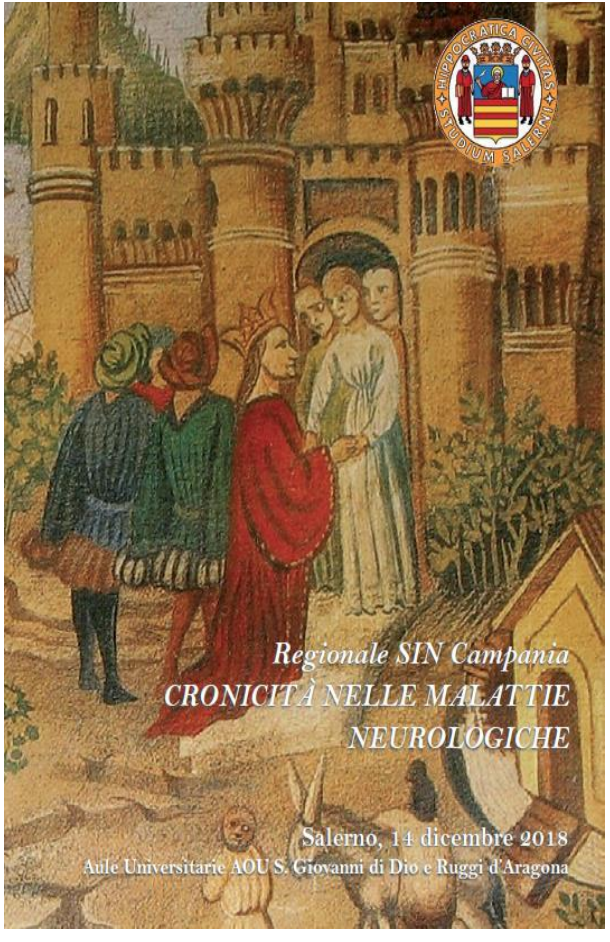
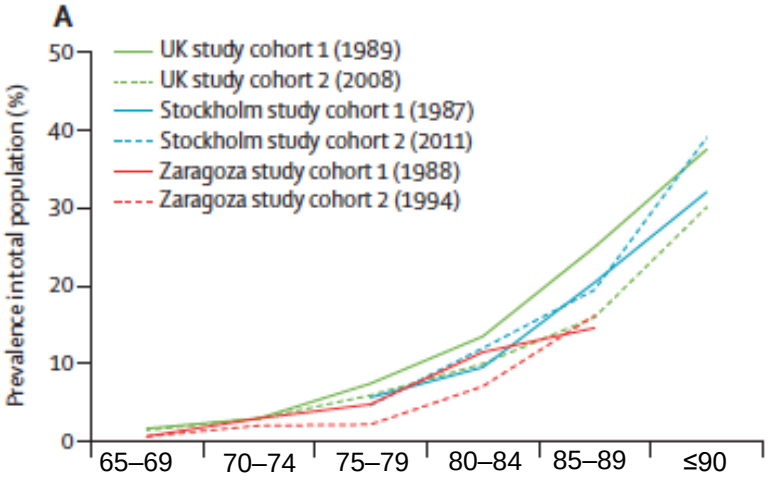


Il contributo vascolare nelle malattie neurodegenerative

Arturo de Falco

UOC di Neurologia e Stroke Unit

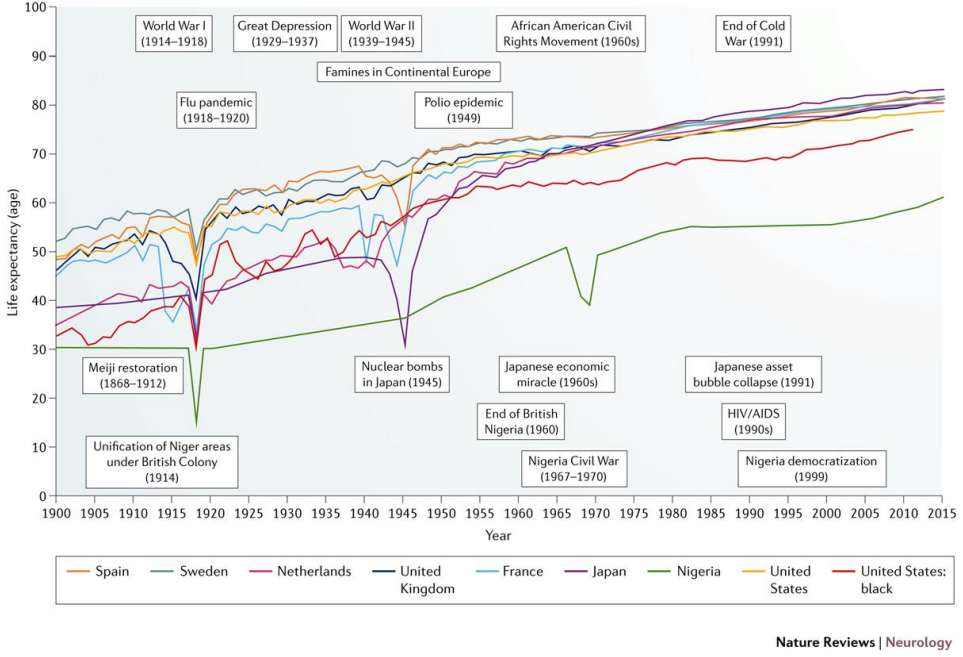
San Giuseppe Moscati - Avellino
Azienda Ospedaliera di Rilievo Nazionale e di Alta Specializzazione



Dementia in western Europe: epidemiological evidence andimplications for policy making

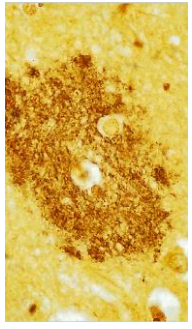
Lancet Neurol 2015

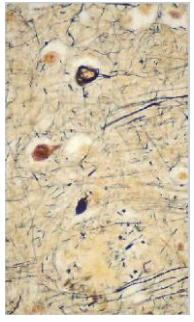
Life expectancy at birth in all countries included in population-based studies of dementia incidence and prevalence

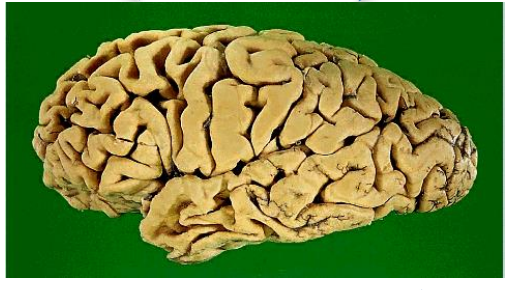


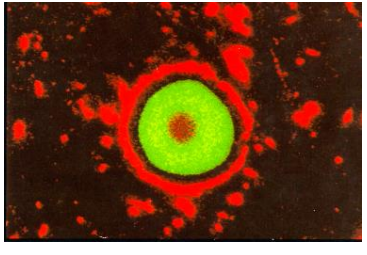
Nature Reviews | Neurology

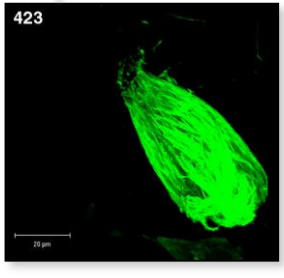
Wu, Y.-T. *et al.* (2017) The changing prevalence and incidence of dementia over time — current evidence *Nat. Rev. Neurol.* doi:10.1038/nrneurol.2017.63







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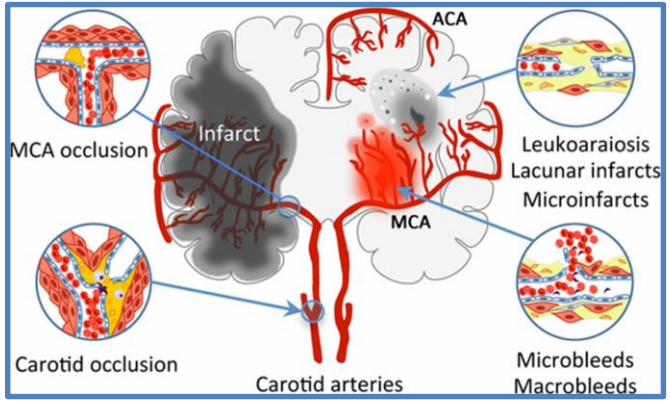
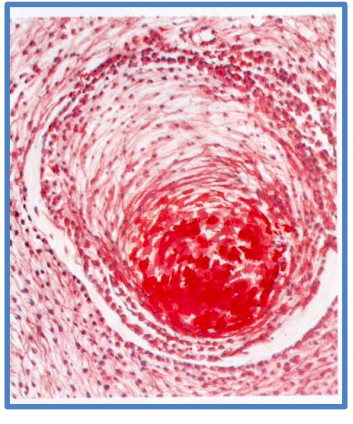
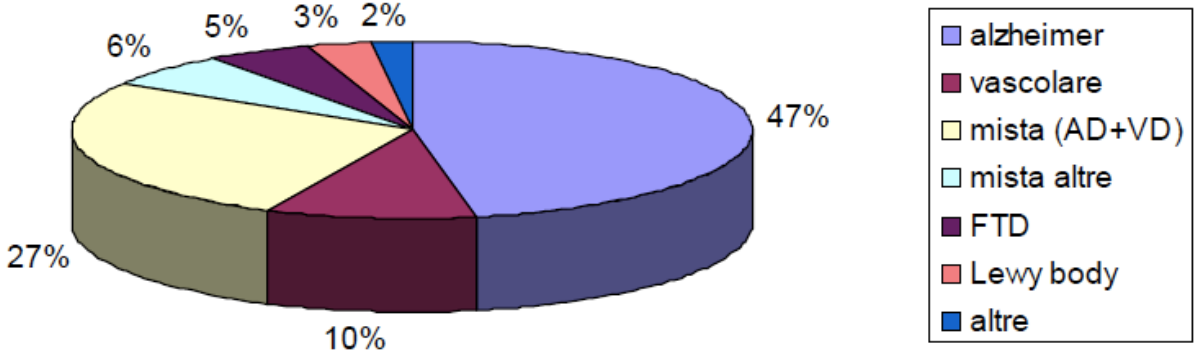
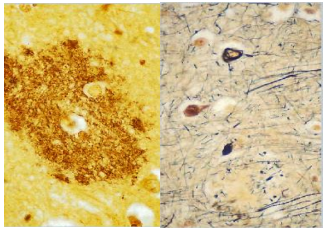
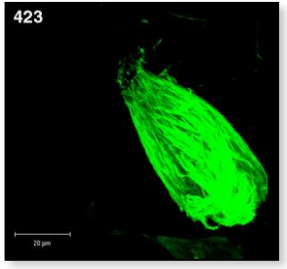

ACA
MCA occlusion
Infarct
Leukoaraiosis
Lacunar infarcts
Microinfarcts
MCA
Carotid occlusion
Carotid arteries
Microbleeds
Macrobleeds





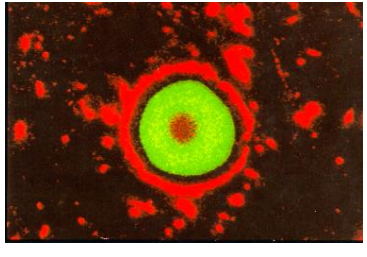
Feldman H, Levy AR, Hsiung G-Y, et al. A Canadian Cohort Study of Cognitive Impairment and Related Dementias (ACCORD): study methods and baseline results. Neuroepidemiology 2003;22:265-74.

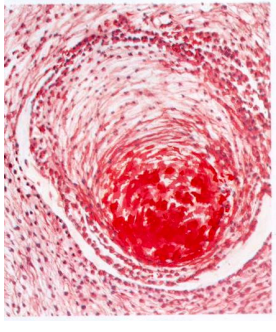




Characteristics for patients with different dementia subtypes and for all demented

Dementia subtype	Patients [*n* (%)]	Sex (% female)	Age [median (range)]
AD	220 (42.0)	59.5	79 (55–96)
VaD	124 (23.7)	43.5	81 (52–102)
AD + VaD	113 (21.6)	61.1	83 (67–97)
FTD	21 (4.0)	71.4	73 (52–86)
Other dementia	46 (8.8)	45.7	74 (39–87)
All demented	524 (100)	55.3	80 (39–102)





Prevalence of dementia subtypes: A 30-year retrospective survey of neuropathological reports

Archives of Gerontology and Geriatrics 49 (2009) 146–149

SOCIETÀ ITALIANA DI NEUROLOGIA

doi:10.1093/brain/awt188 Brain 2013: 136; 2697–2706 | 2697

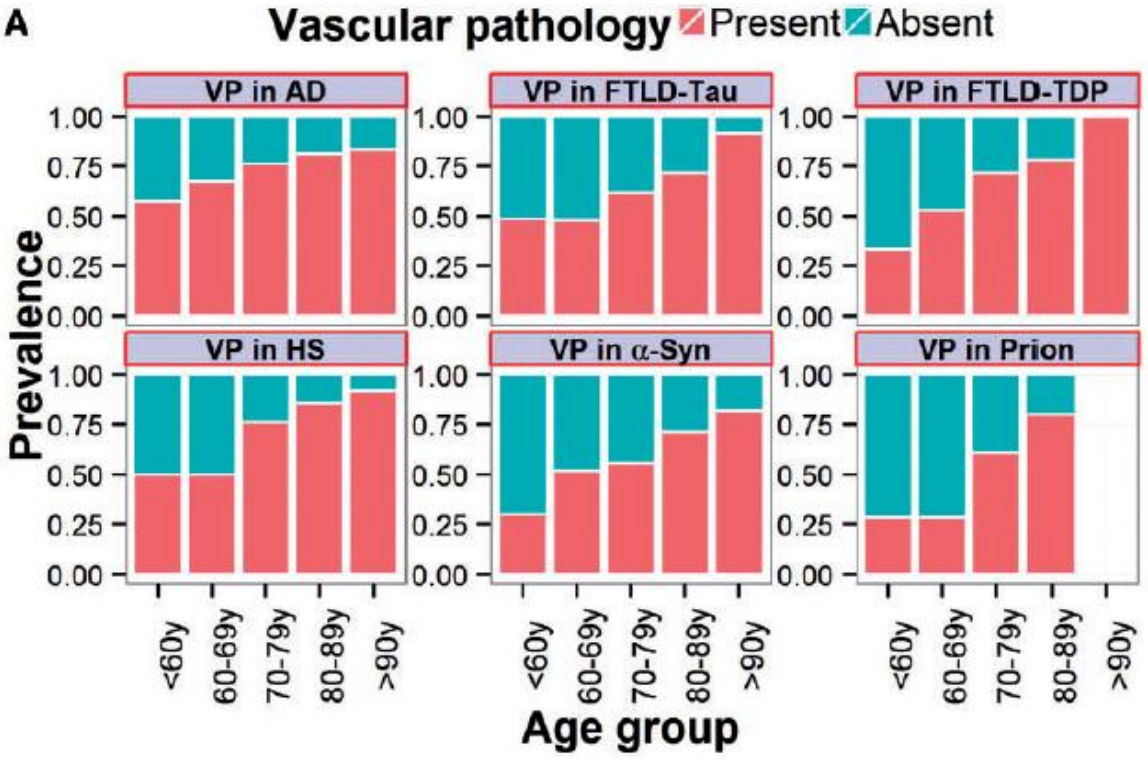
BRAIN
A JOURNAL OF NEUROLOGY

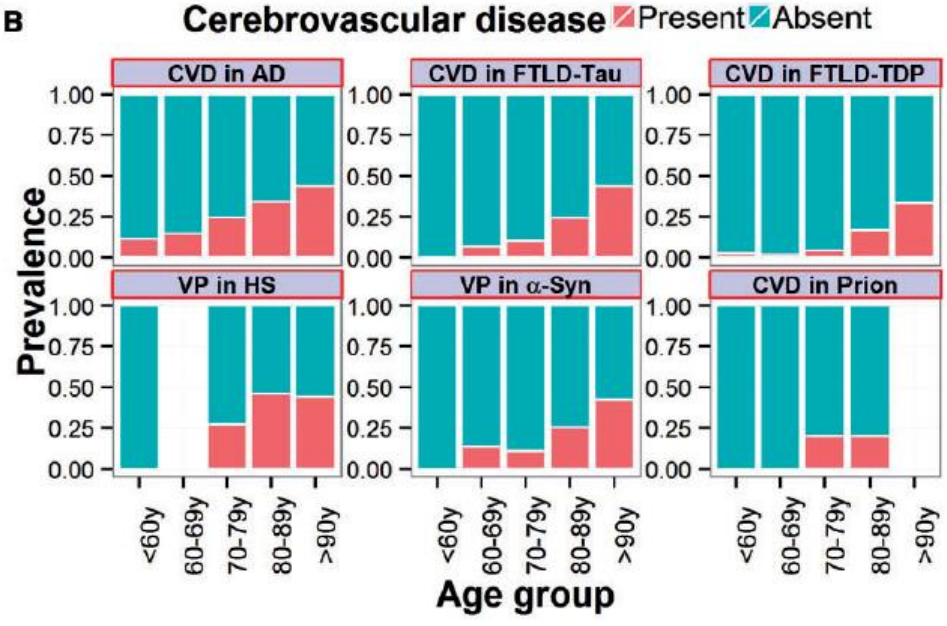
Contribution of cerebrovascular disease in autopsy confirmed neurodegenerative disease cases in the National Alzheimer's Coordinating Centre

Jon B. Toledo,[1,*] Steven E. Arnold,[2,3,*] Kevin Raible,[1] Johannes Brettschneider,[1] Sharon X. Xie,[4] Murray Grossman,[2] Sarah E. Monsell,[5] Walter A. Kukull[5] and John Q. Trojanowski[1]

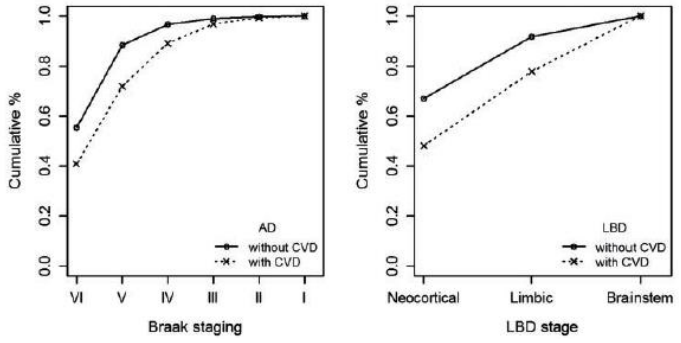
	Alzheimer's disease	FTLD-Tau	FTLD-TDP	α-Synucleinopathy	Hippocampal sclerosis	Prion	Unremarkable brain	Cerebrovascular disease	*P*-value
Number of cases	4629	379	207	323	77	100	210	280	
Age at death, years	81.1 (10.4)	73.7 (12.0)	66.8 (10.3)	77.9 (9.5)	86.5 (10.8)	61.8 (11.4)	83.1 (9.5)	84.2 (8.2)	0.0001
Gender, % male	44.5	55.7	56.2	73.1	41.6	52.0	48.1	50.3	0.0005
APOE ε4, %	56.4	23.8	28.3	34.1	18.9	14.3	16.9	19.6	0.0005
Demented, %	85.7	89.0	83.7	80.5	67.5	91.7	0	44.3	0.0005
Cerebrovascular disease, %	32.3	17.3	5.2	20.2	39.2	4.8	–	100	<0.0001
Vascular pathology, %	79.9	64.7	60.9	66.2	84.9	41.3	67.3	100	0.0005
Large infarcts, %	12.7	5.4	3.6	8.3	17.9	1.3	10.0	28.3	0.0005
Lacunes, %	19.9	12.5	5.7	15.0	34.3	2.6	16.1	46.3	0.0005
Multiple microinfarcts, %	20.1	8.4	6.8	12.2	32.8	3.8	17.5	39.6	0.0005
Arteriosclerotic leukoencephalopathy, %	9.3	11.1	11.8	7.7	13.0	1.2	2.0	18.1	0.0005
Haemorrhages, %	6.8	3.0	3.0	4.8	4.4	0	4.0	11.8	0.0005
Atherosclerosis, %	39.8	25.2	20.5	27.0	50.7	6.3	22.6	51.5	0.0005
Arteriolosclerosis, %	34.6	35.2	18.1	28.8	46.8	7.7	10.3	54.8	0.0005
Cerebral amyloid angiopathy, %	40.8	7.2	9.2	11.9	10.5	4.1	10.7	9.1	0.0005

- ☑ Large infarcts
- ☑ Multiple microinfarts lacunes
- ☑ Subcortical arteriosclerotic leukoencephalopathy
- ☑ Haemorrhages





Reference category for analysis	Analysed category	OR (95% confidence interval) for vascular pathology	*P*-value for vascular pathology
Alzheimer's disease	FTLD-Tau	0.37 (0.28–0.50)	<0.0001
Alzheimer's disease	FTLD-TDP	0.40 (0.28–0.58)	<0.0001
Alzheimer's disease	Hippocampal sclerosis	1.37 (0.64–2.98)	0.41
Alzheimer's disease	α-Synucleinopathy	0.38 (0.28–0.52)	<0.0001
Alzheimer's disease	Prion disease	0.13 (0.08–0.23)	<0.0001
Alzheimer's disease	Unremarkable Brain	0.49 (0.39–0.61)	<0.0001
α-Synucleinopathy	FTLD-TDP	1.16 (0.71–1.91)	0.56
α-Synucleinopathy	FTLD-Tau	0.96 (0.63–1.45)	0.85
FTLD-TDP	FTLD-Tau	0.84 (0.53–1.33)	0.46



J Neural Transm (2016) 123:241–250
DOI 10.1007/s00702-015-1470-9

CrossMark

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - REVIEW ARTICLE

The contribution of white matter lesions to Parkinson's disease motor and gait symptoms: a critical review of the literature

Branislav Veselý[1] · Angelo Antonini[2] · Ivan Rektor[3]

The review found association between WML severity and axial motor performance (freezing of gait and postural instability), less significant to responsiveness to dopaminergic treatment. Inconsistent impact on tremor, bardykinesia and rigidity.

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

The contribution of white matter lesions (WML) to Parkinson's disease cognitive impairment symptoms: A critical review of the literature

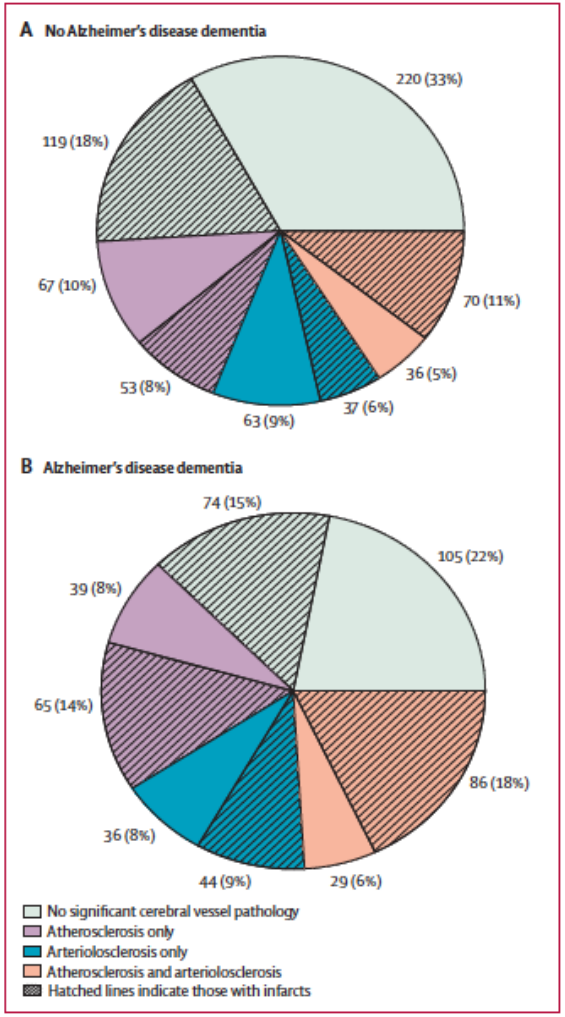
Branislav Veselý [a], Ivan Rektor [b,*]

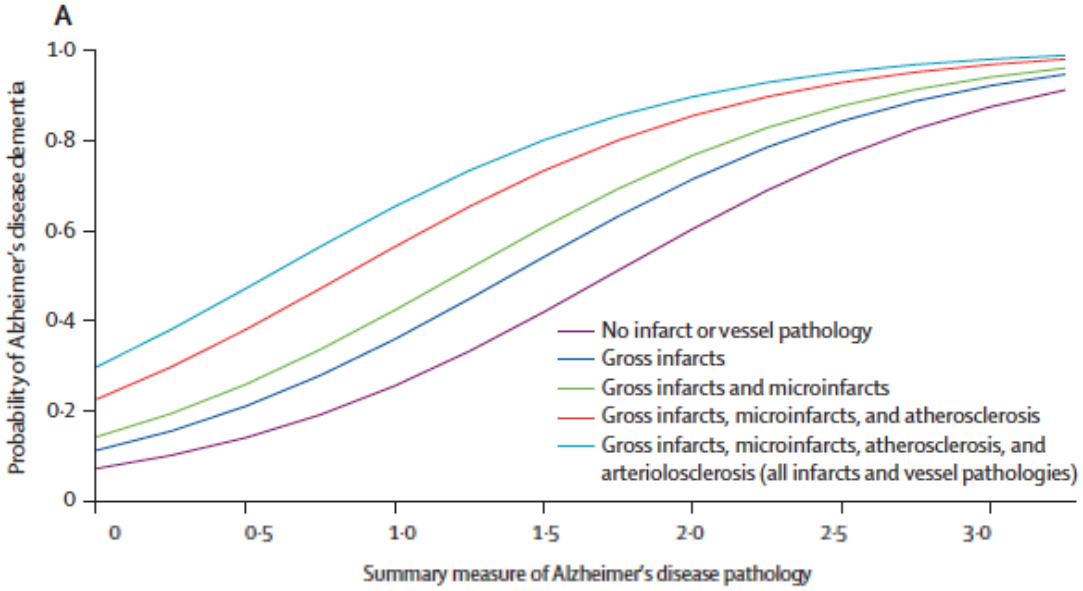
- ☑ **Patients with MCI-PD and PD-dementia had significantly more WML** than the group without MCI and dementia
- ☑ There was significant relationship between increasing total WML volume and **worse performance on executive function, memory and language**
- ☑ Although the progression of neurodegenerative process in advanced stage of PD has been recognized as being mainly responsible for cognitive impairment in PD, WML may also be a contributing factor.
- ☑ It is possible that by reducing the vascular risk factors that cause WML cognitive impairment could be prevented or slowed down

Relation of cerebral vessel disease to Alzheimer's disease dementia and cognitive function in elderly people: a cross-sectional study

Zoe Arvanitakis, Ana W Capuano, Sue E Leurgans, David A Bennett, Julie A Schneider

	No Alzheimer's disease dementia (n=665)	Alzheimer's disease dementia (n=478)	Total (n=1143)
Demographic			
Age at death (years)	87·7 (83·0–91·8)	90·3 (86·2–4·3)	88·8 (84·4–93·0)
Sex			
Women	411 (62%)	326 (68%)	737 (64%)
Men	254 (38%)	152 (32%)	406 (36%)
Education (years)	16 (13–19)	16 (13–18)	16 (13–19)
Clinical			
APOE ε4*	123 (19%)	163 (36%)	286 (26%)
Vascular risk factors†	485 (74%)	314 (68%)	799 (71%)
MMSE score	28 (26–29)	14 (5–20)	25 (16–28)
Global cognitive score‡	–0·1 (–0·5 to +0·2)	–1·8 (–2·6 to –1·3)	–0·7 (–1·6 to –0·01)
Time from last clinical assessment to death (months)	8·4 (4·8–12·3)	9·8 (5·0–16·8)	9·2 (5·0–13·4)
Neuropathological			
Vessel pathology§			
Atherosclerosis	226 (34%)	219 (46%)	445 (39%)
Arteriolosclerosis	206 (31%)	195 (41%)	401 (35%)
Brain infarcts			
Gross infarct(s)	186 (28%)	207 (43%)	393 (35%)
Microinfarct(s)	168 (25%)	154 (32%)	322 (28%)
Alzheimer's disease pathology			
Global score¶	0·4 (0·1–0·8)	1·0 (0·5–1·5)	0·6 (0·2–1·1)





☑ La malattia cerebrovascolare peggiora le performance cognitive in pz con AD e con MP

☑ La presenza di malattia cerebrovascolare abbassa la soglia di Demenza nei soggetti con diagnosi neuropatologica di AD e LBD

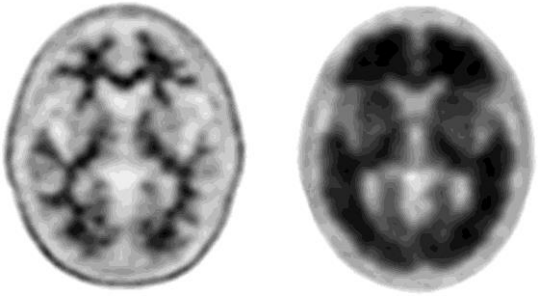
Relation of cerebral vessel disease to Alzheimer's disease dementia and cognitive function in elderly people: a cross-sectional study. Lancet Neurol 2016

☑ La neurodegenerazione di tipo Alzheimer e Malattia cerebrovascolare hanno **effetti additivi** o **interattivi** sulla Demenza

☑ Si pensa che La malattia cerebrovascolare contribuisca ai processi neuropatologici tipici dell'AD compresa l'atrofia cerebrale e l'accumulo di Beta-amiloide (*Zlokovic, 2011; Kalaria et al., 2012; Toledo et al 2013)*

JAMA | Original Investigation

Association Between Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition

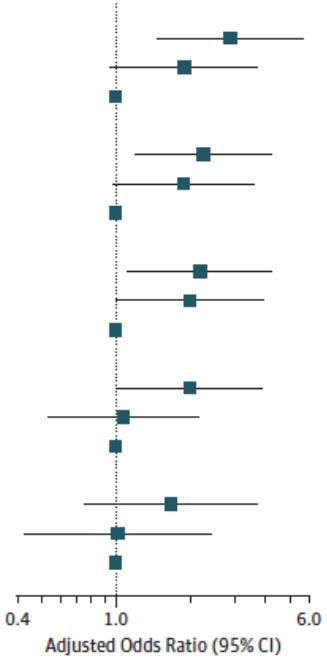


Rebecca F. Gottesman, MD, PhD; Andrea L. C. Schneider, MD, PhD; Yun Zhou, PhD; Josef Coresh, MD, PhD; Edward Green, MD; Naresh Gupta, MD; David S. Knopman, MD; Akiva Mintz, MD; Arman Rahmim, PhD; A. Richey Sharrett, MD, DrPH; Lynne E. Wagenknecht, DrPH; Dean F. Wong, MD, PhD; Thomas H. Mosley, PhD

	Midlife (Study Visit 1, 1987-1989)			Late Life (Study Visit 5, 2011-2013)		
Risk Factors	No. With Vascular Risk Factor and SUVR >1.2/Total No. With Vascular Risk Factor (%)	No. Without Vascular Risk Factor and SUVR >1.2/Total No. Without Vascular Risk Factor (%)	Adjusted OR (95% CI)[a]	No. With Vascular Risk Factor and SUVR >1.2/Total No. With Vascular Risk Factor (%)	No. Without Vascular Risk Factor and SUVR >1.2/Total No. Without Vascular Risk Factor (%)	Adjusted OR (95% CI)[a]
Body mass index ≥30[b]	54/83 (65.1)	110/239 (46.0)	2.06 (1.16-3.65)	66/121 (54.6)	98/201 (48.8)	1.44 (0.85-2.44)
Current smoking	30/55 (54.6)	134/267 (50.2)	1.15 (0.61-2.19)	9/16 (56.3)	155/306 (50.7)	1.53 (0.50-4.62)
Hypertension	55/95 (57.9)	109/227 (48.0)	1.30 (0.75-2.28)	125/230 (54.4)	39/92 (42.4)	1.29 (0.74-2.26)
Diabetes	10/20 (50.0)	154/302 (51.0)	1.06 (0.39-2.86)	68/130 (52.3)	96/192 (50.0)	1.06 (0.65-1.74)
Total cholesterol ≥200 mg/dL	101/180 (56.1)	63/142 (44.4)	1.33 (0.82-2.19)	54/94 (57.5)	110/228 (48.3)	1.17 (0.67-2.05)

Figure 1. Adjusted Odds Ratios for Global Cortex Florbetapir SUVRs >1.2 by Number of Vascular Risk Factors, Midlife Through Late Life

No. of Risk Factors by Study Visit	No. With Elevated SUVR/Total No. (%)	Adjusted Odds Ratio (95% CI)
Visit 1 (1987-1989)		
≥2	82/134 (61.2)	2.88 (1.46-5.69)
1	62/123 (50.4)	1.88 (0.95-3.73)
0	20/65 (30.8)	1 [Reference]
Visit 2 (1990-1992)		
≥2	80/137 (58.4)	2.24 (1.19-4.23)
1	57/108 (52.8)	1.88 (0.97-3.62)
0	27/77 (35.1)	1 [Reference]
Visit 3 (1993-1995)		
≥2	83/146 (56.9)	2.18 (1.12-4.26)
1	60/111 (54.1)	1.98 (1.00-3.92)
0	21/65 (32.3)	1 [Reference]
Visit 4 (1996-1998)		
≥2	93/153 (60.8)	1.98 (1.01-3.89)
1	47/111 (42.3)	1.07 (0.53-2.14)
0	24/58 (41.4)	1 [Reference]
Visit 5 (2011-2013)		
≥2	114/205 (55.6)	1.66 (0.75-3.69)
1	37/82 (45.1)	1.02 (0.43-2.43)
0	13/35 (37.1)	1 [Reference]



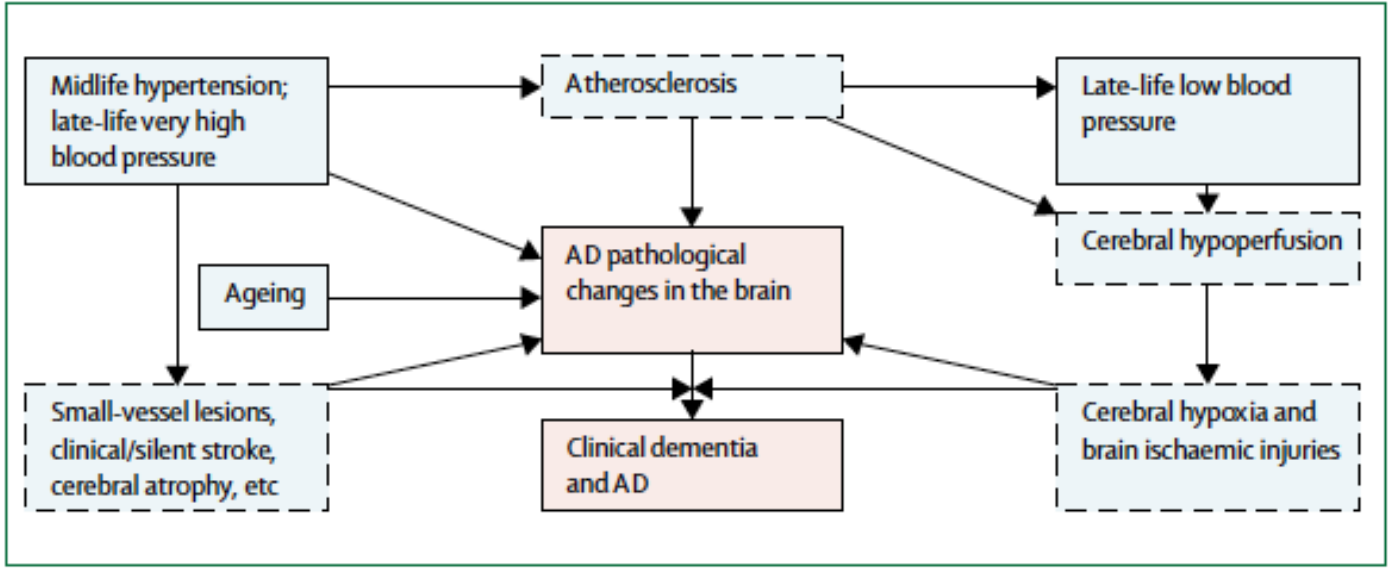
Findings In a prospective cohort study of 346 members of the community-based Atherosclerosis Risk in Communities (ARIC)–PET cohort without dementia, having 2 or more midlife vascular risk factors compared with none was significantly associated with elevated amyloid deposition in the brain (61.2% vs 30.8%). There was no significant association for late-life risk factors.

☑ AD e Malattia cerebrovascolare condividono i principali fattori di rischio tra cui l'età e i fattori di rischio vascolari (*Kling et al, 2013*)

Vascular Risk Factors

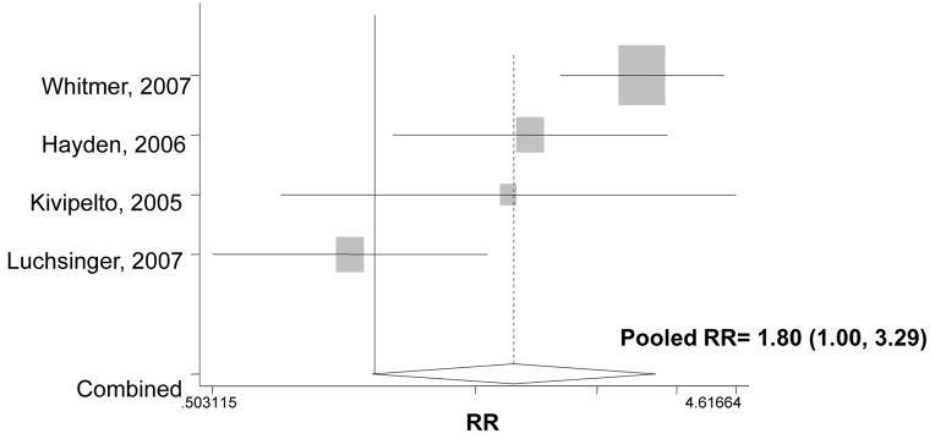
- ☑ **Hypertension in midlife was consistently associated with increased risk of AD and dementia in late life**, with five studies reporting a significant association in fully adjusted models
- ☑ **Hypertension in late life was not consistently associated with risk of AD or dementia**, with 8/13 studies reporting no significant association
- ☑ **Hypotension in late life was consistently associated with increased risk of AD and dementia**, particularly in individuals who took antihypertensive drugs suggesting that **low blood pressure later in life can be both a predictor and a contributor to AD**

Lancet Neurol 2005; 4: 487–99



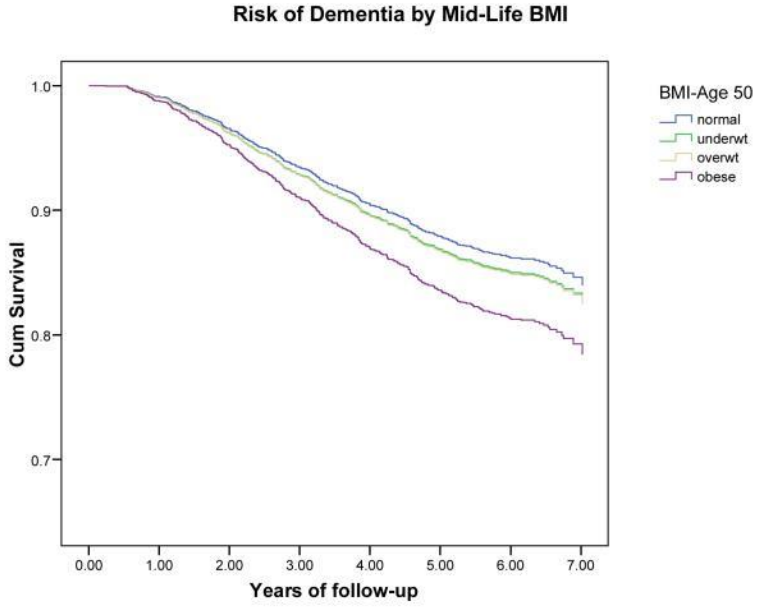
Lancet Neurol 2005; 4: 487–99

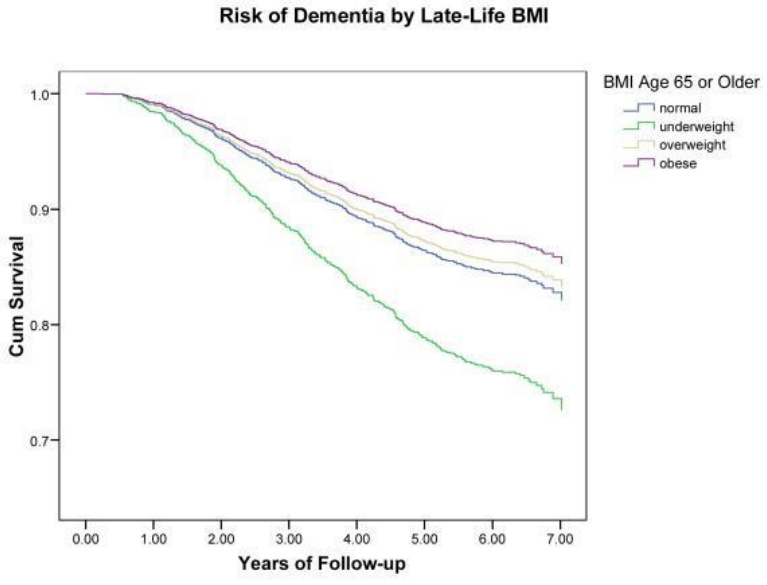
a) Obesity (BMI≥30 kgm^{-2}) vs. AD



☑ Obesity at midlife (~~☐50y) was related to a higher risk of late-life development of dementia in meta-analysis and systematic reviews

☑ The pooled OR for the association between obesity and AD was statistically significant (1.80, 95% CI 1.00–3.29) (*Beydoun MA et al, Obes Rev 2008*)



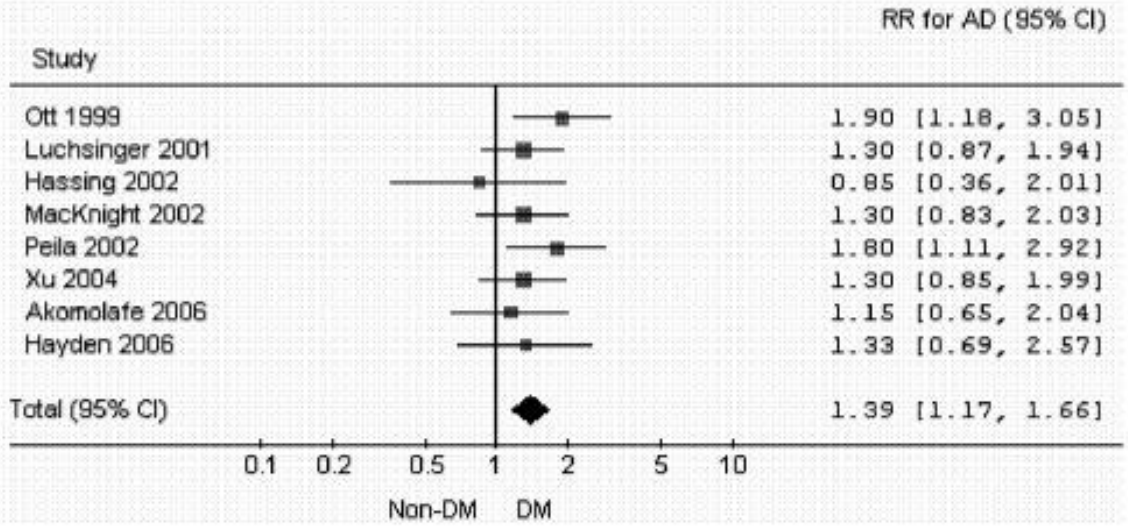


in late life, **obesity was associated with reduced dementia risk** (0.63, 0.44–0.91), whereas **being underweight was associated with increased risk** (1.62, 1.02–2.64)

Obesity in midlife seems to be a risk factor for late-life AD and late-life low BMI and weight loss can be a marker for the preclinical stage of the dementia syndrome

Fitzpatrick AL, Kuller LH, Lopez OL, et al. *Midlife and late-life obesity and the risk of dementia: cardiovascular health study*. Arch Neurol 2009; 66: 336–42.

- ☑ Pooled analysis of 8 follow-up studies has shown that diabetes was associated with a 39% increased risk of AD (RR 1.39; CI 1.16-1.66)
- ☑ Midlife diabetes is associated with an elevated risk of late-life AD



Lu, Feng-Ping et al. “Diabetes and the risk of multi-system aging phenotypes: a systematic review and meta-analysis” *PloS one* vol. 4,1 (2009)

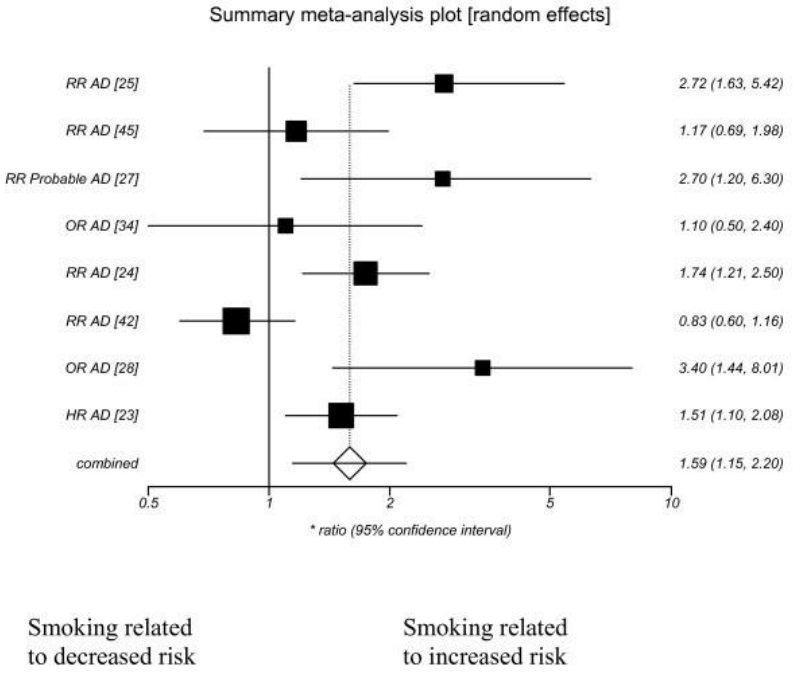
REVIEW

Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies

G. Cheng,[1] C. Huang,[2] H. Deng[1] and H. Wang[2]

	Heterogeneity test			Random effects		Fixed effects	
	Chi	d.f.	*P*	RR	95%CI	RR	95%CI
Risk for AD	47.3	15	<0.0001	1.46	1.20–1.77	1.54	1.40–1.70
Risk for VD	6.3	9	0.71	2.49	2.09–2.97	2.48	2.08–2.96
Risk for any dementia	28.9	10	0.001	1.51	1.31–1.74	1.54	1.41–1.67
Risk for mild cognitive impairment	0.1	1	0.76	1.22	1.0–1.45	1.21	1.02–1.45

95%CI, 95% confidence interval; AD, Alzheimer's disease; RR, relative risk; VD, vascular dementia.



- ☑ Early case-control studies reported that smoking was associated with a reduced risk of AD (*Almeida OP at al, Addiction 2002*)
- ☑ Recent longitudianl studies found that present smoking is associated whit increased risk of dementia [RR 1.27, 95% VI 1.02-1.60] (*Anstey KJ et al. Am J Epidem*, 2007)

CLINICAL REVIEW

Cholesterol as a Risk Factor for Dementia and Cognitive Decline: A Systematic Review of Prospective Studies With Meta-Analysis

Kaarin J. Anstey, Ph.D., Darren M. Lipnicki, Ph.D., Lee-Fay Low, Ph.D.

- ☑ High total cholesterol at midlife was more consistently associated with an increased risk of AD diagnosed more than 20 years later
- ☑ No or inverse association in older people
- ☑ Decreasing total cholesterol in late life may reflect ongoing disease process and thus could be a marker for future devlopment of AD

SOCIETÀ ITALIANA DI NEUROLOGIA

ELSEVIER

Alzheimer's & Dementia 10 (2014) 562–570

Alzheimer's & Dementia

Midlife risk score for the prediction of dementia four decades later

Lieza G. Exalto[a,b], Charles P. Quesenberry[a], Deborah Barnes[c], Miia Kivipelto[d], Geert Jan Biessels[a], Rachel A. Whitmer[b,*]

Step 1

Age, y	Points
40–46	0
47–53	3
54–55	4

Step 2

Education, y	Points
0–6	3
7–9	2
>9	0

Step 3

Sex	Points
Men	1
Female	0

Step 4

Cholesterol, mg/dL	Points
<251	0
≥251	2

Step 5

BMI, kg/m²	Points
<30	0
≥ 30	2

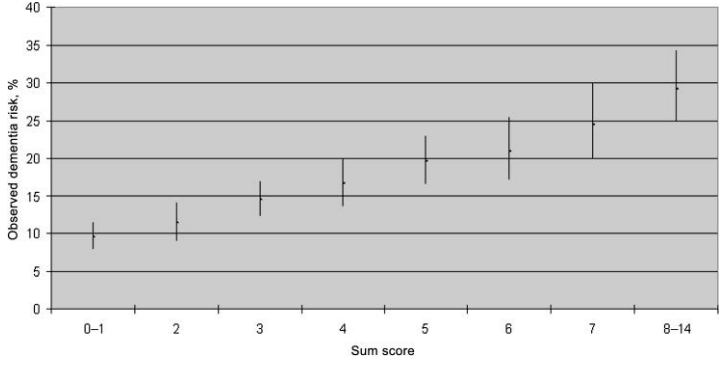
Step 6

Systolic blood Pressure, mm/Hg	Points
<140	0
>140	2

Add up points from stepts 1 through 6, then look up predicted 40-years risk of dementia.

Predicted 40-year risk of dementia

Total points	40–Year risk, %
0–1	10
2	11
3	15
4	17
5	20
6	21
7	25
8 –14	29



	WMH volume *Standardized β-coefficient (p-value)*	MTA score(visual rating) *RR (95% CI)*	GM volume *Standardized β-coefficient (p-value)*
CAIDE Risk Score			
• <10 points ($n=41$)	ref.	ref.	ref.
• ≥10 points ($n=25$)	**0.27 (0.036)**	**1.91 (1.16–2.34)**	0.01 (0.885)

Potential for primary prevention of Alzheimer's disease: an analysis of population-based data

Sam Norton, Fiona E Matthews, Deborah E Barnes, Kristine Yaffe, Carol Brayne

	Relative risk (95% CI)*	Communality (%)†
Diabetes mellitus	1·46 (1·20–1·77)	50·9%
Midlife hypertension	1·61 (1·16–2·24)	65·0%
Midlife obesity	1·60 (1·34–1·92)	43·7%
Physical inactivity	1·82 (1·19–2·78)	49·0%
Depression	1·65 (1·42–1·92)	37·4%
Smoking	1·59 (1·15–2·20)	58·1%
Low educational attainment	1·59 (1·35–1·86)	45·6%

Lancet Neurol 2014; 13: 788–94

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälahti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilkka Soininen, Miia Kivipelto

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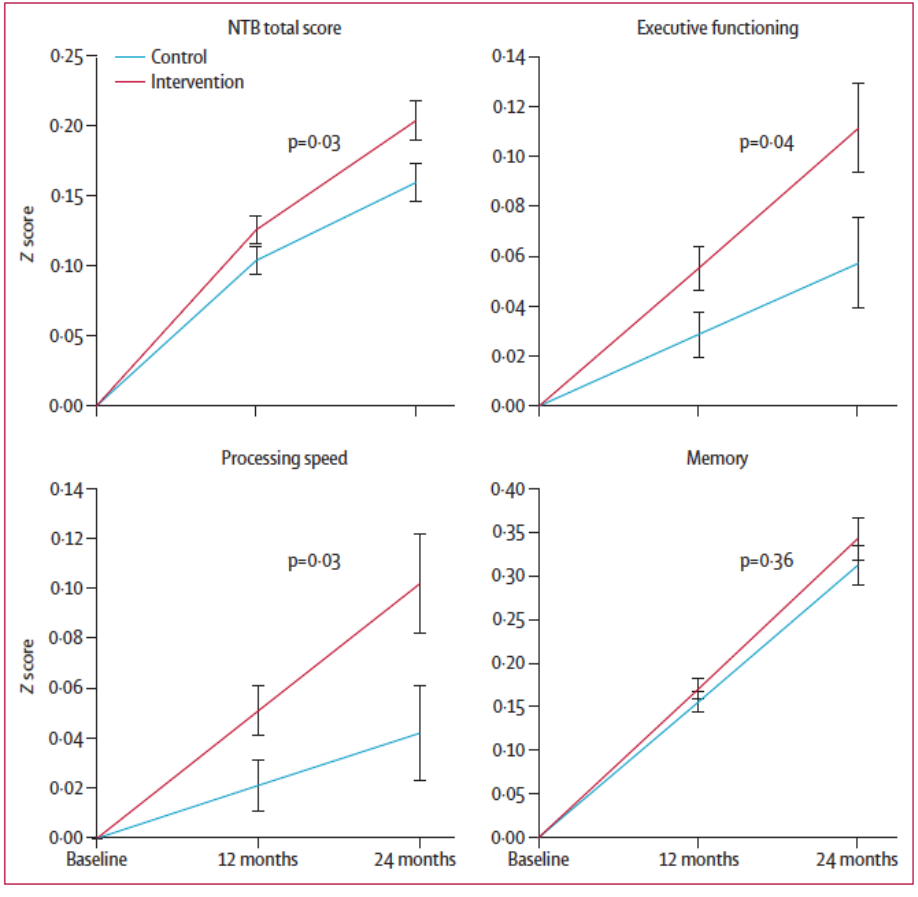

Lancet 2015; 385: 2255–63

	Odds ratio (95% CI)		p value
	Intervention (n=554)	Control (n=565)	
Overall cognitive decline			
NTB total score	1 (reference)	1·31 (1·01–1·71)	0·04
Cognitive decline per domain			
NTB memory score	1 (reference)	1·23 (0·95–1·60)	0·12
NTB executive functioning score	1 (reference)	1·29 (1·02–1·64)	0·04
NTB processing speed score	1 (reference)	1·35 (1·06–1·71)	0·01

The projected effect of risk factor reduction on Alzheimer's disease prevalence

Deborah E Barnes, Kristine Yaffe

	Relative risk (95% CI)*	Communality (%)†
Diabetes mellitus	1·46 (1·20–1·77)	50·9%
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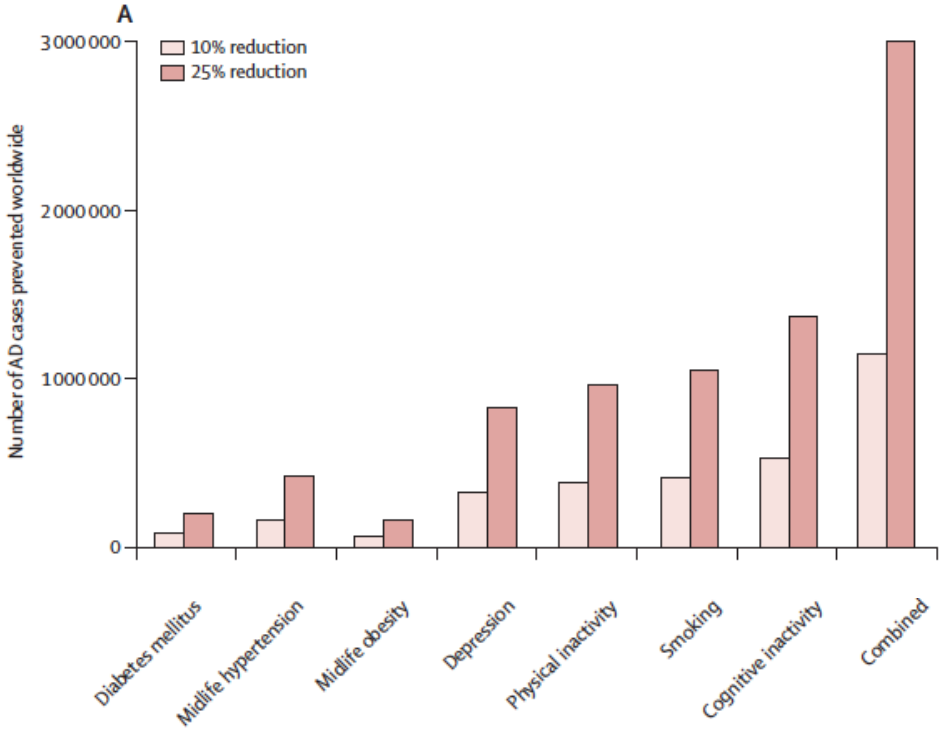


Lancet Neurol 2011; 10: 819–28

Potential for primary prevention of Alzheimer's disease: an analysis of population-based data

Sam Norton, Fiona E Matthews, Deborah E Barnes, Kristine Yaffe, Carol Brayne

Diabetes mellitus
Adult prevalence of diagnosed diabetes mellitus between the ages of 20 years and 79 years

Midlife hypertension
Adult midlife prevalence of hypertension between the ages of 35 years and 64 years

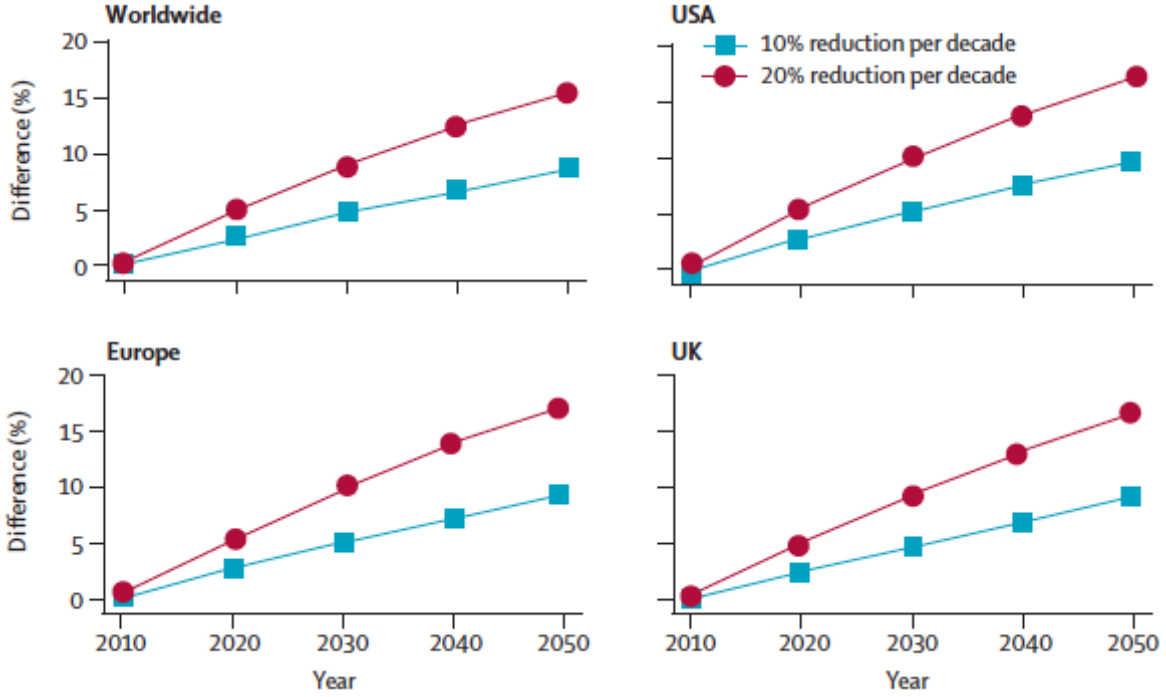
Midlife obesity
Adult midlife prevalence of body-mass index greater than 30 kg/m² between the ages of 35 years and 64 years

Physical inactivity
Proportion of adults who do not do either 20 min of vigorous activity on 3 or more days or 30 min of moderate activity on 5 or more days per week

Depression
Lifetime prevalence of major depressive disorder using Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases criteria

Smoking
The proportion of adult smokers

Low educational attainment
The proportion of adults with an International Standard Classification of Education[15] level of 2 or less (pre-primary, primary, and lower secondary education)



Lancet Neurol 2014; 13: 788–94

Take-home message

- ☑ La malattia cerebrovascolare è strettamente correlata con i processi di neurodegenerazione sia in senso epidemiologico e che patogenetico
- ☑ Il fallimento dei trial clinici delle *disease-modifying therapies* per l'AD potrebbe essere dovuto all'esclusione della patologia vascolare sia nei target farmacologici che nella selezione dei pazienti
- ☑ I nuovi trial dovranno tenere in considerazione anche la patologia vascolare
- ☑ Il trattamento delle malattie neurodegenerative deve necessariamente passare attraverso una corretta individuazione e trattamento di tutti i fattori di rischio vascolari soprattutto nelle fasi precoci di malattia e in prevenzione primaria durante la *mid-life.*

The projected effect of risk factor reduction on Alzheimer's disease prevalence

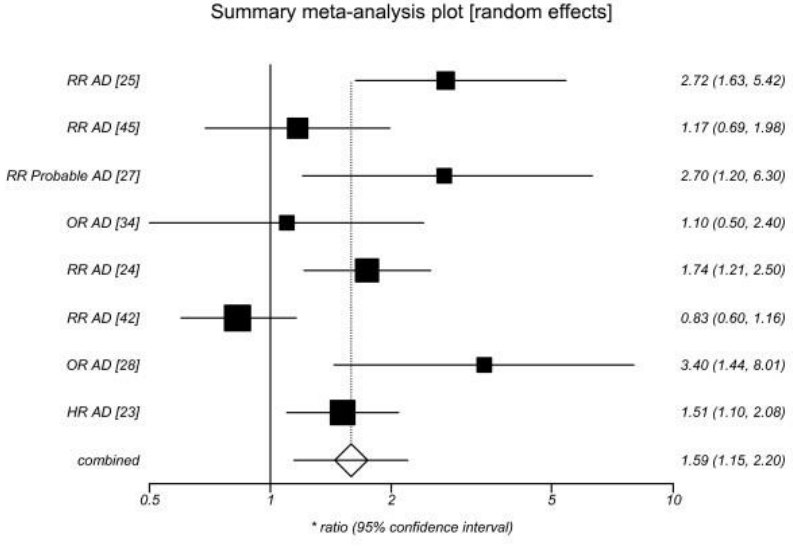
Deborah E Barnes, Kristine Yaffe

The top six relative risk factors for dementia

Risk factor	Relative risk (RR)[1]
Diabetes mellitus	1.39
Midlife Hypertension (untreated)	1.61
Midlife Obesity (BMI>=30)	1.60
Depression	1.90
Physical Inactivity	1.82
Smoking	1.59

[1] D Barnes and K Yaffe, "The projected effect of risk factor reduction on Alzheimer's disease prevalence", The Lancet Neurology 2011:10:9;819-828

Lancet Neurol 2011; 10: 819–28



Smoking related
to decreased risk

Smoking related
to increased risk

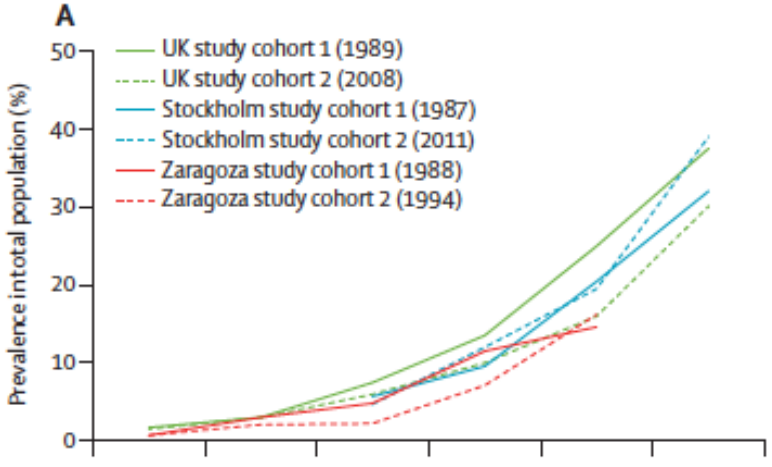
Cochrane Library

Cochrane Database of Systematic Reviews

Effect of the treatment of Type 2 diabetes mellitus on the development of cognitive impairment and dementia (Review)

Areosa Sastre A, Vernooij RWM, González-Colaço Harmand M, Martínez G

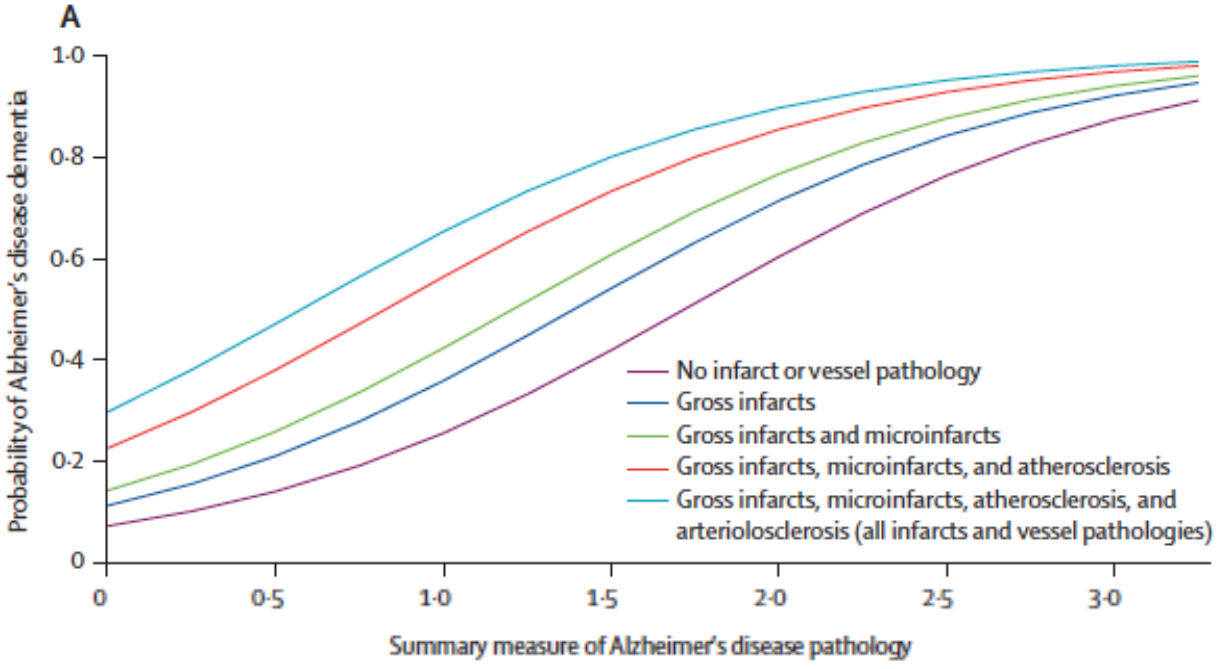
We found no good evidence that any specific treatment or treatment strategy for Type 2 diabetes can prevent or delay cognitive impairment



Dementia in western Europe: epidemiological evidence andimplications for policy making

Lancet Neurol 2015

	Odds ratio (95% CI)	p value
Alzheimer's disease pathology	4·40 (3·45–5·61)	<0·0001
Gross infarcts	1·63 (1·21–2·20)	0·0014
Microinfarcts	1·31 (0·96–1·78)	0·084
Atherosclerosis	1·33 (1·11–1·58)	0·0020
Arteriolosclerosis	1·20 (1·04–1·40)	0·016



Relation of cerebral vessel disease to Alzheimer's disease dementia and cognitive function in elderly people: a cross-sectional study. Lancet Neurol 2016

☑La malattia cerebrovascolare aumenta la probabilità di diagnosi di AD in modo indipendente dalla neurodegenerazione di tipo Alzheimer

Variable	FTLD-Tau	FTLD-TDP	α-Synucleinopathy	Hippocampal sclerosis	Prion	Unremarkable brain	Cerebrovascular disease
Large infarcts	2.0 (0.006)	2.3 (0.036)	1.4 (0.10)	0.9 (0.79)	–[a]	1.5 (0.12)	0.42 (<0.0001)
Multiple microinfarcts	2.4 (<0.0001)	2.4 (0.004)	2.0 (0.0006)	0.6 (0.79)	–[a]	1.5 (0.06)	0.4 (<0.0001)
Lacunes	1.3 (0.17)	2.3 (0.01)	1.3 (0.19)	0.7 (0.19)	–[a]	1.5 (0.05)	0.4 (<0.0001)
Arteriosclerotic leukoencephalopathy	1.6 (0.07)	1.5 (0.20)	1.1 (0.74)	0.3 (0.004)	–[a]	5.5 (0.003)	0.2 (<0.0001)
Haemorrhage	2.1 (0.03)	1.9 (0.15)	1.4 (0.26)	1.9 (0.30)	–[a]	1.8 (0.10)	0.6 (0.022)
Atherosclerosis	1.4 (0.02)	1.2 (0.38)	1.4 (0.01)	1.0 (0.89)	4.0 (0.004)	2.8 (<0.0001)	0.7 (0.006)
Arteriolosclerosis	1.3 (0.13)	2.4 (0.0001)	1.6 (0.005)	0.7 (0.22)	4.8 (0.0005)	3.6 (<0.0001)	0.4 (<0.0001)
Cerebral amyloid angiopathy	12.4 (<0.0001)	9.2 (<0.0001)	6.6 (<0.0001)	9.1 (<0.0001)	20.0 (<0.0001)	6.2 (<0.0001)	7.2 (<0.0001)

Table 4 Prevalence of vascular risk factors and cardiovascular disease

	Alzheimer's disease	FTLD-Tau	FTLD-TDP	α-Synucleinopathy	Hippocampal sclerosis	Prion	Unremarkable brain	Cerebrovascular disease	*P*-value
Number of cases	845	118	86	102	24	44	35	87	
Coronary heart disease, %	18.0	12.7	4.7	16.7	20.8	6.8	37.1	23.0	0.0008
Atrial fibrillation, %	13.7	8.5	3.5	17.6	20.8	2.3	22.8	26.7	0.0008
Hypertension, %	56.2	55.1	36.5	52.0	75.0	45.5	70.6	75.6	0.0008
Hypercholesterolaemia, %	47.4	45.1	35.3	45.5	45.8	43.2	51.4	46.5	0.65
Diabetes, %	12.2	8.5	8.1	10.8	16.7	13.6	20.0	14.9	0.61
Smoking history, %	44.2	56.1	42.9	46.5	62.5	39.0	58.8	49.4	0.13