



UNIVERSITÉ  
DE LORRAINE



# Are frail, very old subjects overtreated for their hypertension?

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15° Πανελλήνιο Συνέδριο Αρτηριακής Υπέρτασης  
Θεσσαλονίκη 7 Μαρτίου 2015

# Disclosures

- Honoraria

- Boehringer

- Fukuda

- Novartis

- Servier

- Sanofi

# Specificities of arterial hypertension in the very elderly

10° Πανελλήνιο Συνέδριο Αρτηριακής Υπέρτασης  
Θεσσαλονίκη, Ιανουάριος 2010



# **No association between SBP and CV morbidity in very old frail populations**

- **No association between SBP/DBP and total/CV mortality in elderly (87 yo) hospitalized in long stay hospital**

**Meaume et al, Arterioscler Thromb Vasc Biol. 2001;21:2046-50**

- **No association between SBP and morbidity in a frail elderly nursing home population**

**Askari M et al; Aging Clin Exp Res. 2004 16:206-11.**

# Lower Systolic Blood Pressure Is Associated with Greater Mortality in People Aged 85 and Older

Lena Molander, Bsc, Hugo Lövheim, MD, PhD, Tove Norman, MD, Peter Nordström, MD, PhD, and Yngve Gustafson, MD, PhD

JAGS OCTOBER 2008-VOL. 56, NO. 10

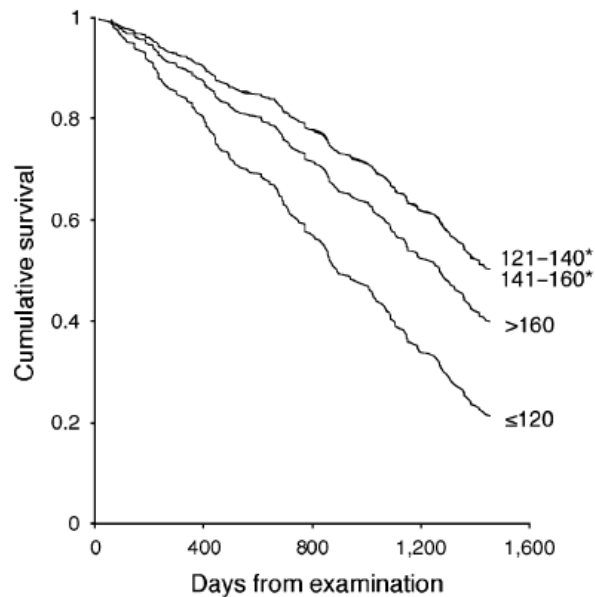


Figure 1. Survival curve based on multivariate Cox regression. *P*-values of comparison with the  $\le 120$  mmHg group: 121–140 mmHg,  $P < .001$ ; 141–160 mmHg,  $P < .001$ ;  $> 160$  mmHg,  $P = .03$ . \*The curves for these two groups overlap.

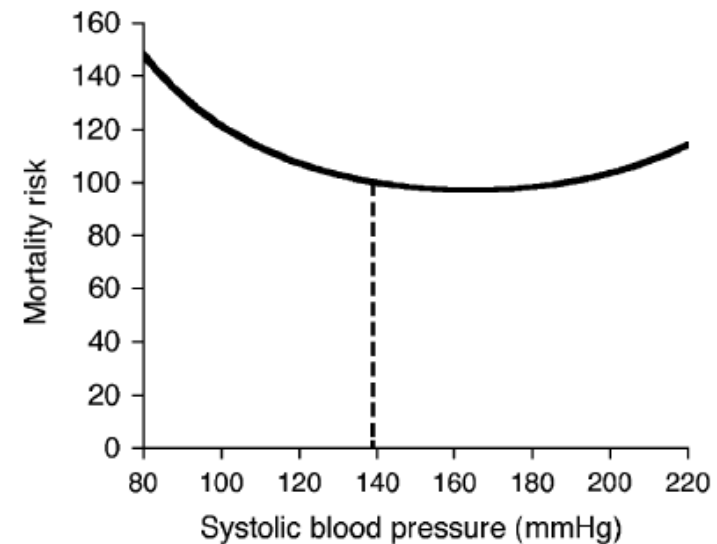
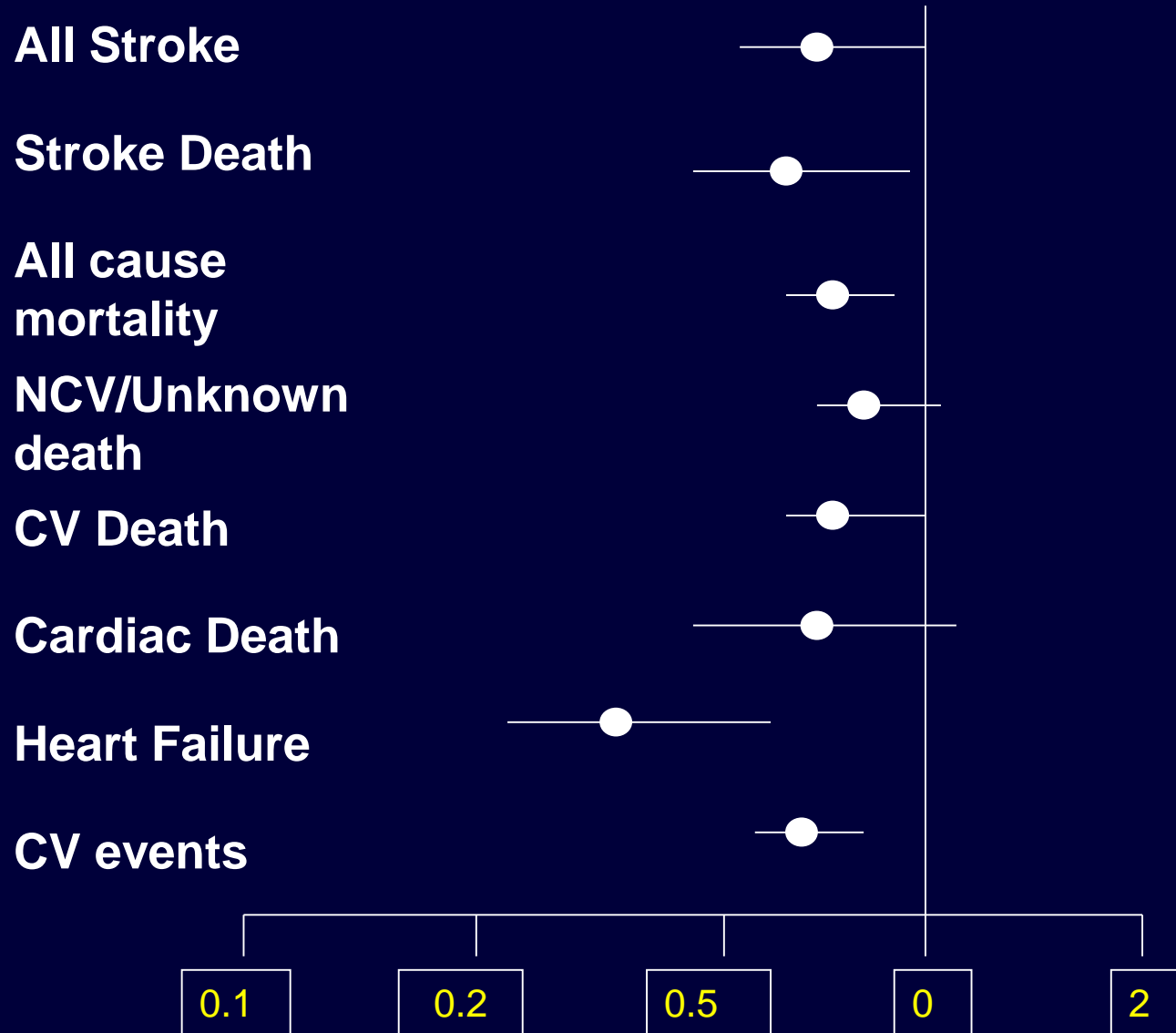


Figure 2. Graph of multivariate Cox regression. Adjusted for sex, age, Mini-Mental State Examination score, activities of daily living according to Barthel score, atrial fibrillation, and diabetes mellitus. Risk associated with systolic blood pressure 140 mmHg (dotted line) was used as index (= 100).

# Hypertension after 80 Actifit (indapamide ± perindopril) vs. placebo: The HYVET study



# Specificities of arterial hypertension in the very old

## Conclusions

(Thessaloniki January 2010)

- Treat all “robuste” hypertensives
- Target SBP < 150 mmHg
- Individual approach for the disabled elderly: Quality of life is the first goal
- Gerontological evaluation for all elderly
- Start low (one drug for starting); Go slow
- Not more than 3 anti-Htn drugs
- Check for orthostatic hypotension
- Attention to the interactions (poly-medication, frailty)



## 2007: PARTAGE

Etude de la Pression ARTérielle des personnes AGées  
vivant en EHPAD

French Ministry of Health Grant for Clinical Research  
PHRC/DCV20070409250

**Rôle of blood pressure and arterial stiffness  
on morbidity, mortality and cognitive impairment  
in very old people living in nursing homes**

**Pr A. Benetos**                      Nancy, France  
**(Coordination)**

**Pr O Hanon**                        Broca, Paris

**Pr P. Manckoundia**            Dijon

**Pr Y. Rolland**                    Toulouse

**Pr P Salvi**                         Cesena

**Pr M Zamboni**                  Verona

- **1126 subjects**
- **78% women**
- **Age: 87y at baseline**
- **7.2 drugs/day**
- **2-year follow up**

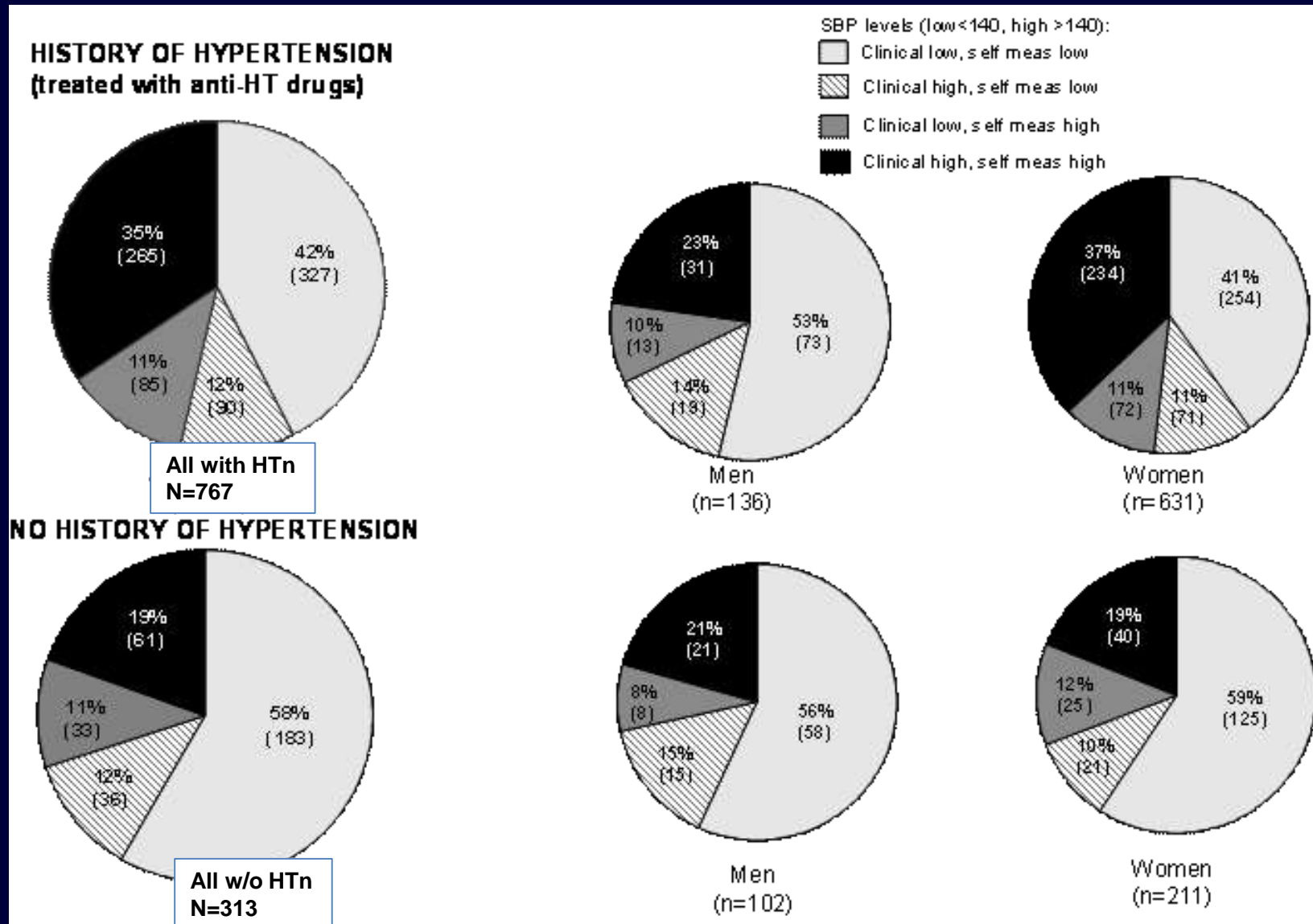




## **PARTAGE Study: Publications 2010-2015**

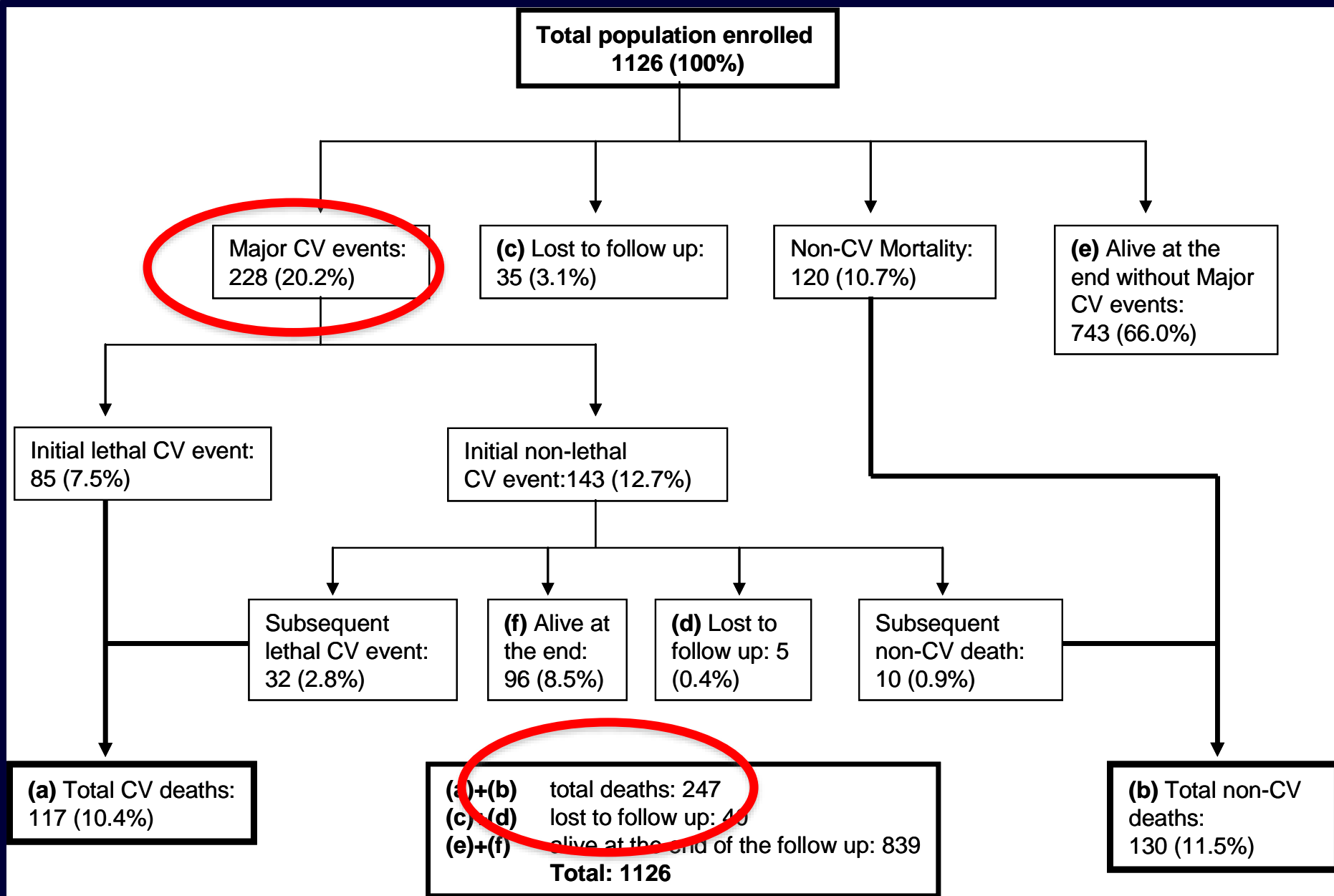
- 1. BENETOS A, et al. Blood pressure and pulse wave velocity values in the institutionalized elderly aged 80 and over: baseline of the PARTAGE study. *J Hypertens.* 2010;28:41-50**
- 2. SALVI P, et al. PARTAGE Study Investigators. Heart disease and changes in pulse wave velocity and pulse pressure amplification in the elderly over 80 years: the PARTAGE Study. *J Hypertens.* 2010;28:2127-33**
- 3. VALBUSA F, et al. Orthostatic hypotension in very old individuals living in nursing homes: the PARTAGE study. *J Hypertens.* 2012;30:53-60.**
- 4. BENETOS A et al. Pulse Wave Velocity is Associated With 1-Year Cognitive Decline in the Elderly Older than 80 years: the PARTAGE Study; *J Am Med Dir Assoc.* 2012;13:239-43.**
- 5. BENETOS A, et al. Mortality and cardiovascular events are best predicted by low central/peripheral pulse pressure amplification but not by high blood pressure levels in elderly nursing home subjects: the PARTAGE study. *J Am Coll Cardiol.* 2012;60:1503-11.**
- 6. MILJKOVIC D, et al. Correlation Between Peripheral Blood Pressure and Pulse-Wave Velocity Values in the Institutionalized Elderly Persons 80 Years of Age and Older: The PARTAGE Study. *Am J Hypert* 2013; 26:163-73**
- 7. BENETOS A. et al. Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in Older Nursing Home Residents The PARTAGE Study. *JAMA Int Med* 2015;doi:10.1001**
- 8. WATFA G et al. Do arterial hemodynamic parameters predict cognitive decline over a period of 2 years in individuals older than 80 years living in nursing homes? The PARTAGE study; *JAMDA* in press**

# SBP levels in treated hypertensive subjects (upper panel) and in subjects without history of hypertension (lower panel). The PARTAGE study





# Flow chart with the data concerning deaths and major CV events during the follow up period.



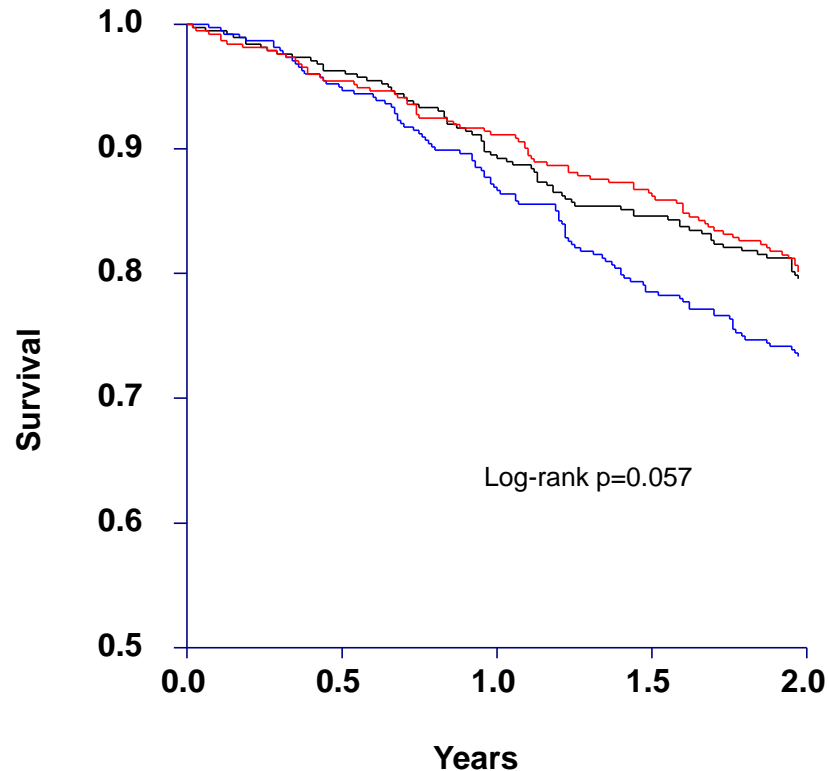
# SBP and total mortality during the 2-year follow-up period



## TOTAL MORTALITY

### SBP tertiles

- L
- M
- H



L: PAS = 85-130 mmHg



**Table 3**

**Risk Ratio (Cox Regression Analysis) for Total Mortality and Major CV Events According to Blood Pressure and Pulse Wave Velocity**

	Risk Ratio	95% CI	p Value
<b>Total mortality</b>			
PWV, +1 m/s	1.00	0.97-1.03	0.792
SBP, +10 mm Hg	0.91	0.84-0.98	0.017
DBP, +10 mm Hg	0.84	0.72-0.99	0.037
MAP, +10 mm Hg	0.85	0.75-0.97	0.016
PP, +10 mm Hg	0.90	0.81-1.00	0.057
<b>Major CV events</b>			
PWV, +1 m/s	1.00	0.98-1.03	0.797
SBP, +10 mm Hg	0.98	0.91-1.06	0.674
DBP, +10 mm Hg	0.97	0.84-1.13	0.716
MAP, +10 mm Hg	0.96	0.84-1.09	0.524
PP, +10 mm Hg	0.98	0.89-1.09	0.741

Each variable presented in this table was included in a multivariate Cox model with the following covariates: age, sex, body mass index, activities of daily living, Charlson comorbidity index, and history of CV disease for total mortality; age, activities of daily living, Charlson comorbidity index, history of CV disease, and antihypertensive treatment for major CV events. For PWV, mean arterial pressure and heart rate were added in the multivariate models.

CI = confidence interval; other abbreviations as in Tables 1 and 2.

**What is the profile of the subjects with low BP  
having increased total mortality?**

Research

Original Investigation

# Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in Older Nursing Home Residents

## The PARTAGE Study

Athanase Benetos, MD, PhD; Carlos Labat, BSc; Patrick Rossignol, MD, PhD; Renaud Fay, PharmD; Yves Rolland, MD, PhD; Filippo Valbusa, MD; Paolo Salvi, MD, PhD; Mauro Zamboni, MD, PhD; Patrick Manckoundia, MD, PhD; Olivier Hanon, MD, PhD; Sylvie Gautier, MD

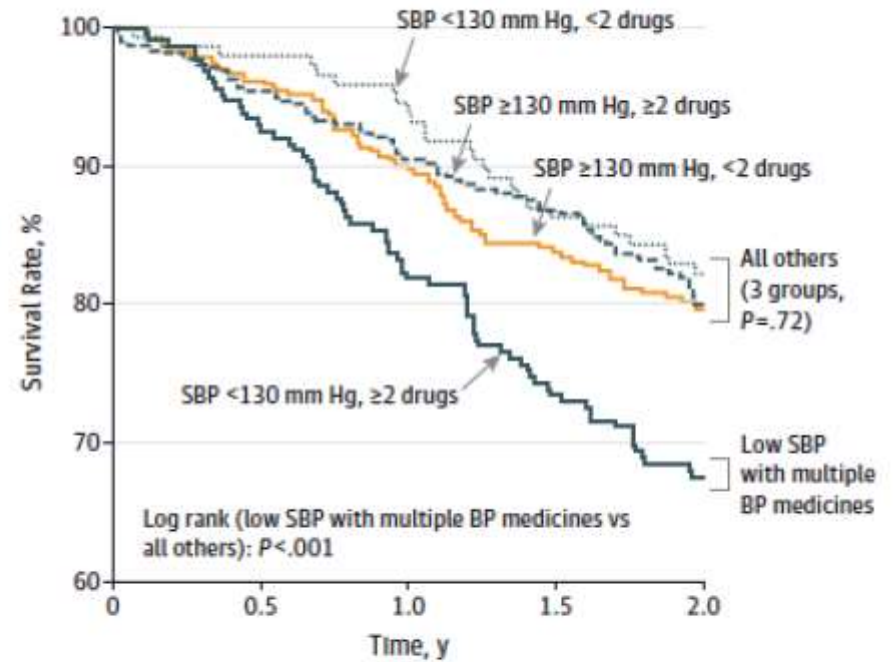
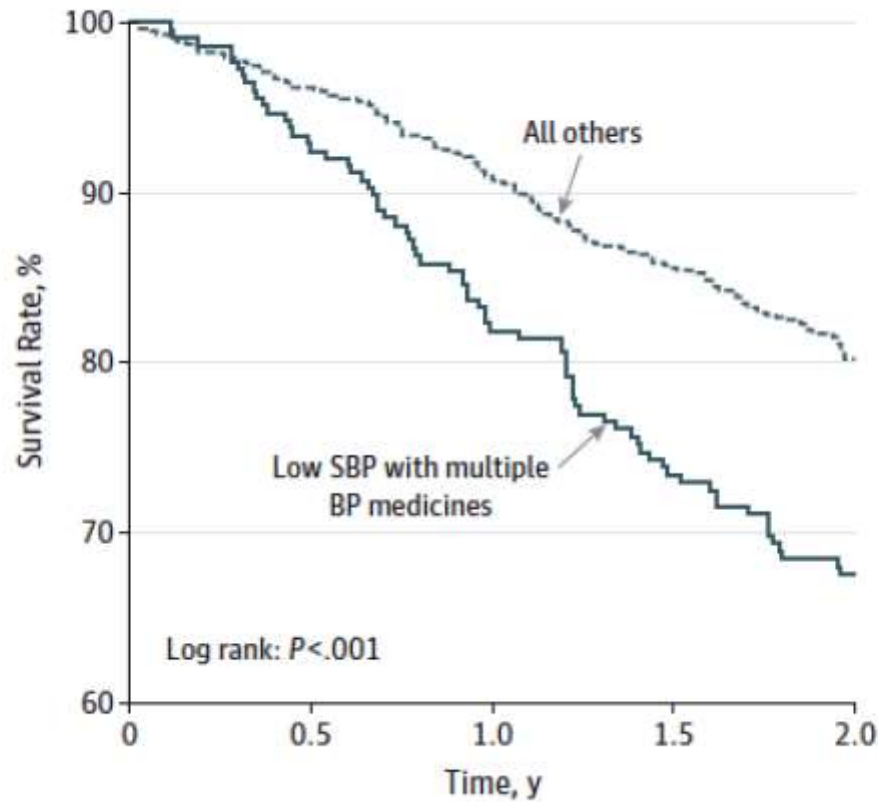
*JAMA Intern Med.* doi:10.1001/jamainternmed.2014.8012  
Published online February 16, 2015.

# Over-Mortality (X2) in patients with low SBP (<130 mmHg) under combination anti-hypertensive therapy

**20% of the entire population**

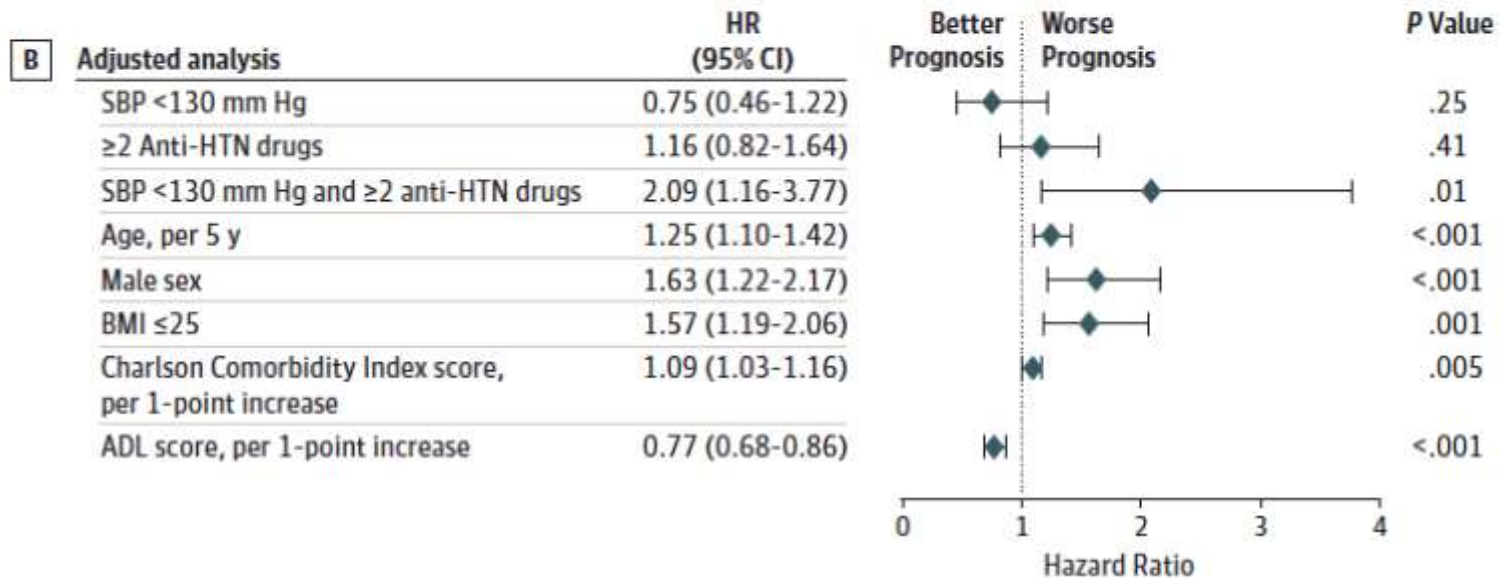
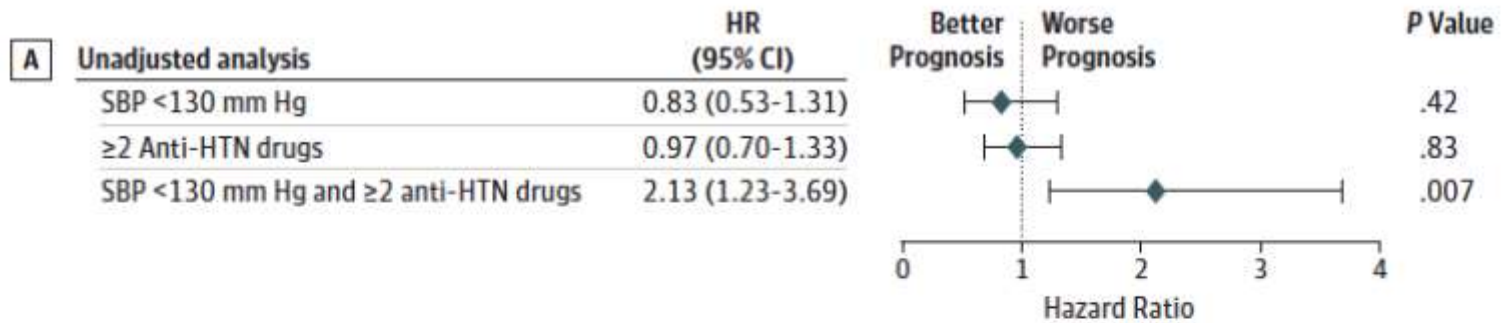


Kaplan-Meier Survival Curves in Patients With Low Systolic Blood Pressure (SBP) Receiving Multiple BP Medicines and All Other Groups





**Hazard ratios for all-cause mortality according to SBP levels, number of antihypertensive drugs and their interaction, both unadjusted (panel A) and after adjustment for several co-founders.**



# Effects of Low Blood Pressure in Cognitively Impaired Elderly Patients Treated With Antihypertensive Drugs

E Mossello et al: *JAMA Intern Med.* Published online March 02, 2015. doi:10.1001/

- Low daytime SBP was independently associated with a greater progression of cognitive decline in older patients with dementia and MCI among those treated with AHDs.
- Excessive SBP lowering may be harmful for older patients with cognitive impairment. Ambulatory blood pressure monitoring can be useful to help avoid high blood pressure overtreatment in this population.

**Drug-induced low BP may be responsible for decreased perfusion of key organs (heart, brain, kidney...) in very old frail subjects**

**Should we modify our therapeutic strategy in these patients?**

**What do the guidelines propose  
in the presence of low BP  
under anti-Htn treatment?**

# 2013 ESH/ESC Guidelines for the management of arterial hypertension (Mancia et al J. Hypert 2013)

## Antihypertensive treatment strategies in the elderly

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref. <sup>c</sup>
In elderly hypertensives with SBP $\geq 160$ mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	141, 265
In fit elderly patients <80 years old antihypertensive treatment may be considered at SBP values $\geq 140$ mmHg with a target SBP <140 mmHg if treatment is well tolerated.	IIb	C	-
In individuals older than 80 years with an initial SBP $\geq 160$ mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B	287

# 2013 ESH/ESC Guidelines for the management of arterial hypertension

## Anti-hypertensive treatment strategies in old people

<p>In frail elderly patients, it is recommended to leave decisions on antihypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment.</p>	I	C	-
<p>Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian.</p>	IIa	C	-

# **THM (1): TREATING HYPERTENSIVE INDIVIDUALS OVER 80 YEARS OLD**

## **ROBUST SUBJECTS**

- Focus on SBP and PP, target SBP 130-150 mmHg
- Start with monotherapy; avoid using more than 3 antihypertensive drugs
- Always check for orthostatic hypotension
- Optimize treatment for global CVD protection

# THM (2): TREATING HYPERTENSIVE INDIVIDUALS OVER 80 YEARS OLD

## FRAIL SUBJECTS

- Reconciliation and revision of the prescription
- Evaluation (CGA) of the risk/benefit ratio (life expectancy, geriatric syndromes, polypharmacy, etc.)
- Start anti-HTn treatment with one drug; start low and go slowly, SBP goal 150 mmHg
- Identify/correct other factors/drugs decreasing BP
- If SBP < 130 mmHg or orthostatic hypertension under treatment:** Consider reducing antihypertensive treatment, especially in case of combination therapy

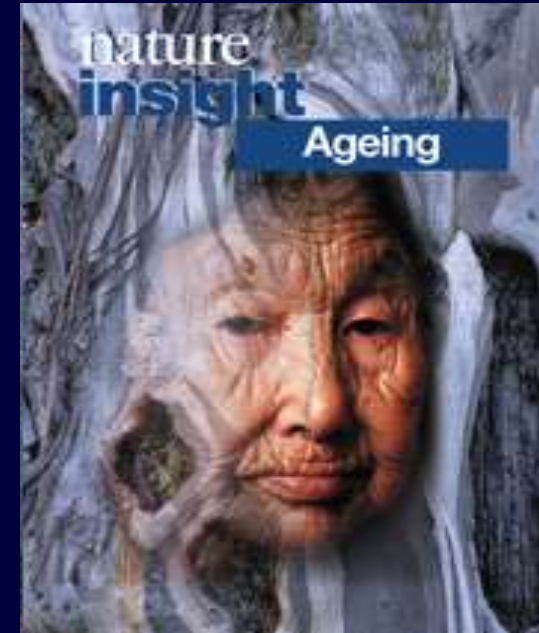


# Conclusions

- **SBP<130 under combination anti-HTn therapy is associated with a 2-fold increase in all-cause mortality**
- **This result persists even after several adjustments**
- **Interventional studies are warranted to assess the benefits/risks ratio of multi-drug antihypertensive treatment in the growing population of elderly frail patients.**

## Research Group and main collaborations

- Dpt of Geriatrics, CHU de Nancy
- and INSERM U1116, Univ. Lorraine
  
- Sylvie Gautier
- Anna Kearny-Schwartz
- Laure Joly
- Carlos Labat
- Paolo Salvi
- Mohamed Temmar
- Ghassan Watfa



•Ευχαριστώ