Optimal BP levels in older adults?

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High Blood pressure in older adults

- Prevalence and risks of high BP

- Interest of reducing BP in old persons and target BP levels

-Management of very old people with hypertension

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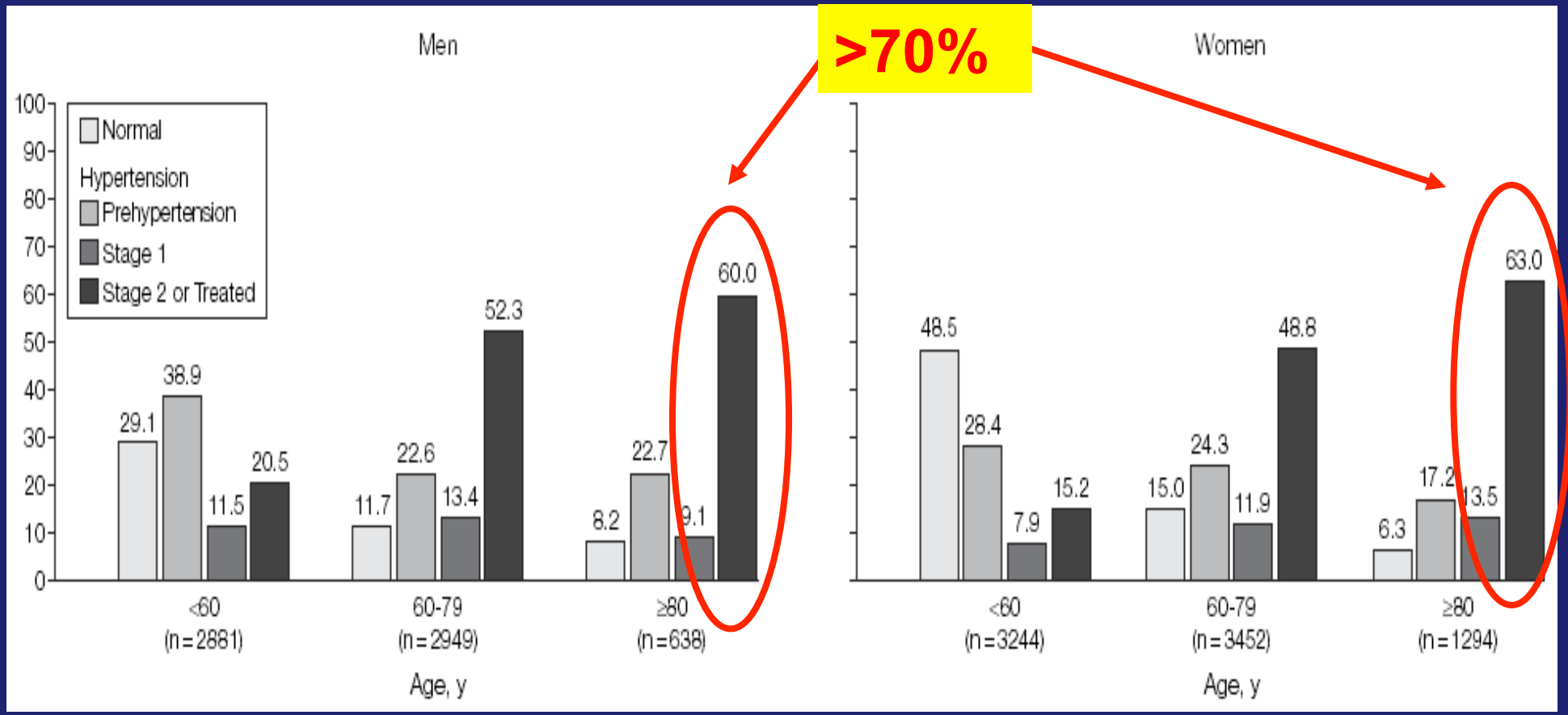
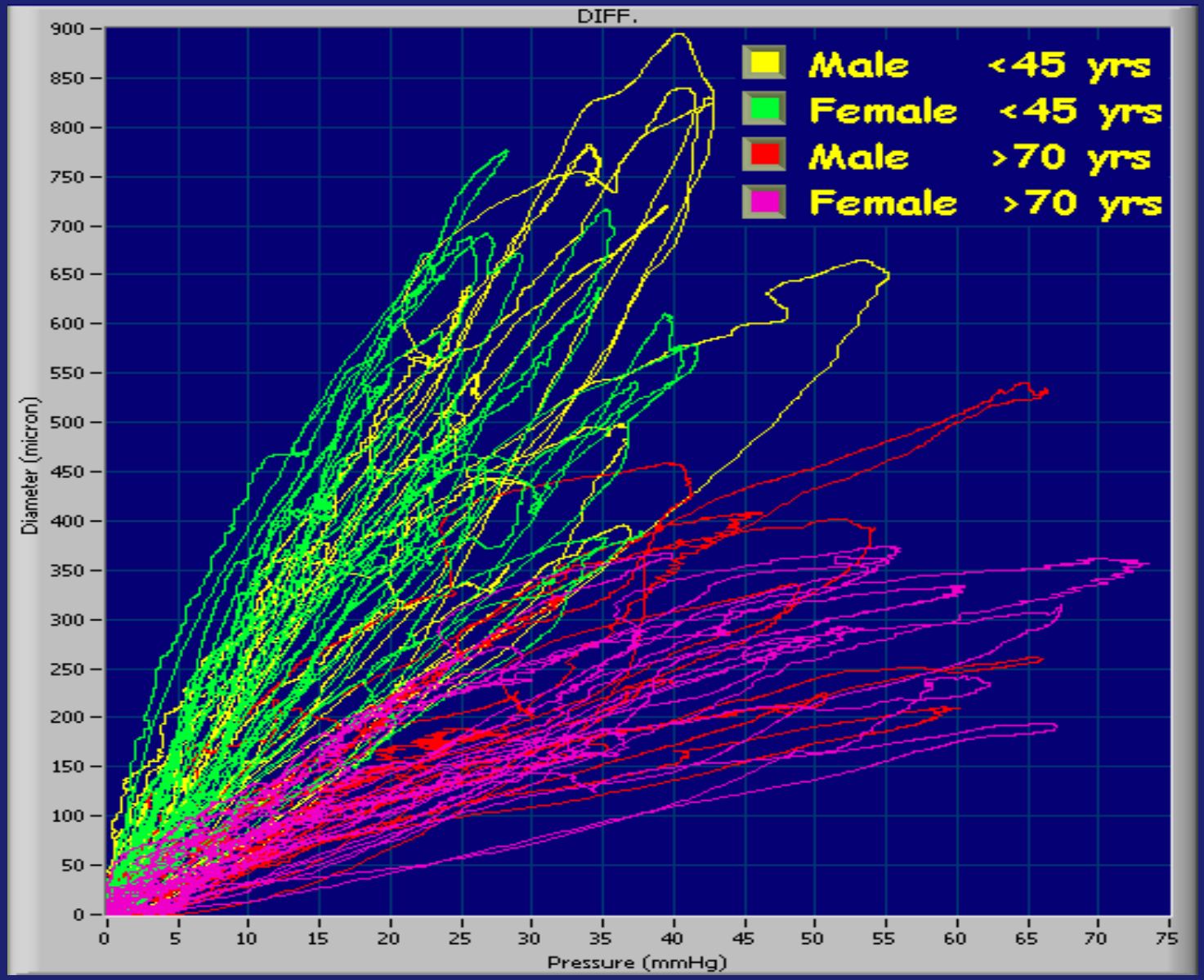
Prevalence of hypertension after 80



JAMA. 2005;294:466-472

Systole-Diastole changes in the Pressure/Diameter relationship



P. Salvi and A. Benetos

Honolulu-Asia Aging Study

3703 subjects
BP at middle age (45-65 years)
Evaluation of cognitives functions 20-25 years later

SBP >160 vs. 110<SBP<140 mmHg
Risk of dementia X 4.8 (2.0-11.0)

DBP>95 vs. 80<DBP<89 mmHg
Risk of dementia X 4.3 (2.0-11.0)

Launer et al, Neurobiol Aging, 2000

Risk factors for COGNITIVE DECLINE AND DEMENTIA

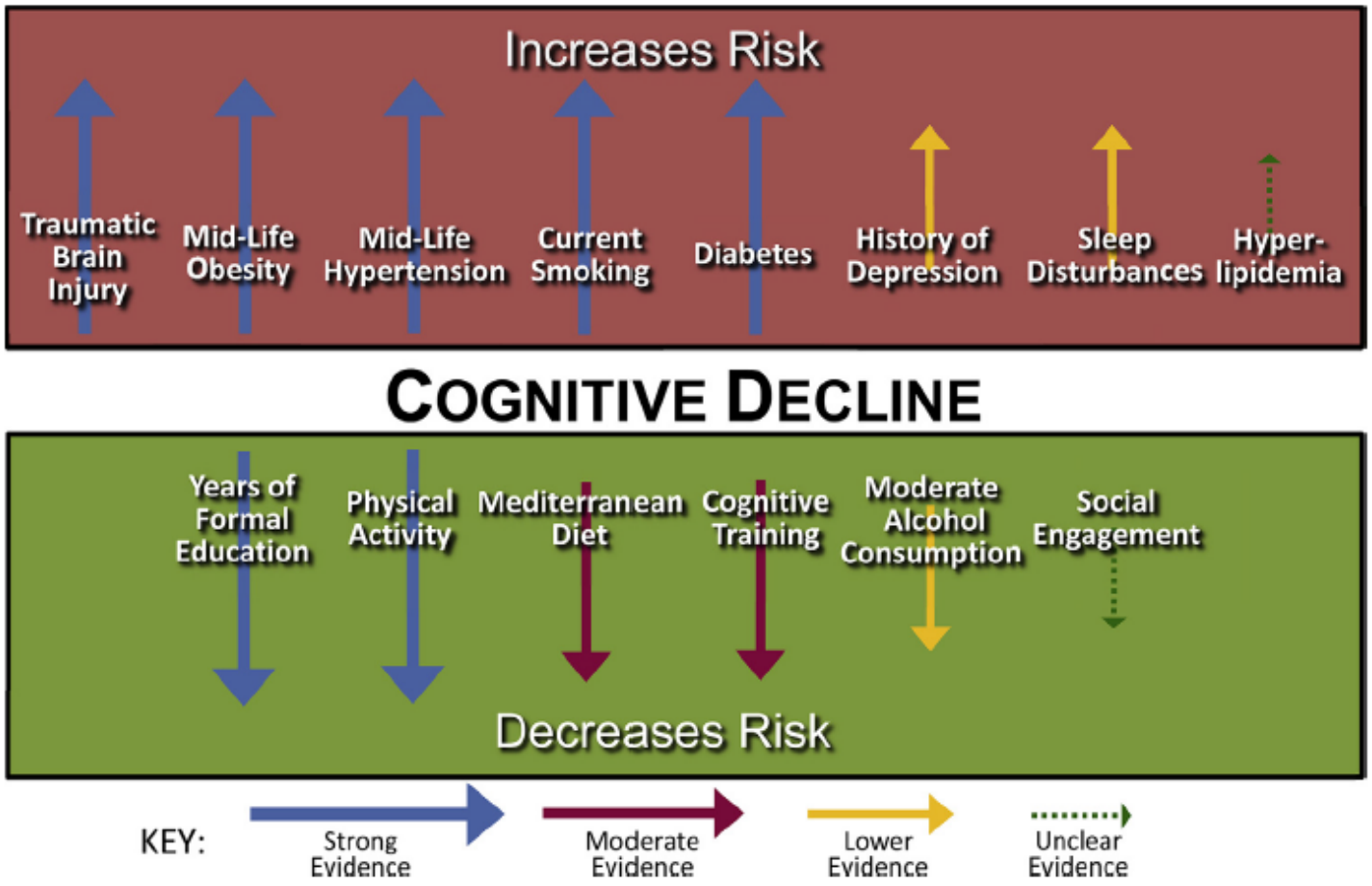


Fig. 1. Strength of evidence on risk factors for cognitive decline.

M. Baumgart et al Alzheimer's & Dementia 11 (2015) 718-726

Temporal Trends in the Incidence of Dementia.

Table 2. Temporal Trends in the Incidence of Dementia.*

Subtype	No. of Cases	Total No. of Observation Periods	5-Yr Cumulative Hazard Rate (95% CI)†				5-Yr Hazard Ratio (95% CI)‡				P Value for Trend
			Epoch 1	Epoch 2	Epoch 3	Epoch 4	Epoch 2	Epoch 3	Epoch 4	Trend§	
Overall dementia	371	9015	3.6 (2.9–4.4)	2.8 (2.2–3.5)	2.2 (1.8–2.8)	2.0 (1.5–2.6)	0.78 (0.59–1.04)	0.62 (0.47–0.83)	0.56 (0.41–0.77)	0.80 (0.72–0.90)	<0.001
Alzheimer's disease	264	9015	2.0 (1.5–2.6)	2.0 (1.5–2.6)	1.7 (1.3–2.3)	1.4 (1.0–1.9)	1.00 (0.70–1.43)	0.88 (0.62–1.25)	0.70 (0.48–1.03)	0.88 (0.77–1.00)	0.052
Vascular dementia	84	9014	0.8 (0.6–1.3)	0.8 (0.5–1.2)	0.4 (0.2–0.7)	0.4 (0.2–0.7)	0.89 (0.51–1.56)	0.46 (0.25–0.86)	0.45 (0.23–0.87)	0.71 (0.56–0.90)	0.004

* The baseline examination period was between 1977 and 1983 for the first epoch, between 1986 and 1991 for the second epoch, between 1992 and 1998 for the third epoch, and between 2004 and 2008 for the fourth epoch.
† The 5-year cumulative hazard rates (the cumulative incidence of dementia per 100 persons over a period of 5 years) are adjusted for age and sex.
‡ The 5-year hazard ratios (the incidence of dementia during each epoch relative to the incidence during the first epoch) are adjusted for age and sex.
§ We estimated linear trends (the decline per decade in the 5-year incidence of dementia) using the elapsed mean time (in decades) between the first epoch and each consecutive epoch.

Satizabal CL et al. N Engl J Med 2016;374:523-532

Reduction of the Incidence of the neurocognitive syndromes in the Framingham study between 1977 et 2008

-Relative to the incidence during the first epoch, the incidence declined by 22%, 38%, and 44% during the second, third, and fourth epochs, respectively.

This risk reduction was observed only among persons who had at least a high school diploma.

The prevalence of most vascular risk factors (except obesity and diabetes) have decreased over time, but none of these trends completely explain the decrease in the incidence of dementia.

Satizabal CL et al. N Engl J Med 2016;374:523-532

High Blood pressure in older adults

- Prevalence and risks of high BP

- Interest of reducing BP in old persons and target BP levels

-Management of very old people with hypertension

Blood pressure lowering in the elderly

or…

Should we adapt antihypertensive strategies in old patients

Question N°1

- What is the evidence of the benefit when lowering BP in old patients?

Benefits of antihypertensive treatment on stroke mortality and cardiac diseases in patients aged 60-79

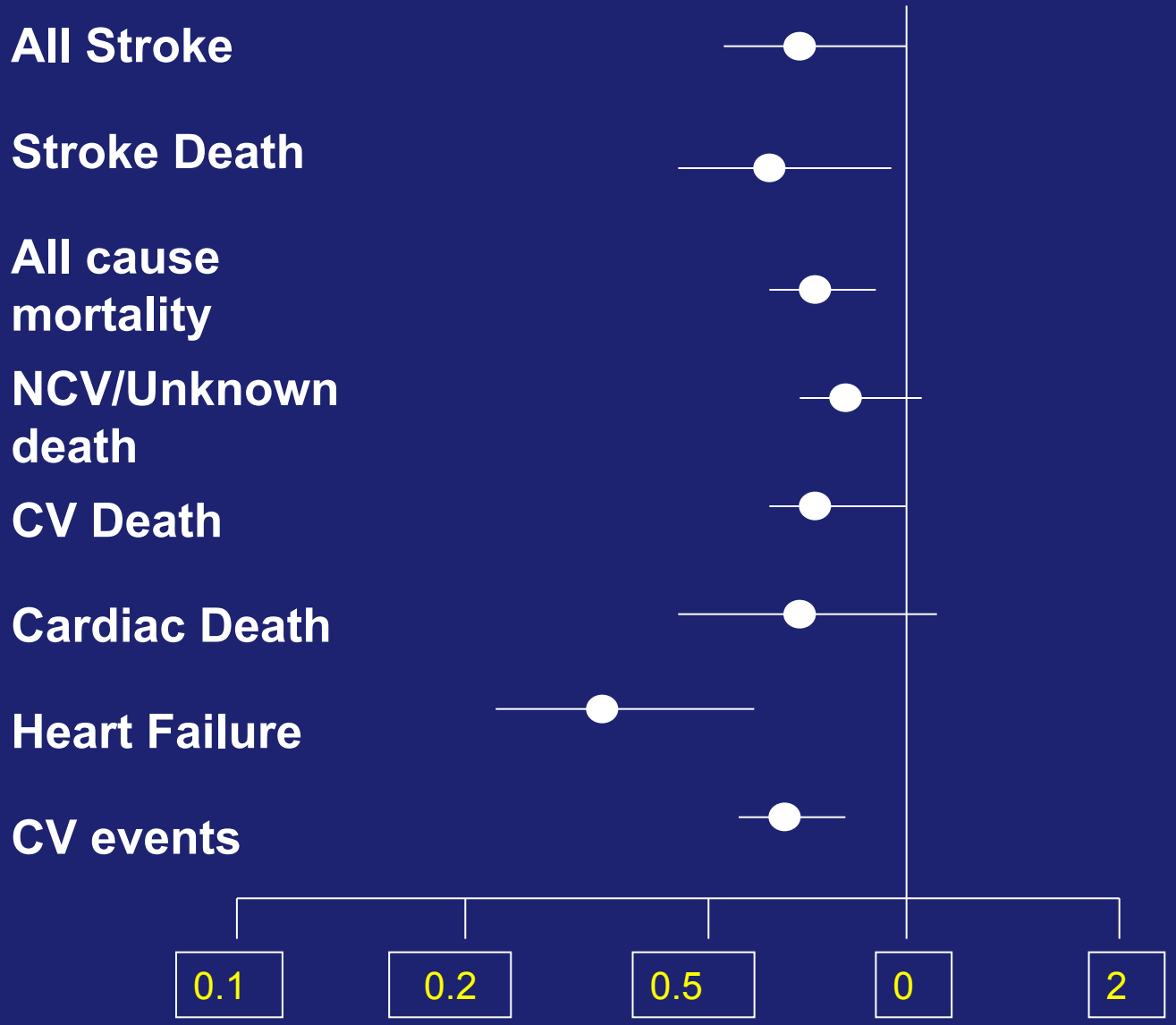
Fatal strokes		p < 0.001 (-51 à -38)
Non fatal strokes		p < 0.001 (-45 à -24)
Fatal cardiac disease	- 25 %	p < 0.001 (-36 à -12)
Non fatal cardiac	- 15 %	p = 0.036 (-27 à -1)
Total mortality	- 12 %	p = 0.009 (-27 à -1)

60-79 years: clear benefits from BP reduction

Insua JT et al. a meta-analysis. Ann Intern Med 1994

Treating hypertension in patients 80+: Actif tt vs. Placebo

The HYVET study



Beckett NS, et al.

NEJM 2008;358

Question N°2

Should we apply the HYVET conclusions to all 80+ patients?

>80 years

The most growing and the most heterogeneous population

HYVET

Warwick *et al. BMC Medicine* (2015) 13:78
DOI 10.1186/s12916-015-0328-1

BMC Medicine

RESEARCH ARTICLE Open Access

No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over

Jane Warwick[1*], Emanuela Falaschetti[2], Kenneth Rockwood[3], Arnold Mitnitski[4], Lutgarde Thijs[5], Nigel Beckett[6], Christopher Bulpitt[6] and Ruth Peters[2]

SPRINT

‘Among ambulatory adults aged 75 years or older, treating to an SBP target of less than 120mmHg compared with an SBP target of less than 140 mmHg resulted in significantly lower rates of fatal and nonfatal major cardiovascular events and death from any cause.’

In addition, exploratory analysis suggested that the benefit of intensive BP control was consistent among persons in this age range who were frail....

Williamson J et al JAMA. 2016;315:2673.

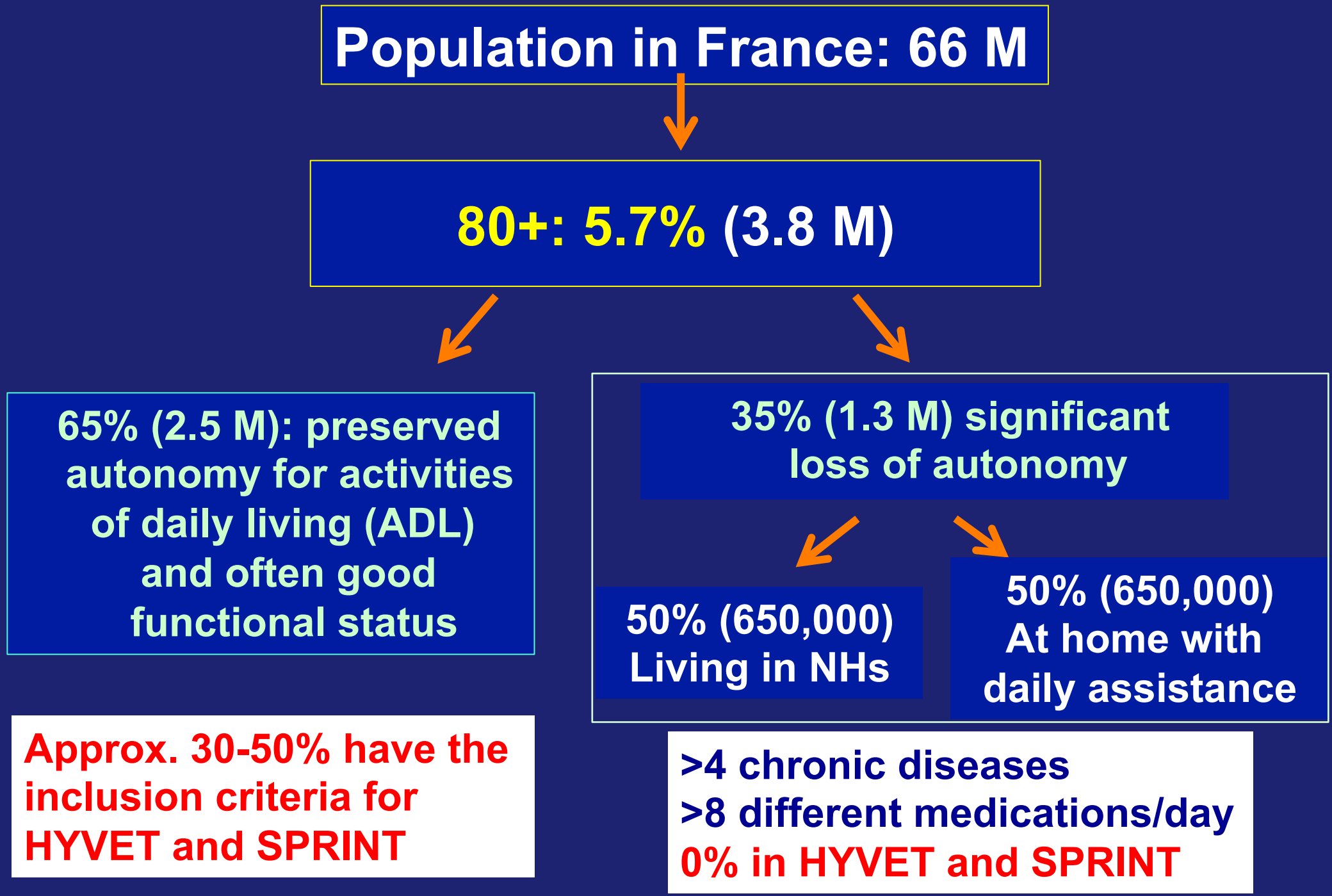
Main exclusion criteria in HYVET and SPRINT

Main Exclusion Criteria in HYVET:

- Living in NHs
- Limited autonomy
- Clinical dementia
- Heart failure needing treatment with ACEI, ARA, Diuretics
- SBP<140mmHg in upright position
- Renal failure
- Patients presenting a high probability of having a major health problem during the 5 year follow-up period

Main Exclusion Criteria in SPRINT:

- Type 2 diabetes
- History of stroke
- Symptomatic heart failure within the past 6 months or reduced LVEF (<35%)
- Clinical diagnosis of/or treatment for dementia
- Expected survival of less than 3 years
- Unintentional weight loss (>10% of body weight) during the last 6 months,
- SBP of less than 110 mm Hg following 1 minute of standing
- Living in NHs.


Population in France: 66 M
80+: 5.7% (3.8 M)
65% (2.5 M): preserved autonomy for activities of daily living (ADL) and often good functional status
35% (1.3 M) significant loss of autonomy
50% (650,000) Living in NHs
50% (650,000) At home with daily assistance
Approx. 30-50% have the inclusion criteria for HYVET and SPRINT
>4 chronic diseases
>8 different medications/day
0% in HYVET and SPRINT

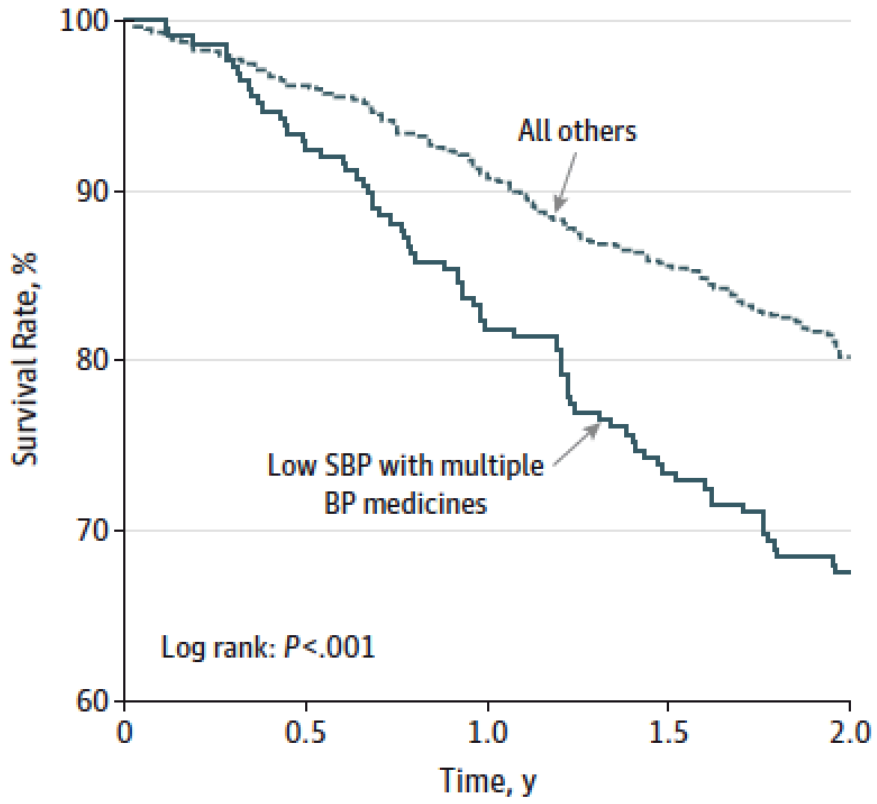
Question N°3

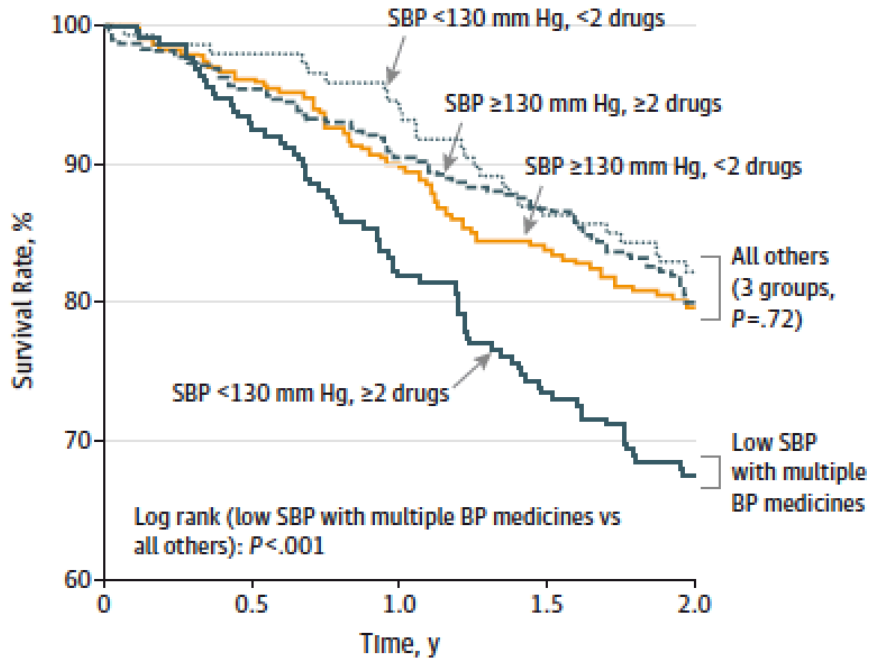
What is the evidence for the benefits of BP lowering in the subgroups who do not have the HYVET/SPRINT 'profile'?

PARTAGE study: Patients 80+ living in NHs

Two-fold increase in mortality in the group with SBP<130mmHg under combination anti-hypertensive therapy (20% of the NHs population)

Kaplan-Meier Survival Curves in Patients With Low Systolic Blood Pressure (SBP) Receiving Multiple BP Medicines and All Other Groups

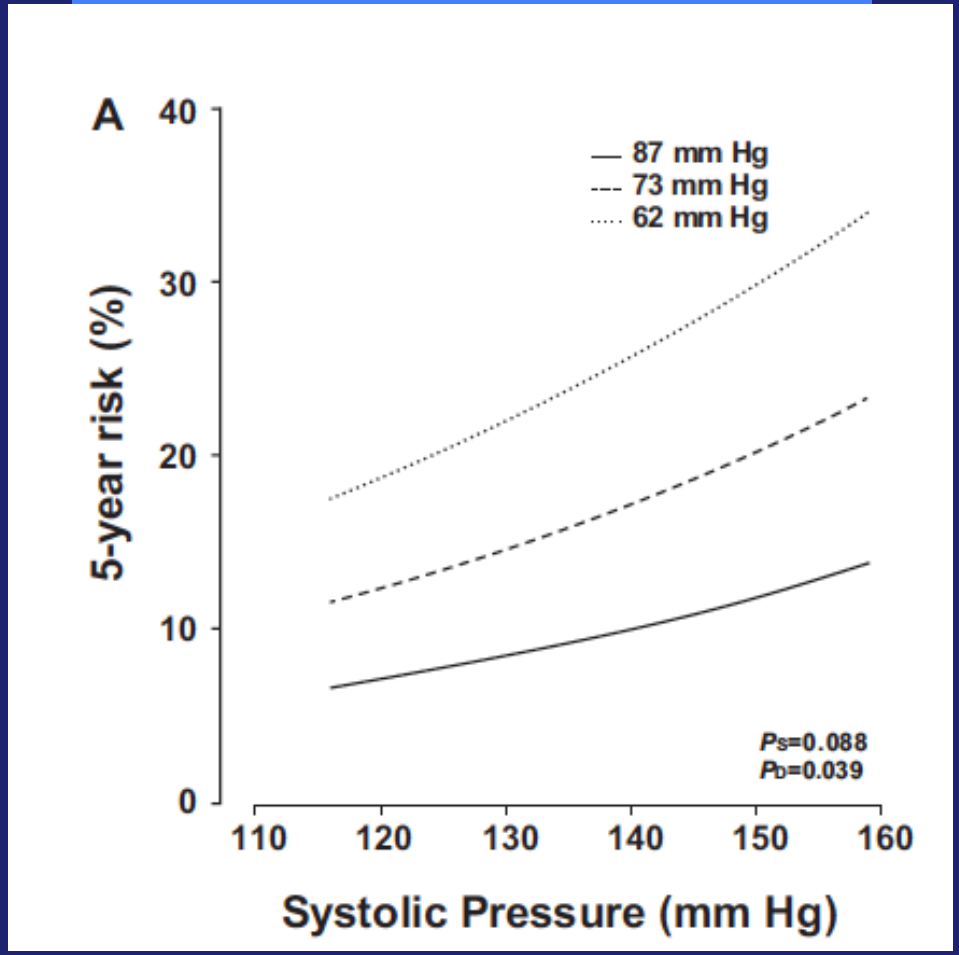




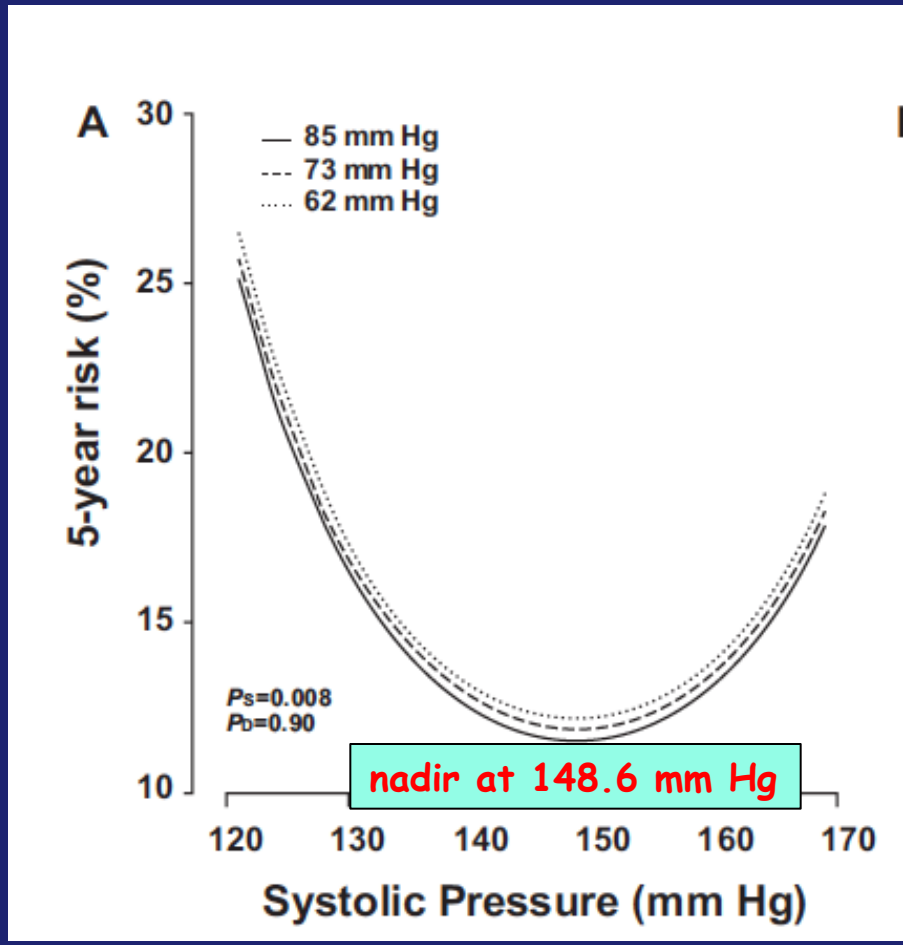
Benetos et al, *JAMA* Int Med 2015

Five-year risk of a cardiovascular event according to home SBP in untreated and treated for Htn subjects

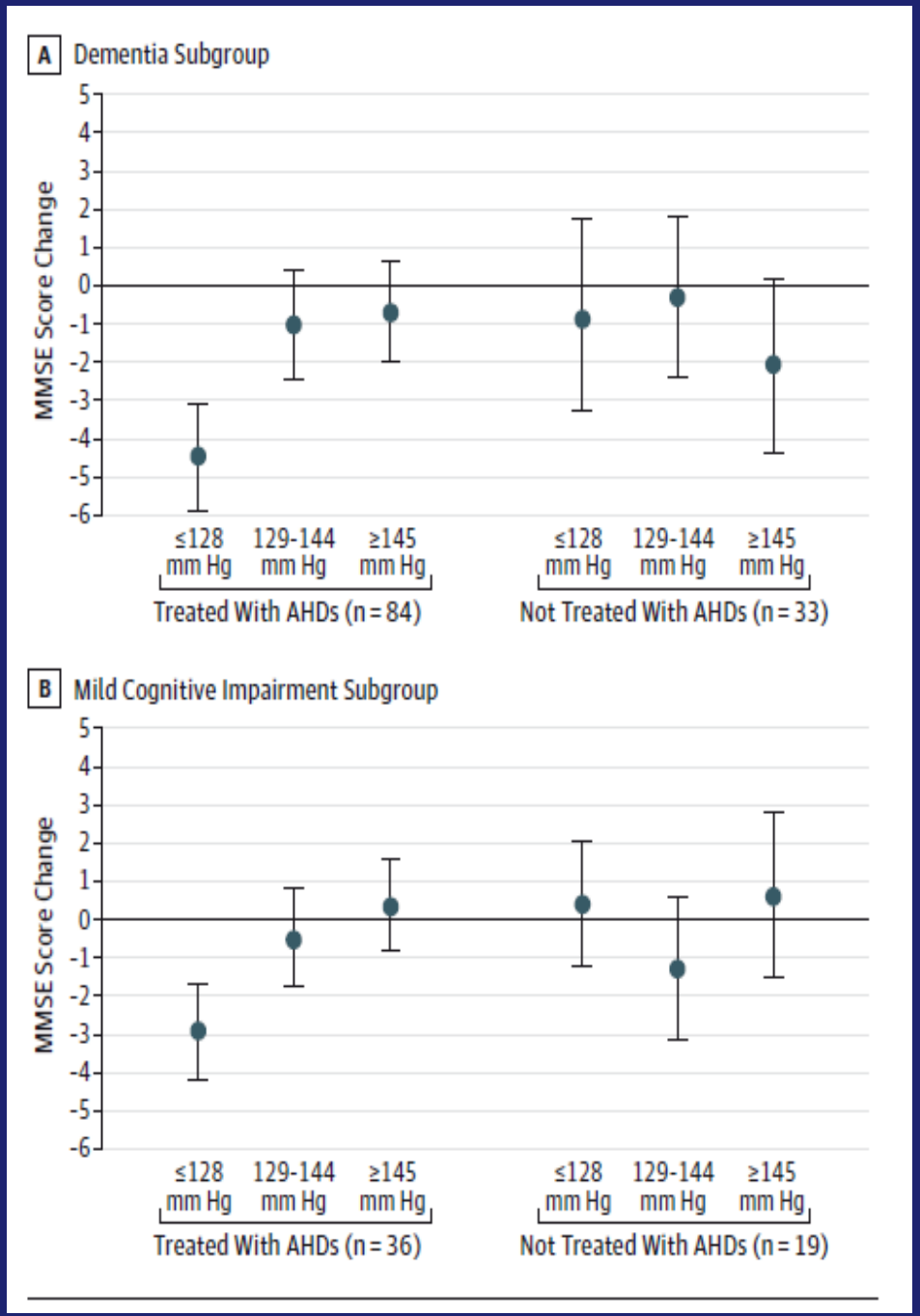
Untreated octogenarians



Treated octogenarians



Aparicio LS et al, Hypertension. 2015



Patients with DEMENTIA or MCI:
More pronounced cognitive decline in old individuals with low SBP under antihypertensive medication

Mossello E et al, JAMA Intern Med 2015

Subgroup analysis for hand grip strength and associations of SBP and all-cause mortality per 10 mmHg lower SBP (n = 570)

		Hazard ratio (95% CI) per 10 mmHg lower SBP	*P*-value
Treatment			
Overall[a] ($n = 249$)		1.29 (1.15, 1.46)	<0.001
By hand grip strength[b]	Low ($n = 161$)	1.24 (1.08, 1.42)	0.002
	High ($n = 88$)	1.40 (1.09, 1.80)	0.009
No treatment			
Overall[a] ($n = 321$)		1.08 (1.00, 1.18)	0.057
By hand grip strength[b]	Low ($n = 201$)	1.10 (1.00, 1.21)	0.060
	High ($n = 120$)	0.99 (0.86, 1.15)	0.90

adjusted for sex and CVD.

Streit S et al, Age and Ageing 2018; 47: 545–550

Lower blood pressure during antihypertensive treatment is associated with higher all-cause mortality and accelerated cognitive decline in the oldest-old. Data from the Leiden 85-plus Study

Sven Streit[1], Rosalinde K. E. Poortvliet[2], Jacobijn Gussekloo[2,3]
Age and Ageing 2018; 47: 545

In this population-based cohort of individuals aged 85 years with a 5-year follow-up, we found lower SBP was associated with higher all-cause mortality and faster annual cognitive decline in participants prescribed antihypertensive therapy.

In participants without antihypertensive treatment, no relation was found between SBP and mortality or cognitive decline.

Question N°4

Does medication-induced BP lowering contribute to the increased morbidity and mortality in people with altered function and loss of autonomy?

No data concerning causality

Question N°5

Should we modify our therapeutic strategy in these patients?

An Expert Opinion From the European Society of Hypertension–European Union Geriatric Medicine Society Working Group on the Management of Hypertension in Very Old, Frail Subjects

Athanase Benetos,* Christopher J. Bulpitt,* Mirko Petrovic, Andrea Ungar, Enrico Agabiti Rosei, Antonio Cherubini, Josep Redon, Tomasz Grodzicki, Anna Dominiczak, Timo Strandberg, Giuseppe Mancia

Two years after the publication of the 2013 guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC),[1] the ESH and the European Union Geriatric Medicine Society have created a common working group to examine the management of hypertensive subjects aged >80 years. The general term hypertension in the elderly is not sufficiently accurate because it mixes younger old patients (60–70 years) with the oldest old. Our group believes that the management of hypertension in individuals aged ≥80 years should be specifically addressed. Although arbitrary, this cutoff value identifies a population that is expanding faster than any other age group with a 50% increase of life expectancy during the past 50 years[2,3]; furthermore, the incidence and prevalence of comorbidities, frailty, and loss of autonomy greatly increases after the age of 80 years[4]; finally, although there is limited evidence on the management of hypertension in this age group, the latest clinical studies indicate that in these patients, treatment may not be the same as in patients in the lower age strata.

The aim of this Working Group was to discuss more in-depth treatment aspects of hypertensive patients aged ≥80 years or older, with special focus on the difficulties and uncertainties posed by very old frail individuals. We focused, in particular, on the following points of the 2013 ESH/ESC guidelines:

Benefits of treatment.
Blood pressure (BP) thresholds and targets.
The choice of treatment.

Benefits of Treatment

The 2013 ESH/ESC guidelines[1] reported the results of the Hypertension in the Very Elderly Double Blind Trial (HYVET). This showed that in hypertensive patients aged ≥80 years, the administration of the thiazide-like diuretic indapamide supplemented, if necessary, by the angiotensin-converting enzyme inhibitor perindopril led to a significant reduction in the risk of major cardiovascular events and all-cause death when compared with placebo.[2] From this, the guidelines concluded that there is evidence that antihypertensive treatment is beneficial in octogenarians in whom BP is elevated and that, therefore, BP-lowering interventions can be strongly recommended within this age range. However, both the ESH/ESC guidelines[1] and other publications[5–8] also point out limitations in the demonstration that treatment is beneficial in octogenarians and this need to be addressed. First, the HYVET is to date the only randomized clinical trial that has addressed this important issue, making confirmation by a second trial highly desirable. Second, the age of the HYVET patients was for the most part closer to 80 years (73% in the 80–84 and 22% in the 85–89 range), leaving the effect of treatment in patients close to or >90 years of age largely unexplored. Third, because the trial was prematurely interrupted by the Safety Monitoring Board (because of the evidence of protective effect of BP reduction in the treated group), the follow-up was rather short (median, 1.8 years). Despite the observation that in the HYVET patients the rate of events remained lower in the originally treated group 1 year after the trial termination,[9] this

Hypertension. 2016;67:820-5

Old Frail Patients

2013 ESH/ESC guidelines: ‘In frail older patients, it is recommended to leave decisions on antihypertensive therapy to the treating physician, and base them on monitoring of the clinical effects of treatment’.

2016 ESH/EUGMS Expert Group: Therapeutic decisions should be preceded by:

A- Accurate information on functional capacity and cognitive status;

B- Attention to multiple drug administration so common in this age stratum;

C- Stratification of the frailty status by one of the available rapid methods.

Benetos et al; Hypertension 2016;67:820-5

Assessment of Frailty

A rapid (<10 minutes) assessment of frailty is feasible.

The most frequently employed is the Fried frailty phenotype.

Other scales used in different countries may also be referred to.

A systematic screening for frailty, which we propose for people >80 years, might take place in younger individuals only when a clinical and functional problem become imminent.

Benetos et al, Hypertension. 2016;67:820-5.

Management of arterial hypertension in individuals 80+ at high frailty

- - For very frail with multiple co-morbidities, the risk/ benefice balance of treatment is unknown
- - Individual approach for the very frail and disabled older patients: Quality of life is the first goal

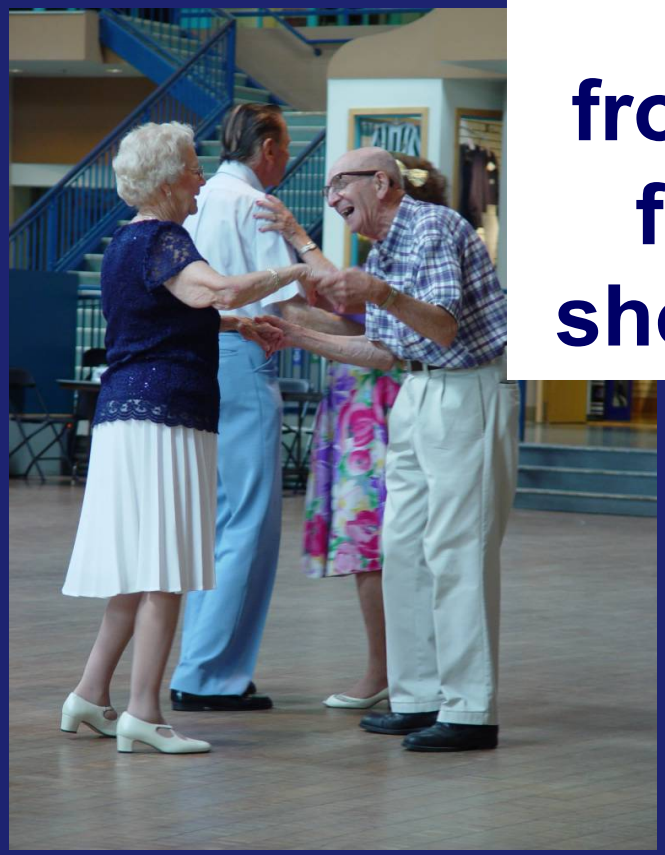
- - Revise prescription: High risk for medication-related problems
- - Reduce therapy if SBP<130 mmHg

Benetos et al; Hypertension 2016;67:820-5

Should the presence of frailty modify antihypertensive treatment?

Discordant points of view!

Who is frail?
…or
from which level of frailty treatment should be adapted?



Canadian Study of Health and Ageing Score:

Rockwood et al: CMAJ 2005;173:489-495

Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

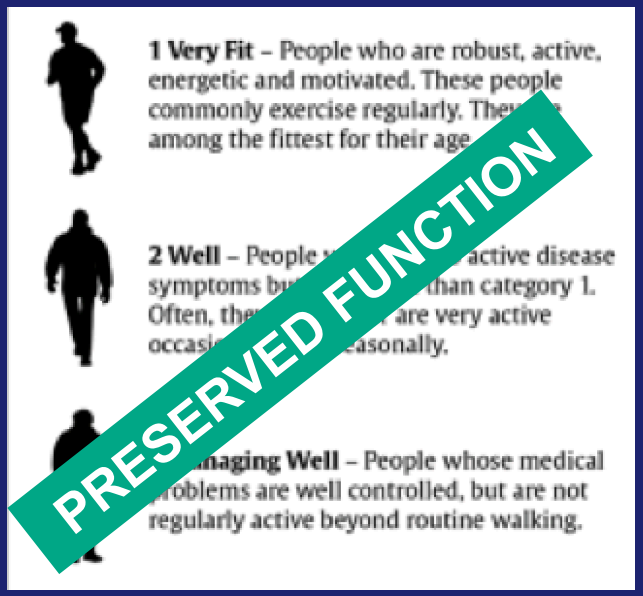
Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

‘VISUAL’ EVALUATION: THREE PROFILES ACCORDING TO FUNCTION/AUTONOMY STATUS



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PRESERVED FUNCTION

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LOSS OF FUNCTION/ PRESERVED AUTONOMY

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LOSS OF AUTONOMY

Benetos A, Petrovic M, Strandberg T, under revision

ADAPTING ANTIHYPERTENSIVE STRATEGIES ACCORDING TO THE PROFILE OF THE 'FRAILTY/FUNCTION/AUTONOMY' STATUS

'PRESERVED FUNCTION'

-Therapeutic approach similar to younger adults with treatment goal: SBP 130-140 mmHg
-Start with monotherapy and titrate antihypertensive medication cautiously
-Always check for orthostatic hypotension

'LOSS OF FUNCTION/ PRESERVED AUTONOMY' (FOR THE ADL)

Tailor antihypertensive strategy after a detailed geriatric assessment.

Moderately altered functional status

Significantly altered functional status

'LOSS OF AUTONOMY' (FOR THE ADL)

-Revision of the prescription
-If BP lowering tt is considered, SBP goal 140-150 mmHg ;
-Under treatment: SBP < 130 mmHg or orthostatic hypotension: Consider reducing antihypertensive treatment.
-Correct other factors and medications decreasing BP

Benetos A, Petrovic M, Strandberg T, under revision

BP targets and treatment strategies?

2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines indicate that a BP <130/80 mmHg should be targeted after the age of 65. *Hypertension*. 2018;71:1269-1324

2018 European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines propose a BP goal of <140/90 mmHg for individuals older than 65 years. *Eur Heart J* 2018 ; 39, 3021–3104

Lifestyle modifications >80 years

Table 5. Lifestyle Modifications to Manage Hypertension

Lifestyle Modifications to Manage Hypertension*		
Modification	**Recommendation**	**Approximate Systolic BP Reduction, Range**
Weight reduction	Maintain normal body weight (BMI, 18.5–24.9 kg/m^2)	5–20 mm Hg/10-kg weight loss (160,514,515)
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8–14 mm Hg (516,517)
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride	2–8 mm Hg (160,516–518)
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 min/d, most days of the week)	4–9 mm Hg (477,511,519)
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks/d (1 oz or 30 mL ethanol [e.g., 24-oz beer, 10-oz wine, or 3-oz 80-proof whiskey]) in most men and no more than 1 drink/d in women and lighter-weight persons	2–4 mm Hg (478)

ACCF/AHA 2011 Expert Consensus Document on Hypertension in the Elderly

Lifestyle modifications in frail >80 years

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ACCF/AHA 2011 Expert Consensus Document on Hypertension in the Elderly

Anti-hypertensive treatment strategies in old people

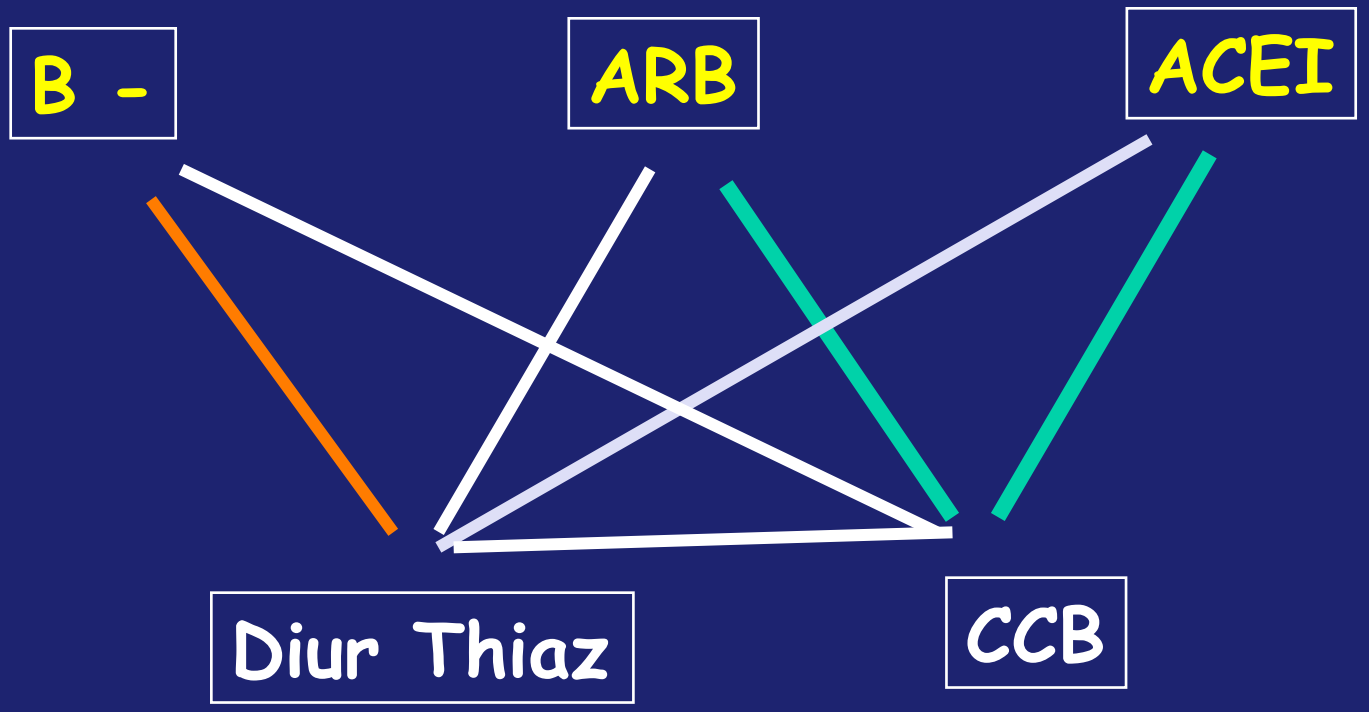
All hypertensive agents are recommended and can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension.	I	A	444, 449, 451, 452

Mancia et al, J. Hypertens 2013

Anti-hypertensive treatment in old individuals

- Start with 1 drug at low doses (Diuretics or CCB)
- Combine if necessary a second drug (ACEI, ARBs)
- Most hypertensives will need a combination therapy
- Use a third drug if necessary
- Do not exceed 3 drugs

French Guidelines for combination therapy



Anti-hypertensive treatment in old individuals: Drugs

Thiazides: do not exceed 25 mg/d, think about urine incontinence

Furosemide: if clearance <60 ml/min

Anti-aldosterone: Only if resistant Htn or HF st. IV; check for renal function and K+. Do not associate with anti-RAS drugs.

CCB: use mainly Dihydropyridines (unless Coronary Disease)

ACEI, ARBs: first choice if HF, diabetes; do not associated them; don't initiate in case of dehydration; check for renal function and K+

Beta blockers: first or second choice if HF, CHD; check for bradycardia and conduction problems especially if anti-cholinesterase drugs.

Other drugs (central anti-Ht, alpha blockers) if necessary

Drug associations that are at high risk for side effects in older adults

- ACEI (or ARB) + anti-Aldo : Renal function and hyperkalemia
- ACEI+ NSAID : Renal failure
- Betablockers + antidiabetic drugs : mask hypoglycemia
- Betablockers + anti-cholinestase : negative chronotropic and dromotropic effects

Question N° 6

How to obtain solid evidence in the profiles with loss of function and/or loss of autonomy ?

Management of arterial hypertension in individuals 80+

NEED FOR INTERVENTIONAL CONTROLLED STUDIES TO DEFINE THE TARGET BP LEVELS IN VERY OLD FRAIL PERSONS

RETREAT-FRAIL
French Multi-Center project

Coordinator A. Benetos (CHRU Nancy)

The central goal this multi-center, trial is to examine in nursing-home settings the change in overall mortality as the primary outcome of intervention over the course of 3 years.

This randomized case-control trial will consist of two parallel arms, focusing on patients ≥ 80 years with a SBP<130 mmHg with >1 anti-Htn drugs.

The intervention arm will entail antihypertensive drug step-down, while the control arm will comprise the standard anti-hypertensive treatment.

National Grants
- RHU FIGHT-HF
- PHRC National

Management of arterial hypertension in individuals 80+

THoM (1)

Frailty, function, autonomy and multi-morbidity (not age) are the main determinants of our strategies

- Treat all “robuste” hypertensives
- Target SBP 140/90 mmHg
- Start low (one drug for starting); Go slow
- Not more than 3 anti-Htn drugs
- Use tools for better prescribing
- Check for orthostatic hypotension
- Check for renal function

Management of arterial hypertension in individuals 80+

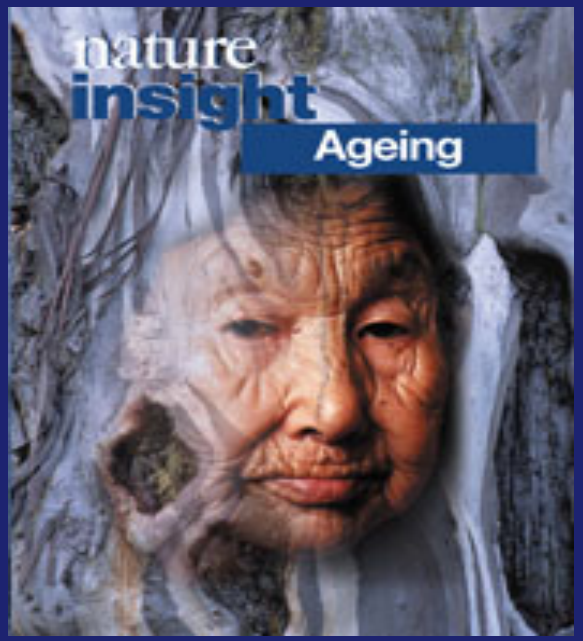
THoM (2)

- For very frail, with multiple co-morbidities the risk/benefice balance of treatment is unknown
- High risk for iatrogenic problems (poly-medication, frailty)
- Reduce therapy if SBP<130 mmHg
- Individual approach for the very frail and disabled elderly : Quality of life is the first goal

NEED FOR INRVENTIONAL STUDIES TO INVESTIGATE THE TARGET BP LEVELS IN VERY OLD FRAIL PERSONS

спасибо

ΕΥΧΑΡΙΣΤΩ



Merci

Thank you