

Online supplement

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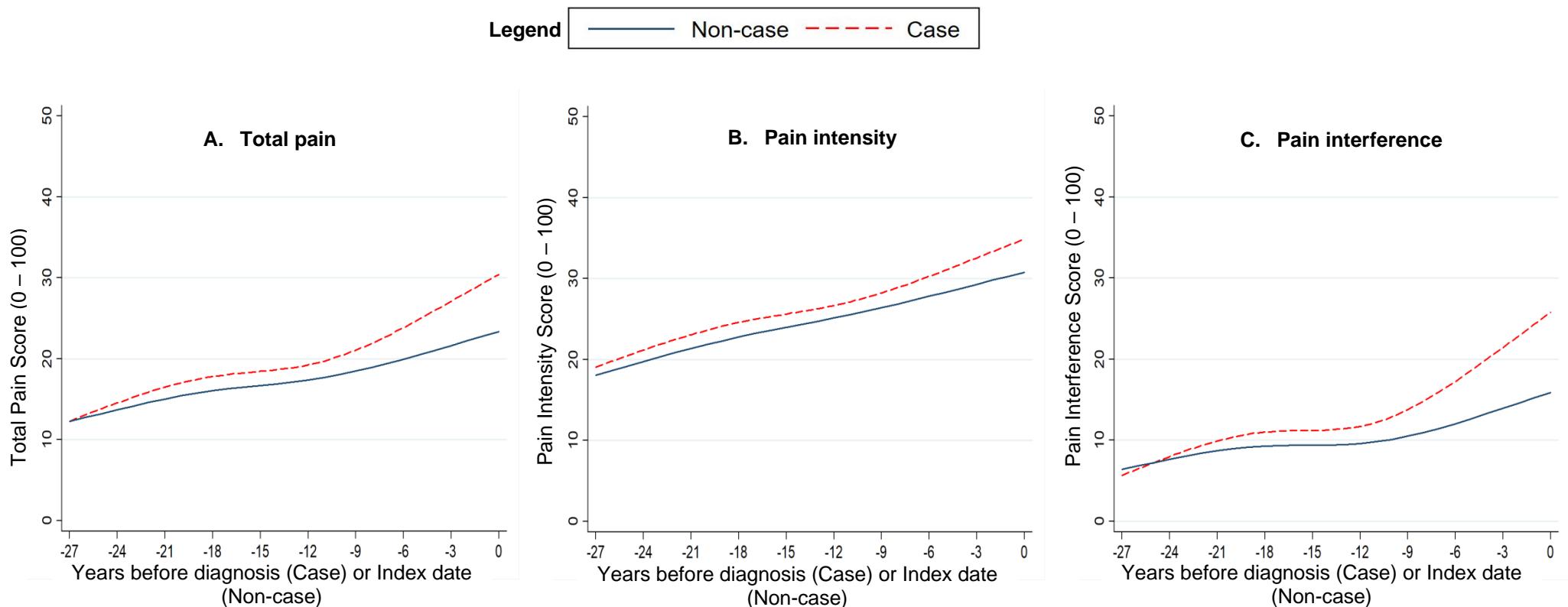
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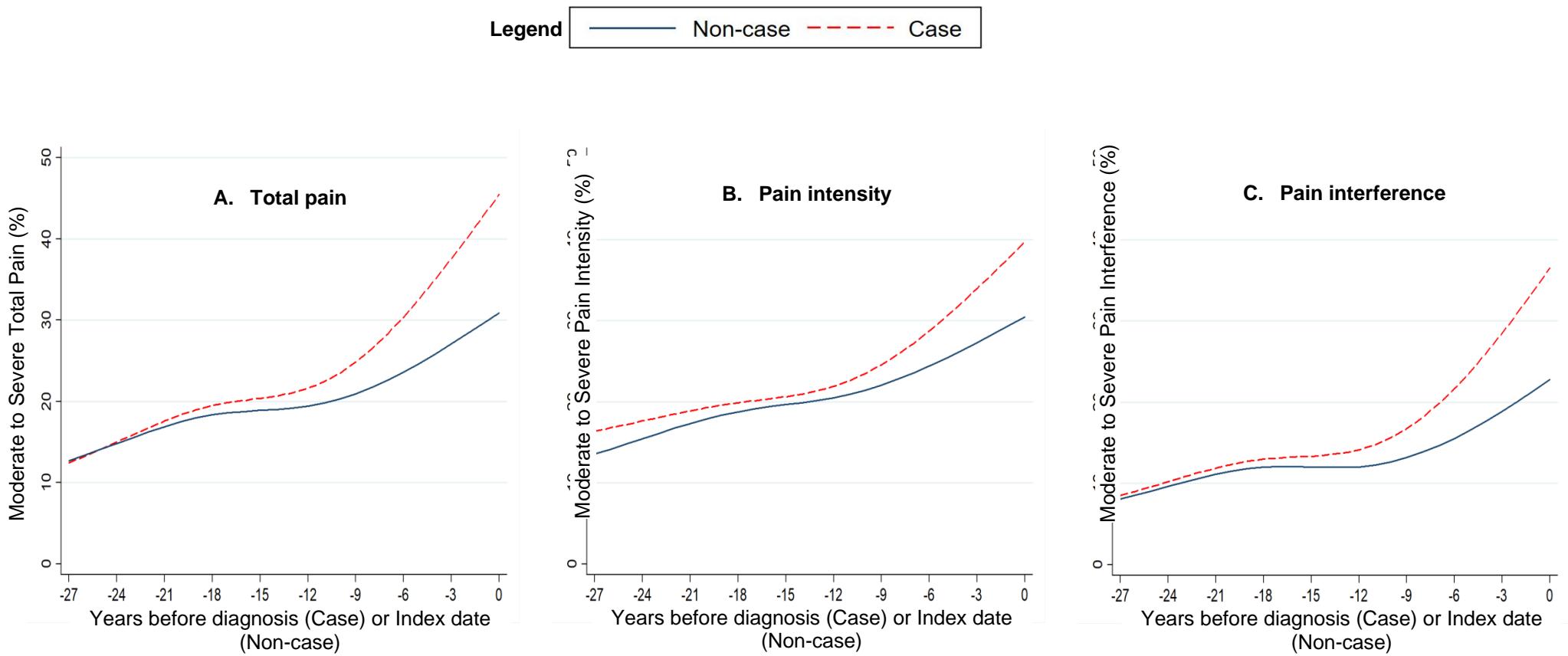
Figure S1. Twenty-seven year trajectories of pain before dementia diagnosis: exploratory analyses using cubic splines regression.



Estimated from linear mixed models adjusted for age at Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), interaction of these covariates with slope terms and birth cohort.

Higher scores correspond to higher pain.

Figure S2. Twenty-seven year trajectories of moderate to severe pain before dementia diagnosis: exploratory analyses using cubic splines regression.



Estimated from logistic mixed models adjusted for Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), interaction of these covariates with slope terms and birth cohort.

Figure S3. Flow chart describing the selection of population.

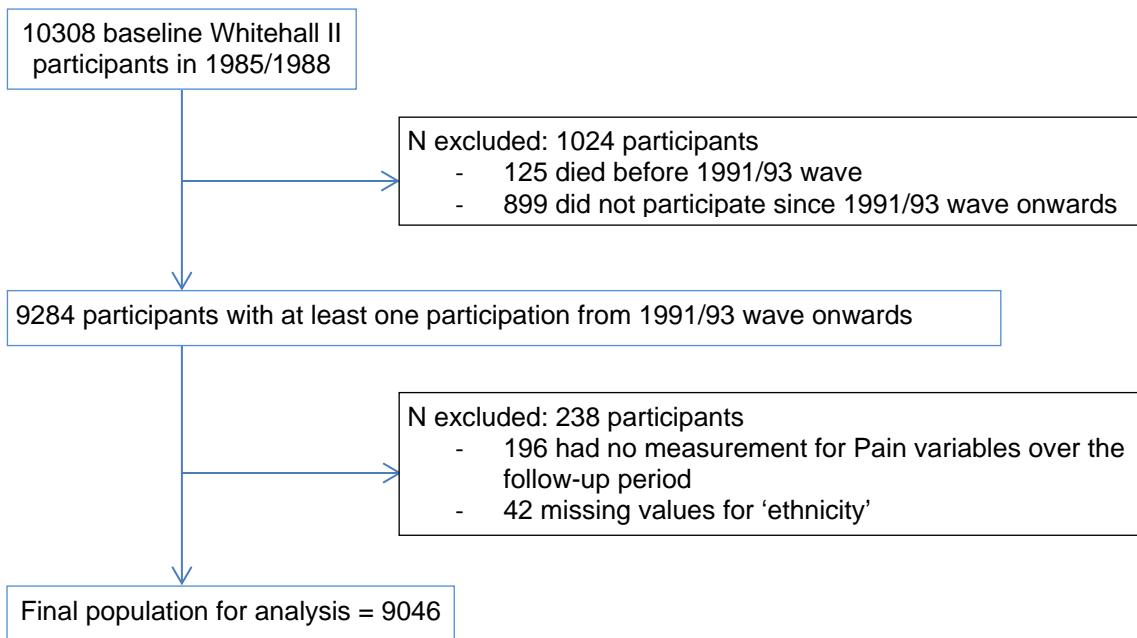
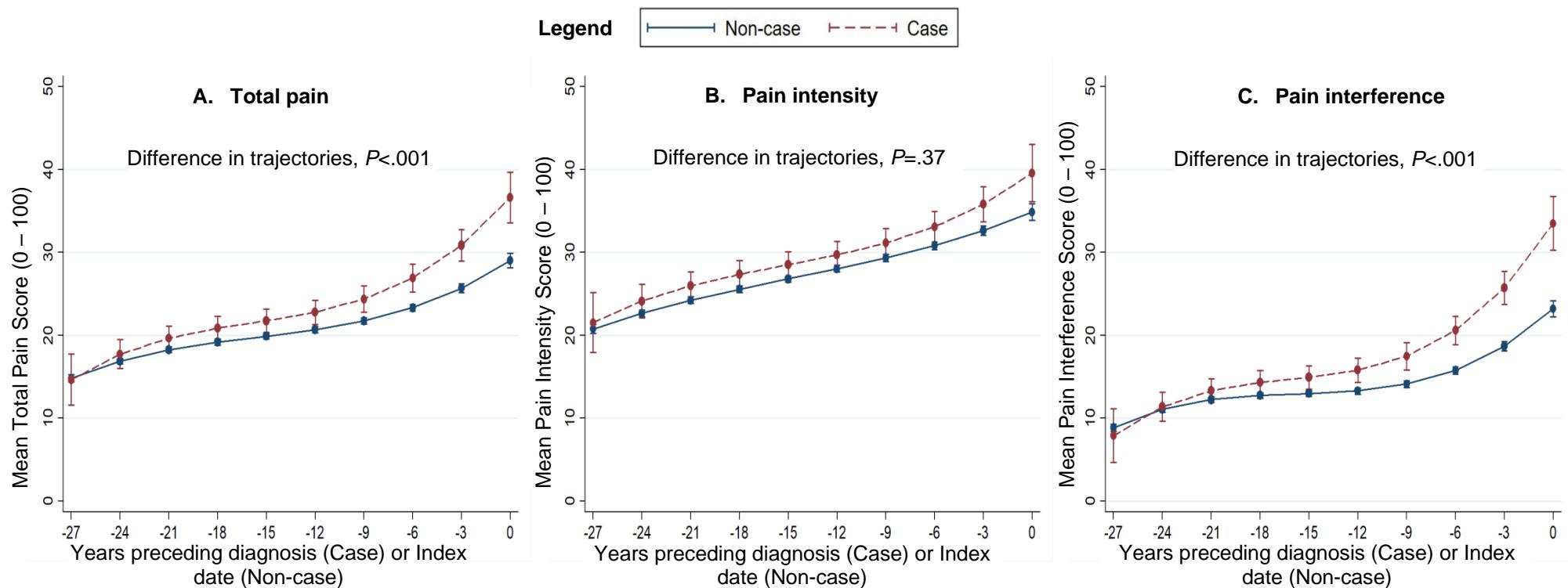


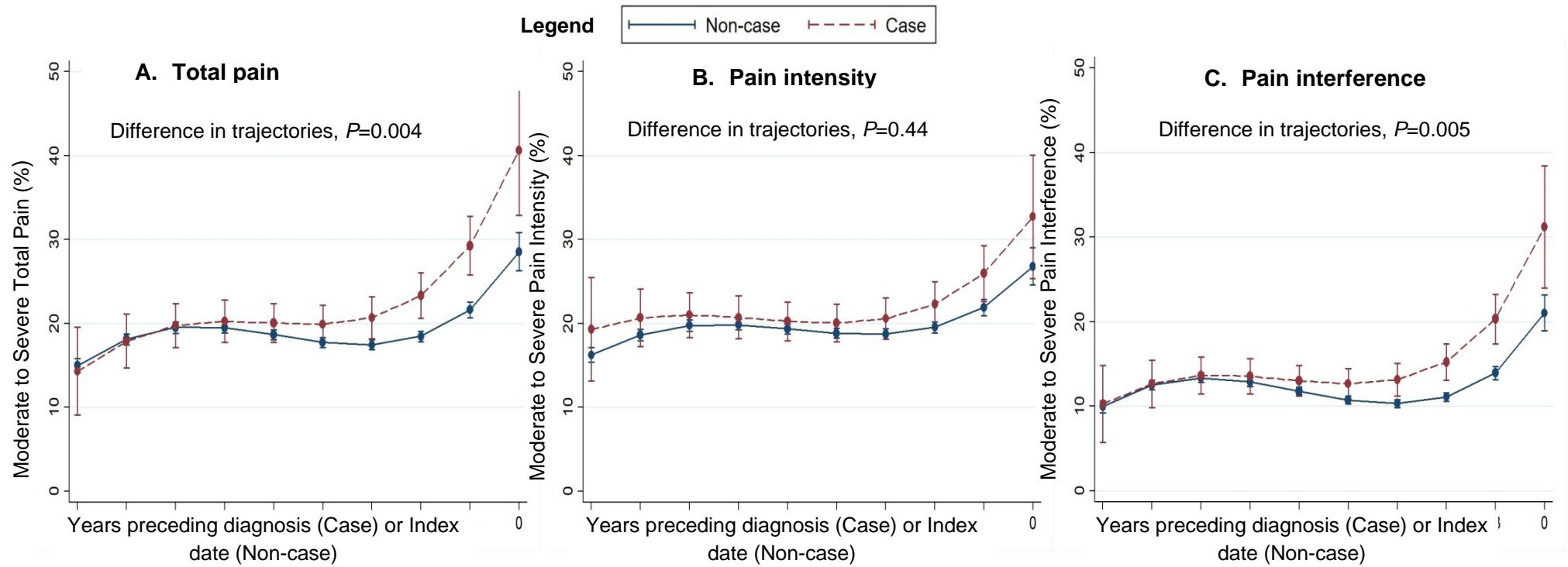
Figure S4. Twenty-seven year trajectories of pain, using continuous measures, before dementia diagnosis (Model 1).



Years	Number of observations in the analysis from year -27 to year 0										
	-27 to -24	-24 to -18	-18 to -12	-12 to -6	-6 to 0	-27 to -24	-24 to -18	-18 to -12	-12 to -6	-6 to 0	
	Case N = 567	168	715	904	882	604	168	715	904	882	604
Non-case N = 8479	3947	17594	13599	12713	7669	3947	17594	13599	12713	7669	3947

Estimated from linear mixed models adjusted for age at Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), interaction of these covariates with slope terms and birth cohort (Model 1). Estimates came from Margins command in STATA. See corresponding difference in pain scores for each year of the 27 years of follow-up in Table S2. Higher scores correspond to higher pain.

Figure S5. Twenty-seven year trajectories of moderate to severe pain before dementia diagnosis.



Number of observations in the analysis from year -27 to year 0												
Years	-27	-24	-18	-12	-6	-27	-24	-18	-12	-6	-27	-24
	to	to	to	to	to	to	to	to	to	to	to	to
Case	-24	-18	-12	-6	0	-24	-18	-12	-6	0	-24	-18
	N Pain	29	149	221	237	220	35	159	218	230	198	20
N Total	168	715	904	882	604	168	715	904	882	604	168	715
	Case											
Non-case	-27	-24	-18	-12	-6	-27	-24	-18	-12	-6	-27	-24
	N Pain	459	2823	2478	2528	1939	550	2823	2639	2658	1973	277
N Total	3947	17594	13599	12713	7669	3947	17594	13599	12713	7669	3947	17594
	Non-case											

Estimated from logistic mixed models adjusted for age at Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), interaction of these covariates with slope terms, birth cohort, pain medication use, multi-morbidity index, and depression assessed at the time of pain measurement. Estimates came from Margins command in STATA.

Table S1. ICD 10 codes used for dementia diagnosis.

ICD 10 codes	Disease
F00	Dementia in Alzheimer disease
F01	Vascular dementia
F02	Dementia in other diseases classified elsewhere
F03	Unspecified dementia
F05.1	Delirium superimposed on dementia
G30	Alzheimer disease
G31.0	Frontotemporal dementia
G31.1	Senile degeneration of brain, not elsewhere classified
G31.8	Other specified degenerative diseases of nervous system (Alpers disease, Lewy body dementia, Leigh's disease)

Table S2. Comparison of characteristics in 1985/88 of participants included and excluded from the analysis.

Variables	Participants included N=9046		Participants excluded N=1262		<i>P</i> value
	Mean	SD	Mean	SD	
Age at inclusion, y	44.8	6.0	45.7	6.2	<0.001
	N	%	N	%	
Women, N (%)	2840	31.4	573	45.4	<0.001
Caucasian ^a , N (%)	8203	90.7	978	77.5	<0.001
University education, N (%)	2448	27.1	216	17.1	<0.001
Married/cohabiting ^b , N (%)	6788	75.0	847	67.1	<0.001
Depression, N (%)	109	1.2	13	1.0	0.59
Dementia, N (%)	567	6.3	89	7.1	0.29

Abbreviations: SD, Standard Deviation.

^a 92 missing values for ethnicity

^b 4 missing values for marital status

Table S3. Differences in pain score between dementia cases and non-cases in the years preceding dementia diagnosis (Model 1).

Years before index date	Total pain			Pain intensity			Pain interference		
	Diff	95% CI	P value	Diff	95% CI	P value	Diff	95% CI	P value
-27	-0.2	-3.3, 3.0	0.92	0.8	-2.9, 4.4	0.68	-1.0	-4.2, 2.3	0.56
-26	0.2	-2.3, 2.8	0.85	1.1	-1.9, 4.0	0.48	-0.5	-3.1, 2.1	0.72
-25	0.6	-1.5, 2.7	0.58	1.3	-1.1, 3.7	0.30	0.0	-2.2, 2.1	0.97
-24	0.9	-0.9, 2.6	0.35	1.5	-0.6, 3.6	0.17	0.3	-1.5, 2.1	0.73
-23	1.1	-0.5, 2.7	0.19	1.6	-0.3, 3.5	0.09	0.6	-1.0, 2.2	0.45
-22	1.3	-0.3, 2.8	0.11	1.7	-0.1, 3.5	0.06	0.9	-0.6, 2.4	0.26
-21	1.4	-0.1, 2.9	0.07	1.8	0.0, 3.5	0.05	1.1	-0.4, 2.6	0.15
-20	1.5	0.0, 3.0	0.05	1.8	0.1, 3.5	0.04	1.3	-0.2, 2.8	0.10
-19	1.6	0.1, 3.1	0.04	1.8	0.1, 3.5	0.04	1.4	-0.1, 2.9	0.06
-18	1.7	0.2, 3.2	0.03	1.8	0.1, 3.5	0.04	1.6	0.1, 3.0	0.04
-17	1.7	0.3, 3.2	0.02	1.8	0.1, 3.5	0.04	1.7	0.2, 3.2	0.02
-16	1.8	0.3, 3.3	0.02	1.8	0.1, 3.4	0.04	1.8	0.4, 3.3	0.01
-15	1.9	0.4, 3.3	0.01	1.7	0.1, 3.4	0.04	2.0	0.5, 3.4	0.008
-14	1.9	0.5, 3.4	0.01	1.7	0.1, 3.3	0.04	2.1	0.7, 3.6	0.005
-13	2.0	0.5, 3.5	0.008	1.7	0.0, 3.3	0.05	2.3	0.8, 3.8	0.002
-12	2.1	0.6, 3.6	0.006	1.7	0.0, 3.4	0.05	2.5	1.0, 4.0	0.001
-11	2.2	0.7, 3.8	0.005	1.7	0.0, 3.4	0.05	2.7	1.2, 4.3	0.001
-10	2.4	0.8, 4.0	0.003	1.7	0.0, 3.5	0.05	3.0	1.4, 4.7	<0.001
-9	2.6	1.0, 4.3	0.002	1.8	0.0, 3.6	0.05	3.4	1.7, 5.1	<0.001
-8	2.9	1.2, 4.6	0.001	1.9	0.1, 3.8	0.04	3.8	2.1, 5.5	<0.001
-7	3.2	1.5, 4.9	<0.001	2.1	0.2, 4.0	0.03	4.3	2.5, 6.0	<0.001
-6	3.6	1.9, 5.3	<0.001	2.3	0.4, 4.2	0.02	4.8	3.1, 6.6	<0.001
-5	4.1	2.3, 5.8	<0.001	2.5	0.6, 4.5	0.01	5.5	3.7, 7.3	<0.001
-4	4.6	2.7, 6.4	<0.001	2.8	0.8, 4.8	0.006	6.2	4.3, 8.1	<0.001
-3	5.2	3.2, 7.2	<0.001	3.2	1.0, 5.4	0.004	7.1	5.0, 9.1	<0.001
-2	5.9	3.7, 8.2	<0.001	3.6	1.1, 6.1	0.004	8.0	5.7, 10.4	<0.001
-1	6.7	4.1, 9.3	<0.001	4.1	1.2, 7.1	0.006	9.1	6.3, 11.9	<0.001
0	7.6	4.4, 10.8	<0.001	4.7	1.1, 8.3	0.01	10.3	6.9, 13.7	<0.001
Difference in trajectories		<i>P</i> <0.001			<i>P</i> =0.37			<i>P</i> <0.001	

Estimated from linear mixed models adjusted for age at Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), and interaction of these covariates with slope terms, and birth cohort.

Table S4. Differences in the probability (%) of moderate to severe pain between dementia cases and non-cases in the years preceding diagnosis.

Years before index date	Total pain			Pain intensity			Pain interference		
	Diff	95% CI	P value	Diff	95% CI	P value	Diff	95% CI	P value
-27	-0.7	-6.0, 4.6	0.80	3.1	-3.1, 9.3	0.33	0.3	-4.3, 4.9	0.89
-26	-0.6	-5.0, 3.9	0.81	2.7	-2.3, 7.7	0.29	0.2	-3.7, 4.2	0.90
-25	-0.4	-4.2, 3.4	0.83	2.4	-1.8, 6.5	0.26	0.2	-3.1, 3.5	0.91
-24	-0.3	-3.5, 3.0	0.88	2.0	-1.4, 5.5	0.25	0.2	-2.7, 3.0	0.91
-23	-0.1	-3.0, 2.8	0.95	1.7	-1.3, 4.8	0.27	0.2	-2.3, 2.7	0.89
-22	0.1	-2.7, 2.8	0.96	1.5	-1.4, 4.3	0.31	0.2	-2.1, 2.5	0.86
-21	0.2	-2.4, 2.9	0.86	1.3	-1.5, 4.0	0.37	0.3	-2.0, 2.5	0.81
-20	0.4	-2.2, 3.1	0.76	1.1	-1.6, 3.8	0.43	0.4	-1.8, 2.6	0.73
-19	0.6	-2.0, 3.2	0.66	1.0	-1.7, 3.7	0.48	0.5	-1.7, 2.7	0.64
-18	0.8	-1.8, 3.4	0.55	0.9	-1.7, 3.5	0.51	0.7	-1.5, 2.8	0.54
-17	1.0	-1.6, 3.5	0.45	0.8	-1.7, 3.4	0.52	0.8	-1.2, 2.9	0.42
-16	1.2	-1.3, 3.6	0.34	0.8	-1.6, 3.3	0.50	1.0	-0.9, 3.0	0.30
-15	1.4	-1.0, 3.8	0.25	0.9	-1.5, 3.3	0.46	1.2	-0.6, 3.1	0.20
-14	1.6	-0.7, 4.0	0.17	1.0	-1.4, 3.3	0.42	1.5	-0.4, 3.3	0.12
-13	1.9	-0.4, 4.2	0.11	1.1	-1.2, 3.4	0.36	1.7	-0.1, 3.5	0.06
-12	2.2	-0.2, 4.5	0.07	1.2	-1.1, 3.6	0.31	1.9	0.1, 3.7	0.03
-11	2.5	0.1, 4.8	0.04	1.4	-1.0, 3.8	0.25	2.2	0.4, 4.0	0.02
-10	2.8	0.4, 5.3	0.02	1.6	-0.9, 4.1	0.20	2.5	0.6, 4.4	0.01
-9	3.2	0.7, 5.8	0.01	1.8	-0.7, 4.4	0.16	2.8	0.9, 4.8	0.005
-8	3.7	1.1, 6.3	0.006	2.1	-0.5, 4.7	0.12	3.2	1.2, 5.3	0.002
-7	4.2	1.5, 6.9	0.002	2.4	-0.3, 5.1	0.08	3.6	1.5, 5.8	0.001
-6	4.9	2.1, 7.6	0.001	2.7	0.0, 5.5	0.05	4.2	1.9, 6.4	<0.001
-5	5.6	2.8, 8.5	<0.001	3.1	0.3, 5.9	0.03	4.8	2.4, 7.1	<0.001
-4	6.5	3.4, 9.6	<0.001	3.6	0.6, 6.6	0.02	5.5	3.0, 8.0	<0.001
-3	7.6	4.1, 11.2	<0.001	4.1	0.6, 7.5	0.02	6.4	3.4, 9.3	<0.001
-2	8.9	4.4, 13.4	<0.001	4.6	0.3, 8.9	0.04	7.4	3.6, 11.3	<0.001
-1	10.4	4.5, 16.3	0.001	5.2	-0.4, 10.9	0.07	8.7	3.4, 14.0	0.001
0	12.1	4.1, 20.1	0.003	5.9	-1.7, 13.5	0.13	10.2	2.7, 17.6	0.008
Difference in trajectories	P=0.004			P=0.44			P=0.005		

Estimated from logistic mixed models adjusted for age at Year 0, sex, education, ethnicity, marital status, dementia status, slope terms (time, time², and time³), interaction of these covariates with slope terms, birth cohort, pain medication use, multi-morbidity index, and depression assessed at the time of pain measurement.