55° Congresso SIGG
Invecchiamento e longevità: più geni o più ambiente?

Firenze, 30/11/2010 - 04/12/2010
Palazzo dei Congressi

SIMPOSIO SIGG-SIIA

IPERTENSIONE ARTERIOSA:
GLI ASPETTI PECULIARI NELL'ANZIANO

IPERTENSIONE E DECADIMENTO COGNITIVO

F. Cacciatore, MD, PhD

Fondazione Salvatore Maugeri, IRCCS

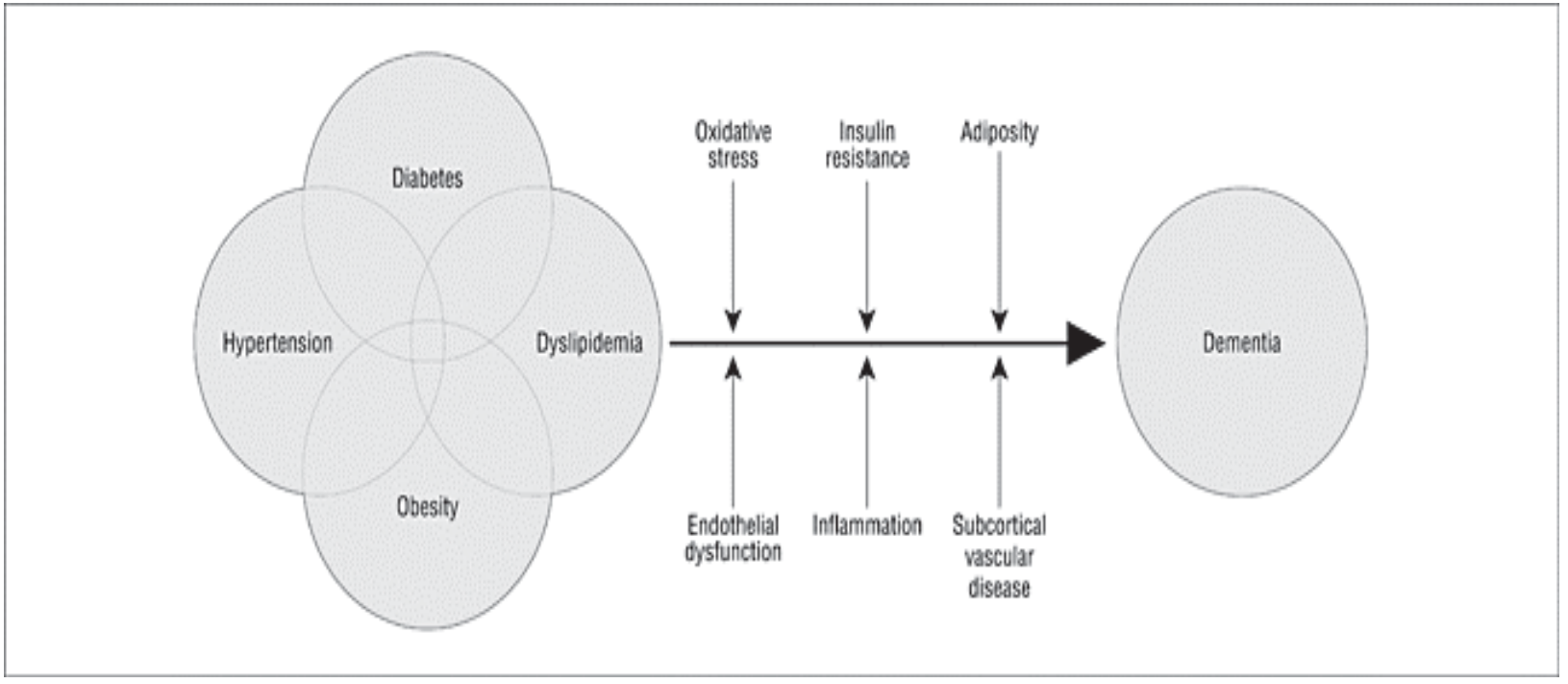
Le previsioni epidemiologiche

- Ad oggi si stima che 1 ultra-65 enne su 3 ha disturbi della sfera cognitiva.

- L'aumento della quota di ultra-85enni potrebbe modificare questo rapporto ad 1:2 visto l'aumento di questa fascia di popolazione.

- Sono quindi necessari interventi di prevenzione primaria per modificare queste previsioni.

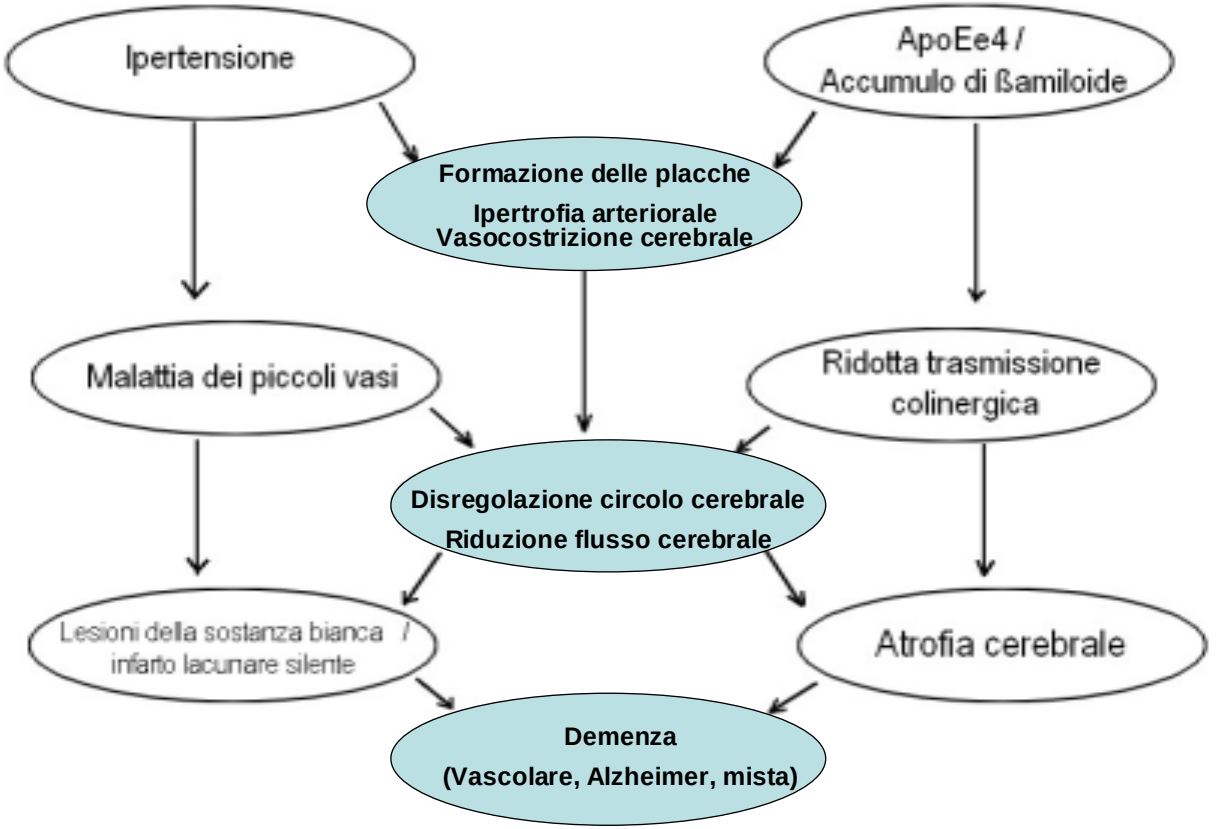
Possible mechanisms that may explain the association between vascular risk factors and an increased risk of developing dementia



Middleton, L. E. et al. Arch Neurol 2009;66:1210-1215.

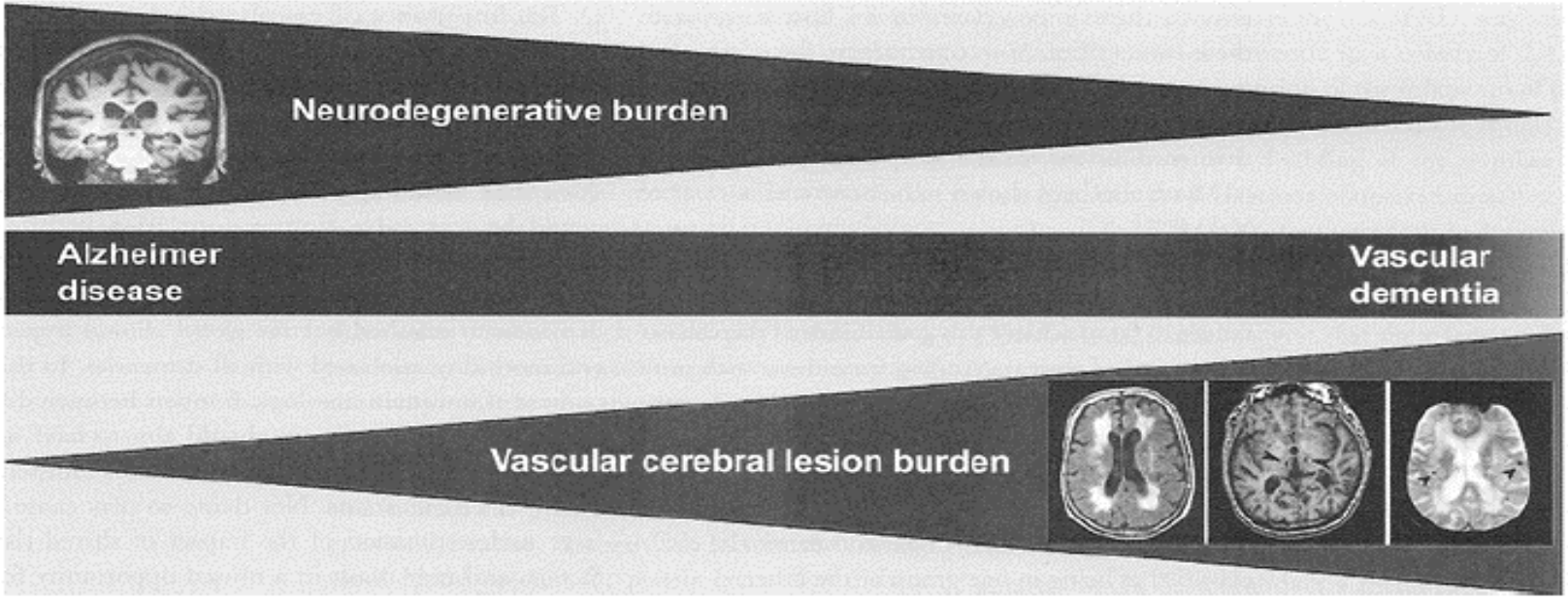
ARCHIVES OF NEUROLOGY

Momenti fisiopatologici comuni per Demenza Vascolare e Malattia di Alzheimer ed ipertensione

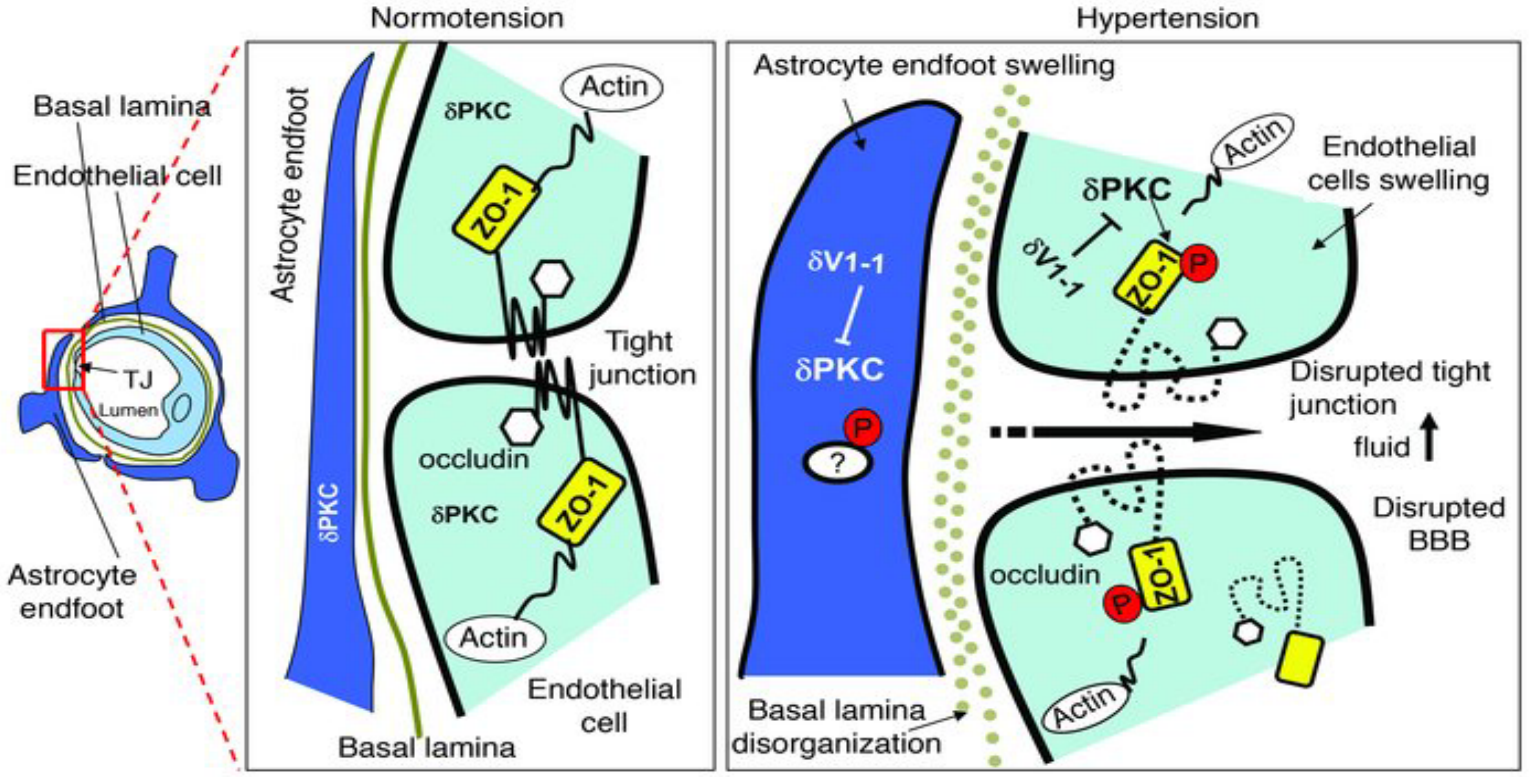


The Vascular Dementia Continuum

Viswanathan A, Rocca WA, Tzourio C. Neurology 2009;72:368-374



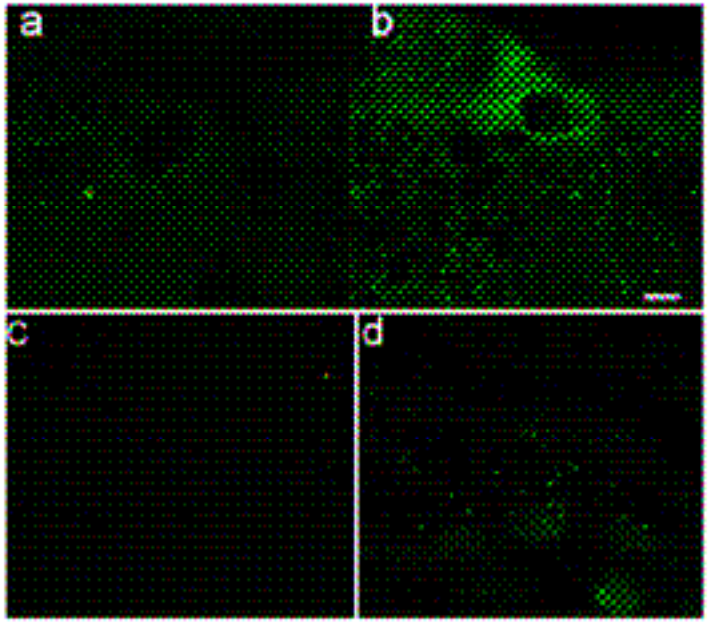
Blood brain barrier dysfunction

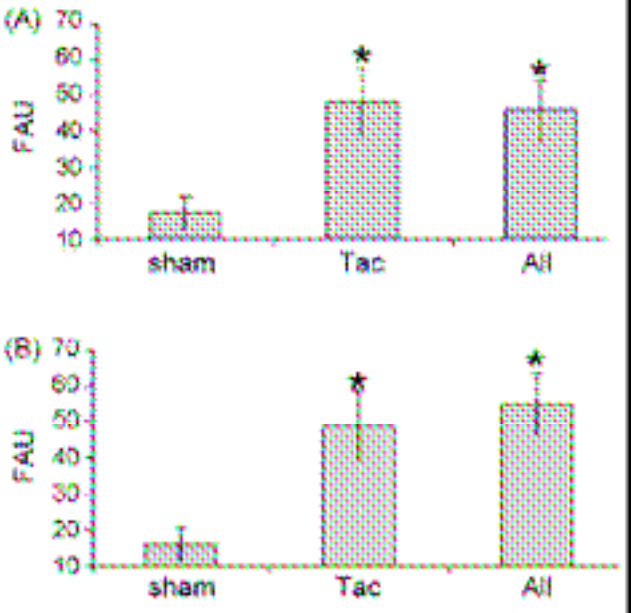


Scheme of a cerebral microvessel. Hypertension causes swelling of endothelial and endfeet of astrocytes surrounding the small vessels of brain and increases immunoreactivity of δPKC (right versus middle). Consequently, BBB permeability increased.

X Qi et al J Clin Invest, 2008

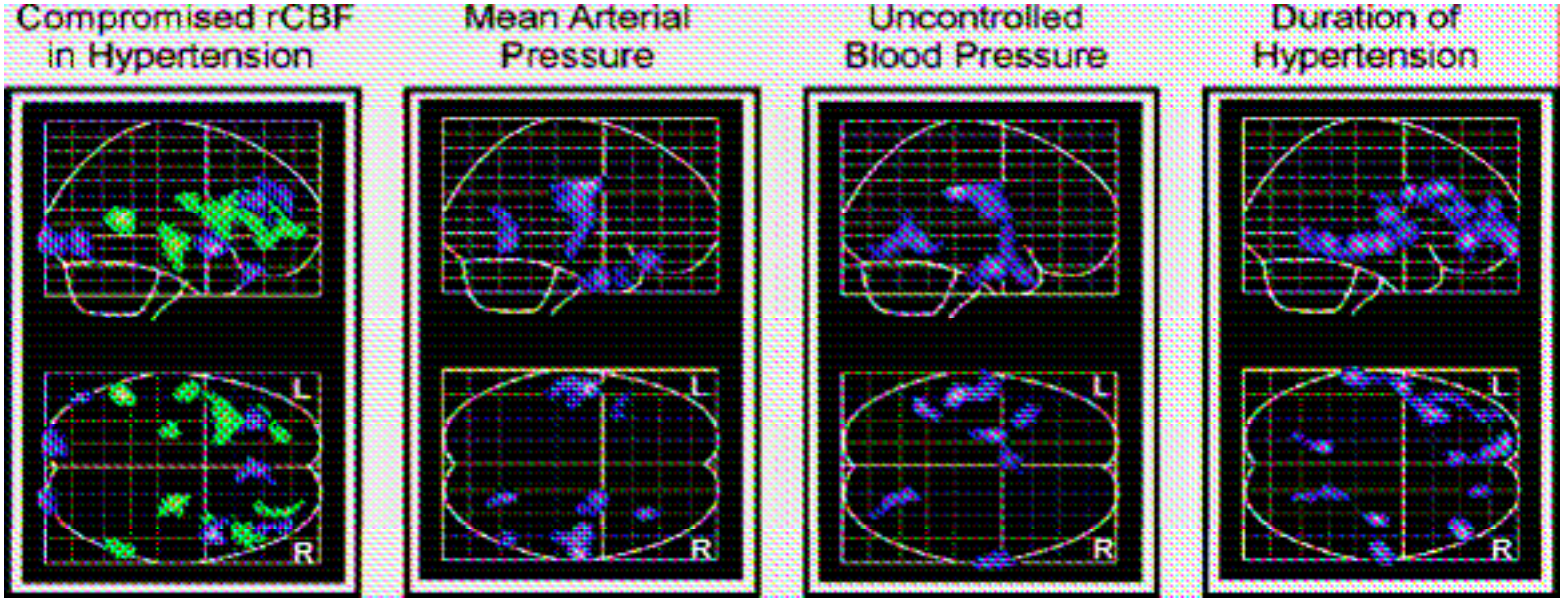
β-Amyloid deposition in brain is enhanced in mouse models of arterial hypertension





Neurobiol of Aging, 2007

Longitudinal Changes in Cerebral Blood Flow in the Older Hypertensive Brain



Hypertensive variables and rCBF. Maps of the effect of different variables on the patterns of rCBF change from over 7 years of follow-up. Blue represents greater declines in HTNs, green represents regions that do not increase flow in HTN to the same extent as Healthy Controls

Beason et al, Stroke 2007

EPIDEMIOLOGIA

- Studi Trasversali
- Studi Longitudinali

EPIDEMIOLOGIA

- Studi Trasversali

Ipertensione arteriosa e deficit cognitivo

Studio	Soggetti	Pressione arteriosa	Test neuropsicologico	Follow-Up	Risultati
Starr (4)	598 soggetti senza trattamento anti-ipertensivo. Età > 70 anni	Media PA 160/86 mmHg	MMSE	Caso-controllo	Punteggio più basso nel MMSE per i soggetti con alti valori di PA.
Kuusisto (5)	744 senza ictus e non diabetici; età media 73 anni	PA ≥ 160/95 mm Hg o in trattamento anti-ipertensivo	MMSE, TMT, BSR HVR, VFT	Caso-controllo	Funzione cognitiva compromessa per i soggeti con alti valori di pressione arteriosa
Guo (6)	1736 soggetti; età > 75 anni	Quattro gruppi PAS ≥ 180; 160-179; 130-159; < 130 mmHg	MMSE	Caso-controllo	Correlazione positiva tra valori di pressione arteriosa sistolica e diastolica.
Cacciatore (7)	1106 soggetti senza ictus; età 65-95 anni	N/A	MMSE	Trasversale	Alti valori di pressione arteriosa diastolica sono associati con il deficit cognitivo.
Kilander (8)	999 soggetti; età 69–75 anni	N/A	MMSE, TMT,	20 (anni)	Alti valori di pressione arteriosa diastolica in età adulta predicono la funzione cognitiva all'età di 70 anni. La misura della pressione arteriosa all'età di 70 anni con holter PA è associata a deficit cognitivo
Seux (9)	2252 soggetti; età ≥ 60 anni	PAS ≥160-219 mm Hg;	MMSE	Trasversale	Correlazione negativa tra valori di pressione arteriosa e deficit cognitivo
Suhr (10)	2727 soggetti Età 20-59 anni	N/A	Symbol Digit, Serial Digit, Learning Visuomotor reaction time	Trasversale	Alti valori di pressione arteriosa predicono i valori dei test cognitivi all'età di 40 anni.
Elias (11)	529 anni; 2 gruppi d'età 18-46 e 47-83	N/A	WAIS	20 anni	Alti valori di PAD e PAS al baseline sono predittivi di declino cognitivo sia in adulti che in anziani
Waldstein (12)	847 soggetti senza ictus; età > 75 anni	N/A	WAIS, TMT A e B, BVRT	11 anni	Relazione ad U e J shaped tra PA e funzione cognitiva
Robbins (13)	147 Afro-Americani 1416 Caucasici < 80 anni	N/A	WAIS	Trasversale	PAS e PAD sono negativamente associate alla performance cognitiva in entrambe le razze anche se l'effetto è più evidente per gli afro-americani
Obisesan (14)	6163 soggetti, età ≥ 60 anni	N/A	Short Portale MMSE	Trasversale	Alti valori pressione arteriosa sistolica mostrano una peggiore funzione cognitiva tranne che per gli > 80 anni

The role of blood pressure in cognitive impairment in an elderly population

Francesco Cacciatore, Pasquale Abete, Nicola Ferrara*, Giuseppe Paolisso†, Laura Amato†, Silvestro Canonico‡, Stefania Maggi**, Michele Varricchio† and Franco Rengo, for the 'Osservatorio Geriatrico Campano Group'

Objective The aim of this study was to investigate the cross-sectional relationship between arterial blood pressure and cognitive impairment in a group of elderly subjects, controlling for such confounding variables as age, education, depression, drug use and antihypertensive treatment.

Design and setting A cross-sectional survey in Campania, a region in southern Italy.

Subjects and methods A random sample of 1339 elderly subjects aged 65–95 years (mean 73.9 ± 6.2 years) selected from the electoral rolls was interviewed by trained physicians. Sociodemographic characteristics, results of Mini-Mental State Examination (MMSE), Geriatric Depression Scale (GDS), blood pressure and whether antihypertensive treatment was being administered were recorded. When subjects with neurological diseases and those under psychotropic therapy were excluded from the analyses, the population numbered 1106.

Results The MMSE score was less than 24 for 27.9% of the subjects and the mean GDS score was 10.8 ± 6.3. The mean systolic blood pressure (SBP) was 145.3 ± 19.0 mmHg and the mean diastolic blood pressure (DBP) was 82.0 ± 9.2 mmHg. Logistic regression analysis showed that female sex, age, GDS score and DBP but not SBP were predictive of cognitive impairment. Educational level and antihypertensive treatment, on the contrary, play a protective role. DBP was associated with cognitive impairment in subjects aged 75 years (odds ratio 1.62, 95% confidence interval 1.16–2.25) and over (odds ratio 5.16, 95% confidence interval 1.50–17.71) but not in those aged 65–74 years.

Conclusion DBP but not SBP is predictive of cognitive impairment in subjects aged 75 years and over without neurological disorders independently from sex, age, education, GDS and antihypertensive treatment.

Journal of Hypertension 1997, 15:135–142

Keywords: ageing, blood pressure, cognitive impairment

From the Cattedra di Geriatria, Università degli Studi di Napoli 'Federico II', †Fondazione Salvatore Maugeri, Centro Medico di Campoli, IRCCS, Benevento, the ‡Dipartimento di Geriatria and the *Cattedra di Chirurgia Geriatrica II, Università degli Studi di Napoli, and the **Progetto Finalizzato Invecchiamento Consiglio Nazionale delle Ricerche, Italy.

Sponsorship: This study was supported by a grant from the Regione Campania to the Osservatorio Geriatrico Regione Campano.

Requests for reprints to Dr Franco Rengo, Istituto di Medicina Interna, Cardiologia e Chirurgia Cardiovascolare, Cattedra di Geriatria, Università degli Studi di Napoli 'Federico II', Via S. Pansini 5, 80131 Napoli, Italy.

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Table 3 Distribution of variables according to the Mini-Mental State Examination results < 24 and ≥ 24

Variables	MMSE < 24	MMSE ≥ 24	Significance (*P*)
Age (years)	75.3 ± 6.7	72.1 ± 5.1	0.0001
Educational level	2.8 ± 1.3	4.2 ± 1.2	0.0001
GDS score	12.6 ± 6.2	8.6 ± 5.8	0.0001
SBP (mmHg)	146.6 ± 19.3	143.7 ± 18.4	0.01
DBP (mmHg)	82.8 ± 9.1	81.0 ± 9.0	0.001

Values are expressed as means ± SD. GDS, Geriatric Depression Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure.

F.Cacciatore et al. J Hypertension. 1997

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F.Cacciatore et al. J Hypertension. 1997

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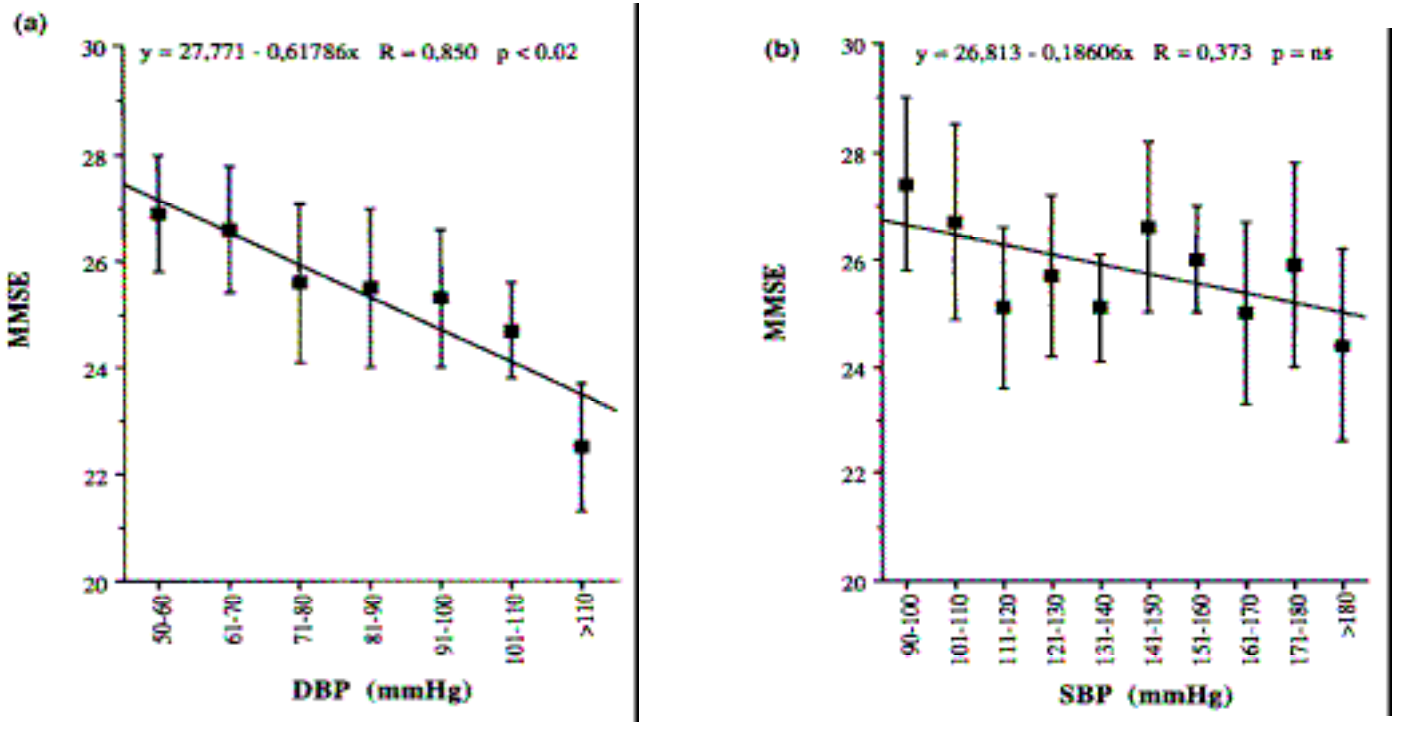

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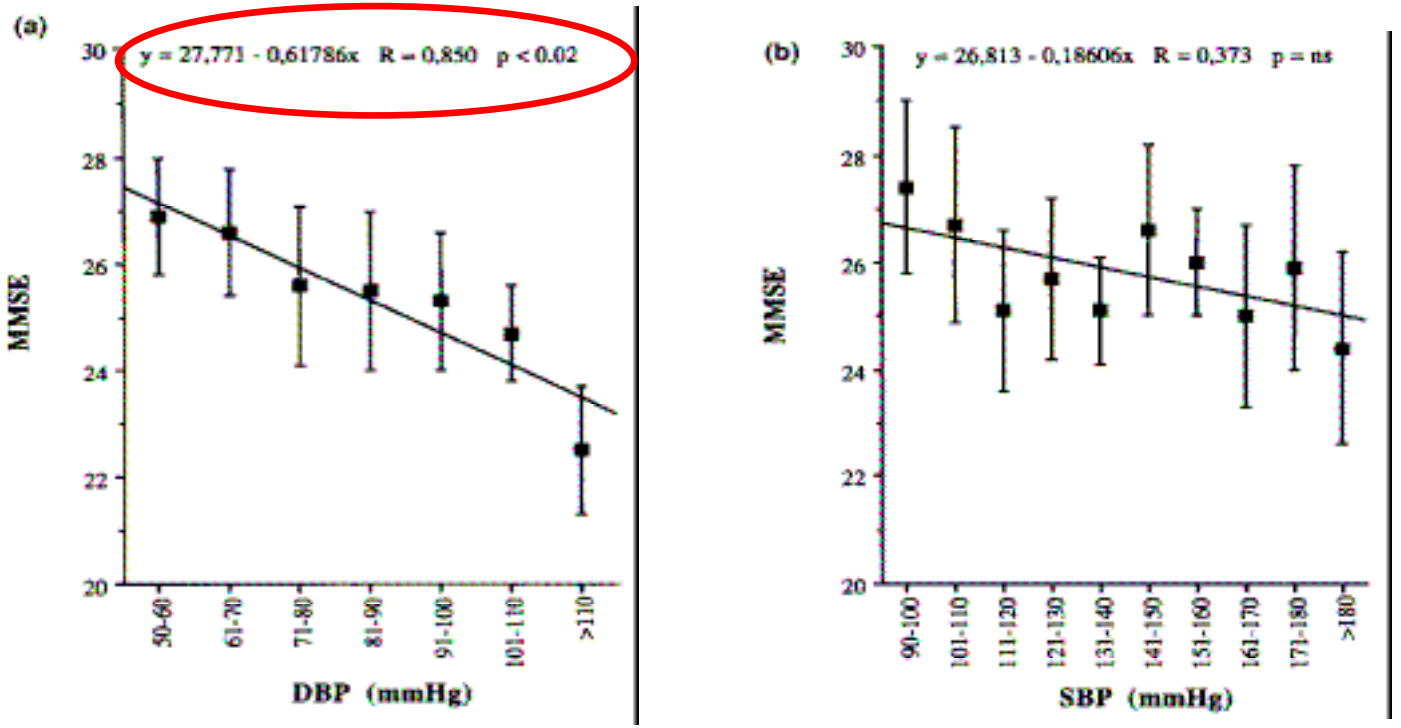

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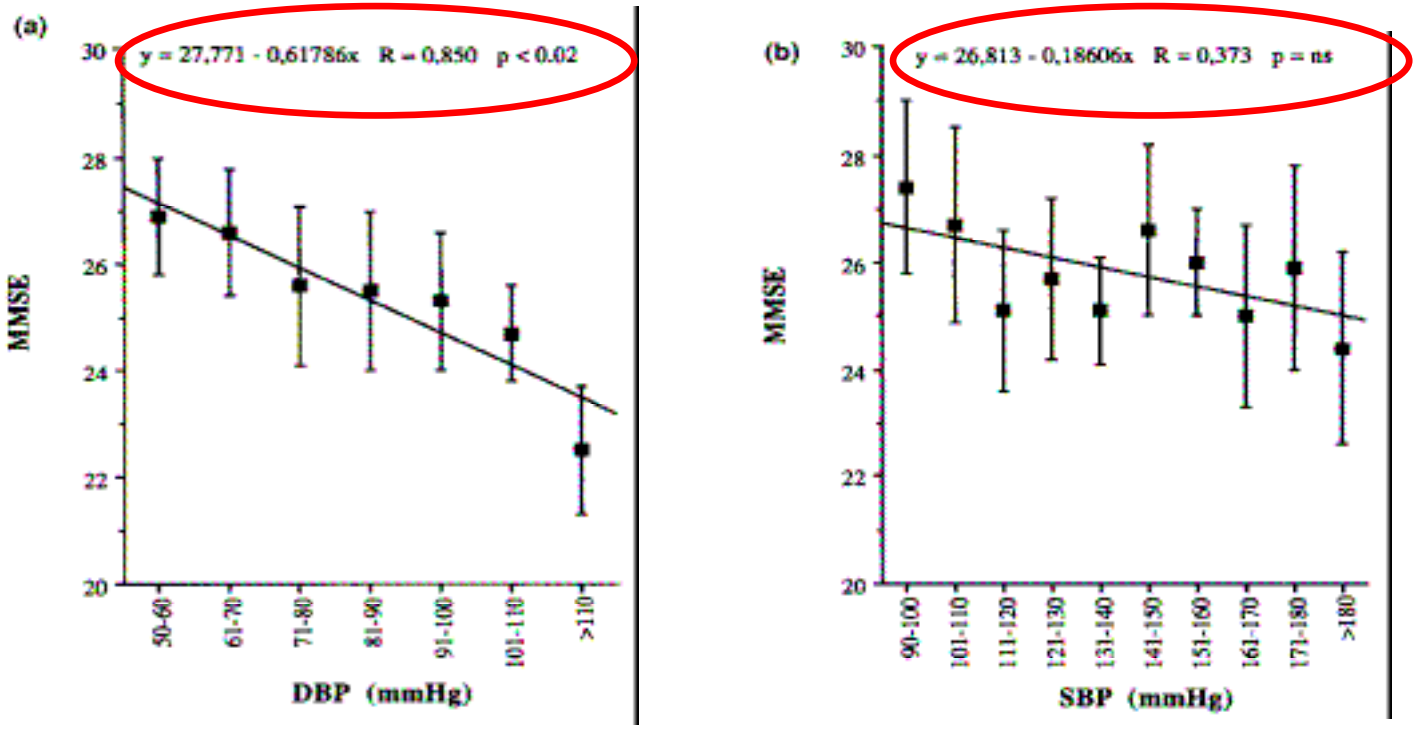
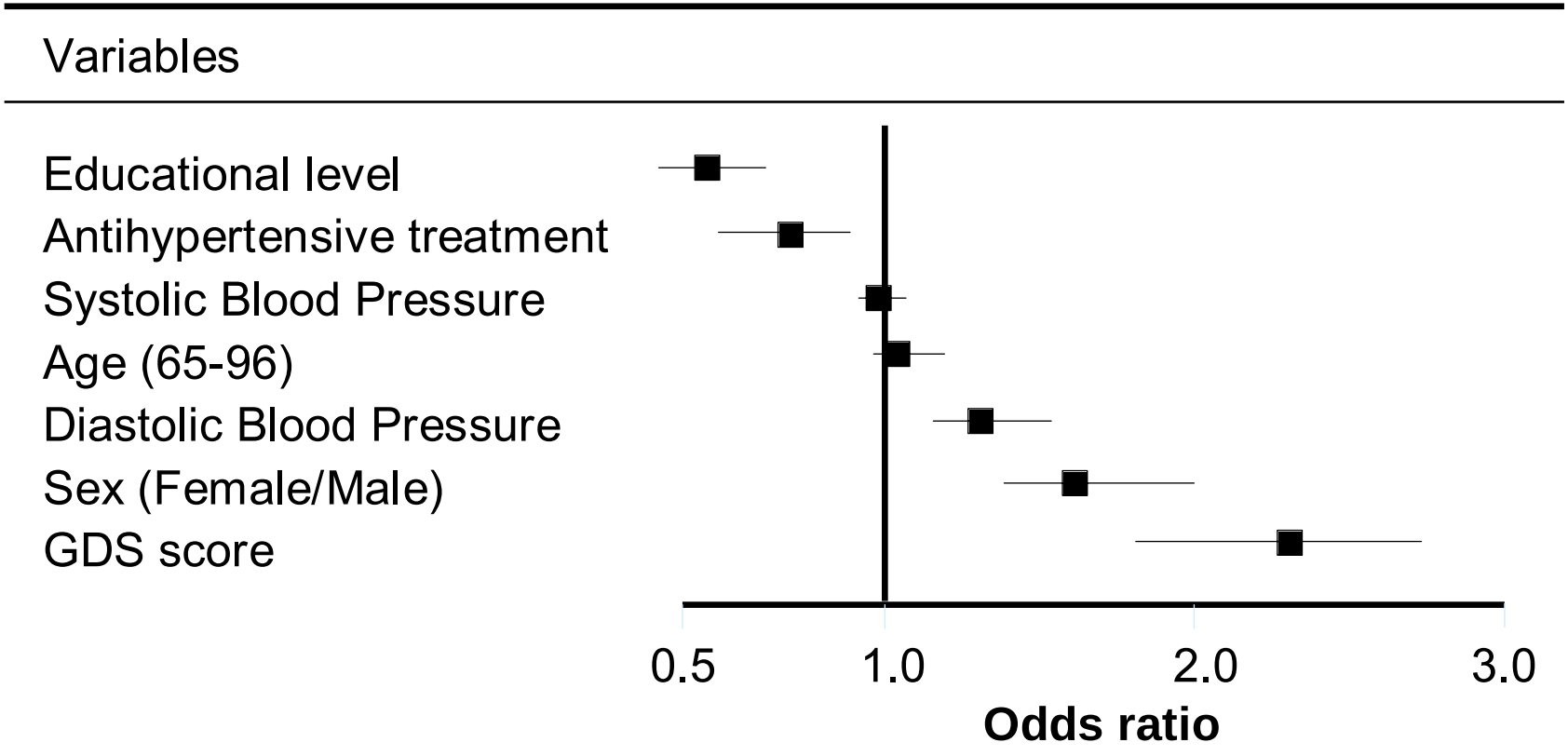


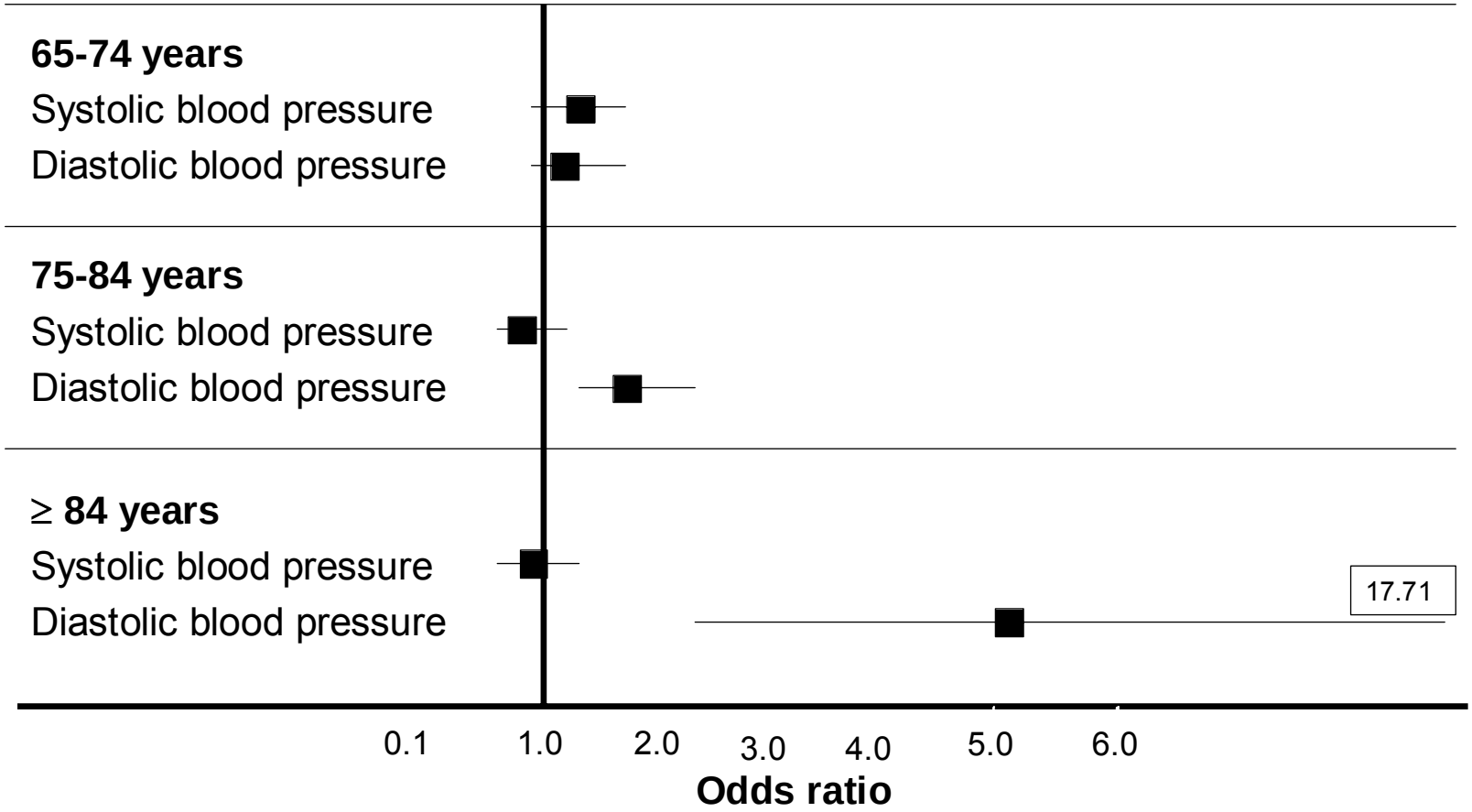
F.Cacciatore et al. J Hypertension. 1997

Logistic regression analysis considering the role of sex, age, educational level, GDS score, SBP, DBP and antihypertensive treatment on MMSE.



Cacciatore F et al., J Hypertens 1997

Logistic regression analysis considering the role SBP and DBP on MMSE stratified by age.



Cacciatore F et al., J Hypertens 1997

EPIDEMIOLOGIA

- Studi Longitudinali

Ipertensione arteriosa ed incidenza di demenza e Malattia di Alzheimer

Studio	Soggetti	Pressione arteriosa	Outcome	Follow-Up	Risultati Odds Ratio o Rischio Relativo
Launer (15)	3703 uomini Americani-Giapponesi- mai trattati con farmaci 57%	PAD: severe high (≥95 mm Hg); high (90–94 mm Hg); normal (80–89 mm Hg). PAS: severe high (≥160 mm Hg); high (140–159 mm Hg); normal (110–139 mm Hg)	Demenza	**2.7 (anni)**	Tra i pazienti mai trattati, il rischio di demenza è 3.8 (1.6–8.7) per PAD ≥95 mm Hg, e 4.3 (1.7–10.8) per PAD 90–94 mm Hg; il rischio di demenza è 4.8 (2.0–11.0) in quelli con PAS ≥160 mm Hg. PA non è associate al rischio di demenza in soggetti trattati.
Kivipelto (16)	1449 soggetti; età 65–79	PAS ≥ 160 mm Hg	Demenza	**21 (anni)**	Il rischio di demenza 2.3 (1.0–5.5) per SBP ≥ 160 mm Hg
Li (21)	2356 soggetti; età ≥ 65	PAD; borderline-high (80–89 mm Hg); normal (<80 mm Hg), PAS; high (≥160 mm Hg); normal (<140 mm Hg)	Demenza	**8 (anni)**	Nel gruppo con età più giovane (65–74), un rischio maggiore è presente in soggetti con PAS (≥160 mm Hg) (1.60, 1.01–2.55) o PAD (80–89 mm Hg) (1.59, 1.07–2.35) rispetto ai soggetti con pressione normale
Kivipelto (19)	1449 soggetti; età 65–79	PAS > 140 mm Hg	Demenza, AD	**21 (anni)**	**Ipertensione non predice AD ma demenza**
Posner (18)	1259 soggetti; età ≥ 65	N/A	AD, VaD	**7 (anni)**	**Ipertensione non predice AD ma demenza vascolare**
Kivipelto (17)	1449 soggetti; età 65–79	PAS ≥ 160 mm Hg	AD	**21 (anni)**	**Sistolica isolata predice l'Alzheimer**
Luchsinger (20)	1138 soggetti; età media 76.2	N/A	AD	**5.5 (anni)**	**Ipertensione non predice l'Alzheimer**

Ipertensione arteriosa ed incidenza di demenza e Malattia di Alzheimer

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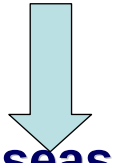
LONGITUDINAL STUDIES ON BLOOD PRESSURE AND ALZHEIMER'S DISEASE

Previous high blood pressure



Alzheimer's disease in late life

5-15 years

The H70-study in Gothenburg

Skoog et al. Lancet 1996

The Honolulu-Asia Aging Study

Launer et al. Neurobiol Aging 2000

The Rotterdam Study

Ruitenberg et al. Dissertation 2000

Kaiser Permanente, USA

Whitmer et al. Neurology 2005

Kuopio, Finland

Kivipelto et al. BMJ 2001

Kungsholmen Study

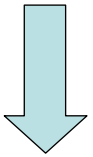
Qiu et al Arch Neurol 2003

Chinese Study

Wu et al Life Science 2003

HONOLULU-ASIA AGING STUDY

High midlife systolic blood pressure



Neuritic plaque ↑

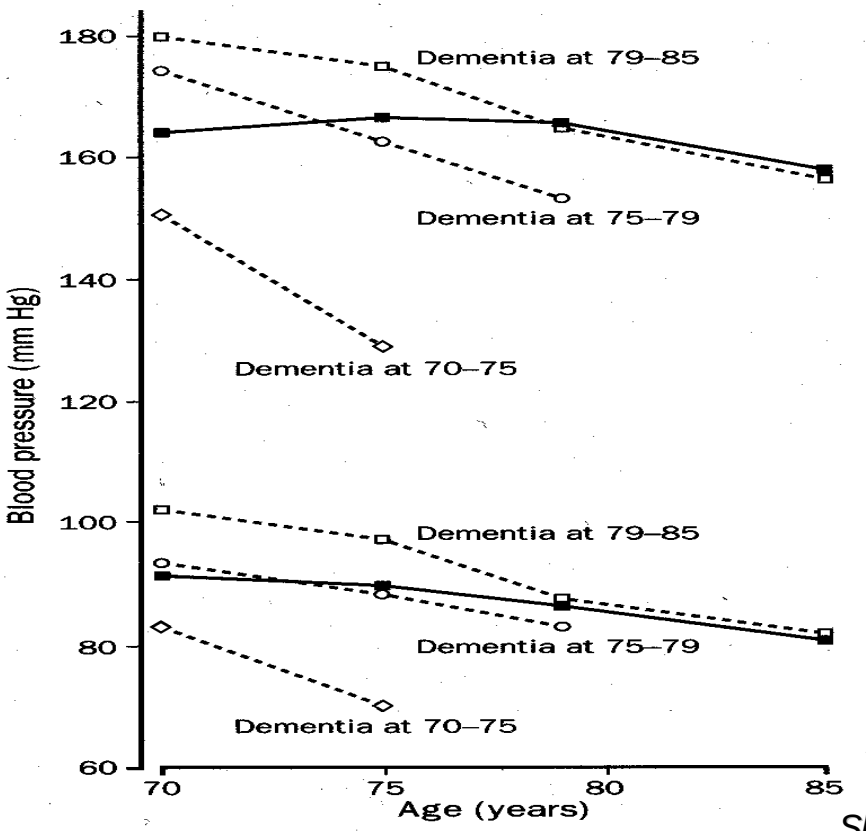
in old age

Petrovitch et al. Neurobiology of Aging 2000

Low blood pressure and dementia

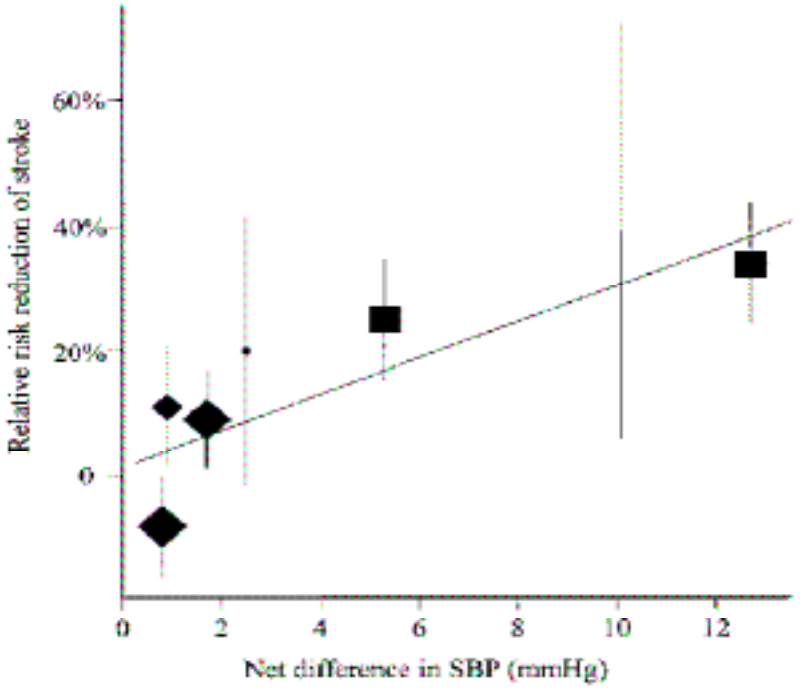
- It has been shown that blood pressure begins to decrease approximately 3 years before the diagnosis of dementia
  - » [Qiu C, Lancet Neurol 2005]
- continues to decline in AD
  - » [Verghese J, Neurology 2005]
- with increasing severity
  - » [Guo Z, BMJ 1995].

A 15-year follow-up of blood pressure and dementia



Skoog et al. Lancet 1996

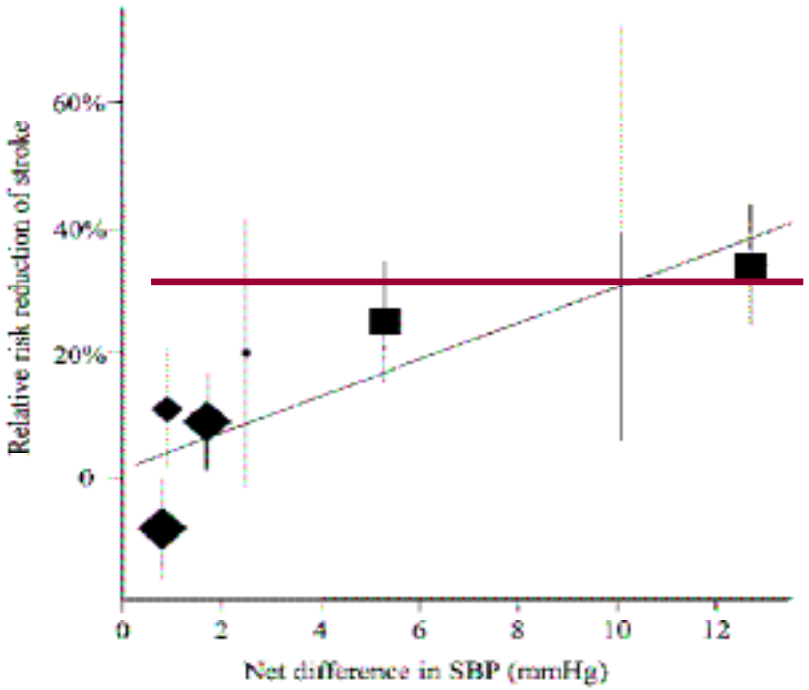
Riduzione del rischio di ictus e trattamento antipertensivo



La riduzione netta dei valori di PAS e la riduzione del rischio relativo di stroke ottenuta dai trial clinici randomizzati sono valutatati mediante una meta-regressione, ovvero una relazione diretta tra la riduzione dei valori di PAS plottati verso la riduzione del rischio di stroke per ognuna delle 7 meta-analisi. Lo slope della curva indica che per una riduzione di 10 mmHg si osserva una riduzione del rischio di stroke del 31%. R^2=71%

Lawes, Stroke 2004

Riduzione del rischio di ictus e trattamento antipertensivo



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Lawes, Stroke 2004

BMJ

RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M R Law, professor of epidemiology | K Morris, professor of medical statistics | N J Wald, professor of environmental and preventive medicine

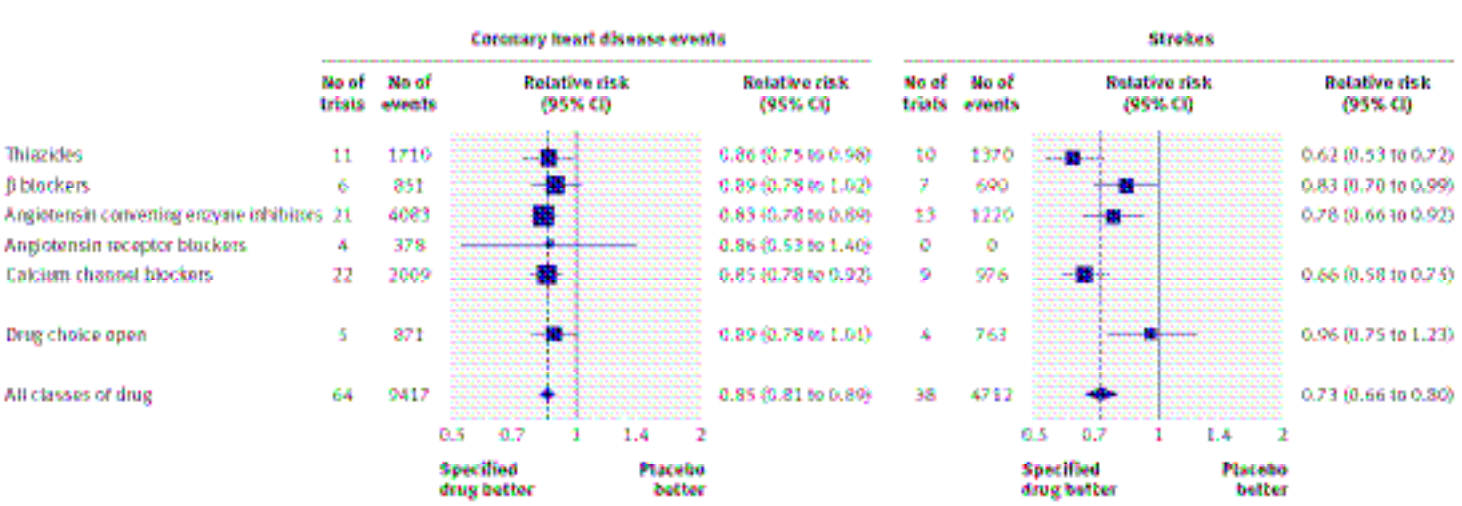

Fig 3 | Relative risk estimates of coronary heart disease events and stroke in single drug blood pressure difference trials according to class of drug (excluding CHD events in trials of β blockers in people with history of coronary heart disease). (Totals are less than the sum of the individual categories because some trials include more than one category; see web extra figures 3a-i for individual trial results and summary estimates)

Law et al. BMJ, 2009

BMJ

RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

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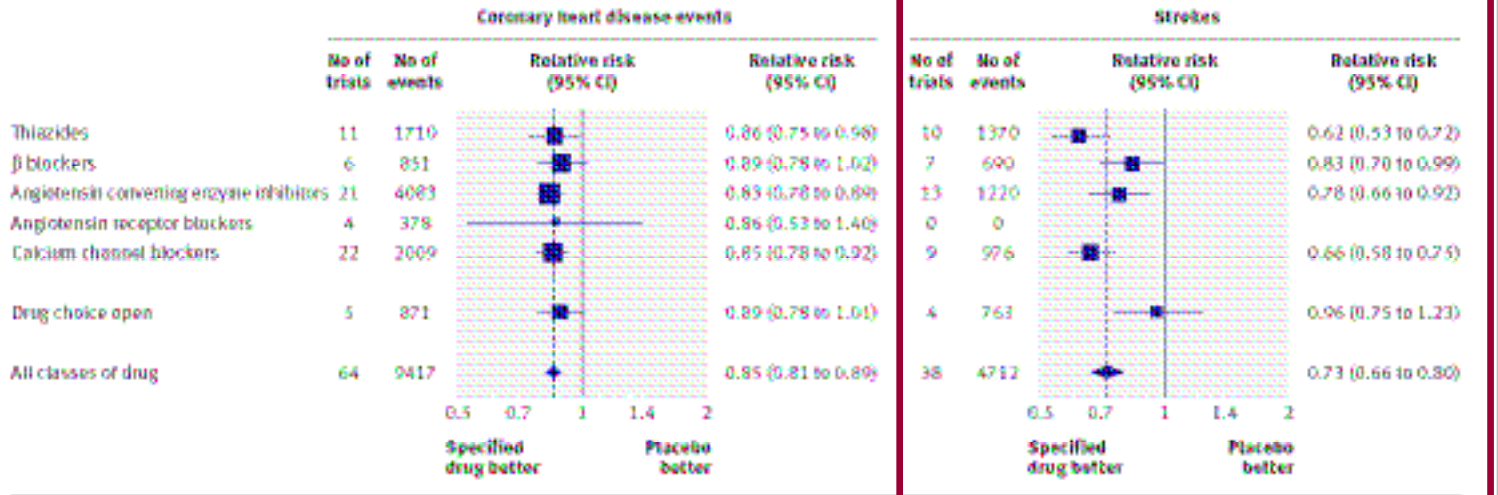

Fig 3 | Relative risk estimates of coronary heart disease events and stroke in single drug blood pressure difference trials according to class of drug (excluding CHD events in trials of β blockers in people with history of coronary heart disease). (Totals are less than the sum of the individual categories because some trials include more than one category; see web extra figures 3a-i for individual trial results and summary estimates)

Law et al. BMJ, 2009

BMJ

RESEARCH

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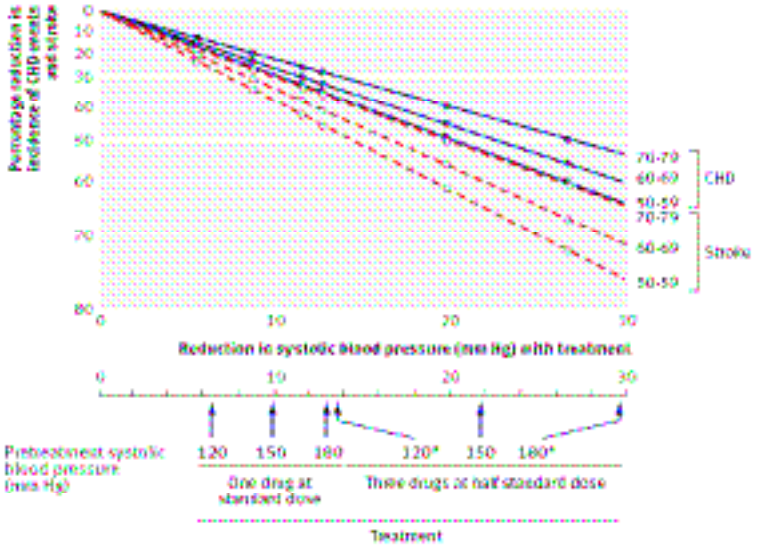


Fig 7 | Reduction in incidence of coronary heart disease (CHD) events and stroke in relation to reduction in systolic blood pressure according to dose and combination of drugs, pretreatment systolic blood pressure, and age. *Blood pressure reductions are more uncertain and hence also reductions in disease incidence

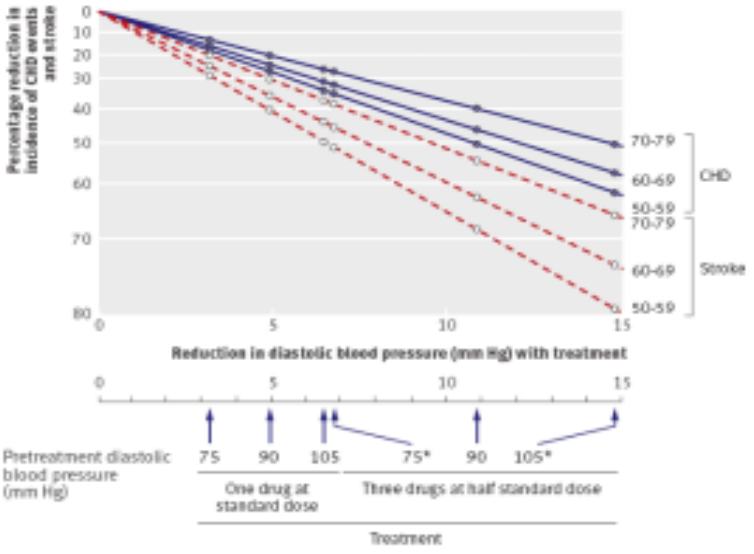
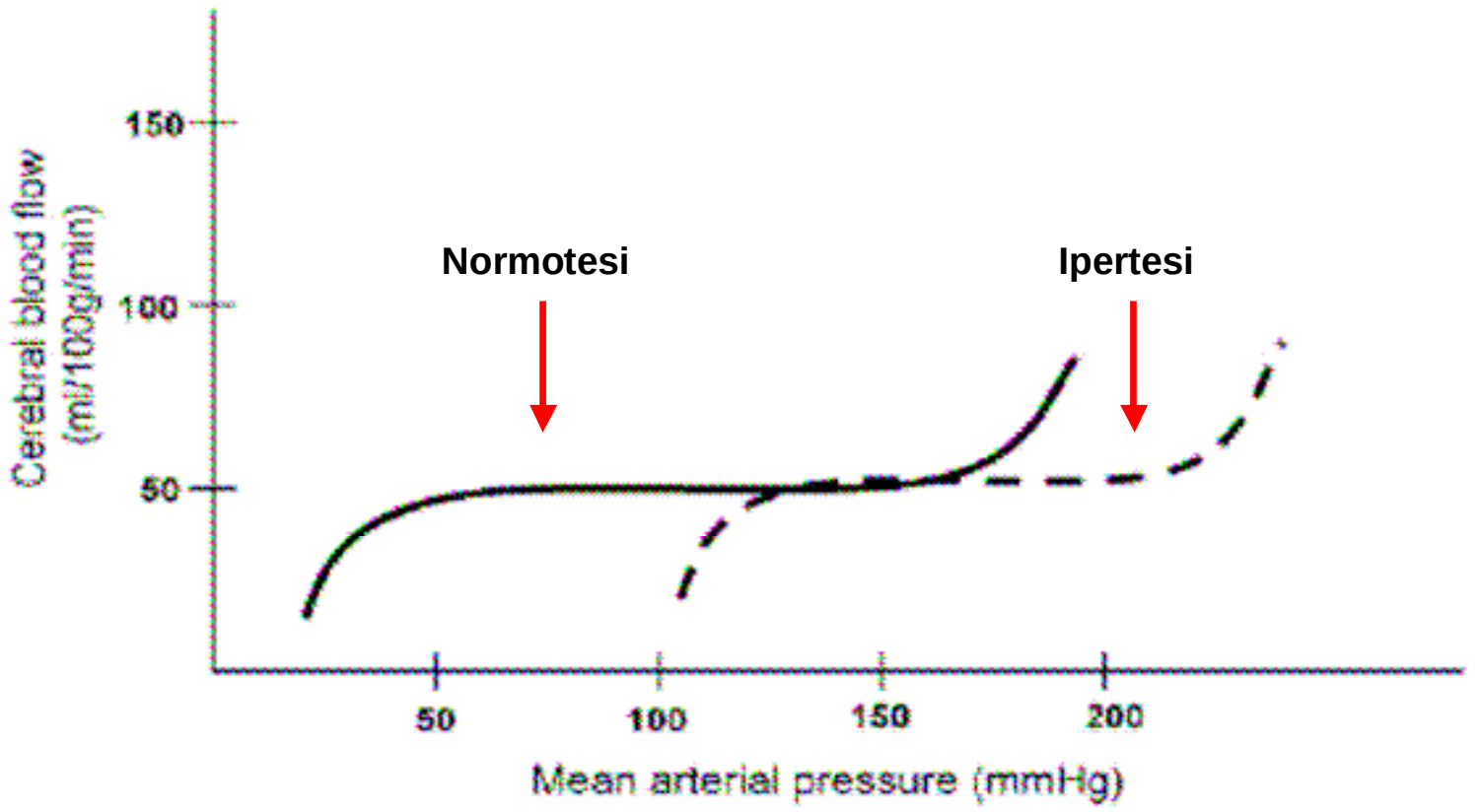


Fig 6 | Reduction in incidence of coronary heart disease (CHD) events and stroke in relation to reduction in diastolic blood pressure according to drug dose, number of drugs, pretreatment diastolic blood pressure, and age. *Blood pressure reductions are more uncertain and hence also reductions in disease incidence

Law et al. BMJ, 2009

Modifiche flusso cerebrale ed ipertensione



Mortality and Blood Pressure in Elderly People with and without Cognitive Impairment

Gerontology

Clinical Section

Gerontology 2005;51:53–61
DOI: 10.1159/000081436

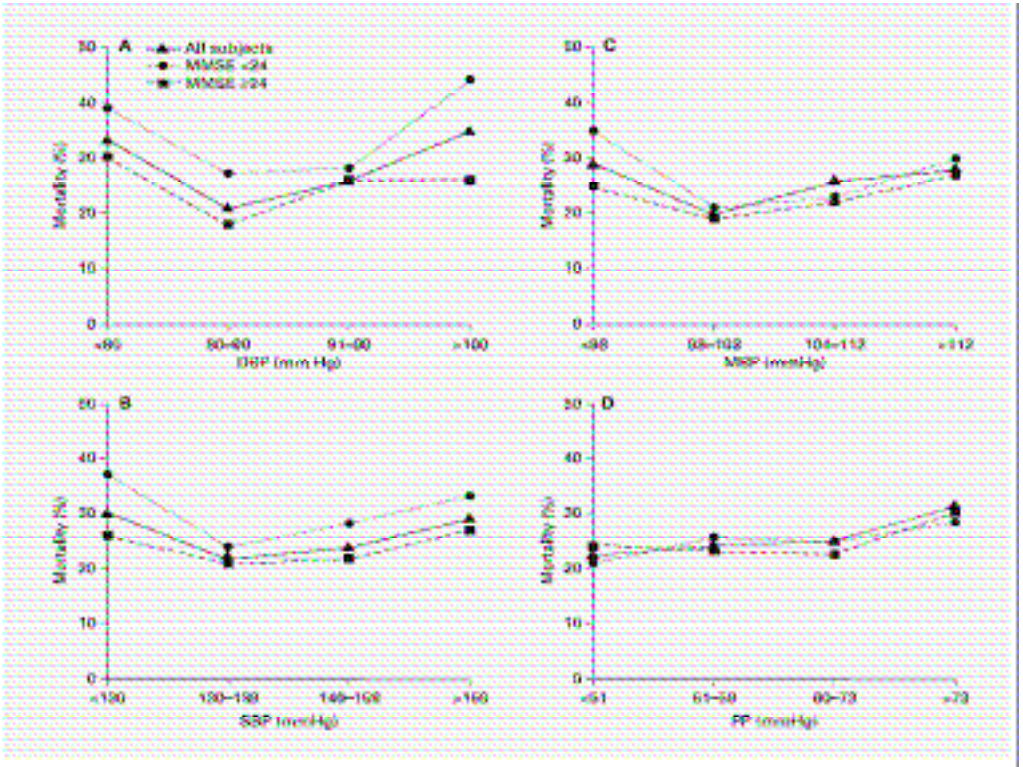


Fig. 1. Relationship between mortality and diastolic (DPB; **A**), systolic (SBP; **B**), mean (MBP; **C**), and pulse (PP; **D**) blood pressure in all elderly subjects (▲), in those with MMSE of less than 24 (< 24; ●), and in those with MMSE of equal to or more than 24 (≥ 24; ■).

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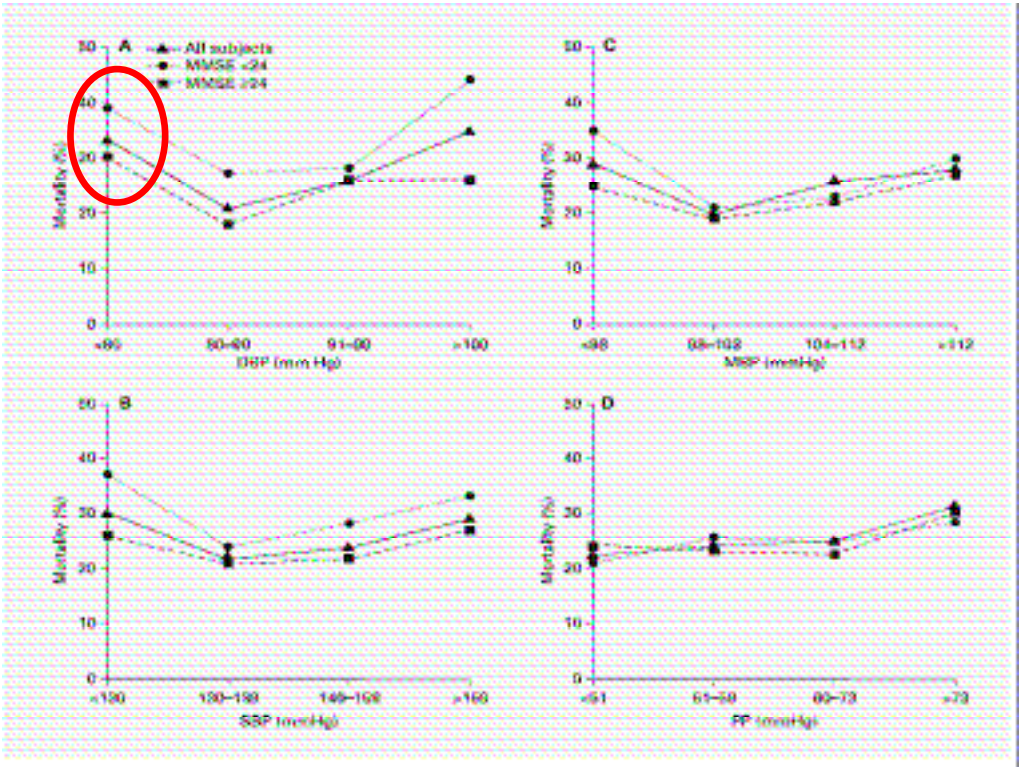

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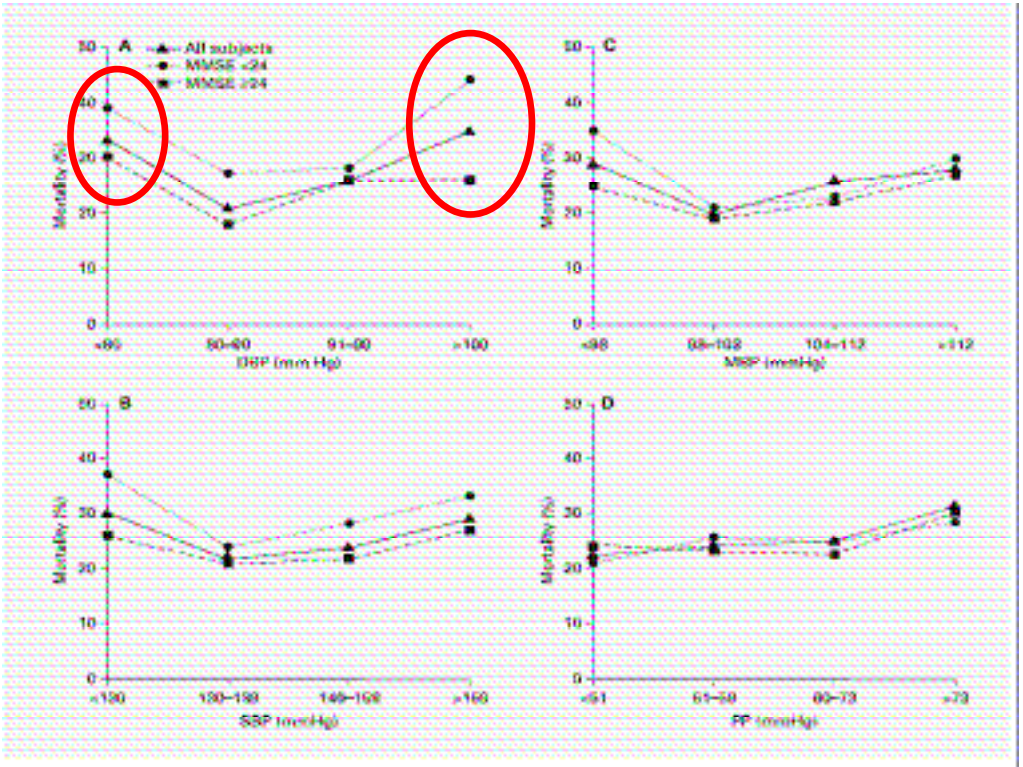

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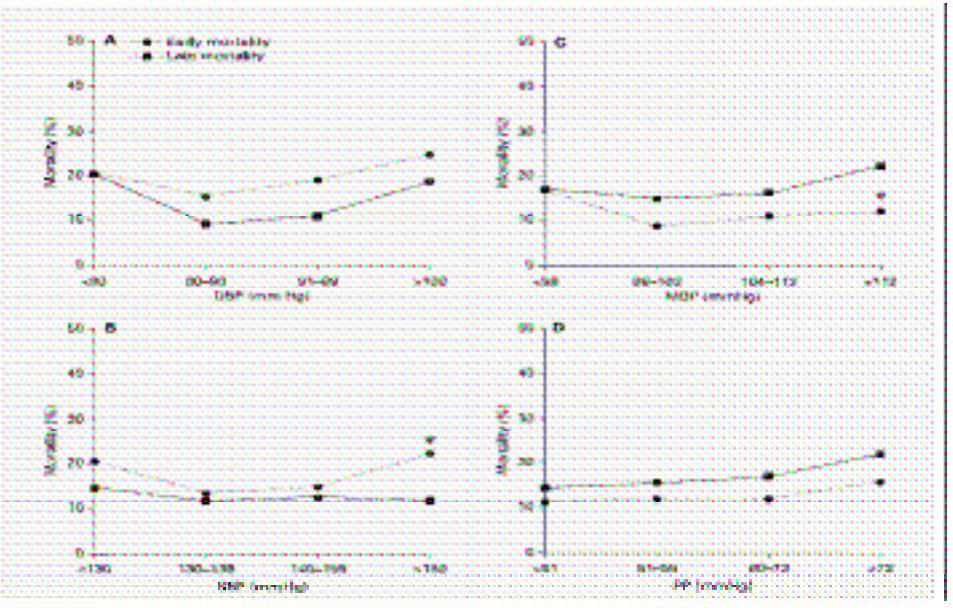

Fig. 2. Relationship between early (first 3 years; ●) and late (last 3 years; ■) mortality and diastolic (DPB; **A**), systolic (SBP; **B**), mean (MBP; **C**), and pulse (PP; **D**) blood pressure. * $p < 0.05$ vs. late mortality.

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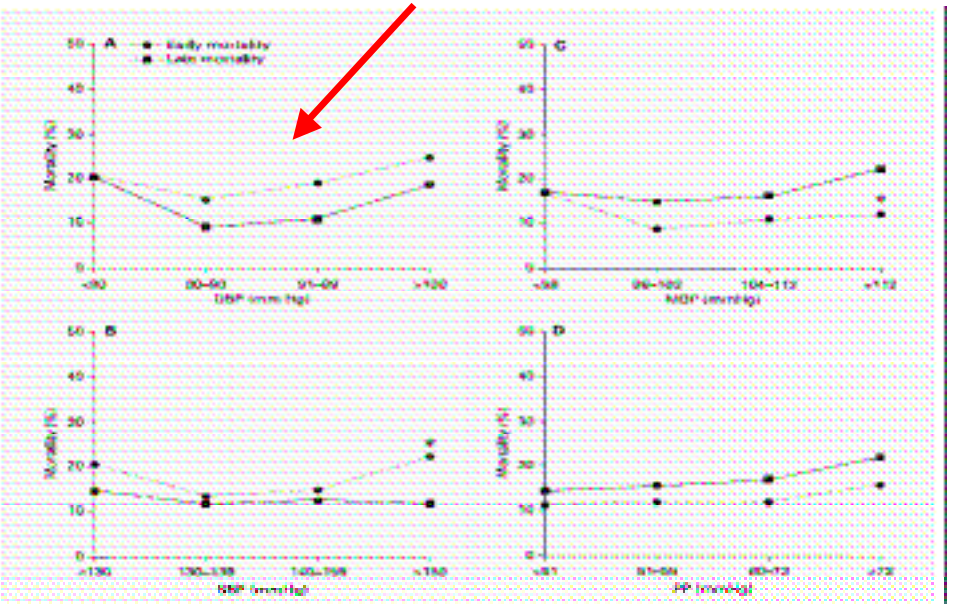

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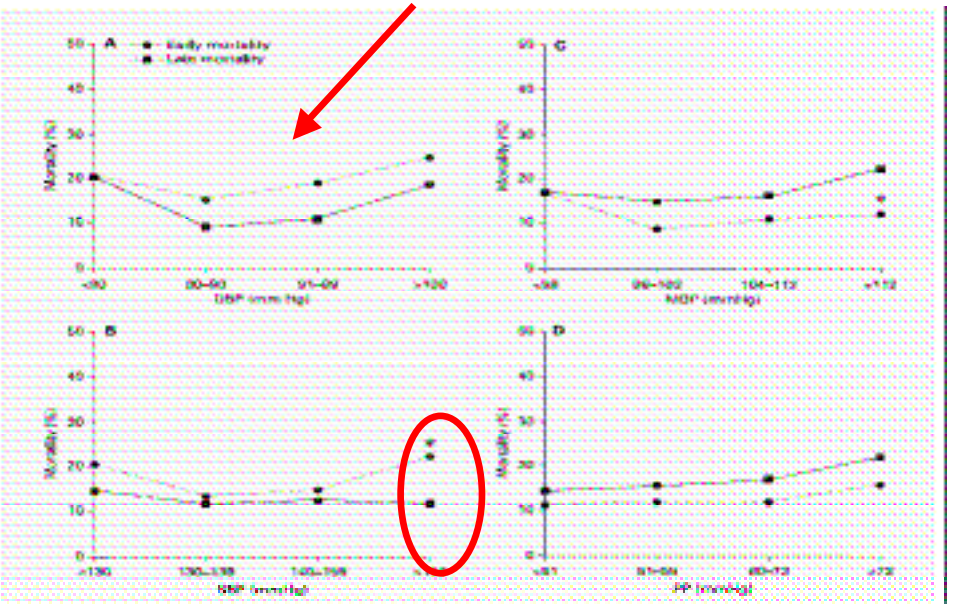

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Table 3. Relative risk and 95% confidence interval on mortality controlled for age, sex, MMSE, ADLs, comorbidity, antihypertensive therapy, coronary artery disease, congestive heart failure, and diabetes for diastolic (DBP), systolic (SBP), mean (MBP), and pulse blood pressure (PP)

	DBP (mm Hg)			
	<80	80–89	90–99	>99
All subjects	1.95 (1.38–2.76)	1 (referent)	1.43 (0.97–2.10)	2.35 (1.26–4.39)
MMSE ≥24	1.64 (1.11–2.41)	1 (referent)	1.39 (0.88–2.19)	1.60 (0.68–3.76)
MMSE <24	2.84 (2.53–5.24)	1 (referent)	1.51 (0.83–2.74)	3.41 (1.40–8.29)
	SBP (mm Hg)			
	<130	130–139	140–159	>159
All subjects	0.74 (0.44–1.24)	1 (referent)	0.90 (0.59–1.39)	0.81(0.50–1.30)
MMSE ≥24	0.85 (0.48–1.52)	1 (referent)	1.09 (0.68–1.63)	0.93 (0.55–1.57)
MMSE <24	0.53 (0.25–1.10)	1 (referent)	0.66 (0.38–1.14)	0.53 (0.28–1.02)
	MBP (mm Hg)			
	<98	98–103	104–112	>112
All subjects	1.90 (0.92–3.94)	1 (referent)	1.15 (0.75–1.78)	1.22 (0.79–1.89)
MMSE ≥24	1.26 (0.79–2.00)	1 (referent)	0.90 (0.55–1.49)	1.07 (0.66–1.45)
MMSE <24	1.86 (1.02–3.40)	1 (referent)	1.57 (0.86–2.87)	1.49 (0.82–2.72)
	PP (mm Hg)			
	0–50	51–60	61–74	>74
All subjects	1 (referent)	1.15 (0.76–1.75)	1.27 (0.84–1.92)	1.29 (0.85–1.95)
MMSE ≥24	1 (referent)	1.13 (0.72–1.78)	1.15 (0.73–1.81)	0.93 (0.60–1.53)
MMSE <24	1 (referent)	1.13 (0.59–2.16)	1.47 (0.75–2.88)	2.35 (1.31–4.2)

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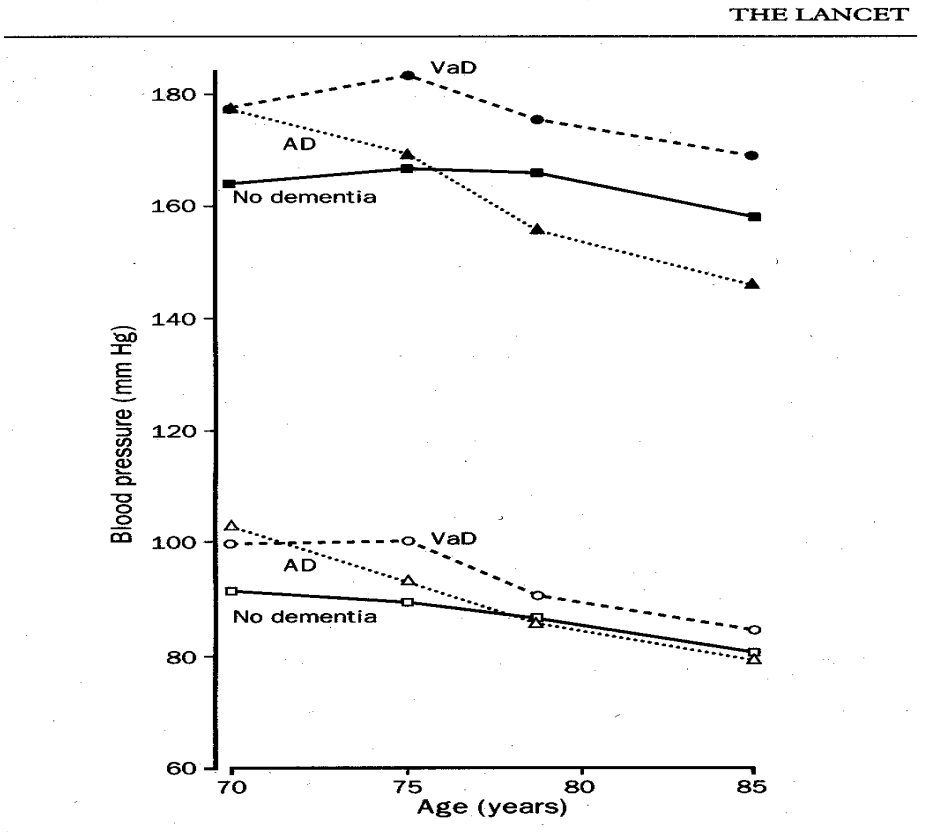
BLOOD PRESSURE AND DEMENTIA

IS IT DANGEROUS TO TREAT HYPERTENSION IN THE ELDERLY?

A 15-year follow-up of blood pressure and Alzheimer's disease

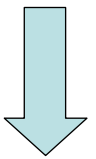


Skoog et al. Lancet 1996

HONOLULU-ASIA AGING STUDY

High midlife blood pressure

in men not treated for hypertension



Alzheimer's disease in old age

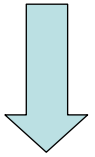
Vascular dementia in old age

Launer et al. Neurobiology of Aging 2000

Prospective Population Study of Women in Gothenburg

High midlife blood pressure

in women not treated for hypertension



Dementia in old age

Skoog et al 2008

ANTIHYPERTENSIVE DRUGS AND RISK OF DEMENTIA

Indianapolis (prevalence)	OR
Dementia	0.67
Alzheimer's Disease	0.59

(Richards et al. J Am Geriatr Soc 2000;48:1035-41)

Kungsholmen (incidence)	RR (95%-CI)
Dementia	0.7 (0.6-1.0)

(Guo et al. Arch Neurol 1999;56:991-996)

Rotterdam (incidence)	RR (95%-CI)
Dementia	0.76 (0.52-1.12)
Vascular dementia	0.30 (0.11-0.99)

(In`t Veld et al. Neurobiol Aging, 2001; 22:407-412)

Cashe County Study (incidence)	RR (95%-CI)
Alzheimer's disease	0.64 (0.41-0.98)

(Khachaturian et al . Arch Neurol 2006;63:686-92)

Honolulu Asia Study

- For each additional year of antihypertensive treatment there was a reduction in the risk of incident dementia (hazard ratio [HR]=0.94, 95% CI, 0.89 to 0.99)
- Same result for incident Alzheimer's disease
- Thus, the longer time on treatment, the lower risk of dementia

Peila et al. Stroke 2006

RCT OF ANTI-HYPERTENSIVE TREATMENT ON COGNITIVE IMPAIRMENT OR DEMENTIA – POSITIVE RESULTS

Study	Subjects	Treatment	Neuropsychological test	Follow-up period	Results
MRC[60]	2,584 subjects; aged 65–74; SBP 160–209/ DBP < 115 mm Hg	Diuretic (hydrochlorothiazide), β blocker (atenolol) vs. placebo	PALT, TMT-A	4.5 (years)	Significant difference in the mean SBP fall between groups: diuretic 33.5, β blocker 30.9, placebo 16.4 mm Hg; no difference in the mean learning test coefficients (rate of change of score over time) between groups: diuretic −0.31 (95% CI −0.23 to −0.39), β blocker −0.33 (−0.25 to −0.41), placebo −0.30, (−0.24 to −0.36)
Syst-Eur[64]	2,418 systolic hypertensives; mean age of 70 years	CCB (nitrendipine) with possible addition of ACE-I (enalapril), diuretic (hydrochlorothiazide), or both vs. placebo	MMSE	3.9 (years)	Mean difference in BP between the treatment and placebo groups was 7.0 mm Hg systolic and 3.2 mm Hg diastolic; the rates of dementia incidence on placebo and active treatment were 7.4 and 3.3 cases per 1,000 patient-years (risk reduction: 55% risk reduction; 95% CI: 24–73%) with significance
PROGRESS[65]	6,105 subjects with prior stroke or transient ischemic attack; mean age of 64 years	ACE-I (perindopril) with possible addition of diuretic (indapamide) vs. placebo	MMSE	3.9 (years)	Mean difference in BP between the treatment and placebo groups was 9.0 mm Hg systolic and 4.0 mm Hg diastolic; the rates of dementia incidence on placebo and active treatment were 7.1 and 6.3% (relative risk reduction: 12%; 95% CI: −8 to 28%) without significance; the rates of cognitive decline on placebo and active treatment were 11.0 and 9.1% (risk reduction: 19%; 95% CI: 4–32%) with significance
HOPE[66]	9,297 patients with vascular disease or diabetes plus an additional risk factor; age ≥ 55	ACE-I (ramipril) vs. placebo	—	4.5 (years)	Mean difference in BP between the treatment and placebo groups was 3.8 mm Hg systolic and 2.8 mm Hg diastolic; the rates of cognitive decline on placebo and active treatment were 0.6 and 1.1% (relative risk: 0.59; 95% CI: 0.37–0.94) with significance

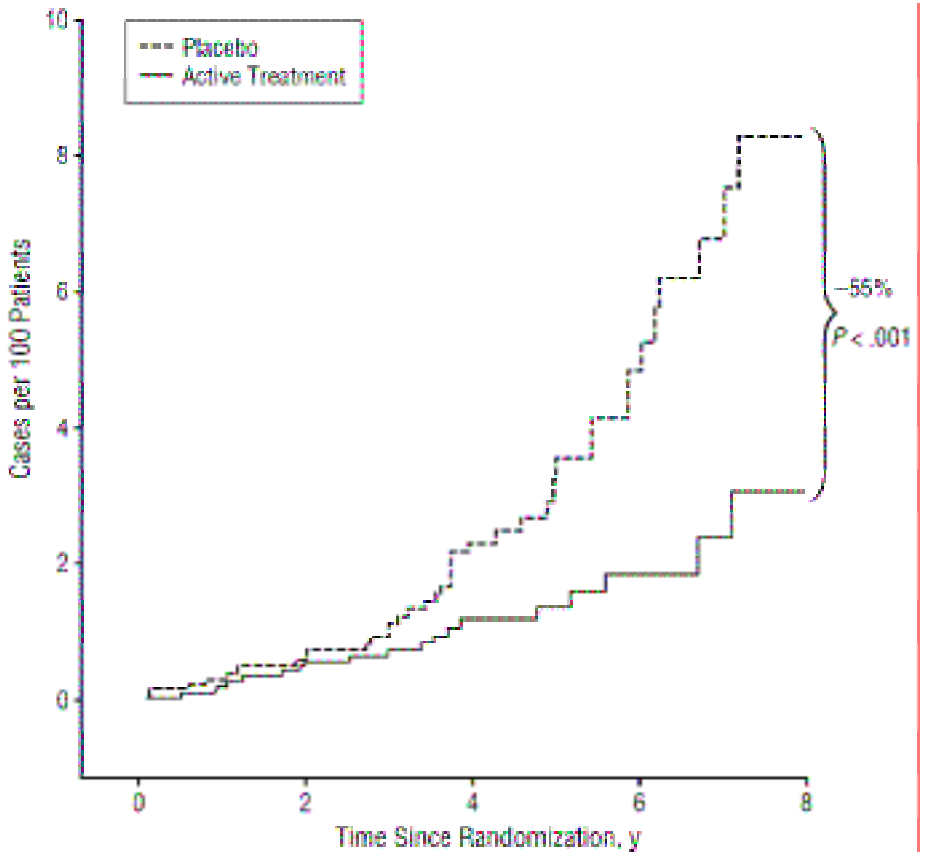
The Prevention of Dementia With Antihypertensive Treatment

New Evidence From the Systolic Hypertension in Europe (Syst-Eur) Study

Arch Intern Med. 2002;162:2046-2052

Treatment consisted of nitrendipine (10-40 mg/d) (70.2%), with the possible addition of enalapril maleate (5-20 mg/d) (35.4%), hydrochlorothiazide (12.5-25 mg/d) (18.4%), or both add-on drugs.

"Nitrendipine" calcium channel Blocker dihydropyridines cross the blood-brain barrier.



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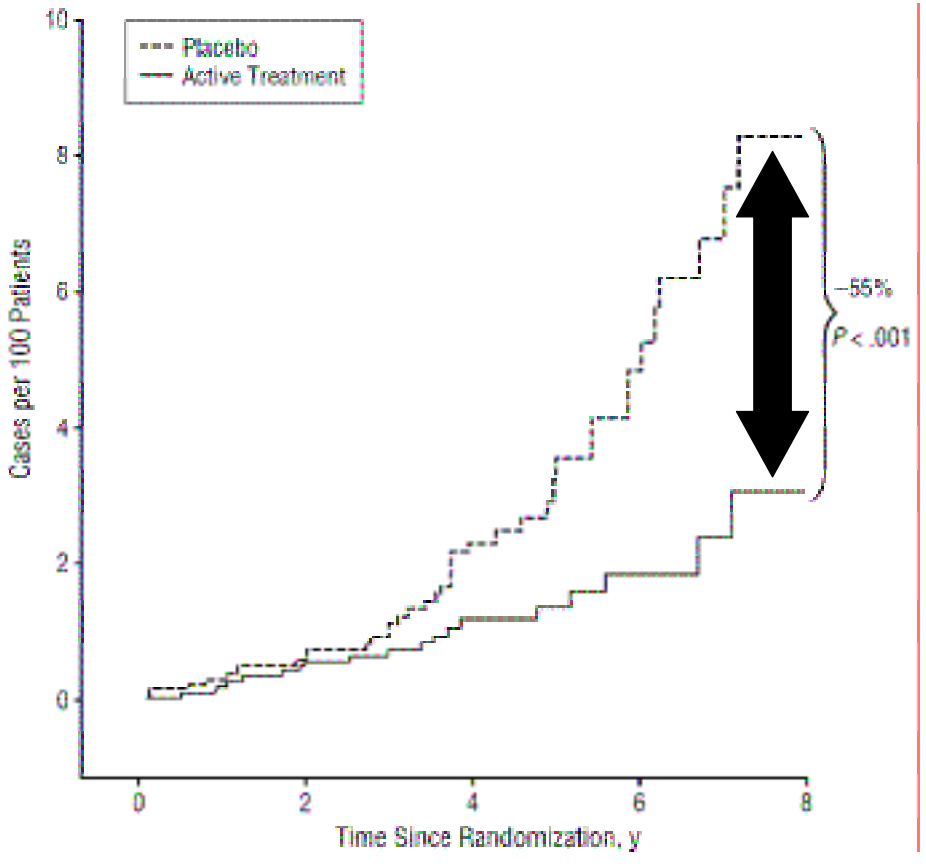
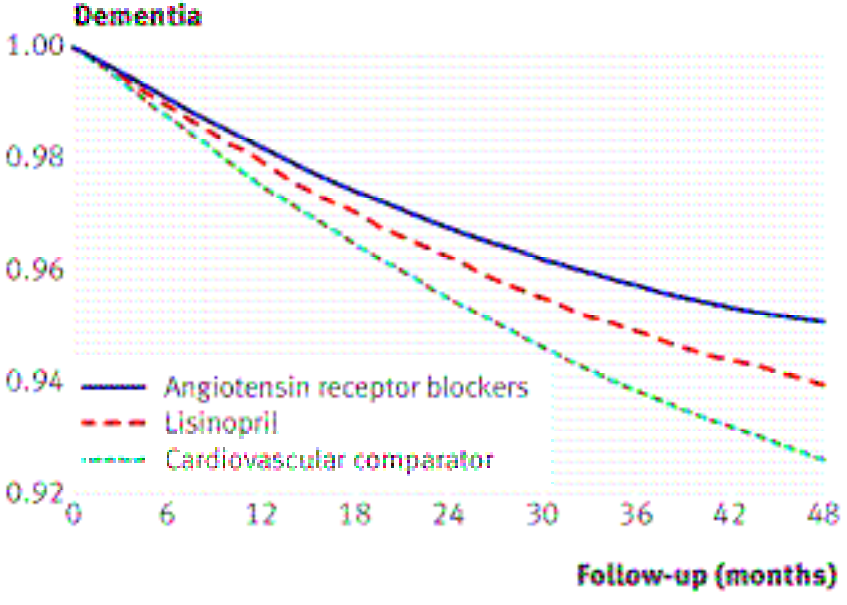


RCT OF ANTI-HYPERTENSIVE TREATMENT ON COGNITIVE IMPAIRMENT OR DEMENTIA – NEGATIVE RESULTS

SHEP[61]	4,736 systolic hypertensives, mean age of 72 years	Diuretic (chlorthalidone) with possible addition of β blocker (atenolol) or sympathetic nervous blocker (reserpine) vs. placebo	Short-CARE	4.5 (years)	Mean difference in BP between the treatment and placebo groups was 12 mm Hg systolic and 4 mm Hg diastolic; the rates of dementia incidence on placebo and active treatment were 4.2 and 3.6 cases per 1,000 patient-years (relative risk reduction: 14%; 95% CI: −26 to 54%) without significance
HYVET-COG[62]	3,336 hypertensives (SBP 160–200 and DBP < 110 mm Hg); age ≥ 80	Diuretic (indapamide) with possible addition of ACE-I (perindopril) vs. placebo	MMSE	2.2 (years)	Mean difference in BP between the treatment and placebo groups was 15 mm Hg systolic and 5.9 mm Hg diastolic; the rates of dementia incidence on placebo and active treatment were 38 and 33 cases per 1,000 patient-years (hazard ratio 0.86; 95% CI: 0.67–1.09) without significance
SCOPE[63]	4,964 hypertensives; aged 70–89; SBP 160–170/DBP 90–99 mm Hg	ARB (candesartan) vs. placebo; Open-label antihypertensive drugs were added to both groups	MMSE	3.7 (years)	Mean difference in BP between the treatment and placebo groups was 3.2 mm Hg systolic and 1.6 mm Hg diastolic; there was no significant difference between the groups in the adjusted change in MMSE score (mean difference 0.15; 95% CI: −0.08 to 0.38); the rates of dementia incidence on placebo and active treatment were 6.8 and 6.3 cases per 1,000 patient-years without significance; the rates of cognitive decline on placebo and active treatment were 15.2 and 13.5 cases per 1,000 patient-years without significance
PRoFESS[58]	20,332 subjects with ischemic stroke; mean age of 66 years	ARB (telmisartan) vs. placebo	MMSE	2.4 (years)	Mean difference in BP between the treatment and placebo groups was 3.8 mm Hg systolic and 2.0 mm Hg diastolic; the rates of cognitive decline on placebo and active treatment were 11 and 11% (relative risk: 0.95; 95% CI: 0.87–1.05) without significance

Use of Angiotensin Receptor Blockers and risk of "DEMENTIA" in a predominantly male population: prospective cohort analysis



	dementia
Variables	Hazard rate* (95% CI)
Angiotensin receptor blocker *v* lisinopril	0.81 (0.73 to 0.90)
Angiotensin receptor blocker *v* cardiovascular comparator	0.76 (0.69 to 0.84)
Lisinopril *v* cardiovascular comparator	0.94 (0.91 to 0.97)

Li NC et al., BMJ 2010

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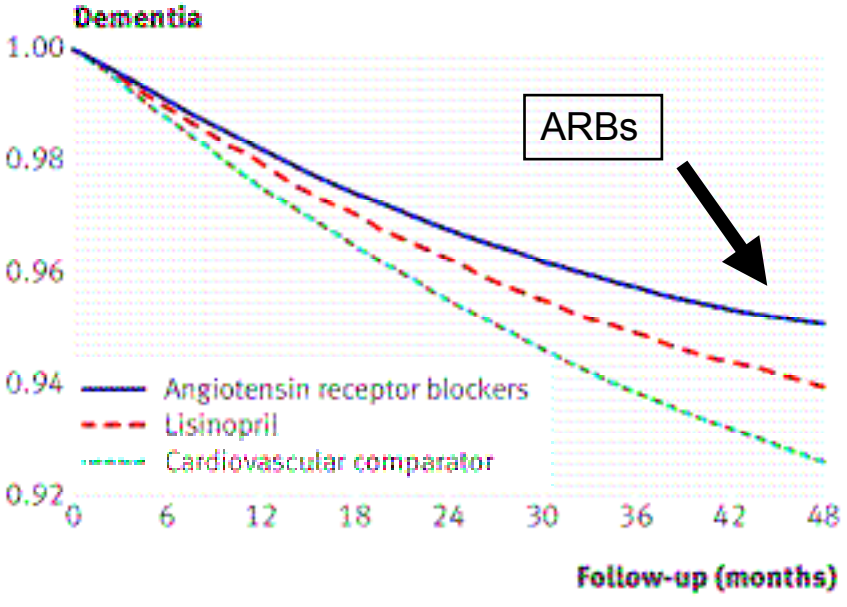

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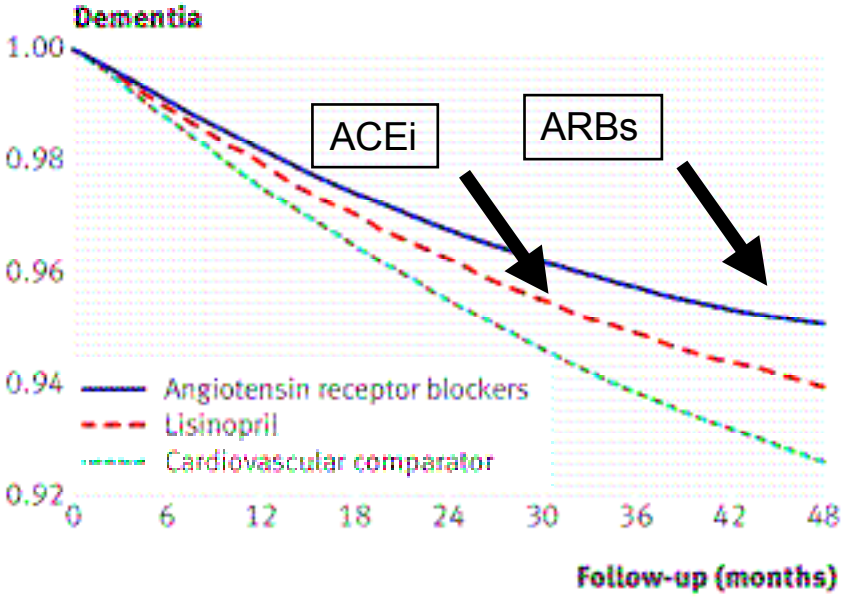

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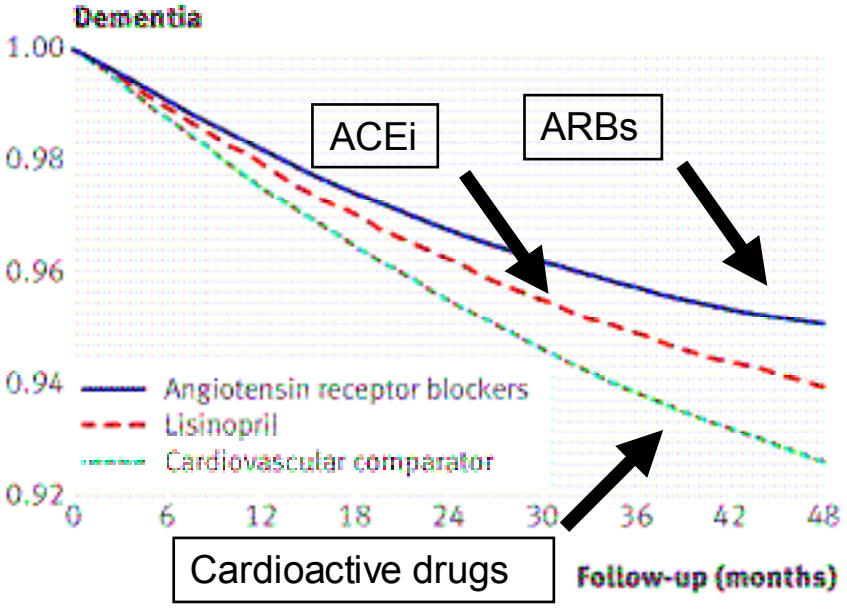

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Li NC et al., BMJ 2010

Conclusioni

- L'ipertensione è una condizione ad alta prevalenza nella popolazione anziana
- Molti soggetti non sanno di essere ipertesi e quindi non sono trattati
- Il trattamento farmacologico dell' ipertensione riduce il rischio di Ictus e malattie cardiovascolari in tutte le fasce d'età.
- Alti valori di pressione arteriosa sono associati e predicono il decadimento cognitivo

Conclusioni

- Il rischio per ipertesi non trattati di sviluppare demenza è circa del 40%.
- Il trattamento anti-ipertensivo riduce il rischio di demenza.
- L'ipertensione va trattata anche in età avanzata indipendentemente dalla presenza di demenza per prevenire la progressione della malattia cerebrovascolare.

Ma ….. Sia l'ipertensione che la demenza devono essere individuate…..

Molte persone non sanno di essere ipertese e molte ritengono che il decadimento cognitivo non sia prevenibile.

Si prevedono circa 106 milioni di casi di demenza nel 2050 di questi 23 milioni potrebbero essere totalmente evitati se potessimo ritardare l'inizio della malattia di almeno 2 anni con misure di prevenzione cardiovascolare *(Alzheimer Statistics)*