (3.21,3.36)	<0.001
> 10 – 20 years	9.62 (9.47,9.77)	6.35 (6.29,6.42)	3.04 (2.97,3.10)	<0.001
> 20 – 39 years	9.82 (8.74,11.0)	9.20 (8.80,9.62)	1.80 (1.58,2.04)	<0.001
0 – 39 years	14.2 (13.6,14.7)	11.9 (11.7,12.2)	2.99 (2.93,3.05)	<0.001

1. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.
2. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder

eTable 12. Adjusted HR for depression and dementia without censoring of comparison cohort members

	Depression Diagnosis Risk (95% CI)	**Comparison Cohort** Risk (95% CI)	**HR (95% CI)**	p-value
1 – 10 years	5.33 (5.23,5.43)	2.69 (2.65,2.72)	2.46 (2.40,2.53)	<0.001
> 10 – 20 years	4.55 (4.37,4.74)	3.78 (3.71,3.85)	1.75 (1.65,1.85)	<0.001
> 20 – 39 years	9.82 (8.74,11.0)	9.42 (9.03,9.83)	1.69 (1.49,1.91)	<0.001
1 – 39 years	13.6 (13.0,14.2)	11.9 (11.6,12.2)	2.28 (2.22,2.33)	<0.001

1. Risk was calculated separately for individuals with depression and members of the comparison cohort using cumulative incidence functions that treated death as a competing risk.
2. We used stratified Cox proportional hazards regression models to compute hazard ratios (HR) for the association between depression and dementia. Variables were chosen for adjustment based on current knowledge regarding common causes of depression and dementia, and restricted to those measured before depression diagnosis, including education, income, CVD, COPD, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder