

Data supplement

Table DS1 Quality assessment of case-control studies using the Newcastle-Ottawa scale^a

Case-control studies	Selection					Exposure		
	Case definition	Representativeness	Controls selection	Definition of controls	Comparability	Ascertainment	Equality of methods	Non-response rate
French <i>et al</i> (1985) ¹⁵	-	*	-	-	**	*	*	*
Agbayewa (1986) ¹⁶	*	*	-	-	**	-	*	*
Shalat <i>et al</i> (1987) ¹⁷	-	-	*	-	**	-	*	*
Broe <i>et al</i> (1990) ¹⁸	*	*	-	*	**	*	*	*
Kokmen <i>et al</i> (1991) ¹⁹	*	*	*	-	**	-	*	*
Speck <i>et al</i> (1995) ²⁰	-	*	*	*	**	*	*	*
Steffens <i>et al</i> (1997) ²⁴	*	-	*	*	**	*	*	*
Tsolaki <i>et al</i> (1997) ²⁵	*	-	*	*	-	-	*	*
Cooper & Holmes (1998) ²⁶	*	*	*	-	**	*	*	*
Wetherell <i>et al</i> (1999) ²⁸	*	*	*	*	**	*	*	*
Hébert <i>et al</i> (2000) ³³	*	*	*	*	**	-	*	*
Zalsman <i>et al</i> (2000) ³²	-	*	-	-	-	-	-	*
Green <i>et al</i> (2003) ³⁷	*	*	*	*	**	-	-	*
Zubenko <i>et al</i> (2003) ³⁶	*	-	-	*	-	*	*	*
Brommelhoff <i>et al</i> (2009) ³⁸	*	*	*	-	**	*	*	*

a. Each study is evaluated from three general perspectives: (a) the selection of the study groups; (b) the comparability of the groups; (c) ascertainment of both exposure and outcome of interest. A star '*' is given if the study fulfills criteria that reflect greater methodological quality and '-' indicates that the study did not achieve the quality threshold for that specific feature. Thus, a higher number of stars indicates better study quality. Only comparability can be scored with two stars (one if age was controlled and another if any other relevant variable was controlled for). Comparability was scored not according to the main results of the studies but according to the data that were extracted from them (for example if a crude odds ratio had to be calculated from the results presented in the article, then no stars were allocated in 'comparability' even if the main results of the study were well controlled for confounding variables).

Table D52 Quality assessment of cohort studies using the Newcastle–Ottawa scale^a

Cohort studies	Selection				Outcome			
	Representativeness (exposed cohort)	Selection (non-exposed cohort)	Ascertainment of exposure	Outcome of interest not present at baseline	Comparability	Assessment	Follow-up length	Adequacy of follow-up
Minami <i>et al.</i> (1995) ²¹	–	*	–	*	**	–	*	–
Buntinx <i>et al.</i> (1996) ²²	*	*	*	*	**	*	*	–
Devanand <i>et al.</i> (1996) ²³	*	*	*	*	**	*	–	*
Chen <i>et al.</i> (1999) ²⁹	*	*	*	*	**	*	*	*
Kessing <i>et al.</i> (1999) ²⁷	*	*	*	*	**	*	*	*
Pálsson <i>et al.</i> (1999) ³⁰	*	*	*	*	**	*	*	*
Geerlings <i>et al.</i> (2000) ³¹	*	*	*	*	**	*	*	*
Lindsay <i>et al.</i> (2002) ³⁴	*	*	–	*	**	*	*	*
Wilson <i>et al.</i> (2002) ³⁵	–	*	*	*	**	*	*	–
Fuhrer <i>et al.</i> (2003) ³⁹	*	*	*	–	**	*	*	–
Kessing & Nilssen (2003) ³⁸	*	*	*	*	**	*	*	*
Kessing & Andersen (2004) ⁴¹	*	*	*	*	**	*	*	*
Steffens <i>et al.</i> (2004) ⁴⁰	–	*	*	*	**	*	–	–
Andersen <i>et al.</i> (2005) ⁴³	*	*	–	*	**	–	*	*
Dal Forno <i>et al.</i> (2005) ⁴²	–	*	*	–	**	–	*	–
Gatz <i>et al.</i> (2005) ⁴⁴	–	*	*	*	**	*	*	*
Baldwin <i>et al.</i> (2006) ⁴⁶	–	*	*	–	–	–	*	*
Kim <i>et al.</i> (2006) ⁴⁵	*	*	*	*	–	*	*	*
Shadlen <i>et al.</i> (2006) ⁴⁷	*	*	*	*	–	–	*	*
Simons <i>et al.</i> (2006) ⁴⁸	*	*	–	*	**	*	*	–
Chen, <i>et al.</i> (2008) ⁵¹ – China	*	*	*	*	**	–	–	–
Chen, <i>et al.</i> (2008) ⁵¹ – UK	*	*	*	*	**	–	*	–
Fischer <i>et al.</i> (2008) ⁵²	*	*	*	*	*–	*	–	–
Geerlings <i>et al.</i> (2008) ⁵⁴	*	*	*	*	**	*	*	–
Irie <i>et al.</i> (2008) ⁵⁰	*	*	*	*	**	*	*	–
Luchsinger <i>et al.</i> (2008) ⁵³	–	*	*	*	**	–	*	–
Stepaniuk <i>et al.</i> (2008) ⁴⁹	*	*	*	*	*–	*	*	–
Becker <i>et al.</i> (2009) ⁵⁵	*	*	*	*	**	*	*	*
Jungwirth <i>et al.</i> (2009) ⁵⁷	*	*	*	*	*–	*	*	*
van den Kommer <i>et al.</i> (2009) ⁵⁶	–	*	*	*	**	*	*	*
Doison <i>et al.</i> (2010) ⁵⁹	–	*	*	*	**	*	*	*
Kim <i>et al.</i> (2010) ⁶¹	*	*	*	*	**	*	–	*
Saczynski <i>et al.</i> (2010) ⁶⁰	*	*	*	*	**	*	*	*
Goveas <i>et al.</i> (2011) ⁶⁵	*	*	*	*	**	*	*	*
Byers <i>et al.</i> (2012) ⁶³	*	*	–	*	**	–	*	*
Köhler <i>et al.</i> (2011) ⁶²	*	*	*	*	**	–	*	*
Lenoir <i>et al.</i> (2011) ⁶⁴	*	*	*	*	**	*	*	*

a. Each study is evaluated from three general perspectives: (a) the selection of the study groups; (b) the comparability of the groups; (c) ascertainment of both exposure and outcome of interest. A star '*' is given if the study fulfils criteria that reflect greater methodological quality and '–' indicates that the study did not achieve the quality threshold for that specific feature. Thus, a higher number of stars indicates better study quality. Only comparability can be scored with two stars (one if age was controlled and another if any other relevant variable was controlled for). Comparability was scored not according to the main results of the studies but according to the data that were extracted from them (for example if a crude odds ratio had to be calculated from the results presented in the article, then no stars were allocated in 'comparability' even if the main results of the study were well controlled for confounding variables). Three years of follow-up was the threshold for star attribution in 'Follow-up length'. Besides other criteria, less than 15% of individuals lost to follow-up was considered enough to award a star in 'Adequacy of follow-up'.

Table D53 Characteristics of case-control studies that evaluated depression as a risk factor for late-life dementia

Source, country	Dementia type (diagnostic criteria)	Depression (diagnosis/assessment)	Onset of depression	Sample size (cases/controls)	Comments
French <i>et al</i> (1983) ¹⁵ USA	Alzheimer's disease (criteria described by the authors)	Structured study interview	Not specified	154 (78/76) All males	Matched design (age, gender, race) Patients with 'history of significant psychiatric disorders' excluded
Agbayewa (1986) ¹⁶ Canada	Dementia: DSM-III-R or ICD-9	Clinical diagnosis	Not specified	368 (188/80)	Matched controls
Shalat <i>et al</i> (1987) ¹⁷ USA	Alzheimer's disease (NINCDS-ADRD)	Informant self-administered questionnaire	Not specified	260 (98/162)	Depression onset occurred within 4 years of dementia onset. Depression onset in controls was on average 6 years earlier
Broe <i>et al</i> (1990) ¹⁸ Australia	Alzheimer's disease (NINCDS-ADRD)	Study questionnaire	Early-onset depression and late-onset depression	340 (170/170)	Matched controls. Antidepressant use was not significantly associated with increased risk
Kokmen <i>et al</i> (1991) ¹⁹ USA	Alzheimer's disease (authors' criteria)	Medical records	Not specified	830 (415/415)	Matched case-control study
Speck <i>et al</i> (1995) ²⁰ USA	Alzheimer's disease (NINCDS-ADRD and DSM-III-R)	Study questionnaire	Early-onset depression and late-onset depression	594 (294/300)	Antidepressant use was not significantly associated with increased risk
Steffens <i>et al</i> (1997) ²⁴ USA	Alzheimer's disease (NINCDS-ADRD)	DSM-III-R	Early-onset depression and late-onset depression	142 (81/61)	Twin cohort based case-control study. Results shown are for unmatched analysis Controlled for APOE ε4
Tsolaki <i>et al</i> (1997) ²⁵ Greece	Alzheimer's disease (NINCDS-ADRD and DSM-IV)	DSM-IV	Not specified	134 (65/69)	Increased risk for developing depression followed by dementia if there was a family history of Alzheimer's disease
Cooper & Holmes (1998) ²⁶ UK	Dementia (CAMDEX; dementia with Lewy bodies criteria)	Records review	> 5 years before dementia onset	1118 (559/559)	Matched case-control study
Wetherell <i>et al</i> (1999) ²⁸ Sweden	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRD)	Informant interview, record review; national psychiatric registry	Any time and early-onset depression (> 10 years before dementia)	60 twin pairs	Twin case-control study 90% CI used in risk calculation. Antidepressant use was not significantly associated with increased risk (in matched analysis)
Hébert <i>et al</i> (2000) ³³ Canada	Vascular dementia (NINDS-AIREN)	Study questionnaire, clinical evaluation	Not specified	721 (66/655)	Nested case-control The risk estimate increased in patients with previous strokes
Zalsman <i>et al</i> (2000) ³² Israel	Dementia (DSM-IV)	DSM-IV	Late-onset depression (> 50 years)	502 (36/466)	In-patient study Bipolar depression cases included
Green <i>et al</i> (2003) ³⁷ USA	Alzheimer's disease (NINCDS-ADRD)	Single yes or no question in study questionnaire	Early-onset depression and late-onset depression considered	4046 (1953/2093)	Nested case-control study
Zubenko <i>et al</i> (2003) ³⁶ USA	Alzheimer's disease (NINCDS-ADRD)	DSM-III-R	Not specified	394 (243/151)	
Brommelhoff <i>et al</i> (2009) ⁵⁸ Sweden	Dementia (DSM-IV and CERAD) Alzheimer's disease (NINCDS-ADRD)	Psychiatric and medical registry review, ICD-7-10 criteria	Early-onset depression and late-onset depression considered	12 680 (547/12 133)	Also included a twin case-control analysis

NINCDS-ADRD, Neurological and Communicative Disorders and Stroke - Alzheimer Disease and Related Disorders Association criteria; CAMDEX, Cambridge Mental Disorders of the Elderly Examination; NINDS-AIREN, Neuroepidemiology Branch of the National Institute of Neurological Disorders and Stroke/Association Internationale pour la Recherche et l'Enseignement en Neurosciences; CERAD, Consortium to Establish a Registry for Alzheimer's Disease.

Table DS4 Characteristics of cohort studies that evaluated depression as a risk factor for late-life dementia

Source, country	Dementia type (diagnostic criteria)	Depression diagnosis method	Onset of depression	Sample size ^a	Comments
Minami <i>et al</i> (1995) ²¹ Japan	Dementia (DSM-III-R)	Self-report	Not specified	2461	3 years of follow-up Controlled for age and gender
Buntinx <i>et al</i> (1996) ²² The Netherlands	Dementia (ICHPPC-2)	ICHPPC	Late-life depression	19103	Retrospective cohort Community-based study
Devanand <i>et al</i> (1996) ²³ USA	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA)	Diagnosed if HRSD mood item present	Late-life depression	478	Mean follow-up of 2.54 years Controlled for age, gender, education, cognitive and functional scores
Chen <i>et al</i> (1999) ²⁹ USA	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA)	mCES-D (DSM-III-R oriented)	Late-life depression	803	Mean follow-up of 4 years Controlled for age, gender and education
Pålsson <i>et al</i> (1999) ³⁰ Sweden	Dementia (no reference to diagnostic criteria)	DSM-III-R (major depression, dysthymia and depression NOS)	Early-onset depression and late-onset depression considered	267	3 years of follow-up Community-based Small sample There were no differences in CT measures of brain atrophy between late- and early-onset depression Mean follow-up of 3.2 years
Geerlings <i>et al</i> (2000) ³¹ The Netherlands	Alzheimer's disease (DSM-IV)	GMSS	Late-life depression	1911	
Lindsay <i>et al</i> (2002) ³⁴ Canada	Alzheimer's disease (DSM-IV)	Study questionnaire	Not specified	3316	5 years of follow-up
Wilson <i>et al</i> (2002) ³⁵ USA	Alzheimer's disease (NINCDS-ADRDA)	10-item CES-D	Late-life depression	651	Mean 5.5 years of follow-up Increase of 19% risk for every one-point increase in CES-D
Fuhrer <i>et al</i> (2003) ³⁹ France	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA)	History of depression (study questionnaire) Late-life depression: CES-D; Men ≥ 16 , women ≥ 23	History of depression (onset not specified), late-life depression	2152	62.2% followed up for 8 years Poor definition of history of depression ORs adjusted for education, gender, MMSE score
Kessing & Niissen (2003) ³⁸ Denmark	Dementia (ICD-8)	ICD-8 (296.09; 296.29)	Not specified	93121	In-patient case register cohort compared with control group with osteoarthritis
Steffens <i>et al</i> (2004) ⁴⁰ USA	Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (NINDS-AIREN) Dementia (DSM-IV)	MADRS	Late-life depression	413	Mean time of follow-up was 4.23 years for individuals with depression
Andersen <i>et al</i> (2005) ⁴³ Denmark	Alzheimer's disease (NINCDS-ADRDA)	Self-report; record review when available	Early-onset depression and late-onset depression	1822	5 year follow-up Controlled for age, gender, intellectual level, diabetes, myocardial infarction
Dal Forno <i>et al</i> (2005) ⁴² USA ^b	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA)	CES-D >20	Late-life depression	1357	Mean follow-up of 6.1 years
Gatz <i>et al</i> (2005) ⁴⁴ Canada	Alzheimer's disease and other dementias (DSM-IV)	History of depression: patient self-report Late-life depression: CES-D ≥ 16	History of depression (lifetime) Late-life depression	766	5-year follow-up Controlled for age, gender and education
Baldwin <i>et al</i> (2006) ⁴⁶ UK	Dementia (ICD-10)	DSM-IV	Late-onset depression	62	
Kim <i>et al</i> (2006) ⁴⁵ Korea	Dementia (DSM-IV)	GMSS	Late-life depression	686	Mean follow-up period of 2.4 years. Crude OR calculated based on the results presented

(continued)

Table DS4 Characteristics of cohort studies that evaluated depression as a risk factor for late-life dementia (*continued*)

Source, country	Dementia type (diagnostic criteria)	Depression diagnosis method	Onset of depression	Sample size ^a	Comments
Shadlen <i>et al</i> (2006) ⁴⁷ USA	Dementia (cardiovascular health study/Modified 10-item CES-D ≥ 8 – cognition study diagnostic criteria)	Modified 10-item CES-D ≥ 8	Late-life depression	2786	6 years of follow-up
Simons <i>et al</i> (2006) ⁴⁸ Australia	Dementia (ICD-10-AM or ICD-9-CM)	Study questionnaire	Late-life depression	2805	16 years of follow-up Adjusted for age and gender, marital status, education, history of stroke and activities of daily living
Chen <i>et al</i> (2008) ⁵¹ UK and China	Dementia (GMSS)	GMSS level 3	Late-life depression	2157 (UK) 1254 (China)	4 years' follow-up in the UK and 1 in China
Fischer <i>et al</i> (2008) ⁵² Austria ^c	Alzheimer's disease (NINCDS-ADRDA)	DSM-IV	History of depression (lifetime)	479	30 months of follow-up At baseline patients were > 75 years old
Geerlings <i>et al</i> (2008) ⁵⁴ The Netherlands	Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (NINDS-AIREN)	Clinical history (depression treated by a GP or mental health specialist)	Early-onset depression and late-onset depression	486	Mean follow-up of 6 years Controlled for gender, age, education, cognition and hippocampal and amygdala volume
Irie <i>et al</i> (2008) ⁵⁰ USA (Hawaii)	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (SCADDTQ)	CES-D > 8	Late-life depression	1932 (all men)	Mean follow-up of 6.1 years Controlled for age, education and vascular risk factors
Luchsinger <i>et al</i> (2008) ⁵³ USA	Dementia (DSM-IV) Alzheimer's disease (NINCDS-ADRDA)	HRSD > 9	Late-life depression	526	Mean follow-up of 5 years Controlled for age, gender, education, ethnicity, APOE $\epsilon 4$, and vascular risk factors
Stepaniuk <i>et al</i> (2008) ⁴⁹ Canada	Dementia (DSM-III-R)	CAMDEX (section H)	Late-life depression	169	5 years of follow-up Depression assessed by informant interview
Becker <i>et al</i> (2009) ⁵⁵ USA	Alzheimer's disease (NINCDS-ADRDA)	10-item CES-D	Late-life depression	288	Mean follow-up of 7.1 years High average age of the participants (77 years) might have lead to a survival bias
Jungwirth <i>et al</i> (2009) ⁵⁷ Austria ^c	Alzheimer's disease (NINCDS-ADRDA)	DSM-IV	Not specified	487	60 months of follow-up At baseline patients were > 75 years old
van den Kommer <i>et al</i> (2009) ⁵⁶ Sweden	Dementia (DSM-III-R)	CES-D ≥ 16	Late-life depression	387	8 years of follow-up All participants were aged 80 and older
Dotson <i>et al</i> (2010) ⁵⁹ USA ^b	Dementia (DSM-III-R) Alzheimer's disease (NINCDS-ADRDA)	CES-D ≥ 16	Late-life depression	1113	Long follow-up (23.6 years median time of follow-up)
Kim <i>et al</i> (2010) ⁶¹ Korea	Dementia (DSM-IV) Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (NINDS-AIREN)	KGDS > 13	Late-life depression	518	3 years of follow-up OR adjusted for age, education, disability and physical activity
Saczynski <i>et al</i> (2010) ⁶⁰ USA	Dementia (DSM-IV) Alzheimer's disease (NINCDS-ADRDA)	CES-D ≥ 16	Late-life depression	949	Long follow-up (14 years) Patients aged 79 (s.d. =5) years at baseline Adjusted for gender, education, homocysteine, APO $\epsilon 4$ Risk even higher when controlling for vascular risk factors

(continued)

Table DS4 Characteristics of cohort studies that evaluated depression as a risk factor for late-life dementia (*continued*)

Source, country	Dementia type (diagnostic criteria)	Depression diagnosis method	Onset of depression	Sample size ^a	Comments
Byers <i>et al</i> (2012) ⁶³ USA	Dementia (ICD-9)	ICD-9 (296.2, 296.3, 311, 300.4)	Late-life depression	281 540, 96% men	All veterans Mean follow-up of 7.2 years HR adjusted for demographics, cardiovascular and psychiatric comorbidity
Goveas <i>et al</i> (2011) ⁶⁵ USA	Dementia (DSM-IV)	Burnam screening algorithm	Late-life depression	6376 all women	Mean follow-up of 5.4 years HR adjusted for demographic and lifestyle variables, comorbid vascular disease, hormone therapy assignment, cognition at baseline and antidepressant therapy
Köhler <i>et al</i> (2011) ⁶² The Netherlands	Dementia (DSM-III-R and DSM-IV) Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (NINDS-AIREN)	SCL-90 upper quartile of depression subscale	Late-life depression	771	9-year follow-up OR adjusted for age, gender and education. Although not reported it is described that results were unchanged when controlling for cognitive score at baseline and the presence of vascular disease
Lenoir <i>et al</i> (2011) ⁶⁴ France	Dementia (DSM-III-R and DSM-IV) Alzheimer's disease (NINCDS-ADRDA) Vascular dementia (NINDS-AIREN)	CES-D > 22 for women and > 16 for men	Late-life depression	7989	4-year follow-up HR adjusted for age, gender, baseline cognition and cardiovascular risk factors

ICHPCC-2, International Classification of Health Problems in Primary Care; HRSD, Hamilton Rating Scale for Depression; NINCDS-ADRDA, Neurological and Communicative Disorders and Stroke - Alzheimer Disease and Related Disorders Association criteria; mCES-D, Interviewer administered version of the original Center for Epidemiologic Studies Depression Scale (CES-D); NOS, not otherwise specified; CT, computed tomography; GMSS, Geriatric Mental State Schedule; MMSE, Mini-Mental State Examination; MADRS, Montgomery-Åsberg Depression Rating Scale; NINDS-AIREN, Neuroepidemiology Branch of the National Institute of Neurological Disorders and Stroke/Association Internationale pour la Recherche et l'Enseignement en Neurosciences; GP, general practitioner; SCADDTIC, State of California Alzheimer's Disease Diagnostic and Treatment Centers criteria; CAMDEX, Cambridge Mental Disorders of the Elderly Examination; KGDS, Geriatric Depression Scale (Korean version); OR, odds ratio; HR, hazard ratio;
a. Number of participants evaluated at least once during follow-up.
b. Samples overlap between Dal Forno *et al* and Dotson *et al*.
c. Samples overlap between Fischer *et al* and Jungwirth *et al*.

Table D55 Characteristics of longitudinal studies that evaluated bipolar disorder as a risk factor for late-life dementia				
Source (country)	Dementia type (diagnostic criteria)	Bipolar disorder diagnosis method	Sample size	Comments
Kokmen <i>et al</i> (1991) ¹⁹ USA	Alzheimer's disease (criteria described by the authors)	Medical records	830 (415 cases; 415 controls)	Case and controls matched by age, gender and duration of medical records
Cooper & Holmes (1998) ²⁶ UK	Dementia (CAMDEX; dementia with Lewy bodies criteria)	Records review	1118	Case and controls matched by age, gender and district of residence
Kessing <i>et al</i> (1999) ²⁷ Denmark ^a	Dementia (ICD-8) diagnosed on readmission	ICD-8 (296.19; 296.39) on first ever discharge between 1970 and 1974	13 852 Bipolar disorder (518) Unipolar disorder (3363) Neurosis (8 946) Schizophrenia (1025)	Case register cohort The probability for developing dementia comparing the different disorders: bipolar disorder > unipolar disorder > schizophrenia > neurosis
Kessing & Niilsen (2003) ³⁸ Denmark ^a	Dementia (ICD-8) diagnosed on readmission	ICD-8 (296.19; 296.39) on first ever discharge	164 277 2007 with bipolar disorder 11 741 with depression 81 380 with osteoarthritis 69 149 with diabetes	Case register cohort
Kessing & Andersen (2004) ⁴¹ Denmark ^a	Dementia (ICD-8) diagnosed on readmission	ICD-8 (296.19; 296.39); ICD-10 (DF30-31.9; DF 38.00) on first ever discharge	22 788 4202 (depressive disorder) 18 586 (bipolar disorder)	Case register cohort
CAMDEX, Cambridge Mental Disorders of the Elderly Examination. a. Samples may overlap.				