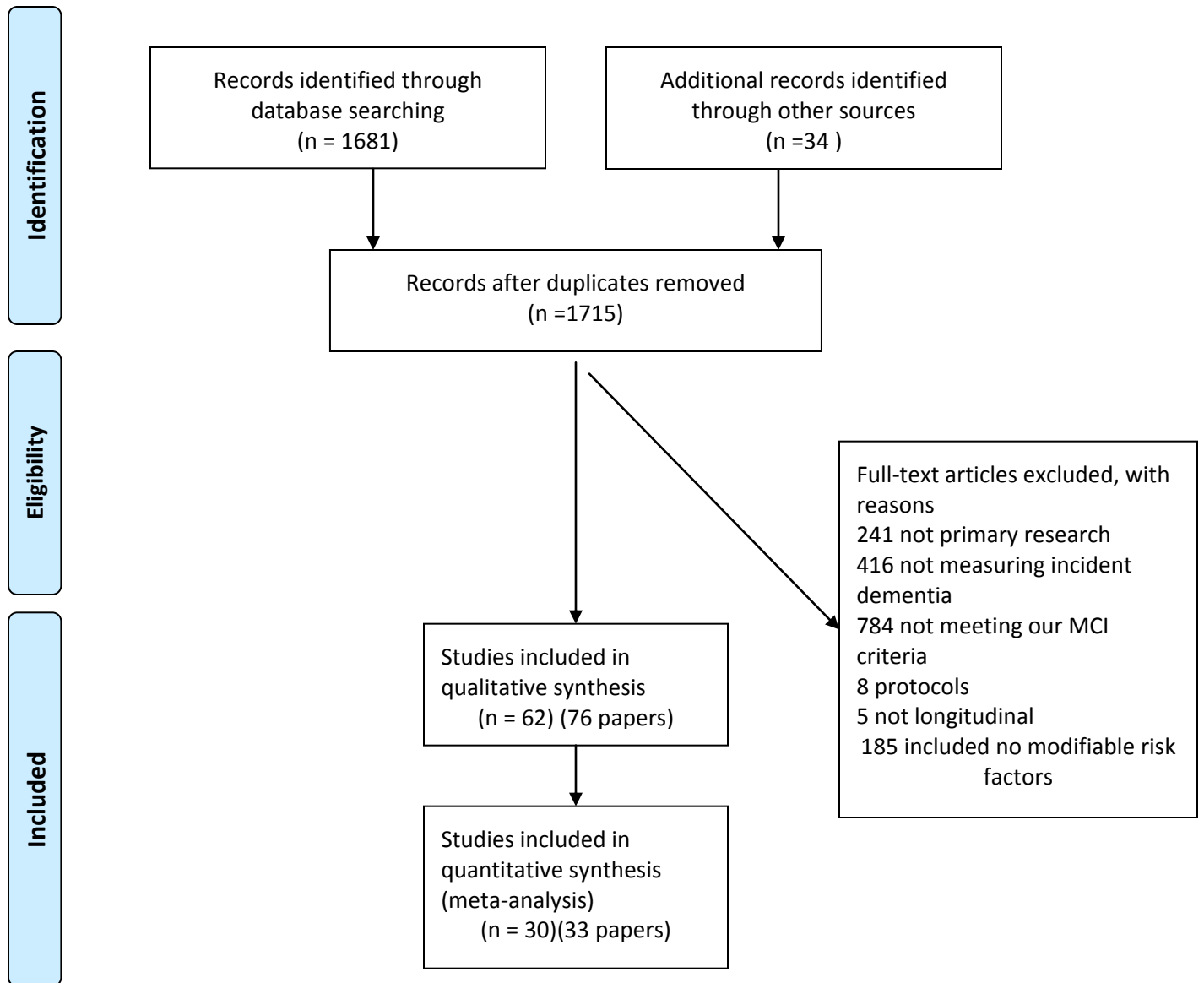


Figure 1: PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Supplemental Tables

Key for all tables

Unless stated, dementia diagnoses met DSM-IV (or DSM-III-R) criteria for dementia, or NINCDS/ARDR criteria for possible or probable AD, or NINDS-AIREN criteria for possible or probable vascular dementia, or DLB Consortium criteria for Lewy body disease or Manchester-Lund criteria for frontotemporal dementia.

*MCI criteria for diagnosis – in addition to objective cognitive (or for aMCI) impairment on testing; absence of dementia and ADL impairment

** Whether meets validity criteria in method: 1. A defined representative sample of participants assembled at a common (usually early) point in the course of their disease, or recruited to be representative of the general older population, with a response rate of at least 60% of eligible potential participants. 2. Participant follow-up for at least a year, with at least 70% followed up. 3. Criteria for diagnosing MCI and dementia were objective or applied in a 'masked' fashion.

AB=abstinence; AD=Alzheimer's Disease; ADASCog=Alzheimer's Disease Assessment Scale-cognitive subscale; ADL=Activities of Daily Living; aMCI=Amnesic Mild Cognitive Impairment; APOE=Apolipoprotein E; b/l=baseline; BMI=Body Mass Index; bp=Blood Pressure; CDR=Clinical Dementia Rating scale; CERAD=Consortium to Establish a Registry for Alzheimer's Disease; CAD=coronary artery disease; ChEI=Cholinesterase Inhibitor; C/NC: Converters (to Dementia) versus Non-Converters; CPH=Cox Proportional Hazards; CSF=Cerebrospinal Fluid; CIRS=Cumulative Illness Rating Scale; CVA=Cerebrovascular Accident; DM=Diabetes Mellitus; FHx=Family History of Dementia; GDS=Geriatric Depression Scale; GLM=Generalized Linear Model; HD=Heart disease; HDL=High Density Lipoprotein; HR=Hazard Ratio; HRT=Hormone replacement Therapy; HT=Hypertension; IADL=Instrumental Activities of Daily Living; IQ=Intelligence Quotient; IWG=International Working Group; KM=Kaplan-Meier analysis; LDL=Low Density Lipoprotein; LEDS=Life events and Difficulties Schedule; LR=Logistic Regression; MCI=Mild Cognitive Impairment; MMSE=Mini Mental State Examination; MADRS=Montgomery-Åsberg Depression Rating Scale; MD-MCI=Multi domain MCI; MeDi=Mediterranean Diet; MPS=Mild Parkinsonian Symptoms; N=number; NINCDS=National Institute of Neurological and Communicative Disorders and Stroke; NP=Neuropsychological test score; NPI=Neuropsychiatric Inventory; NS=Non Significant; OR=Odds Ratio; (P)=Petersen criteria; CT=Randomized Controlled Trial; RR=Risk or Rate Ratio; SD=Standard Deviation; SMC=Subjective memory impairment; S/IMC=Subjective or informant base memory impairment; SCC=Subjective cognitive complaint; S/ICC=Subjective or informant-based cognitive complaint; T1/T2=Time 1 and Time 2; TIA=Transient Ischemic Attack; UC: Univariate comparisons; VaD=Vascular Dementia; WMS-R=Wechsler Memory Scale-Revised; WS=Figure shows response or follow-up rate for whole cohort, not specifically those with MCI

TABLE S1. Characteristics and findings of higher quality epidemiological studies

Study	Recruitment source	% recruited	FU, years	MCI subtypes and criteria*	N (outcome if not dementia)	% follow-up	Analysis adjusted for..	Model	Prognostic factor	Statistics (for all MCI unless stated)
Han (73)	Random sampling in Seongnam, Korea	64%	1.5	All IWG criteria	140	71%	age, sex, education, time, APOE, medications,MMSE, GDS, CIRS	LR	Years education, chronic illness, GDS, medications	All ns (stats not given)
Li (18)	Long term residents aged 55+without depression from 10 randomly selected communities in the city of Chongqing	71%	5	aMCI SMC	638 (AD)	76%	age, sex, education, occupation, depressive symptoms, APOE4, baseline MMSE, and ADL score	CPH	Hypertension	HR 1.84(1.19–2.84) p=0.006
									Diabetes	HR 1.62 (1.00–2.62) p=0.049
									Hypercholesterolemia (HC)	HR 1.11 (1.04–1.18), p=0.001
									Obesity	HR 1.15 (0.45–2.92) p=0.78
									Myocardial infarction	HR 1.05 (0.67–1.65) p=0.83
									Atrial fibrillation	HR 1.09 (0.54–2.20) p=0.815
									Current smoking	HR 1.09 (0.67–1.79) p=0.73
									Daily drinking	HR 1.10 (0.69–1.75) p=0.700
									Vs untreated: HT treated	HR 0.85 (0.80–0.90) p=0.001
									Diabetes treated	HR 0.87 (0.83–0.91) p=0.001
									HC treated	HR 0.88 (0.83–0.93) p=0.001
									Cease smoking	HR 0.91 (0.49–1.70) p=0.78
									Cease drinking	HR 0.89 (0.62–1.27) p=0.51
Luck (25)	A random sample selected from people aged 75+in 6 German towns referred by General Practitioners	75%	4.5	All	745	71%	Age, gender, cognition and other factors listed	CPH	Living alone	HR 1.42 (0.95–2.14) 0.09
									Not married currently	HR 1.52 (0.71–3.23)
									Diabetes Mellitus	HR 1.35 (0.94–1.96) 0.11
									Hypertension	HR 1.05 (0.70–1.59) 0.81
									Cardiac arrhythmia	HR 0.80 (0.53–1.21) 0.30
									Coronary heart disease	HR 1.25 (0.82–1.90) 0.29
									Myocardial infarction	HR 0.59 (0.31–1.15) 0.12
									Peripheral artery disease	HR 0.95 (0.53–1.69) 0.85
									Carotid artery stenosis	HR 0.61 (0.21–1.79) 0.37
									TIA	HR 1.55 (0.91–2.64) 0.10
									Hyperlipidemia	HR 1.27 (0.82–1.95) 0.29
									Hypercholesterolemia	HR 1.16 (0.76–1.78) 0.48
									Epilepsy	HR 0.14 (0.02–1.12) 0.06
									Hyperthyroidism	HR 0.94 (0.45–1.96) 0.87
									Hypothyroidism	HR 0.88 (0.34–2.32) 0.80
									GDS 6+	HR 1.60 (1.03–2.48) 0.04
									Impaired vision	HR 1.02 (0.65–1.58) 0.95
									Impaired hearing	HR 1.44 (1.01–2.05) 0.05
Former versus nonsmoker	HR 0.69 (0.45–1.08) 0.10									
Current versus nonsmoker	HR 0.94 (0.47–1.87) 0.86									
Normal versus no drinking	HR 1.13 (0.78–1.65) 0.51									
Harmful versus no	HR 0.47 (0.06–3.59) 0.46									

									drinking	
									Antidementia drugs	HR 1.19 (0.78–1.84) 0.42
Peltz (78)	Members of a large USA retirement community, aged 90+	61%	2.5	All	395	94%	Age	CPH	Education (being college graduate)	HR 1.03 (0.6–1.6)
Richard (102)	Participants identified from a probability sample of Medicare beneficiaries in New York 1999–2001	98.9%	5.1	All MCI SMC	320	74%	Age, sex education, ethnicity	CPH	Depression (CES-D 4+)	HR 1.8 (1.0–3.1)
Scarmeas (61)	Participants identified (via ethnicity and age stratification) from a Medicare probability sample of beneficiaries in New York in 1992 and 1999	64%	4.3	aMCI	482 (AD)	85%	cohort, age, sex, ethnicity, education, APOE, caloric intake, BMI,	CPH	Middle versus lowest MeDi adherence tertile	aMCI/MCI: HR 0.48 (0.22–1.04; p=0.06); HR=0.55 (0.34–0.90); p=0.01
				all					Highest versus lowest tertile	aMCI/MCI: 0.71 (0.32–1.59) p=0.41; 0.52 (0.30–0.91) p=0.02
Panza (103)	Data from Italian Longitudinal Study of aging, a random sample population survey of people aged 65–84 from 8 municipalities	83%	3.5	aMCI normal MMSE for age/ education	121	87%	Sex, age, education, HT, CAD, smoking, stroke, DM, HC	Poisson	Italian GDS 10+	Rate ratio 1.42 (0.48–4.23)
Solfrizzi (39)								CPH	<1 drinks /day alcohol versus abstinence (AB)	HR 0.15 (0.03–0.78)
									1–2 drinks/day versus AB	HR 0.47 (0.08–2.73)
									2+drinks/day versus AB	HR 0.44 (0.05–4.06)
									<1 drinks /day wine versus AB	HR 0.15 (0.03–0.77)
									1–2 drinks/day wine versus AB	HR 0.44 (0.07–2.64)
									2+drinks/day wine versus AB	HR 0.36 (0.03–4.26)
Solfrizzi (41)						Sex, age, education, GDS, alcohol, smoking, fibrinogen, cholesterol, HD, stroke	CPH	Metabolic syndrome	HR 7.80 (1.29–47.20)	
Solfrizzi (24)	None							Univariate Poisson regression	Education (<4 years)	RR 0.79 (0.23–3.44)
									No hypertension	RR 1.74 0.46–9.74
									No coronary artery disease	RR 1.71 0.32–6.78
									No type II DM	RR 0.54 0.01–3.62
									Never smoked	RR 0.46 0.08–1.74
									Cholesterol, versus<4.5: 4.6–5.2	RR 0.75 0.11–4.43
									5.2–6.0	RR 0.97 0.18–5.20
									>6.0	RR 0.75 0.11–4.43
									HDL cholesterol (vs<1.0): 1.0–1.2	RR 1.37 0.27–8.84
									1.2–1.4	RR 1.67 0.32–10.73
>1.4	RR 0.30 0.01–3.75									

St John (72)	Random sample of residents aged 65+ of Manitoba, Canada	61%	5	All; Modified MMSE < 78, CIND on examination	85	90%	Sex, age, education, MMSE, depression, function, SMC	LR	self-rated health good	OR 1.05 (0.30–3.72)
									Educations (years)	OR 0.88 (0.74–1.05)
Caracciolo (104)	Kungsholmen Project, population-based prospective cohort study of all registered inhabitants aged 75+ in a Stockholm district, Sweden, in 1987	76%	3	All,	160	85%	age, sex, education and APOE	CPH	Perceived sadness/ low mood at baseline	aMCI: HR 5.9 (1.4 to 25.0) All MCI: 1.4 (0.8 to 2.4)
Xu (22)			9	aMCI,	302	90%	age, sex, education, MMSE, survival, BMI, HD, stroke, bp, APOE antihypertensive drugs	CPH	Prediabetes (blood glucose 7.8 –11.0 mmol/l)	Dementia: HR 4.96 (2.27–10.84); AD: 5.73 (2.43–13.5)
				Non aMCI					Diabetes Mellitus	HR 2.87 (1.30–6.34) AD: HR 2.83 (1.18–6.78)
									DM or preDM	aMCI: HR 2.24 (0.75– 6.71) non a-MCI: 4.31 (1.97–9.42)
Palmer (60)	3	aMCI MMSE > 19; SMC	47 (AD)	92.4% WS	age, sex, and education		Mood symptoms	RR 0.9 (0.6–1.5)		
								Motivation symptoms	RR 1.1 (0.7–1.8)	
								Anxiety symptoms	RR 1.8 (1.2–2.7)	

TABLE S2. Characteristics and findings for other epidemiological studies

Study	Recruitment source	FU, years	N	Type of MCI	Outcome	Analysis adjusted for..	Model	Prognostic factor	Statistics	Validity*						
										1	2	3				
Artero (26)	Random sample recruited from French electoral roles	4	2882	All	Dementia	None	** UC, LR	Hypertension; coffee, alcohol, tobacco use; HRT Hypercholesterolaemia; head trauma; depression; herpes; anesthesia; cancer; diabetes, vascular risks, asthma, antidepressants, subjective health, insomnia, BMI>27, appetite loss, social isolation,	Not significant on univariate comparisons for men or women (p>0.01; actual stats not shown)	n	y	y				
													IWG criteria	IADL	Subclinical depression	Women: OR 1.95 (1.06–3.58); p<0.03 Men NS
													S/ICC	APOE	Anticholinergic drugs	Women: OR 1.78 (1.00 –3.18) p=0.04; Men: NS
													Age	Age	Low education level	Men: OR 2.26 (1.25 to 4.06); p<0.01; Women: 2.16 (1.31 to 3.56); p<0.01
													Stroke (men)	Stroke (men)		
													Gender-stratified	Gender-stratified		
Blasko (62)	People recruited for a population-based study of 75 year-olds in Vienna, Austria	5	81		Dementia	none	LR	Self-reported folate/B12 supplements versus (1) nonusers (2) inconsistent users	(1) OR 0.15, 0.03–0.77 p=0.023 (2) OR 1.8 (0.6–5.6), p=0.330	n	y	y				
													Serum homocysteine and B12 levels	Not significant		
													sex, APOE, education, creatinine, folate	LR	Ln of serum folate Education (years)	OR 0.17 (0.04–0.69), p=0.013 OR 0.77 (0.58–1.01), p=0.062
Brodsky (47)	70–90 years on Sydney electoral roll	2	319	All (P)	Dementia	age, sex, education	LR	NPI score \geq 1	OR 0.57 (0.1–2.8), p=0.49	n	y	y				
Beaudreau (45)	Adults aged 70+in USA aging study recruited to represent population	4	180	All, panel diagnoses	Dementia	Age, APOE Education, NPI	LR	Education (years) NPI total scores	OR 0.97 (0.88, 1.07) p=0.56 OR 1.01 (0.97, 1.06) p=0.61	n	y	y				
Chan et al (59)	People aged 60+from Hong Kong, and from old age hostels & day centers	2	321	All SMC	Dementia	MMSE, education, age, gender	LR	Education (years) depression/dysphoria apathy/indifference aberrant motor behavior	OR 0.98 (0.87–1.09) p=0.67 OR 2.40 (1.05–5.46) p=0.04 OR 0.31 (0.09–1.13) p=0.08 OR 9.96 (0.57–174.42) p=0.12	n	y	y				
Lopez (105)	Random sampling of Pittsburgh Medicare	Mean 4.3	136	aMCI and MD-MCI		Nil	**UC	> High school education, No. (%)	NS, chi2=2.43	n	y	y				
Meyer (80)	Participants who developed MCI during longitudinal study	mean 3.9	73	SMC	AD and vascular dementia	None	**UC	Education (years)	AD, C/NC: 11.54 versus 14.57, p<0.01	n	y	y				
				All					VaD, C/NC: 13.13 versus 14.57							

					ntia							
Oveisgharan (30)	Participants in Canadian Study of Ageing, recruited to represent population	5	990	All	Dementia	Age, sex, APOE, cognitive impairment subtypes and interaction terms	LR	Hypertension	NS (results not given); in subgroup with executive dysfunction, hypertension, 57.7% versus normotension 28.0%, P=0.02), in UC	y	n	y

TABLE S3. Characteristics and findings for clinical studies

Study	Recruitment source	FU, years	N	Type of MCI	Outcome	Analysis adjusted for..	Model	Prognostic factor	Statistics	Validity (see method)					
										1	2	3			
Abner (29)	Recruits from Kentucky AD center who entered a longitudinal study (BRAiNS), who agreed to brain donation, when cognitively intact and developed MCI	10	101	All, aMCI, S/ICC, Intact global cognition	Dementia	APOE, age, gender, family history, education, hypertension, MCI duration	Markov chain	Hypertension	RR 0.30 (0.10–0.93)	n	y	y			
Abner (37)			649					Vs never smoked: <1–10 pack-years versus never smoked	OR 0.28 (0.08–0.94) p=0.039	n	y	y			
								10–20 pack-years	OR 0.28 (0.08–0.94) 0.04	n	y	y			
								≥20 pack-years	OR 0.31 (0.13–0.71) p=0.005	n	y	y			
Kryscio (75)			554		Dementia	APOE, age, gender, family history, education	polytomous LR	□12 versus □16 years education	Amnestic: OR 1.00 (0.32–3.14) Mixed: 0.38 (0.05–3.12)	n	y	y			
									13–15 versus □16 years education	Amnestic: OR 0.92 (0.39–2.16) Mixed: 1.56 (0.64–3.79)	n	y	y		
Kryscio (36)										Years to diagnosis	HRT	Mean (SD) 1.3±0.5, p=0.0029	n	y	y
											Smoker at baseline	0.66±0.26, p=0.043	n	y	y
Alefret (68)	Clinical convenience sample	4	42	aMCI(P)	AD	Age, gender	CPH	2ndry school education	HR 1.80 (0.70–4.67)	n	y	y			
Amieva (70)	Participants in drug RCT, no history of depression or stroke	2	90	SMC aMCI	Dementia	—	**UC	% primary school diploma	C/NC 89.7% versus 88.5% (p=0.99)	n	y	y			
Aretouli et al (76)	Research centers and clinics in USA	2	104	All	Dementia (CDR□1)	—	**UC	Education (years)	F(1,92)=0.02, p=0.890	n	y	y			
Barabash (69)	Consecutive, Madrid Memory Unit	1.7	89	aMCI, SMC	AD	Age, APOE, genetics	CPH	< 10 years schooling	HR 0.23 (0.05–0.98) p=0.016	n	y	y			
Betterman (106)	Recruited from 4 USA academic centers	6	482	All	Dementia (expert)	age, sex, race, APOE, education, stroke,	CPH	Statin ever	HR 0.88 (0.64–1.21) p=0.43	n	y	y			
							Other lipid lowerer	HR 0.78 (0.36–1.68), p=0.52							

					panel)	HD							
Brodaty (42)	9 Australian memory clinics	3	185	All (P)	Dementia	Age, sex, MMSE	CPH	Depression (NPI subscale)	HR 1.08 (0.98–1.19)				
								NPI (total & 6 m change)	Not significant, results not given				
Chilovi et al (58)	Outpatient aging clinic, Brescia, Italy	2	124	All	Dementia	Age, Barthel Index, ADAS-Cog	LR	Clinical depression	OR 0.10 (0.02–0.39); p=0.001	n	y	y	
				S/ICC				Clinically significant apathy	OR 7.07 (1.99–25.17); p=0.003				
Devanand (67)		4.5	139	All SMC	Dementia	—	**UC	Education (years)	C/NC: mean 14.1(SD 4.5) versus 15.6 (4.0)	n	y	y	
Devier (53)	New York Memory clinic attendees, without psychiatric diagnosis or CVA	1–9	108 148	aMCI	AD	Cognition, education and stratified for age (and other variables tested)	CPH	State anxiety	HR 1.68 (0.75–3.77) p=0.21	n	y	y	
								Trait anxiety	aMCI: 0.35 (0.14–0.85) p=0.02				
									All MCI: HR 0.36 (0.16–0.82) p=0.015				
								Hamilton depression score	All MCI: HR 1.01 (0.92–1.10) p=0.86				
				SMC									
								Education (years)	HR 1.01 (0.93, 1.10) p=0.81				
Edwards (49)	Records, Californian memory clinics	1.6	270	All	Dementia	Age, MMSE, function, site, comorbidity	LR	4+neuropsychiatric symptoms	OR=2.44 (1.07–5.55)	n	n	y	
Farias (74)	Clinic referrals and outreach	2	1111	All	Dementia	memory, age, education	CPH	Education (years)	NS	n	y	y	
Fellows (38)	Canadian memory clinic	3.3	90	aMCI S/IMC	AD	age onset, MMSE, sex, education, function	UC; LR	Smoking (pack years)	OR 0.98 (0.95–1.00) p=0.13	n	y	y	
						None	**UC	Education (years)	C/NC: (mean(SD): 10.6 (3.6) versus 10.9 (3.3))	n	y	y	
								GeDS>6	C/NC 55 versus 62, p=0.53				
								Alcohol consumption	C/NC 45 versus 44, p=0.92				
								Vascular risk factors	C/NC 60 versus 45 p=0.15				
Fleischer (107)	Participants in an RCT	3	539	aMCI	AD	Age, sex, cognition, FHx	GLM	Education (years)	NS	n	y	y	
Gabryelewicz (52)	Participants in a longitudinal study recruited	3	105	All	Dementia	Age	ANC OVA	Higher baseline MADRS score	F=4.83, p=0.010	n	y	n	

Gavrilova (64)	from consecutive referrals to Warsaw clinic MADRS score 28 or less			SMC				Higher baseline homocysteine levels	MD-MCI: 16.53 umol/l versus 14.36 umol/l; U=713, p=0.037 aMCI: ns			
Grande (82)	Milan (Italy) memory clinic	Median 2.6	176	All	Dementia	age, gender, education, MMSE, GDS, MCI subtype, APOE	CPH	Physical activity score (vs lowest tertile): middle 3le	HR 0.59 (0.32 to 1.10)	n	y	y
				SCC				Highest tertile	HR 0.36 (0.18 to 0.75)			
								Social activity score (vs lowest tertile): middle 3le	HR 0.82 (0.54 to 2.15)			
								Highest tertile	HR 0.42 (0.68 to 2.56)			
								Cognitive activity score (vs lowest tertile): middle 3le	HR 0.54 (0.26 to 1.14)			
								Highest tertile	HR 0.89 (0.45 to 1.77)			
Ravaglia (27)	Bologna (Italy) geriatric clinic attendees aged 60+with reliable informant, without psychiatric disorder recruited from March 1999 to March 2004 and August 2005 (Forti	Mean 2.8	165	All	Dementia, deficits in 2+cognitive domains affecting functioning	Age, gender, education	CPH	Ever smoking	HR 0.54 (0.22–1.32) p<0.177	n	y	y
				S/IMC				Diastolic bp (–10mmHg)	HR 0.56 (0.39–0.80) p<0.001			
				MMS E>23				Systolic (–10mmHg)	HR 0.81 (0.69–0.95) p<0.013			
								Hypertension	HR 1.25 (0.70–2.45) p<0.453			
								BMI (vs 25.1–27.6): <25	HR 2.07 (1.04–4.14) p<0.039			
								27.7–29.9	HR 0.53 (0.20–1.37) p=0.189			
								>30	HR 0.62 (0.26–1.46) p=0.270			
								Diabetes	HR 0.75 (0.26–2.13) p<0.593			
								Cardiovascular disease	HR 0.90 (0.44–1.84) p<0.780			
								Chol (Ref 5.3–6.): <5.3:	HR 1.78 (0.85–3.70) p=0.123			
								6.0–6.5 mmol/l	HR 0.38 (0.13–1.07) p=0.068			
								>6.5 mmol/l	HR 0.29 (0.09–0.87) p=0.028			
								Vitamin B12 □217 pmol/l	HR 0.60 (0.26–1.39)			

									p=0.234			
								Serum folate \square 10.4 nmol/l	HR 2.23 (1.12–4.43) p=0.022			
Forti (83)			180			+ MMSE, bp, BMI, folate	CPH	Atrial fibrillation	HR 4.63 (1.72–12.46) p<0.002	n	y	y
						None	**UC	Education>5 years	C/NC: 14 (26.9) versus 29(22.6) p=0.54	n	y	y
Maioli (34)		1.2	52			None	**UC	Serum HDL mg/dl	C/NC 70(25) versus 58 (13), p=0.058	n	y	y
								Serum LDL mg/dl	C/NC: 106 (42) versus 122 (52) p=0.359			
Hansson (32)	Attendees from a Swedish memory clinic, who agreed to provide a sample of CSF	4	137	aMCI SMC	AD	age, sex, education level, APOE E4	CPH	Received higher education	HR 0.80 (0.45–1.43)	n	y	y
								Systolic bp	HR 1.00 (0.98–1.01)			
								Diastolic bp	HR 0.99 (0.97–1.02)			
								Homocysteine	HR 1.08 (1.04–1.12)			
Hsiung (43, 108)		2	68	All; MCI on exami nation	AD, VaD	age, sex	LR	Education (years)	AD: OR 0.82 (0.76–0.89) VaD: 0.62 (0.49–0.79)	n	n	y
	Recruited from 8 Canadian memory clinics						**UC	NPI	C/NC: 4.3(6.3) versus 11.0 (20.1)	n	n	y
								Chronic medical illness	C/NC 5.2 (4.3) versus 5.3 (3.9)			
Jack (28)	Consecutive patients 60–89 from Mayo clinic research registry	2.7	80	S/IMC aMCI	AD	none	nonpa rametr ic CPH	Hypertension	RR 1.63 p=0.272	n	y	y
								Ischemic heart disease	RR 0.55 p=0.272			
								Estrogen replacement	RR 1.09 p=0.864			
Korf (31)	Consecutive attenders at a geriatric clinic, Stockholm, Sweden	2.8	75	All	Demen tia	time	CPH	Education (years)	HR 0.93 (0.82–1.06)	n	y	y
								Hypertension	HR 0.62 (0.27–1.42)			
								Depression	HR 0.76 (0.38–1.52)			
Lee (81)	Aged 55+, \square 1 FU, South Korean study	1.4 7	504	All; SCC	AD	Age, MMSE score	CPH	Education (years)	HR 1.08 (1.04–1.13) p<0.001	n	y	y
Li (19)	Inpatients in a Chinese hospital those with CVA or depressive disorder excluded	3	257	aMCI SMC	AD	Age, covariates listed; carotid stenosis, stroke during follow-up	CPH	diabetes mellitus	HR 2.39 (1.07–5.33) p=0.03	n	y	y
								Education (> 6 years)	HR 0.48 (0.21–1.10) p=0.08			
								Hypertension	HR 0.71 (0.22–2.22) p=0.55			
								Antihypertensives	HR 1.22 (0.48–3.13) 0.68			

						and white matter changes		antihyperglycemic	HR 2.08 (0.66–6.54) p=0.21			
Luis (109)	Record review Miami memory clinic	2.4	134	All SCC	Dementia	Age, sex, MMSE, subtype	CPH	Education (years)	NS (results not given)	n	y	y
Mauri (110)	Italian outpatient clinic patients	3	119	All	Dementia	None	No tests	Mild parkinsonism symptoms at baseline	11/22 (50%) with MPS at baseline and 35/97 without developed dementia; trend (p<0.05) for vascular dementia	n	y	y
Modrego (51)	Consecutive Spanish outpatient clinic patients	3	114	aMCI SMC	Dementia	None	Log-rank test	Depression diagnosed by structured clinical interview	HR: 4.1; 2.4–6.9	n	y	y
Olazaran (77)	Recruited by primary care physicians in a Madrid practice	1	81	All	Dementia	Age, sex	LR	Higher educational level (not illiterate or incomplete education)	OR 0.13 (0.02–0.77) 0.024	n	y	y
Palmer (56)	Consecutive new diagnoses at 3 Rome memory clinics	4	131	aMCI	AD	age, sex, apathy, MMSE, education, depression	CPH	Depression diagnosis	HR 0.6 (0.2–1.8)	n	y	y
								Apathy diagnosis	HR 6.9 (2.3–20.6)			
								NPI apathy score 2+	HR=4.6 (1.3–16.2)			
Peavy (111)	Research center & clinic, aged 65+, no mental illness, 3 follow-ups	2.5	33	All (P)	Dementia	Age, gender, education, cortisol, APOE	LR	Education (years)	NS (data not shown)	n	y	y
Perri (112)	Aged 50–80, USA memory clinics, \geq 5 years education	2	190	aMCI	AD	Age, gender, cognition	LR	Education (years)	NS (p=0.85)	n	y	y
				S+IMC								
Prasad (20)	Patients at a tertiary neurology memory clinic with follow-up information available for 18 months including MRI scans	1.5	79	aMCI	Dementia (all AD)	none	**UC	Education (years)	C/NC: 8.3 versus 10.2 p=0.098	n	n	y
				Diabetes mellitus				C/NC: N=10 (43.5%) versus 15 (28.9) p=0.215				
				Hypertension				C/NC: 11 (47.8) versus 28 (52.8) p=0.094				
				Hyperlipidemia				C/NC: 10 (45.4) versus 36 (67.9) p=0.032				
Mackin (35)	ADNI database, recruited from 50+sites in USA and Canada without depression (GDS<6)	2–3	405	aMCI	AD	ApoE, intracranial volume, white matter lesions,	CPH	GDS score 1–5 (sub syndromal depression) versus GDS=0	NS (statistics not given)	n	y	y
				S+IMC								
				MMS								

				E >23		demographics removed as NS						
		3	227	SMC	Dementia (NINCDS)	None	**UC	Education (years)	C/NC: 15.9 (2.9) versus 16.0 (2.8) p=0.72	n	n	y
				aMCI				GeDS 6+at follow-up	OR=1.88, p=0.15			
								GeDS score	C/NC: 1.6 (1.3) versus 1.5 (1.4) p=0.38			
								Serum LDL mg/dl	C/NC:106 (42) versus 122 (52) p=0.359			
Morris (21)		2	264			Education, age, sex	ANOV A	Impaired glycaemia	C/NC:48.5% versus 32.3% p=0.009	n	y	y
Richard (55)		mean 2.7	151 219 211			age, gender, education and baseline MMSE score	CPH	Apathy symptoms	HR 1.85 (1.09–3.15)	n	y	y
								CES-D score 4+	HR 1.15 (0.72–1.83)			
								Apathy and depression	HR 1.05 (0.91–1.23)			
Schneider (84)		2	402			age, APOE, education ADAS-cog score	Weibul 1 R	ChEI versus no treatment	29.8% reduced time to dementia (p=0.005)	n	y	y
								ChEI and memantine	41.8% reduced time to dementia (p=0.003)			
Robert (57)	Patients from 14 French memory clinics aged 58+, >4 years education, with informant; not MADRS score>20 or significant brain vascular change	1	216	aMCI	AD	age, sex, educational level, MADRS total score and Goldberg anxiety scale	LR	Psychiatric history	C/NC 31.8 versus 19.7, p=0.16	n	y	y
				SMC				Education (% tertiary)	C/NC 31.8 versus 44.3, p=0.22			
				MMS				Goldberg anxiety scale	C/NC 2.6 (2.5) versus 2.9 (2.5) p=0.16			
				E				MADRS total score (% >10)	C/NC 31.8 versus 18.6, p=0.26			
				>24				Apathy	C/NC 59.1 versus 37.6, p=0.10			
Rosenberg (50)	Data from National Alzheimer Coordinating Center database, USA	Median 1.58	1821	All	Dementia	Cognition, age, ethnicity	CPH	NPI middle versus lowest tertile	Dementia/AD: HR 1.43 (1.15–1.80) p=0.002/ 1.48 (1.17–1.88) p=0.001	n	n	y
				Expert diagnosis	AD			NPI top versus lowest tertile	HR 1.5(1.2–1.9)<0.001/1.4(1.1–1.7)			

									0.013			
								GDS mid versus lowest tertile	HR 1.4 (1.1–1.7) 0.003 / 1.3 (1.0–1.6) p=0.05			
								GDS top versus lowest tertile	HR 1.37 (1.1–1.71) p=0.01/1.17 (0.92–1.5)p=0.21			
Rozzini (113)	Consecutive referrals to Italian memory clinic	2	46	Not stated	Dementia	None	**UC	Depression diagnosis at baseline	17/24 without depression developed dementia versus 8/22 with depression	n	y	y
Rozzini (44)		1	119	aMCI	AD	None	**UC	Education (years)	NS	n	y	y
				S/IMC				NPI	C/NC: 14.5 (11.2) versus 12.6 (10.7) NS			
								GeDS	C/NC: 4.3 (3.6) versus 4.7 (3.1) NS			
								Hamilton anxiety scale	C/NC: 8.5 (6.4) versus 10.4 (6.5)			
								Number of drugs	C/NC: 2.8 (2.2) versus 2.5 (1.8)			
Sachdev (79)	Patients at two Australian hospitals, 3–6 months after ischemic stroke / TIA	3	45	All	Vascular dementia	None	**UC	Education (years)	NS (stats not given)	n	n	y
Siuda (63)	Polish Neurology outpatient clinic	1	55	SMC	Dementia	None	**UC	Total homocysteine (μ mol/L)	C/NC: 19.83 (7.31) versus 19.85 (7.64) p=0.645	n	y	y
				Objective cognitive imp				Vitamin B12 (pg/mL)	C/NC: 376.11 (173.44) versus 495.32 (335.78) p=0.143			
								Folic acid (ng/mL)	C/NC: 3.60 (1.72) versus 3.75 (1.90) p=0.752			
Squitti (65)	Italian memory clinic, GDS<14	2–6	141	aMCI	AD	Age, gender, MMSE	CPH	Serum Nonceruloplasmin Copper	HR 1.23 (1.03–1.47), p=0.022	n	y	y
								transferrin, ferritin hypercholesterolemia, hypertension	Not significant (data not shown)			
Taragano (48)	Consecutive patients, Argentinian clinic	5	239	Any SCC	Dementia	None stated	CPH	Psychiatric symptoms	HR 4.01 (2.5–6.3)	n	y	y
Teng (46)	Memory clinic patients aged	2	51	Any	AD	MMSE,	ANC	Any neuropsychiatric	F(1, 40) = 5.23 p=0.028	n	y	y

	50+			SCC		subtype, sex	OVA	symptoms				
Velayudhan (23)	People aged 65+primary care practices in south London, UK	4	61	aMCI SMC	Dementia	Age, gender, APOE, IQ, education, smoking, health	CPH	Diabetes	HR 2.9 (1.1–7.3)	n	y	y
								Duration of diabetes	HR 0.9 (0.7–1.1) 0.29			
						None		Depression	HR 1.4 (0.5–3.9) p=0.5	n	y	y
								Education	HR 1.0 (0.9–1.2) p=0.61			
								Coronary heart disease	HR 1.1 (0.4–2.8) p=0.85			
								Drinking alcohol	HR 2.6 (0.7–8.8) p=0.1			
								Lifetime smoking status	HR 0.8 (0.17–4.3) p=0.8			
Visser (114)	new consecutive patients, Maastricht memory clinic without vascular MCI	10	64	SMC aMCI	Dementia	—	**UC	Education (years)	chi2<1.4, p>0.23	n	y	y
Visser (54)		5	74	SMC aMCI				Dementia (All AD)	**UC			
				Depression (baseline)	C/NC: 26% versus 50%, NS							
				Depression (follow-up)	C/NC: 7% versus 29% NS							
Xu (40)	Male patients from 2 Chinese neurology outpatient clinics	2	163	SMC	Dementia	—	KM	Heavy versus light to moderate alcohol use	P<0.05	n	y	y
				any				Heavy drinkers versus abstainers	P<0.05			
Yasar (33)	Participants with MCI in USA RCT of Ginkgo Biloba	6.1	320	All	AD	age, sex, education, income, no. of vascular diseases, BMI	CPH	Diuretic versus no antihypertensive use	HR 0.38 (0.20–0.73) 0.004	n	y	y
								Other cardiovascular drugs	Not significant predictors			
Ye (71)	Consecutive patients in 31 South Korea memory clinics	Mean 1.43	249	aMCI SMC	AD	age, gender, and baseline MMSE	CPH	Education (>8 years)	HR 2.18 (1.10–4.32); Late-stage: 2.38; p=0.03 Early: NS	n	y	y
Ye (66)	People in National USA MRI study	4	319	aMCI SMC	Probable AD	—	**UC	Education (years)	C/NC: 15.77±2.90 versus 15.65±3.06, p=0.7	n	y	y

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