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SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA
21-24 Novembre 2012

13° Corso Infermieri
22-23 Novembre 2012

Milano

PROGRAMMA



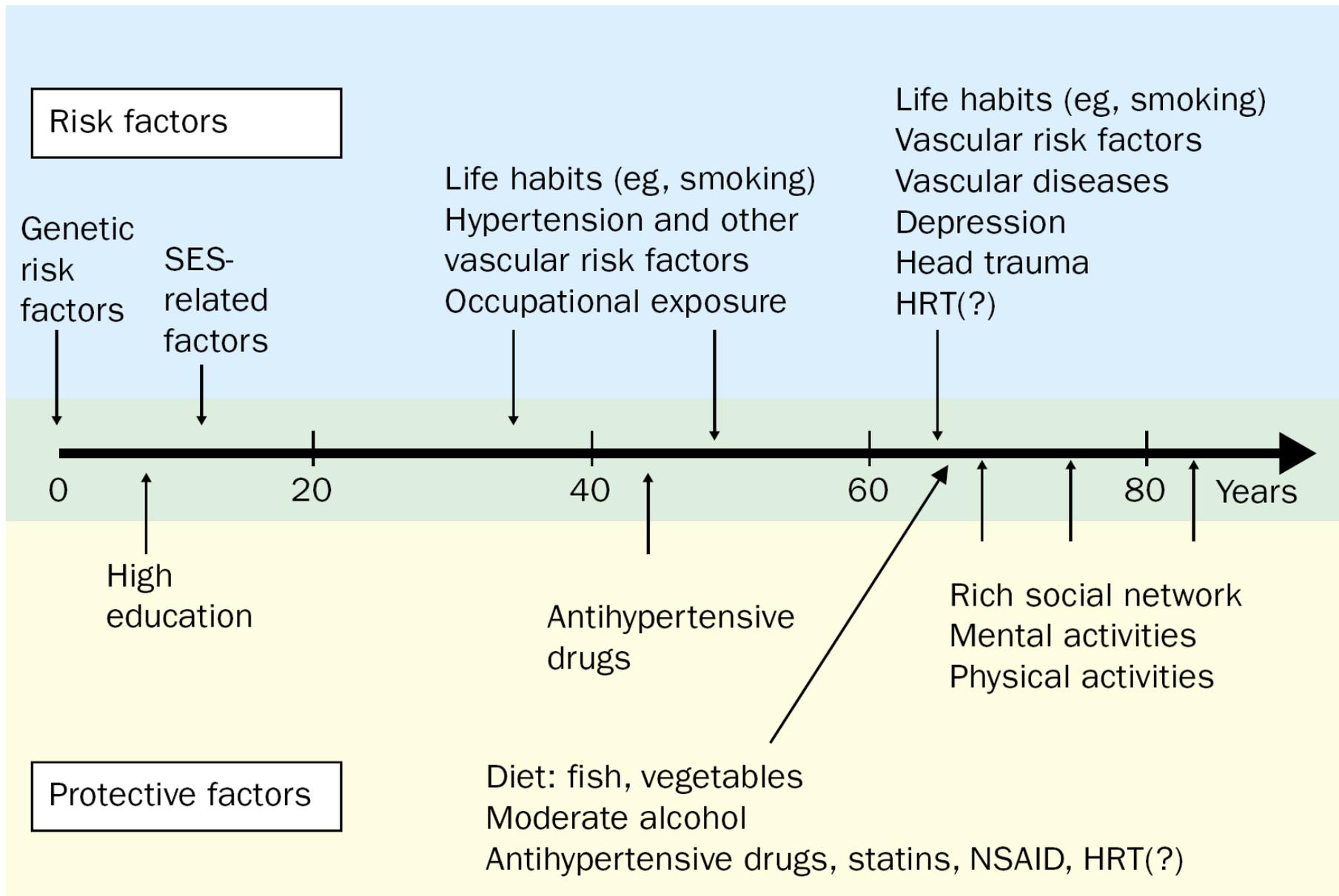
**ASSOCIAZIONE ITALIANA
PSICOGERIATRIA**
Sezione Regionale Campana



**Ipertensione arteriosa e
decadimento cognitivo**

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Hypertension, have a negative correlation with cognitive functions, especially with memory, attention and executive functions (Hanon 2005, Vicario 2005)

Long-term high blood pressure interferes with brain perfusion leading to chronic ischemic lesions and silent strokes (Staessen 1997, Ciobica 2009)

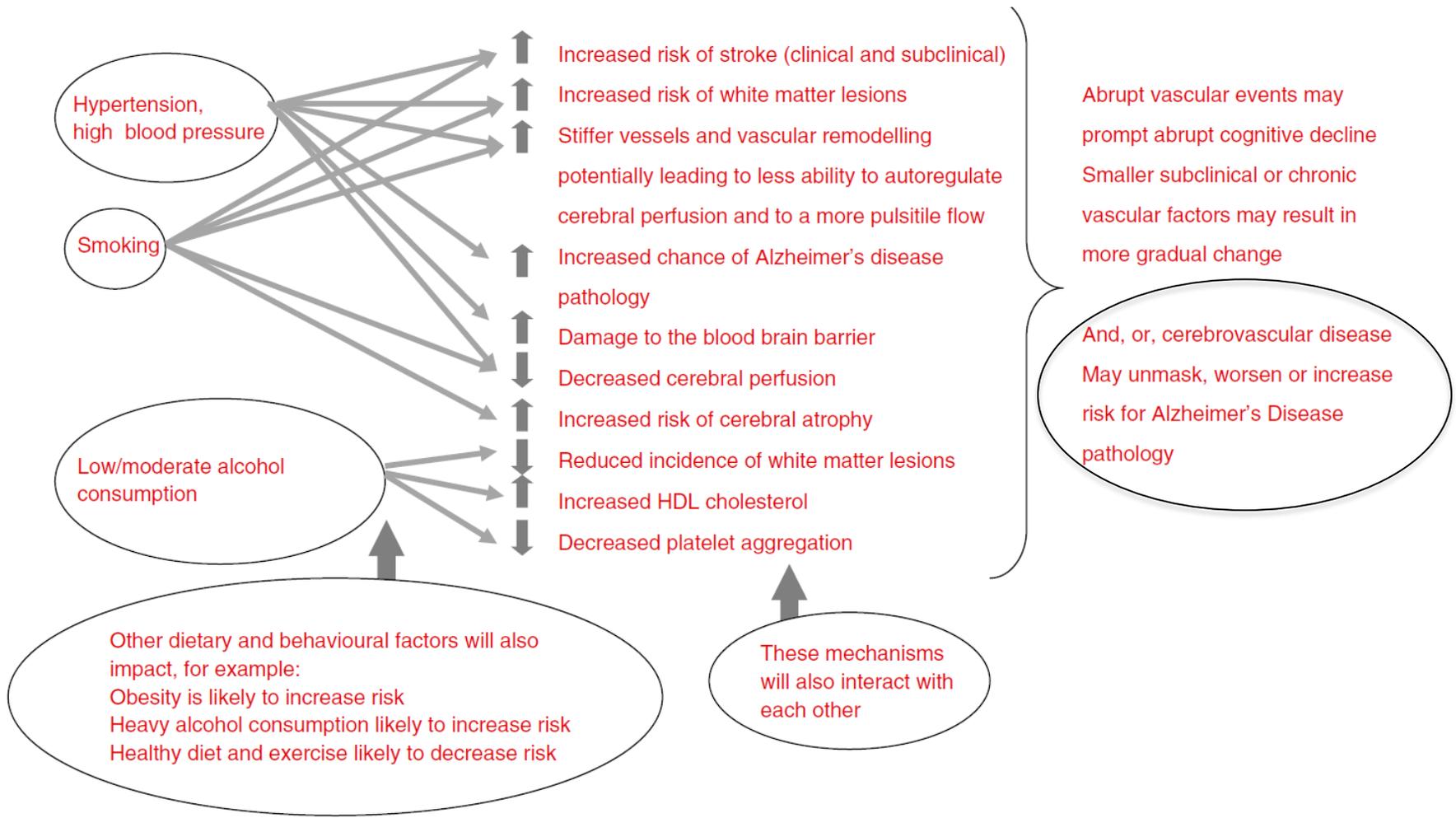
Hypertension can be also involved in amyloid β deposits or neurofibrillary tangles formation (Lee 2003, Bomboi 2010)

Chronic hypertension lead to ventricular enlargement, silent infarct, white matter lesions and brain atrophy, when compared to normotensive individuals Vermeer 2003, Takeda 2008, Nagai 2010). These brain changes could determine cognitive regression which is often found in patients with chronic hypertension (Takeda 2008, Ciobica 2009)

The reduction of systolic blood pressure may have a protective effect against cognitive impairment (Fogari 2003, 2006).

Blood pressure, smoking and alcohol use, association with vascular dementia

Ruth Peters*



Hypertension and dementia.

Nagai M, Hoshida S, Kario K.

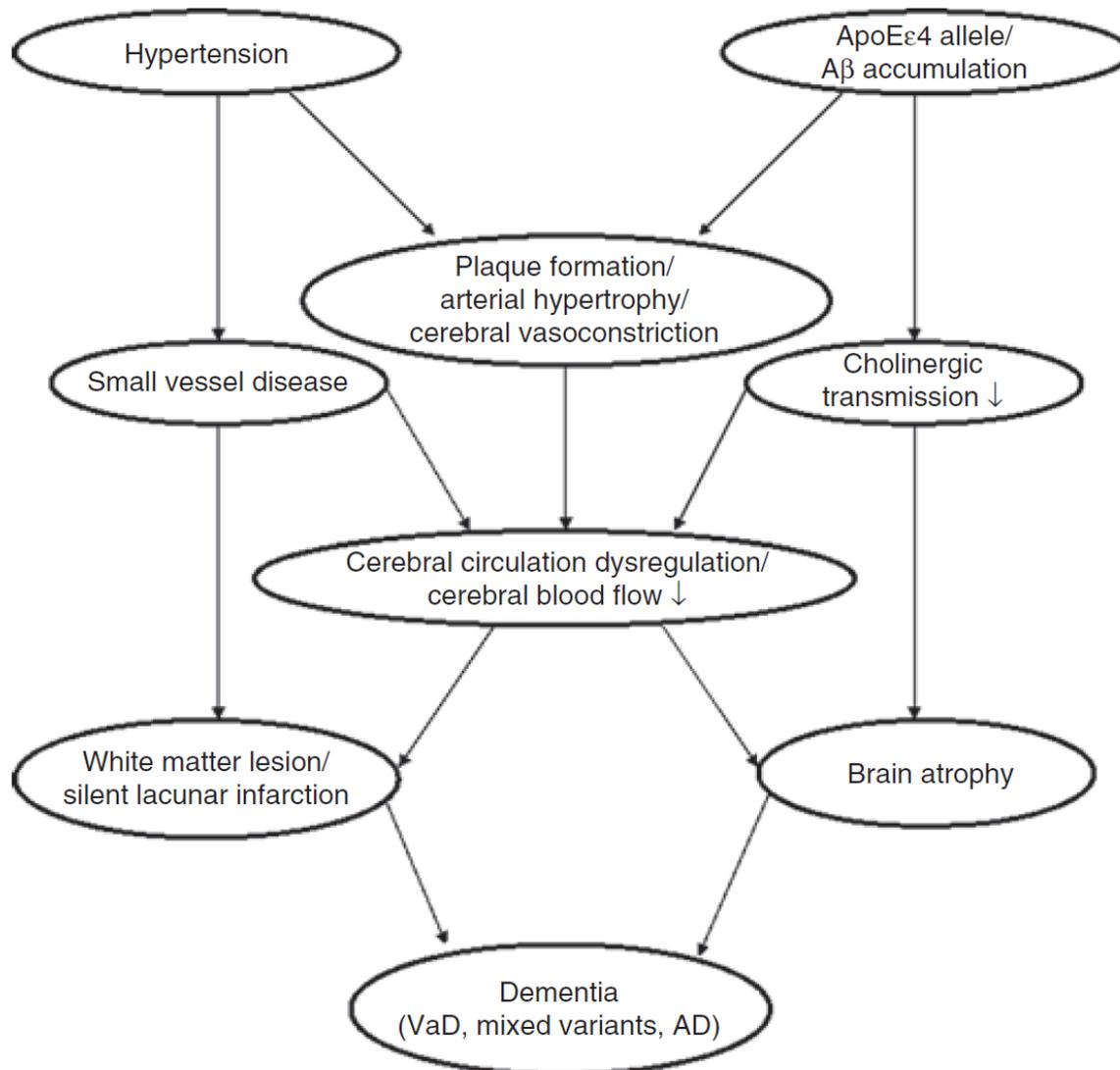
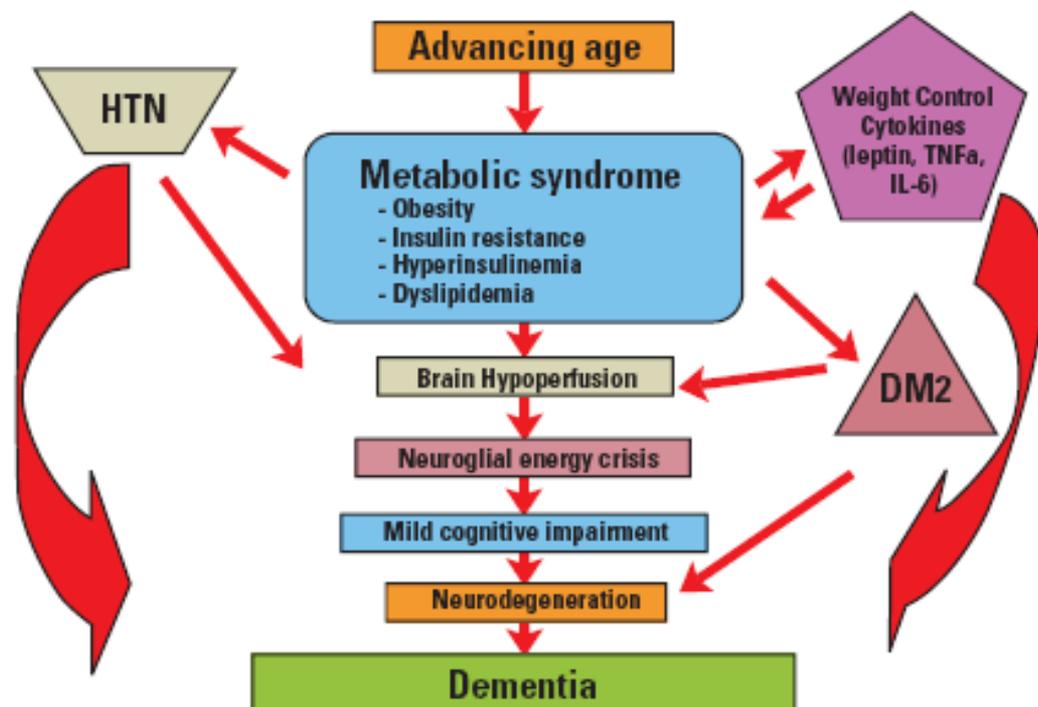


FIGURE.

Potential relationships between components of the metabolic syndrome and the development of Alzheimer's disease: *A link to a vascular etiology?*⁶¹

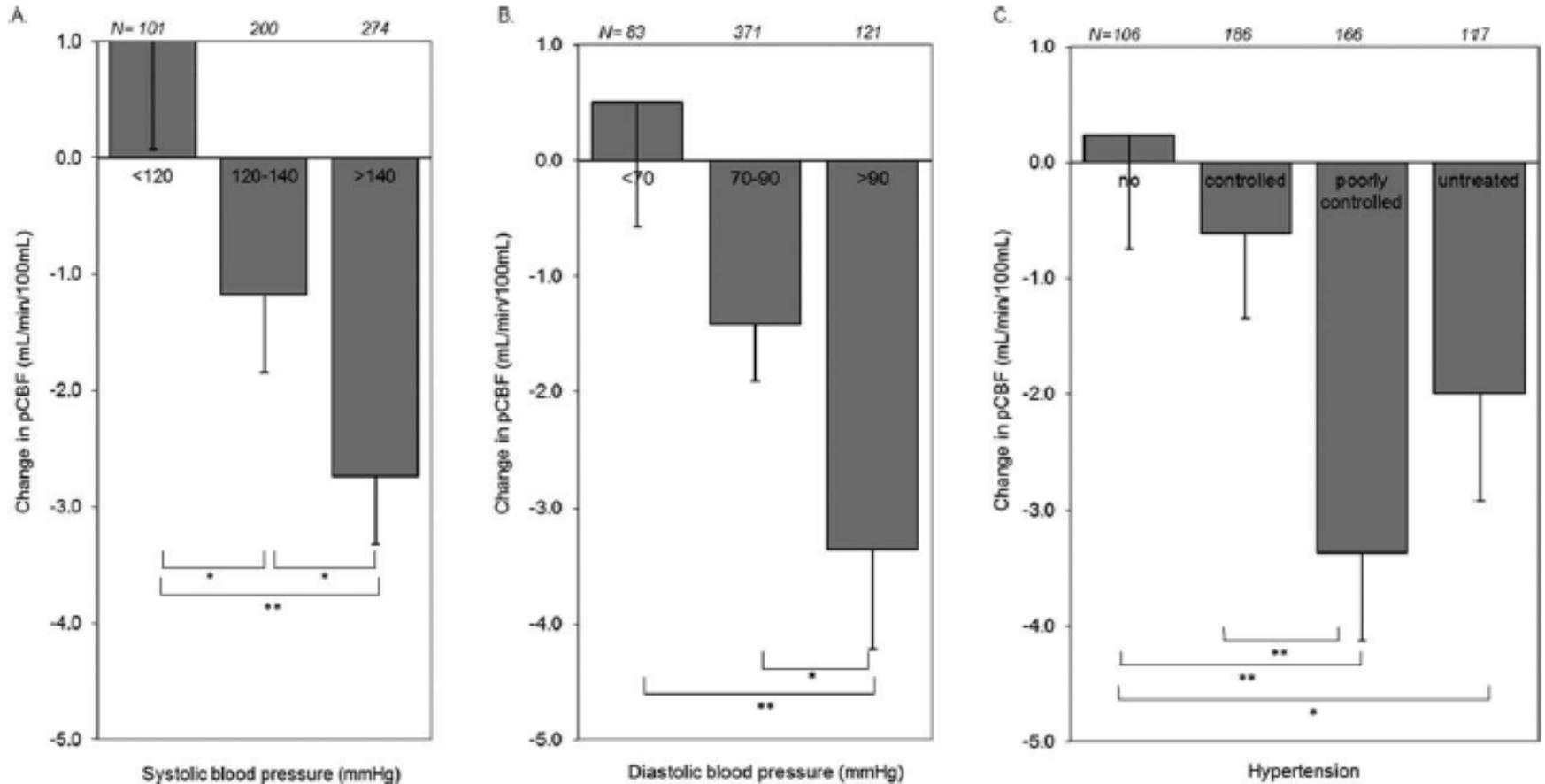


HTN=hypertension; TNF α ; tumor necrosis factor-alpha; IL=interleukin; DM2=type 2 diabetes mellitus.

de la Torre JC. Is Alzheimer's disease a neurodegenerative or a vascular disorder? Data, dogma, and dialectics. *Lancet Neurol.* 2004;3:184-190. Adapted with permission from Elsevier Limited. Copyright 2004.

Milionis HJ, Florentin M, Giannopoulos S. *CNS Spectr.* Vol 13, No 7. 2008.

Hypertension and Longitudinal Changes in Cerebral Blood Flow: The SMART-MR Study



Vascular risk factors promote conversion from mild cognitive impairment to Alzheimer disease

	No. (%)	Crude HR for AD (95% CI)	p ^a	Adjusted HR for AD (95% CI)	p ^b
VRF	414 (53.2)	2.415 (1.189-4.904)	0.015 ^c	2.036 (1.331-3.114)	0.001 ^c
Hypertension	216 (27.8)	1.996 (1.015-3.922)	0.045 ^c	1.835 (1.186-2.840)	0.006 ^c
Diabetes	136 (17.5)	1.917 (1.212-3.031)	0.005 ^c	1.620 (1.003-2.616)	0.049 ^c

All	No. (%)	Crude HR for AD (95% CI)	p ^a	Adjusted HR for AD (95% CI)	p ^b
Treatment of VRF					
Some treated	173 (41.8)	0.627 (0.399-0.986)	0.043 ^c	0.735 (0.579-0.933)	0.017 ^c
All treated	138 (33.3)	0.574 (0.344-0.959)	0.034 ^c	0.614 (0.386-0.976)	0.039 ^c
Treatment of hypertension	137 (63.4)	0.804 (0.764-0.847)	<0.001 ^c	0.847 (0.798-0.900)	<0.001 ^c

Vascular Contributions to Cognitive Impairment and Dementia

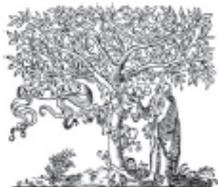
A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

5.1. Cerebral Amyloid Angiopathy (CAA) and Vascular Effects of *A*beta

.....**CAA is a common pathology in the elderly**, appears in 10% to 30% of unselected brain autopsies and 80% to 100% when in the presence of accompanying Alzheimer disease.

Advanced CAA can trigger a series of **destructive changes in the vessel wall**, including loss of smooth muscle cells, development of microaneurysms, and fibrinoid necrosis of the vessel wall.

CAA is most commonly recognized as a cause of spontaneous **intracerebral hemorrhage**, it is an important contributor to age-related cognitive impairment. Population-based clinical pathological studies have identified associations between **advanced CAA and worse cognitive performance**.



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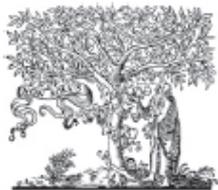
Alzheimer's & Dementia 7 (2011) 280–292

Alzheimer's
&
Dementia

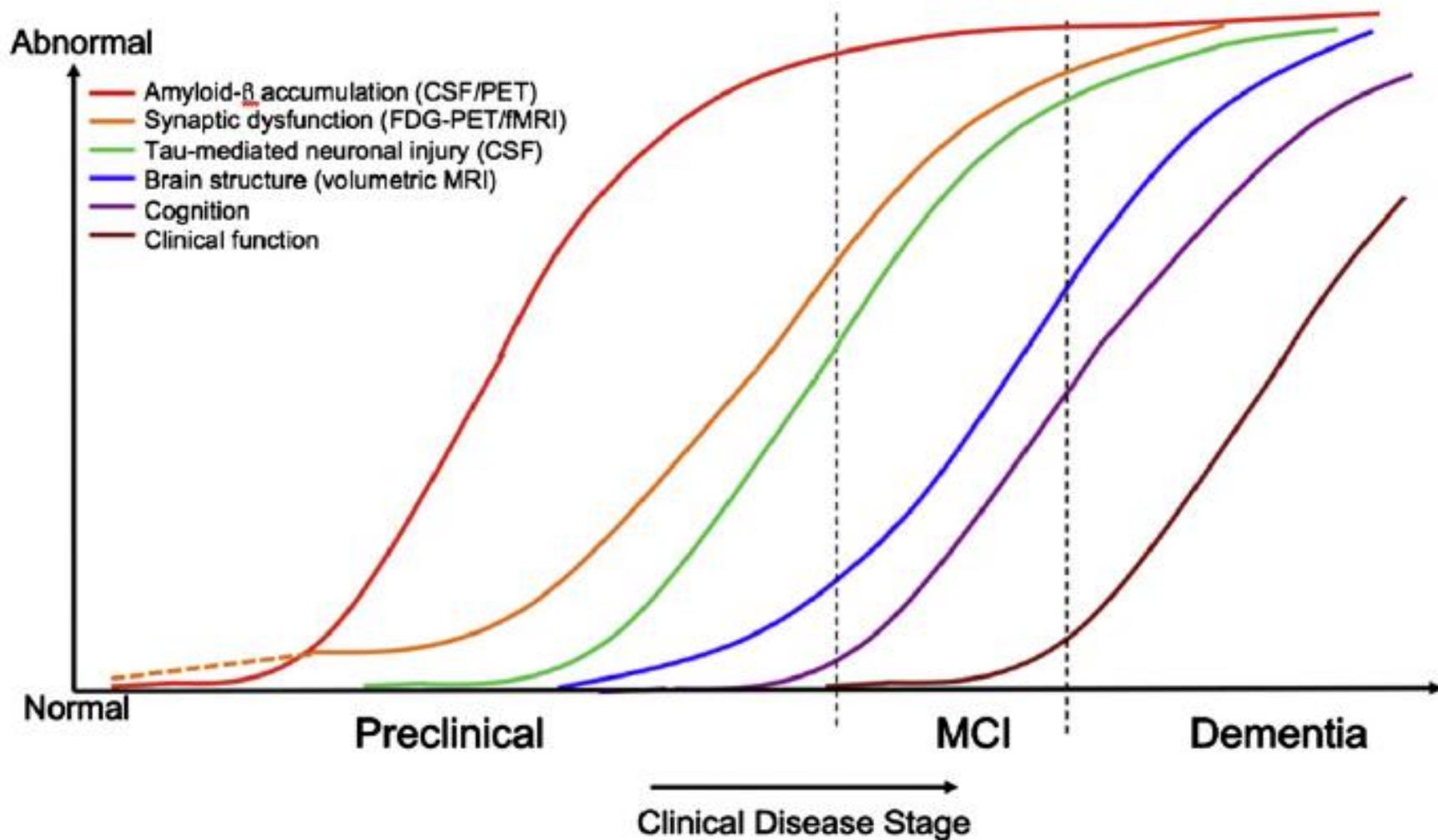
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Toward defining the preclinical stages of Alzheimer's disease:
Recommendations from the National Institute on Aging-Alzheimer's
Association workgroups on diagnostic guidelines
for Alzheimer's disease

Reisa A. Sperling^{a,*}, Paul S. Aisen^b, Laurel A. Beckett^c, David A. Bennett^d, Suzanne Craft^e,
Anne M. Fagan^f, Takeshi Iwatsubo^g, Clifford R. Jack, Jr.^h, Jeffrey Kayeⁱ, Thomas J. Montine^j,
Denise C. Park^k, Eric M. Reiman^l, Christopher C. Rowe^m, Eric Siemersⁿ, Yaakov Stern^o,
Kristine Yaffe^p, Maria C. Carrillo^q, Bill Thies^q, Marcelle Morrison-Bogorad^r, Molly V. Wagster^r,
Creighton H. Phelps^r



ELSEVIER



Int J Geriatr Psychiatry 2012; 27: 313–320.

Discharge diagnosis and comorbidity profile in hospitalized older patients with dementia

Giovanni Zuliani^{1,2}, Matteo Galvani¹, Fotini Sioulis¹, Francesco Bonetti¹, Stefano Prandini¹, Benedetta Boari³, Franco Guerzoni⁴ and Massimo Gallerani³

Table 3 Prevalence of the most common secondary diagnosis clusters in 4466 consecutive hospitalized older patients with a diagnosis of dementia and equivalent prevalence in 47,372 hospitalized older controls

	Dementia (<i>n</i> ^a = 4466)	Controls (<i>n</i> ^a = 47,372)	<i>p</i>
	Secondary diagnosis (%)	Secondary diagnosis (%)	
Atherosclerosis	32.9	27.3	0.001
Hypertension	27.3	34.2	0.001
CAD	19.5	20.2	0.31
BUD	13.8	4.9	0.001
CHF	12.2	12.7	0.29
Ischemic stroke–TIA	11.5	10.1	0.003
Fractures	11.4	8.1	0.001
Pneumonia–pleurisy	11.1	6.8	0.001
COPD	9.9	8.6	0.005
Code V	8.9	16.4	0.001
Cancer	8.9	18.0	0.001
Anemia	8.8	8.2	0.21
Kidney diseases	8.5	8.2	0.51
Hypertensive cardiopathy	8.1	10.0	0.001
Enthesopathies	8.0	1.6	0.001
Delirium	7.5	1.0	0.001
FED	7.3	1.4	0.001
Skin diseases	7.0	3.1	0.001

^aMedian (interquartile range).

CAD, coronary artery disease; BUD, bladder–urethral disorders; CHF, congestive heart failure; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; FED, fluids–electrolytes disorders.

Depression, hypertension, and comorbidity: Disentangling their specific effect on disability and cognitive impairment in older subjects

Angelo Scuteri^{a,*}, Liana Spazzafumo^b, Luca Cipriani^a, Walter Gianni^a, Andrea Corsonello^c, Luca Cravello^d, Lazzaro Repetto^e, Silvia Bustacchini^f, Fabrizia Lattanzio^f, Maurizio Sebastiani^g

.....depression per se' or co-occurrence of hypertension and depression is associated with **higher functional disability** and cognitive impairment in older subjects. This effect is not attributable to the number or to the severity of comorbidities.

Table 2Determinants of disability in the category $ADL \leq 3$, $n=1244$ or 20.1%, OR (95%CI).

	Model 1	<i>p</i> <	Model 2	<i>p</i> <
Age (year)	1.11 (1.09–1.12)	0.001	1.10 (1.08–1.11)	0.001
Female sex	1.48 (1.29–1.70)	0.001	1.61 (1.40–1.85)	0.001
No. of comorbidities			1.09 (1.02–1.17)	0.01
Severity of comorbidities			2.40 (1.67–3.44)	0.001
Normotension (ref)	1.00		1.00	
Hypertension	1.29 (1.06–1.57)	0.01	1.15 (0.95–1.38)	0.149
Depression	2.66 (2.28–3.12)	0.001	2.24 (1.90–2.64)	0.001
Depression and hypertension	2.53 (2.04–3.13)	0.001	2.02 (1.60–2.54)	0.001

Table 3Determinants of disability in the category $IADL \leq 4$: $n=2604$ or 42.1%, OR (95%CI).

	Model 1	<i>p</i> <	Model 2	<i>p</i> <
Age (year)	1.11 (1.10–1.13)	0.001	1.11 (1.09–1.12)	0.001
Female sex	0.62 (0.55–0.69)	0.001	0.64 (0.57–0.72)	0.01
No. of comorbidities			1.07 (1.01–1.13)	0.051
Severity of comorbidities			2.73 (2.00–3.73)	0.001
Normotension (ref)	1.00		1.00	
Hypertension	1.12 (0.96–1.30)	0.146	1.04 (0.90–1.19)	0.629
Depression	2.97 (2.60–3.40)	0.001	2.71 (2.34–3.13)	0.001
Depression and hypertension	2.45 (2.04–2.96)	0.001	1.95 (1.59–2.40)	0.001

Table 4Determinants of cognitive impairment ($MMSE < 21$, $n=1495$ or 24.2%), OR (95%CI).

	Model 1	<i>p</i> <	Model 2	<i>p</i> <
Age (year)	1.07 (1.05–1.08)	0.001	1.06 (1.05–1.07)	0.001
Female sex	1.42 (1.25–1.61)	0.001	1.49 (1.31–1.69)	0.001
No. of comorbidities			1.11 (1.04–1.18)	0.002
Severity of comorbidities			1.28 (0.91–1.83)	0.152
Normotension (ref)	1.00		1.00	
Hypertension	1.10 (0.92–1.32)	0.296	1.03 (0.87–1.22)	0.718
Depression	2.70 (2.33–3.13)	0.001	2.34 (2.01–2.72)	0.001
Depression and hypertension	2.69 (2.21–3.29)	0.001	2.21 (1.79–2.74)	0.001

Hypertension and dementia.

Nagai M, Hoshida S, Kario K.

HYPERTENSION AND DEMENTIA

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Study	Subjects	Blood pressure classification	Outcome	Follow-up period	Results (odds ratio or relative risk; 95% CI)
Launer <i>et al.</i> ¹⁹	3,703 Japanese-American men; never treated hypertensives 57%	DBP; severe high (≥ 95 mm Hg); high (90–94 mm Hg); normal (80–89 mm Hg), SBP; severe high (≥ 160 mm Hg); high (140–159 mm Hg); normal (110–139 mm Hg)	Dementia	27 (years)	Among those never treated, the risk for dementia was 3.8 (1.6–8.7) for severe high DBP, and 4.3 (1.7–10.8) for high DBP; the risk for dementia was 4.8 (2.0–11.0) in those with severe high SBP. BP was not associated with the risk for dementia in treated men
Kivipelto <i>et al.</i> ²⁰	1,449 subjects; age 65–79	High SBP ≥ 160 mm Hg	Dementia	21 (years)	The risk for dementia was 2.3 (1.0–5.5) for high SBP
Kivipelto <i>et al.</i> ²¹	1,449 subjects; age 65–79	High SBP ≥ 160 mm Hg	AD	21 (years)	The risk for AD was 2.6 (1.1–6.6) for high SBP
Posner <i>et al.</i> ²²	1,259 subjects; age ≥ 65	N/A	AD, VaD	7 (years)	A history of hypertension was not associated with an increased risk for AD (0.9, 0.7–1.3), but was with an increased risk for VaD (1.8, 1.0–3.2)
Kivipelto <i>et al.</i> ²³	1,449 subjects; age 65–79	High SBP > 140 mm Hg	Dementia, AD	21 (years)	High SBP was a significant risk for dementia (1.97, 1.03–3.77); no significant risk for AD (1.57, 0.78–3.14)
Luchsinger <i>et al.</i> ²⁴	1,138 subjects; mean age 76.2	N/A	AD	5.5 (years)	Hypertension was not significantly associated with an increased risk for AD (1.4, 0.9–2.1)
Li <i>et al.</i> ²⁵	2,356 subjects; age ≥ 65	DBP; borderline-high (80–89 mm Hg); normal (< 80 mm Hg), SBP; high (≥ 160 mm Hg); normal (< 140 mm Hg)	Dementia	8 (years)	Within the youngest age group (65–74), a greater risk for dementia was found in participants with high SBP (1.60, 1.01–2.55) or borderline-high DBP (1.59, 1.07–2.35) than for those with normal BP

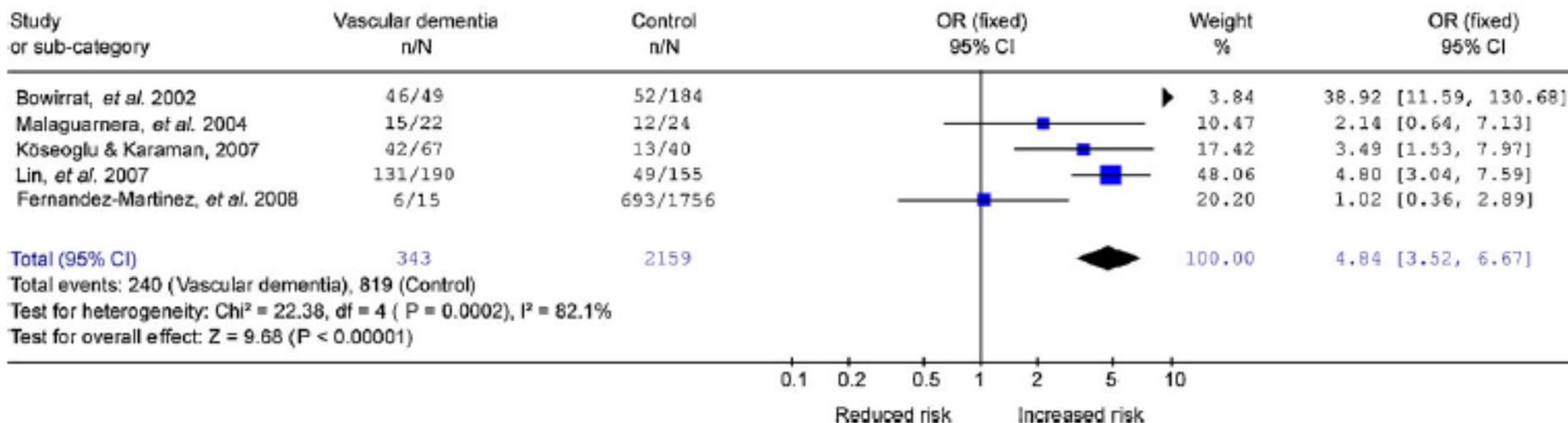
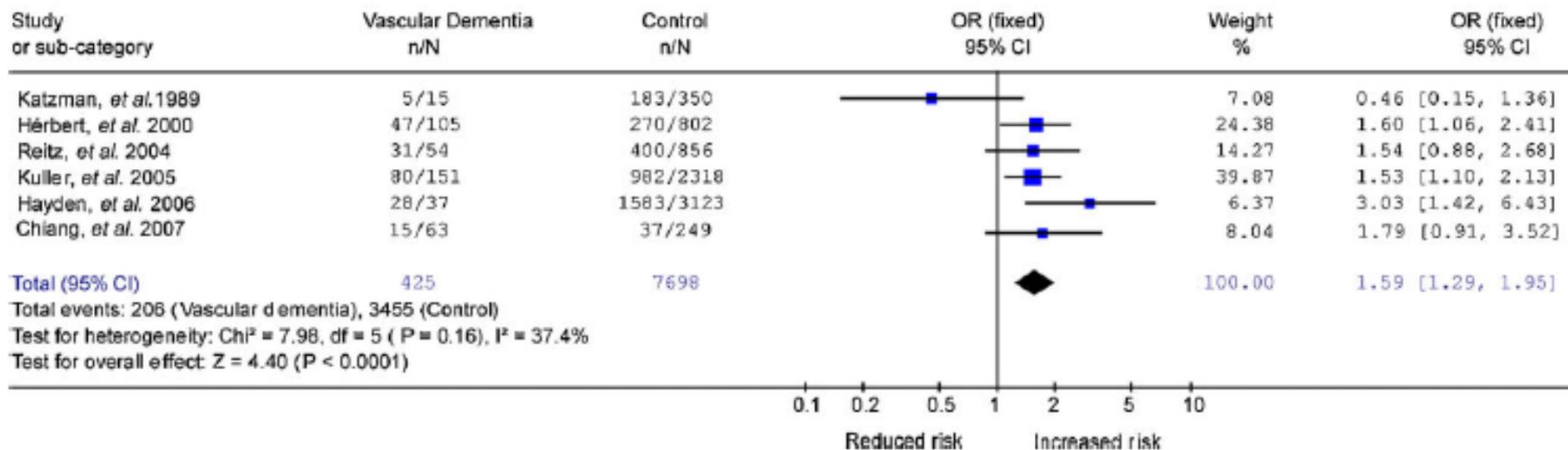
Table 2 | High blood pressure and cognitive impairment

Study	Subjects	Blood pressure classification	Neuropsychological test	Follow-up period	Results
<i>Starr et al.</i> ²⁹	598 subjects; no antihypertensive treatment; age ≥ 70	Mean 160/86 mm Hg, high (>1 s.d. above mean); medium (within 1 s.d. of mean); low (>1 s.d. below mean)	MMSE	(-) (case-control study)	Significant lower cognitive function in patients with high SBP and DBP
<i>Kuusisto et al.</i> ³⁰	744 subjects; stroke-free; nondiabetic; mean age 73	BP $\geq 160/95$ mm Hg or on antihypertensive treatment	MMSE, TMT, BSR HVR, VFT	(-) (case-control study)	Significant lower cognitive function in patients with high SBP and DBP
<i>Guo et al.</i> ³¹	1,736 subjects; age ≥ 75	Four groups (SBP > 180 , 160–179, 130–159, <130 mm Hg)	MMSE	(-) (case-control study)	Positive correlation of cognitive function with SBP and DBP
<i>Cacciatore et al.</i> ³²	1,106 subjects; stroke-free; age 65–95	N/A	MMSE	(-) (cross-sectional design)	Positive correlation between cognitive function and DBP
<i>Kilander et al.</i> ³³	999 subjects; age 69–75	N/A	MMSE, TMT	20 (years)	High DBP at age predicted impaired cognitive function at age 70; cross-sectional measurement at age 70 showed that high 24-h DBP was associated with lower cognitive function

Table 2 | High blood pressure and cognitive impairment

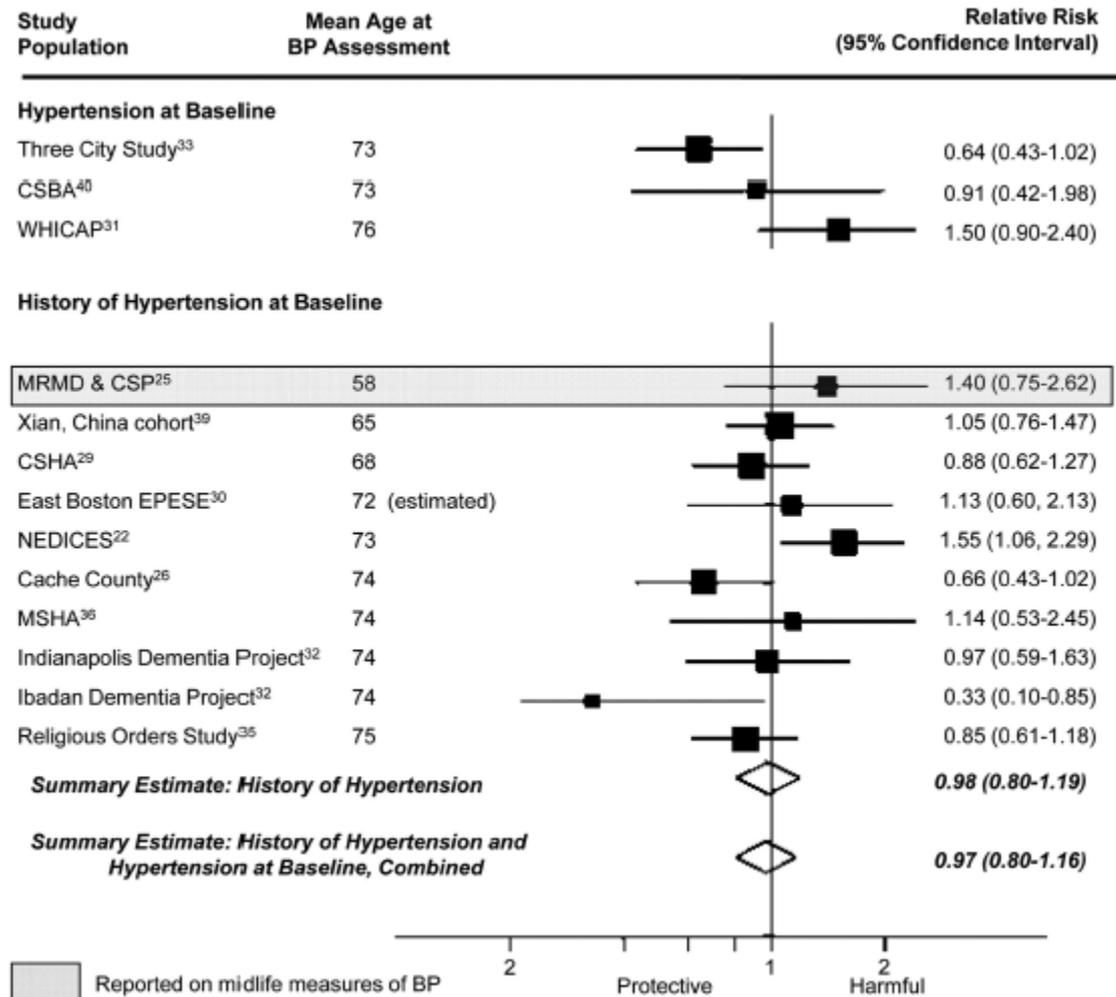
Study	Subjects	Blood pressure classification	Neuropsychological test	Follow-up period	Results
Seux <i>et al.</i> ³⁴	2,252 subjects; age ≥ 60	SBP 160–219 mm Hg (systolic hypertension)	MMSE	(cross-sectional design)	Negative correlation between cognitive function and SBP
Suhr <i>et al.</i> ³⁵	2,727 subjects; age 20–59	N/A	Symbol digit, serial digit learning, visuomotor reaction time	(–) (cross-sectional design)	Higher SBP was associated with poorer cognitive performance in subjects younger than 40 years
Elias <i>et al.</i> ³⁶	529 subjects; two age groups (18–46 years and 47–83 years)	N/A	WAIS	20 (years)	Higher levels of baseline SBP and DBP were significantly associated with decline in visualization/fluid abilities in both younger and older age groups
Waldstein <i>et al.</i> ³⁷	847 subjects; stroke-free; age ≥ 60	N/A	WAIS, BVRT, TMT A and B	11 (years)	Cognitive decline was apparent among older (80 years) individuals with higher systolic BP; cross-sectional findings indicated moderated U- and J-shaped relations between BP and cognitive function
Robbins <i>et al.</i> ³⁸	147 African-Americans, 1,416 Caucasians; age < 80	N/A	WAIS	(cross-sectional design)	SBP and DBP were significantly negatively associated with cognitive performance for both racial cohorts but were generally of higher magnitude for the African-American cohort
Obisesan <i>et al.</i> ³⁹	6,163 subjects; age ≥ 60	N/A	Short-portable MMSE	(–) (cross-sectional design)	Severe hypertension group had the poorest performance in all age groups except the very old (≥80)

Hypertension is a potential risk factor for vascular dementia: systematic review



The Association Between Blood Pressure and Incident Alzheimer Disease

A Systematic Review and Meta-analysis



Midlife and Late-Life Blood Pressure and Dementia in Japanese Elderly

The Hisayama Study

Table 2. Association Between Late-Life Blood Pressure and the Risk of Dementia During 17-Y Follow-Up

Late-Life BP Levels Defined by JNC-7	No. of Events	No. of Participants	Age- and Sex-Adjusted Incidence, per 10 ³ PYs (95% CI)	Age-, Sex-, and Education-Adjusted		Multivariable-Adjusted (Model A)*		
				HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	
<i>All-cause dementia</i>								
Stage 2 hypertension	53	135	37.4 (27.4 to 47.5)	1.28 (0.82 to 1.98)	0.28	1.12 (0.68 to 1.87)	0.65	
<i>P</i> for trend			0.07	0.09		0.25		
<i>Vascular dementia</i>								
Normal	2	106	2.3 (-0.9 to 5.4)	1.00 (reference)		1.00 (reference)		
Prehypertension	19	227	8.4 (4.6 to 12.3)	3.91 (0.91 to 16.85)	0.07	3.01 (0.68 to 13.31)	0.15	
Stage 1 hypertension	29	200	12.6 (8.0 to 17.2)	6.46 (1.53 to 27.21)	0.01	4.46 (1.02 to 19.42)	0.046	
Stage 2 hypertension	26	135	18.9 (11.6 to 26.3)	9.98 (2.35 to 42.35)	0.002	5.57 (1.22 to 25.49)	0.03	
<i>P</i> for trend			<0.001	<0.001		0.009		
<i>Alzheimer disease</i>								
Normal	22	106	17.9 (9.8 to 26.0)	1.00 (reference)		1.00 (reference)		
Prehypertension	39	227	14.0 (9.4 to 18.6)	0.71 (0.42 to 1.20)	0.20	0.73 (0.42 to 1.27)	0.27	
Stage 1 hypertension	39	200	16.8 (11.5 to 22.0)	0.86 (0.51 to 1.47)	0.58	0.95 (0.54 to 1.68)	0.87	
Stage 2 hypertension	23	135	14.7 (8.7 to 20.7)	0.84 (0.46 to 1.52)	0.56	0.84 (0.42 to 1.66)	0.81	
<i>P</i> for trend			0.88	0.92		0.97		

midlife hypertension and late-life hypertension are significant risk factors for the late-life onset of vascular dementia but not for that of Alzheimer disease

No association between hypertension and risk for Alzheimer's disease: a meta-analysis of longitudinal studies.

.... there was **no significant difference** in incidence of AD (RR: 1.02, 95% confidence interval (CI): 0.91-1.14) between subjects with and without hypertension.

There was **no significant difference** in incidence of AD (RR: 0.90, 95% CI: 0.79-1.03) between subjects with and without antihypertensive medication use. The quantitative meta-analysis showed that neither hypertension nor antihypertensive medication use was associated with risk for incident AD.

Risk Factors and Preventive Interventions for Alzheimer Disease

State of the Science

.....When hypertension was defined as systolic blood pressure **higher than 140 mmHg**, there was no consistent association with increased risk. When hypertension was defined as systolic blood pressure **higher than 160 mmHg**, only 1 of 4 studies showed a statistically significant increased risk of AD.

Of 6 studies examining high **diastolic blood pressure** as a risk factor, **only 1 reported significant** results: among middle-aged men who had never been treated with antihypertensive medications, diastolic hypertension (95 mmHg) was significantly associated with incident AD in the Honolulu-Asia Aging Study cohort.

The Association between Hypertension and Dementia in the Elderly

TABLE 1: Randomized controlled trials about antihypertensive treatments and dementia/cognitive decline.

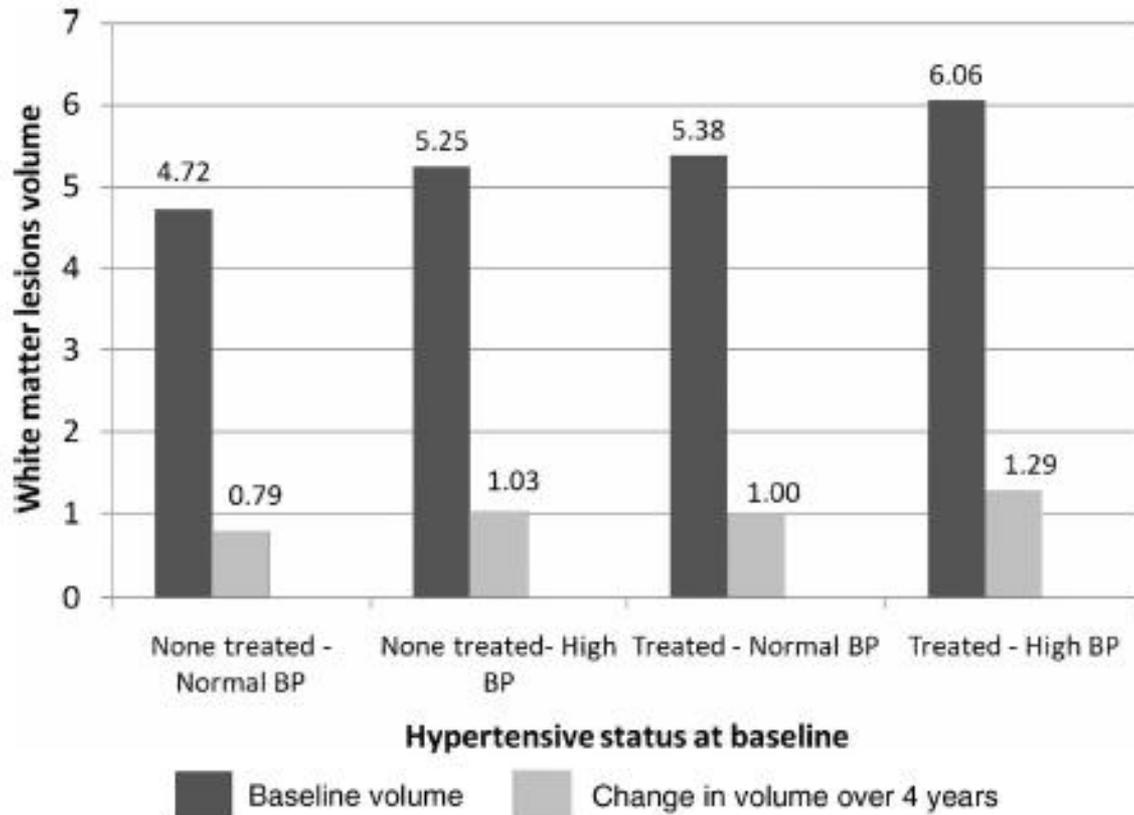
Study setting	Participants and follow up	Treatment	Test	Main results
Systolic hypertension in Europe study (Syst- Eur) [5]	2.418 systolic hypertensives; mean age 70 years, followup 3.9 years	CCB (nitrendipine) with possible addition of ACE-I (enalapril), diuretic (hydrochlorothiazide), or both versus placebo	MMSE	Mean difference in BP between treatment groups and the control was 7.0 mm Hg SBP and 3.2 mm Hg DBP. Rates of dementia for patients in the active treatment groups and the control groups were 3.3 and 7.4 cases per 1.000 patient-years (relative risk reduction: 55%), respectively. <u>Significant.</u>
The perindopril protection against recurrent stroke study (PROGRESS) [6]	6.105 subjects with prior stroke or transient ischemic attack; mean age 64 years, followup 3.9 years	ACE-I (perindopril) with possible addition of diuretic (indapamide) versus placebo	MMSE	Mean difference in BP between treatment groups and the control was 9.0 mm Hg SBP and 4.0 mm Hg DBP. Rates of cognitive decline for patients in the active treatment groups and the control groups were 11.0 and 9.1% (relative risk reduction: 19%), respectively. <u>Significant.</u>

The Association between Hypertension and Dementia in the Elderly

Systolic hypertension in the elderly program (SHEP) [7]	4.736 systolic hypertensives; mean age 72 years, followup 4.5 years	Diuretic (chlorthalidone) with possible addition of β blocker (atenolol) or sympathetic nervous blocker (reserpine) versus placebo	Short CARE	Mean difference in BP between treatment groups and the control was 12.0 mm Hg SBP and 4.0 mm Hg DBP. Rates of dementia incidence for patients in the active treatment groups and the control groups were 3.6 and 4.2 cases per 1.000 patient-years (relative risk reduction: 14%), respectively. Not significant.
Study on cognition and prognosis in the elderly (SCOPE) [8]	4.964 hypertensives; SBP160-170/DBP 90-99 mm Hg; aged 70- 89, followup 3.97 years	ARB (candesartan) versus placebo; open-label antihypertensive drugs were added to both groups	MMSE	Mean difference in BP between treatment groups and the control was 3.2 mm Hg SBP and 1.6 mm Hg DBP. Rates of dementia incidence for patients in the active treatment groups and the control groups were 6.3 and 6.8 cases per 1.000 patient-years, respectively. Not Significant.
Hypertension in the very elderly trial cognitive function assessment (HYVET- COG) [9]	3.336 hypertensives; SBP 160-200 and DBP < 110 mm Hg; age \leq 80, followup 2.2 years	Diuretic (indapamide) with possible addition of ACE-I (perindopril) versus placebo	MMSE	Mean difference in BP between treatment groups and the control was 15 mm Hg SBP and 5.9 mm Hg DBP. Rates of dementia incidence for patients in the active treatment groups and the control groups were 33 and 38 cases per 1.000 patient-years (hazard ratio 0.86). respectively. Not significant.

Antihypertensive Treatment and Change in Blood Pressure Are Associated With the Progression of White Matter Lesion Volumes

The Three-City (3C)–Dijon Magnetic Resonance Imaging Study

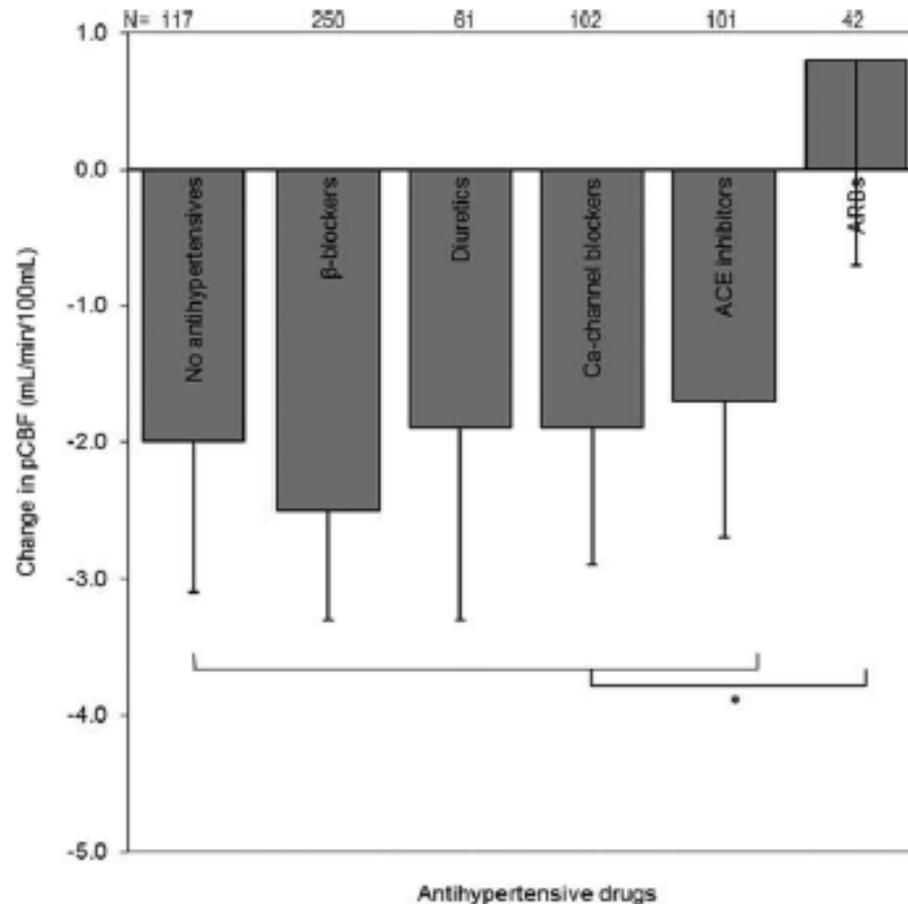


Antihypertensive Treatment and Change in Blood Pressure Are Associated With the Progression of White Matter Lesion Volumes

The Three-City (3C)–Dijon Magnetic Resonance Imaging Study

	n	WML Volume Progression, cm ³	
		Mean (SE)	<i>P</i> *
Treatment status at follow-up			0.21
Never treated	663	0.90 (0.09)	
Treated at 2 y	103	0.60 (0.23)	
SBP at baseline			
<140 mm Hg			0.84
Never treated	373	0.69 (0.13)	
Treated at 2 y	38	0.77 (0.38)	
140–160 mm Hg			0.52
Never treated	206	0.97 (0.16)	
Treated at 2 y	36	0.69 (0.39)	
≥160 mm Hg			0.008
Never treated	84	1.60 (0.26)	
Treated at 2 y	29	0.24 (0.44)	

Hypertension and Longitudinal Changes in Cerebral Blood Flow: The SMART-MR Study



CONCLUSIONI

- L'ipertensione arteriosa ha una stretta correlazione con il deficit cognitivo di natura vascolare soprattutto in associazione ad altri fattori di rischio, meno evidente con la AD
- Il trattamento dell'ipertensione arteriosa nell'anziano viene instaurato indipendentemente dal rischio di deficit cognitivo futuro
- I farmaci antiipertensivi hanno dimostrato un effetto benefico sulla morbilità e complicanze vascolari, meno sul deficit cognitivo
- Non esiste un trattamento di prima scelta, il geriatra decide in base al paziente, alla sua esperienza ed alla presenza di deficit cognitivo
- Particolare attenzione alla ipotensione da farmaci che compromette le prestazioni cognitive