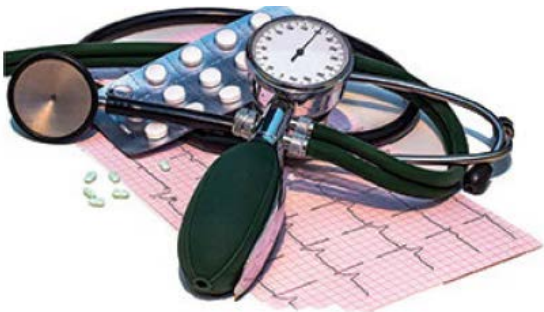




GLEM Neuro 05/03/2018

Actualités sur Hypertension artérielle et AVC

JM KRZESINSKI



Hypertension et AVC

- Epidémiologie de la relation entre HTA et AVC
- Hypertension artérielle et risque d'**AVC primaire**:
Cible de PA pour réduire le risque d'AVC
- Hypertension et **récidive d'un AVC**
- Que faire avec la PA en **phase aiguë** d'un AVC ?
- Take home messages

THE BURDEN OF STROKE IN EUROPE

Report

King's College London

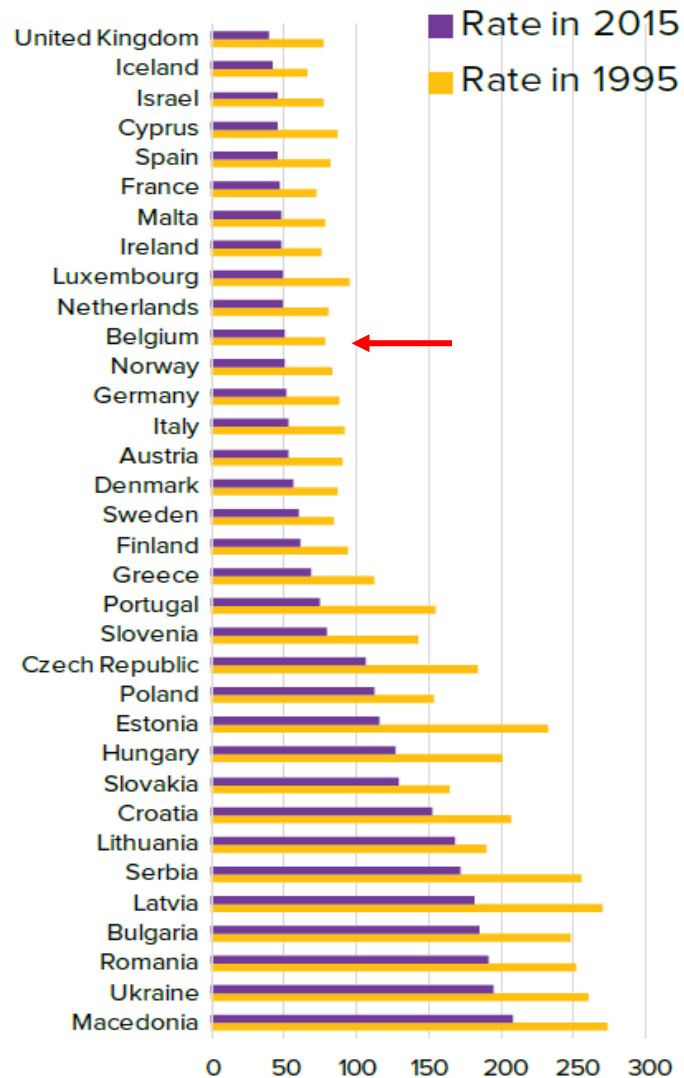
for the

Stroke Alliance for Europe (SAFE)

Dec 2016

Figure 2: Number of new strokes and stroke survivors per 100,000 inhabitants in 1995 and 2015 (age- and sex-standardised to the world standard population, GBD 2015)

New strokes per 100,000 inhabitants, adjusted for age and sex, in 1995 and 2015



Stroke survivors per 100,000 inhabitants, adjusted for age and sex, in 1995 and 2015

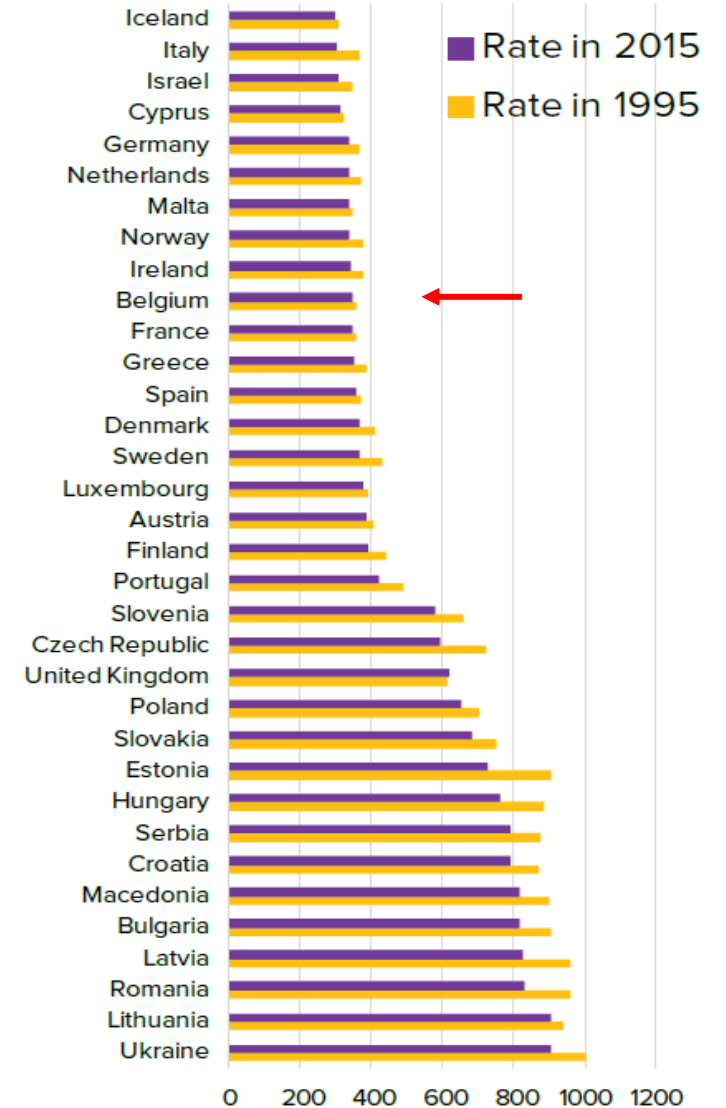
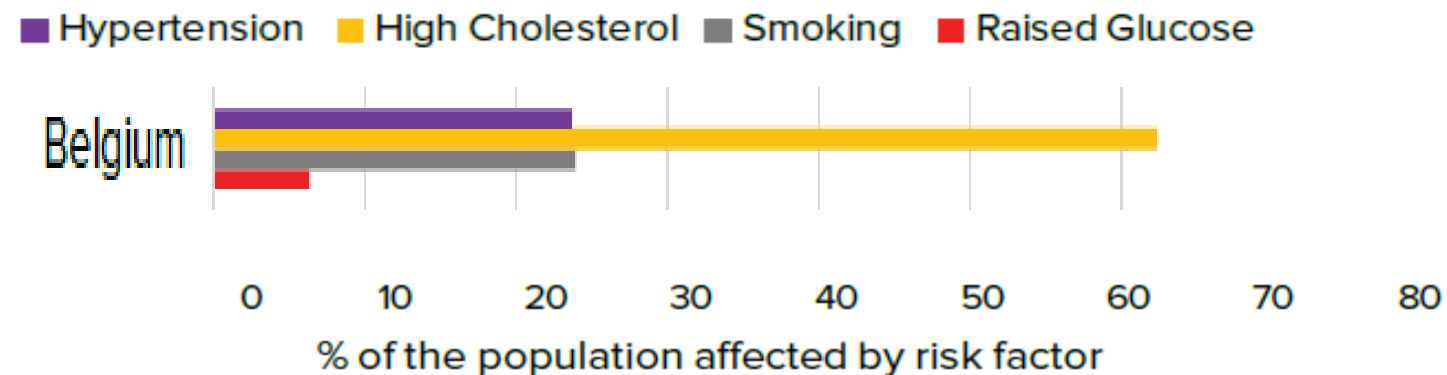
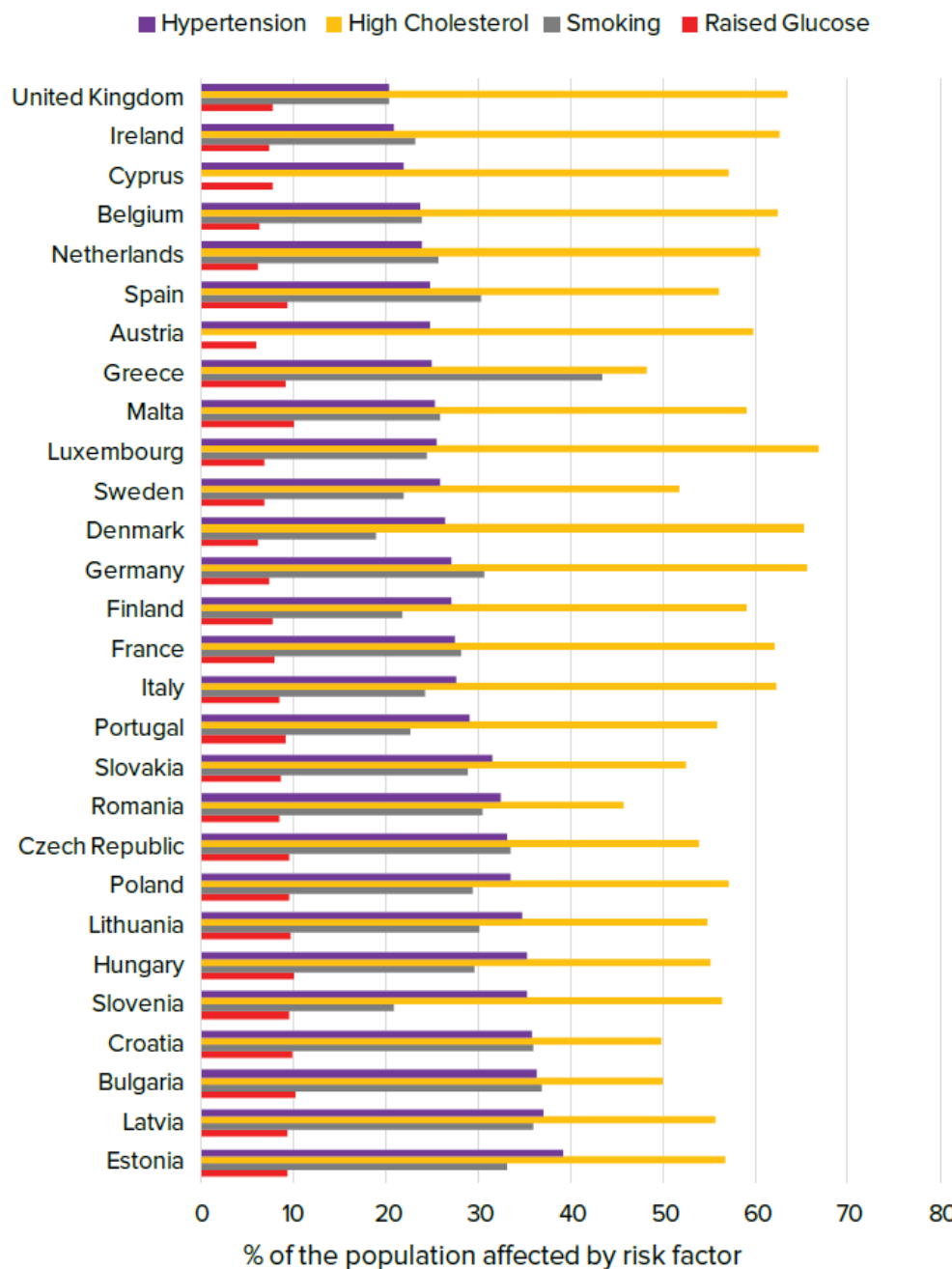


Figure 5: Percentage of the population in European and SAFE member countries affected by some of the major vascular risk factors, ranked by the prevalence of hypertension



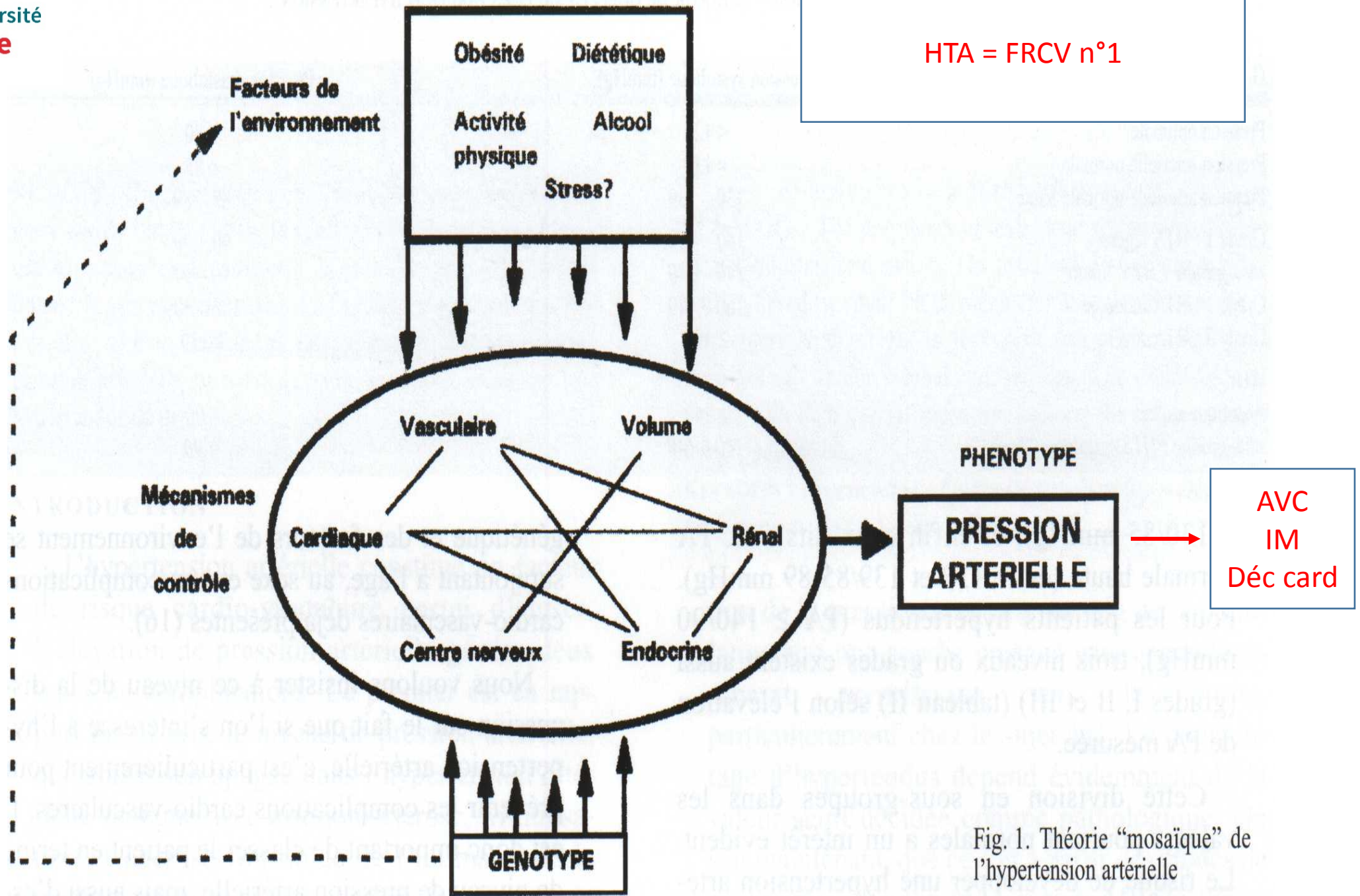


Fig. 1. Théorie "mosaïque" de l'hypertension artérielle

Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study

www.thelancet.com Vol 376 July 10, 2010

- L'hypertension artérielle est un facteur de risque majeur responsable de 44,5 % des AVC dits hémorragiques et de 31,5 % des AVC ischémiques.
- Des antécédents d'hypertension artérielle multiplieraient par 9 le risque de souffrir d'un AVC avant 45 ans.

Autres facteurs modifiables: tabagisme, hypercholestérolémie,
diabète, obésité abdominale, excès d'alcool

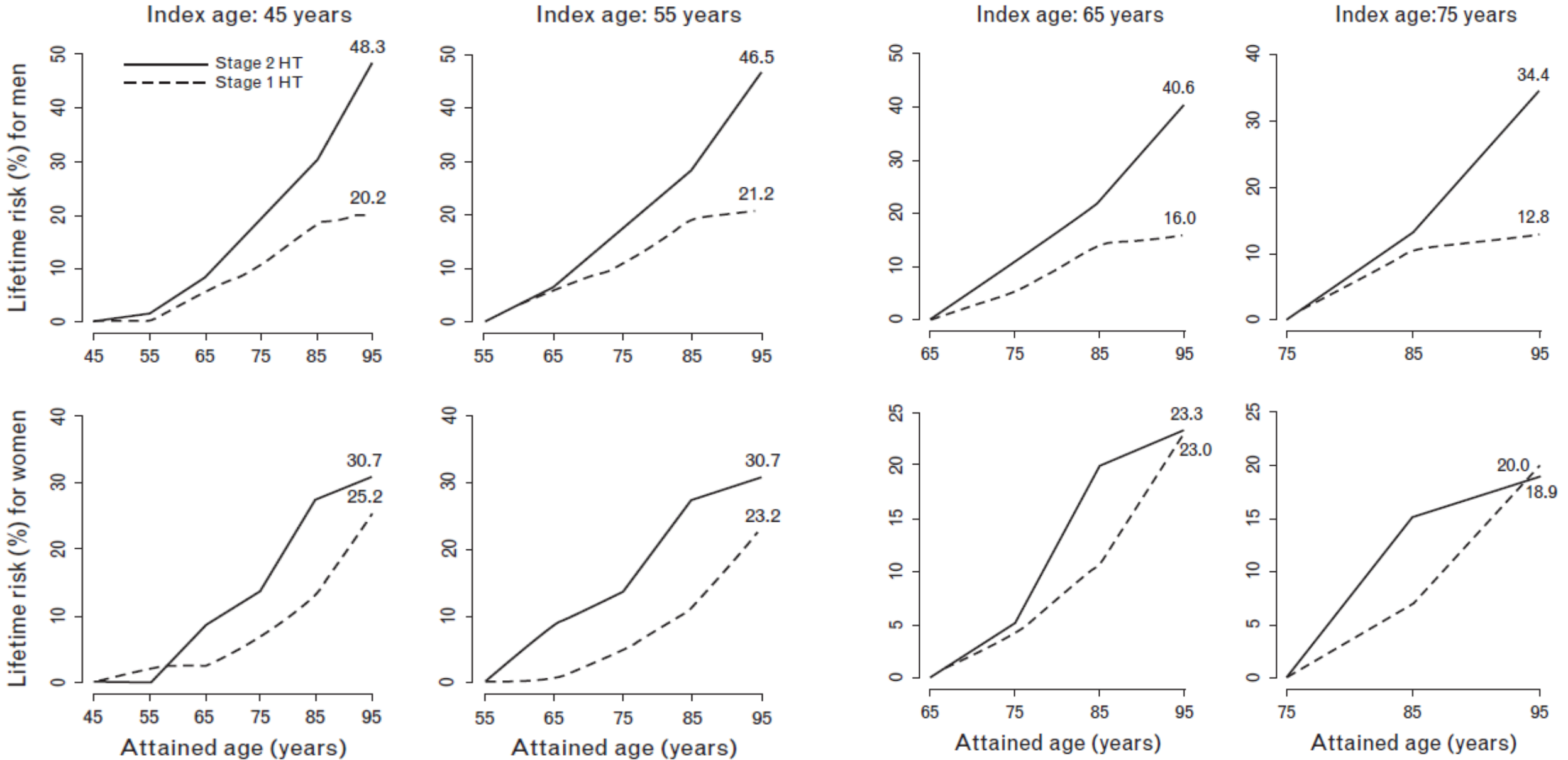
Définition de l'HTA et classification de la pression artérielle (mmHg)

ESH 2013

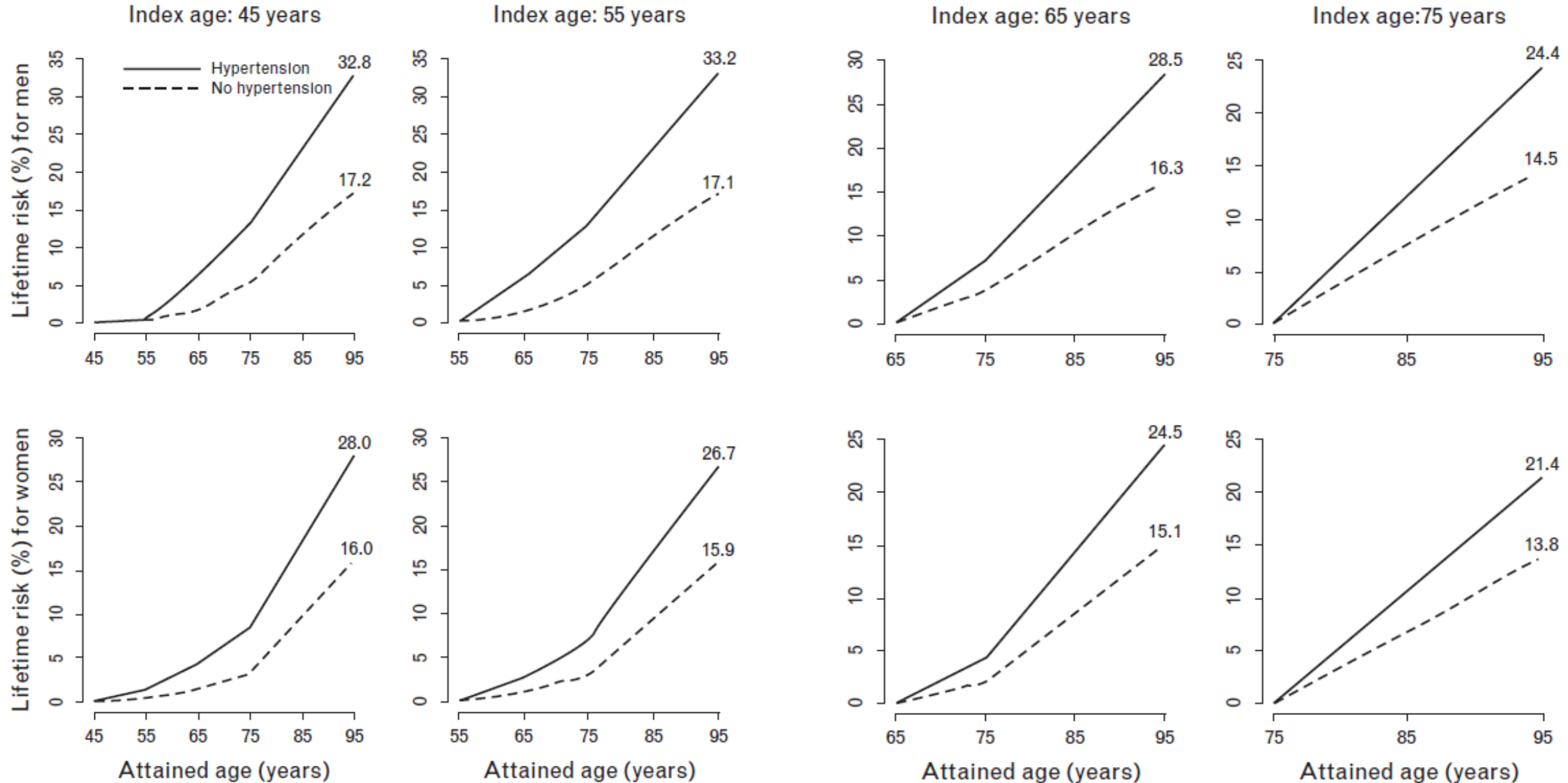
Catégorie	Systolique	Diastolique
Optimal	< 120	< 80
Normal	120-129	80-84
Normal haute	130-139	85-89
Hypertension de Grade 1 (légère)	140-159	90-99
Hypertension de Grade 2 (modérée)	160-179	100-109
Hypertension de Grade 3 (sévère)	≥ 180	≥ 110
Hypertension systolique isolée	≥ 140	< 90

HTA= PA > ou = 140 et/ou 90 mmHg

5600 personnes suivies pendant 18 ans



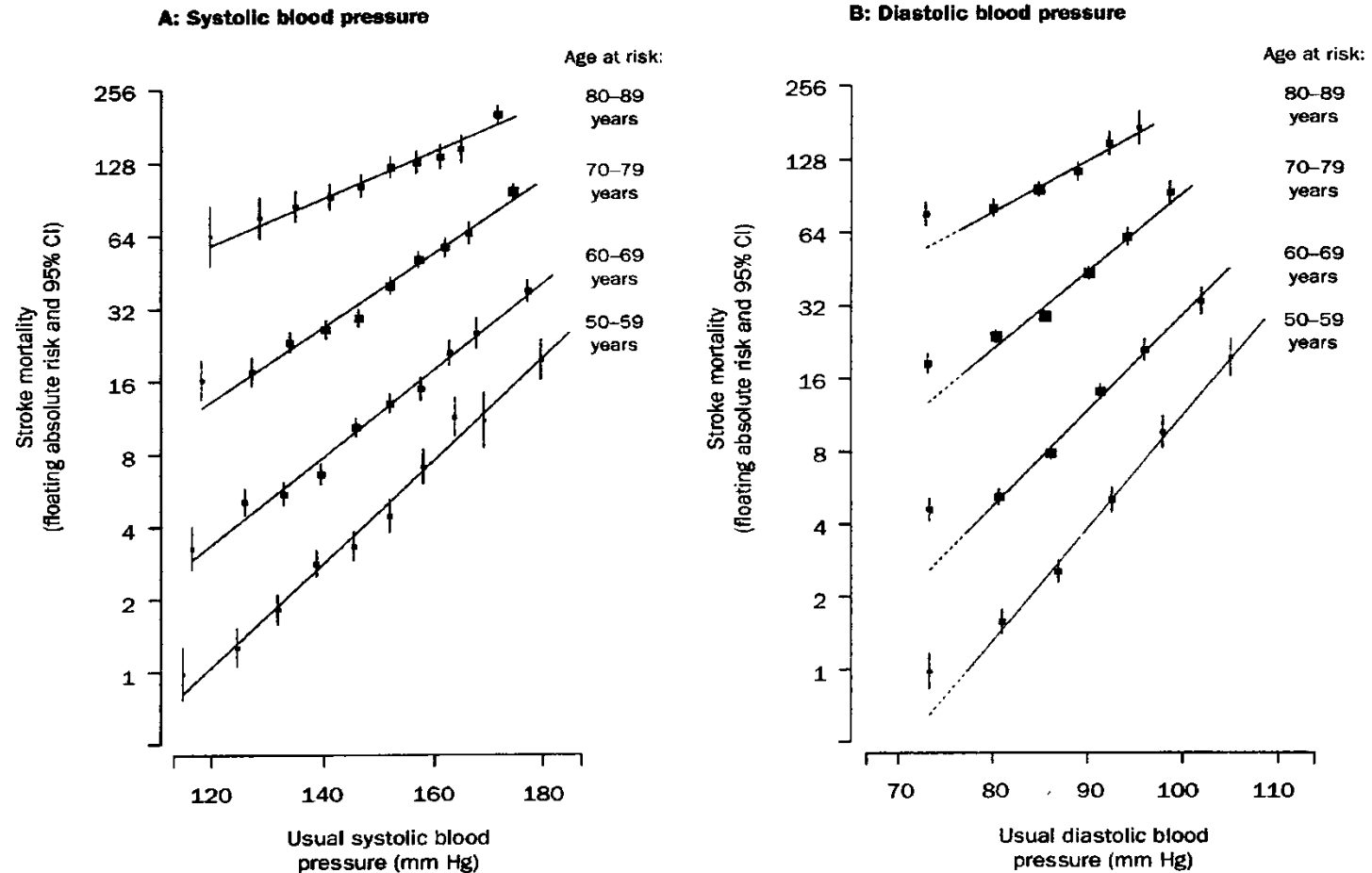
5600 personnes suivies pendant 18 ans



Une méta-analyse de données individuelles en provenance d'un million d'adultes

(Lewington et al Lancet 2002)

Stroke mortality rate



: Stroke mortality rate in each decade of age versus usual blood pressure at the start of that decade

Blood Pressure Trajectories and the Risk of Intracerebral Hemorrhage and Cerebral Infarction

A Prospective Study

Abstract—The association between long-term blood pressure (BP) patterns in community-dwelling adults and risk of intracerebral hemorrhage and cerebral infarction is not well characterized. This prospective study included 79385 participants, free of stroke, myocardial infarction, and cancer in or before 2010 (baseline). Systolic BP trajectories were identified using latent mixture modeling with data from 2006, 2008, and 2010. Incident cases of intracerebral hemorrhage and cerebral infarction occurred during 2010 to 2014, confirmed by review of medical records, by 3 physicians. We identified 5 distinct systolic BP trajectories during 2006 to 2010. Each of the trajectories was labeled according to their BP range and pattern over time: normotensive-stable (n=26740), prehypertension-stable (n=35674), stage 1 hypertension-increasing (n=8215), stage 1 hypertension-decreasing (n=6422), and stage 2 hypertension-stable (n=2334). We documented 1034 incident cases of cerebral infarction and 187 cases of intracerebral hemorrhage. Although the prehypertension-stable trajectory exhibited systolic BP range within the normal range (120–140 mmHg) during 2006 to 2010, this group had higher stroke risk relative to the normotensive-stable group (<120 mmHg) (adjusted hazard ratio was 3.11 for intracerebral hemorrhage and 1.99 for cerebral infarction; $P<0.001$ for both), after adjusting for possible confounders. Individuals in the stage 2 hypertension-stable systolic BP trajectory (175–179 mmHg) had the highest risk of intracerebral hemorrhage (adjusted hazard ratio was 12.4) and cerebral infarction (adjusted hazard ratio was 5.07), relative to the normotensive-stable group ($P<0.001$ for both). BP trajectories were associated with the risk of stroke and increasing BP trajectories within the currently designated normal range may still increase the risk for stroke. (*Hypertension*. 2017;70:508-514.

Blood Pressure Trajectories and the Risk of Intracerebral Hemorrhage and Cerebral Infarction

A Prospective Study

Hypertension. 2017;

Table 2. Adjusted Hazard Ratios and 95% Confidence Intervals for Risks of Cerebral Infarction and Intracerebral Hemorrhage, According to the 5 Subgroups of Different SBP Trajectory Patterns in 79388 Participants of Kailuan Study

Stroke Type	Normotensive-Stable	Prehypertension-Stable	Stage 1 Hypertension-Increasing	Stage 1 Hypertension-Decreasing	Stage 2 Hypertension-Stable
Cerebral infarction	BP<120	BP 120-139			
Case no. (person-year)	102 (101326)	421 (133672)	236 (29786)	170 (23633)	105 (8278)
Age and sex adjusted	1.00	2.36 (1.90–2.94)	4.79 (3.77–6.10)	4.57 (3.55–5.89)	7.15 (5.39–9.48)
Fully adjusted model*	1.00	1.99 (1.60–2.49)	3.61 (2.81–4.63)	3.45 (2.65–4.49)	5.07 (3.77–6.82)
Further adjusted for SBP in 2006*	1.00	1.64 (1.26–2.14)	2.78 (2.03–3.81)	2.56 (1.79–3.65)	3.77 (2.57–5.51)
Further adjusted for SBP in 2010*	1.00	1.88 (1.39–2.53)	2.87 (1.98–4.17)	3.11 (2.19–4.41)	3.80 (2.49–5.80)
Excluding 13280 participants who used antihypertensive during 2006–2010*	1.00	2.00 (1.57–2.54)	3.70 (2.78–4.92)	3.54 (2.59–4.85)	4.96 (3.29–7.47)
Intracerebral hemorrhage					
Case no. (person-year)	14 (101452)	66 (134311)	54 (30109)	31 (23878)	22 (8420)
Age and sex adjusted	1.00	2.96 (1.65–5.30)	9.54 (5.18–17.6)	6.85 (3.57–13.1)	13.3 (6.63–26.7)
Fully adjusted model*	1.00	3.11 (1.72–5.64)	9.66 (5.11–18.3)	6.79 (3.44–13.4)	12.4 (5.95–26.0)
Further adjusted for SBP in 2006*	1.00	3.39 (1.69–6.80)	10.8 (4.89–23.8)	8.20 (3.33–20.2)	15.0 (5.85–38.5)
Further adjusted for SBP in 2010*	1.00	3.21 (1.39–7.41)	7.24 (2.69–19.5)	5.97 (2.30–15.0)	9.82 (3.32–29.1)
Excluding 13280 participants who used antihypertensive during 2006–2010*	1.00	2.44 (1.29–4.62)	8.40 (4.13–17.1)	8.15 (3.84–17.3)	13.0 (5.19–32.7)

Blood Pressure Categories

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Effet du traitement de l'HTA

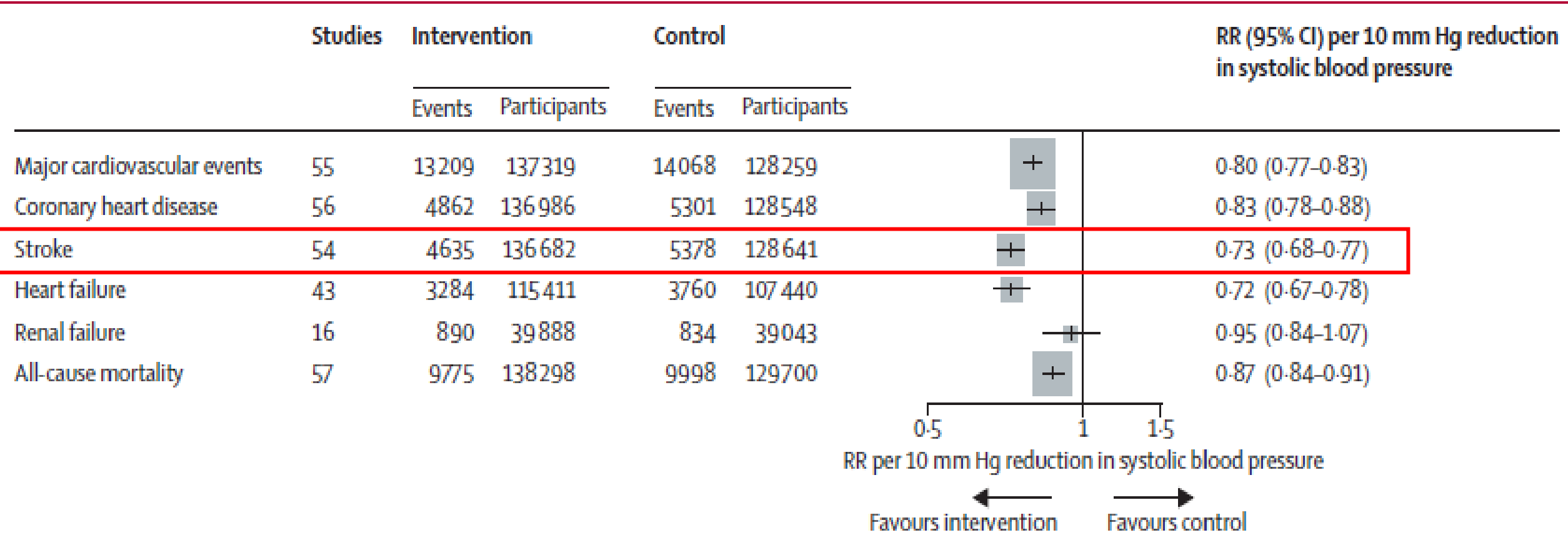


Figure 3: Standardised effects of a 10 mm Hg reduction in systolic blood pressure
RR=relative risk.

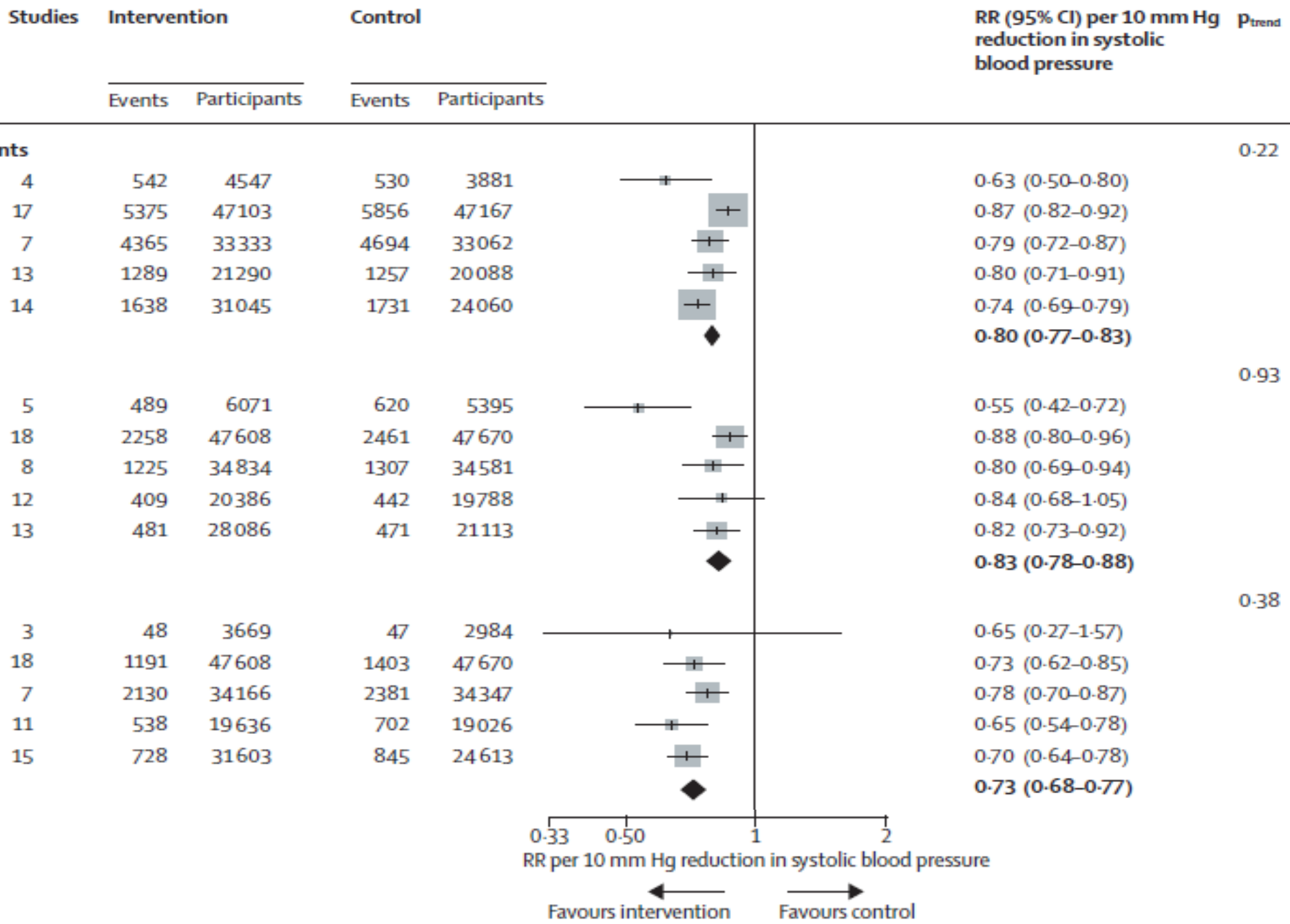


Figure 4: Standardised effects of a 10 mm Hg reduction in systolic blood pressure stratified by blood pressure

Traiter l'HTA



- D'abord valider l'élévation de PA
- Recourir à l'automesure ou la MAPA si HTA de consultation (exclure l'HTA de la blouse blanche) ou PA normale et complications CV (exclure l'HTA masquée)

Suivi de 17 ans chez 1464 patients (60 ans au départ)

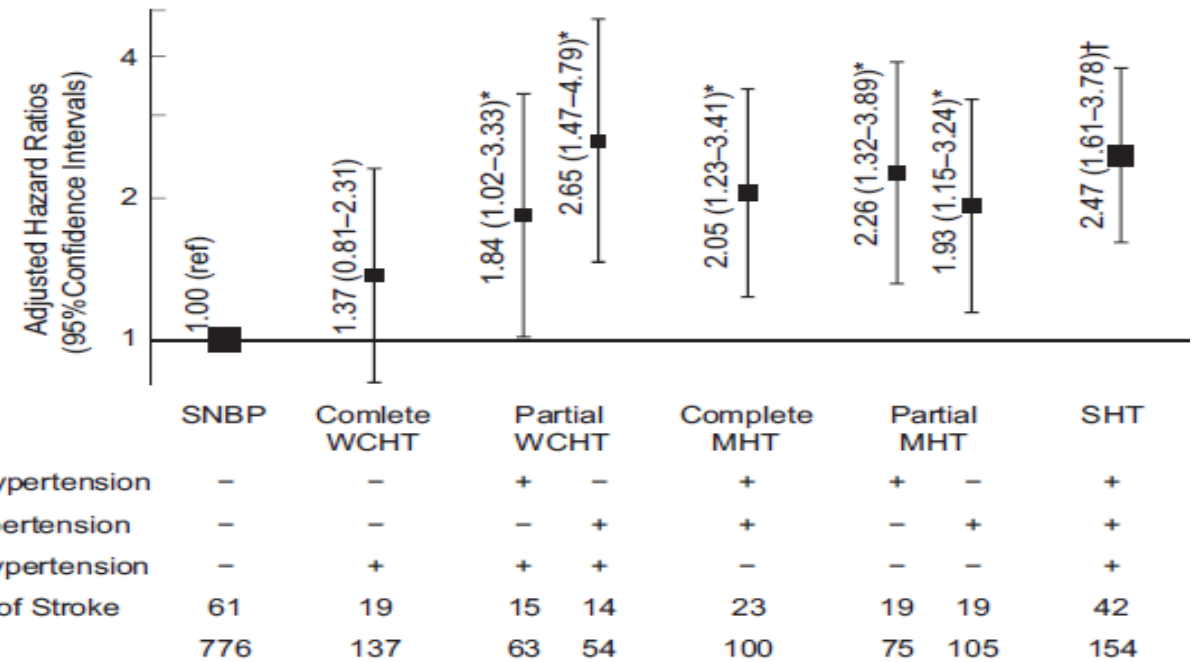


Figure 2. Adjusted hazard ratios among groups after further stratification according to home hypertension and 24-h ambulatory hypertension. Filled squares express adjusted hazard ratios for stroke and are sized in proportion to the number of events observed among hypertension groups. Covariates were sex, age, body mass index, current smoking, alcohol consumption, diabetes mellitus, total cholesterol, history of cardiovascular disease, and use of antihypertensive drugs. Hypertension was defined as systolic/diastolic blood pressure $\geq 135/85$ mm Hg for home, $\geq 130/80$ mm Hg for 24-h ambulatory, and $\geq 140/90$ mm Hg for office. The mark + indicates hypertension. * $P < 0.05$, † $P < 0.0001$ versus sustained normal blood pressure (SNBP) group. MHT indicates masked hypertension; SHT, sustained hypertension; and WCHT, white-coat hypertension.

Traiter l'HTA



Selon ESH 2013:

- Seuil de prise en charge médicamenteuse :
 - <65 ans 140/90 mmHg
 - >65 ans 160/90 ou <140/90 et risque CV >

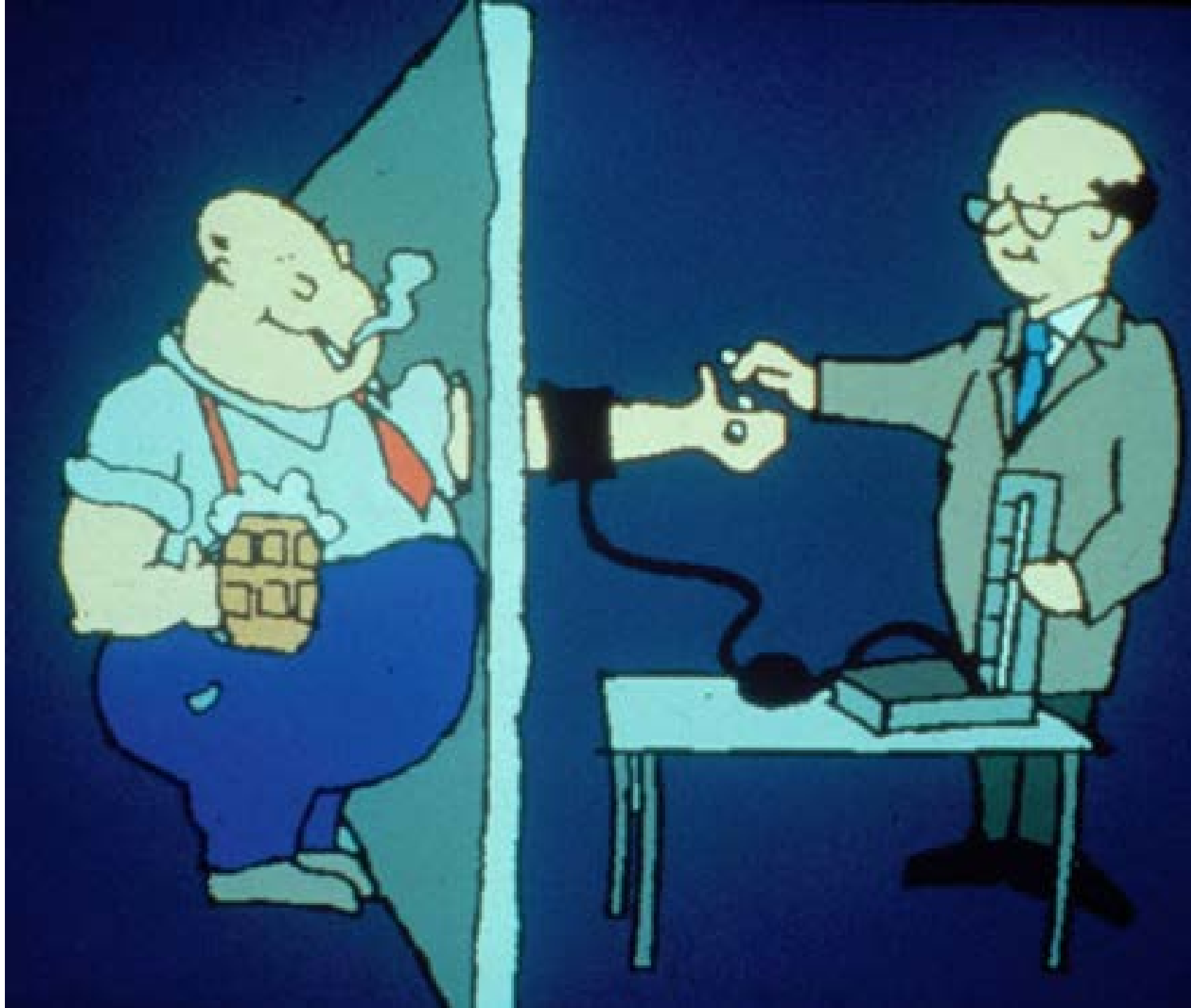
ESH-ESC 2013 recommandations (IA): toujours stimuler les règles H-D



- Salt restriction (5-6g/d)
- Moderation of alcohol intake
- High intake of vegetables, fruits, low fat dairy products
- Regular exercise (5-7 d/ w)
- Reduction of weight if BMI > 25 Kg/m²

Quel médicament?

Prévention
primaire



Traitement pharmacologique de la PA

- En association avec des modifications dues à l'hygiène de vie, le traitement pharmacologique diminue la PA mais diminue surtout par là le risque CV, les AVC et les décès.
- Toutes les molécules sont efficaces mais celles qui diminuent les évènements cliniques doivent être utilisées préférentiellement (thiazides, IEC, sartans et antagonistes calciques)

Nombre de patients à traiter sur 5 ans pour prévenir 1 événement CV
(à partir de méta-analyses de toutes les études en prévention primaire)

AVC, IM, Déc Cardiaque

- Diurétique faible dose 35
- Bêta-bloquant 64
- Antagoniste calcique 34
- IEC 35
- ARAII 50

AVC

- Diurétique faible dose 20
- Bêta-bloquant 136
- Antagoniste calcique 39
- IEC 116
- ARAII 114

Quid de la cible de PA pour la prévention primaire de l'AVC?

Traiter l'HTA



Selon ESH 2013:

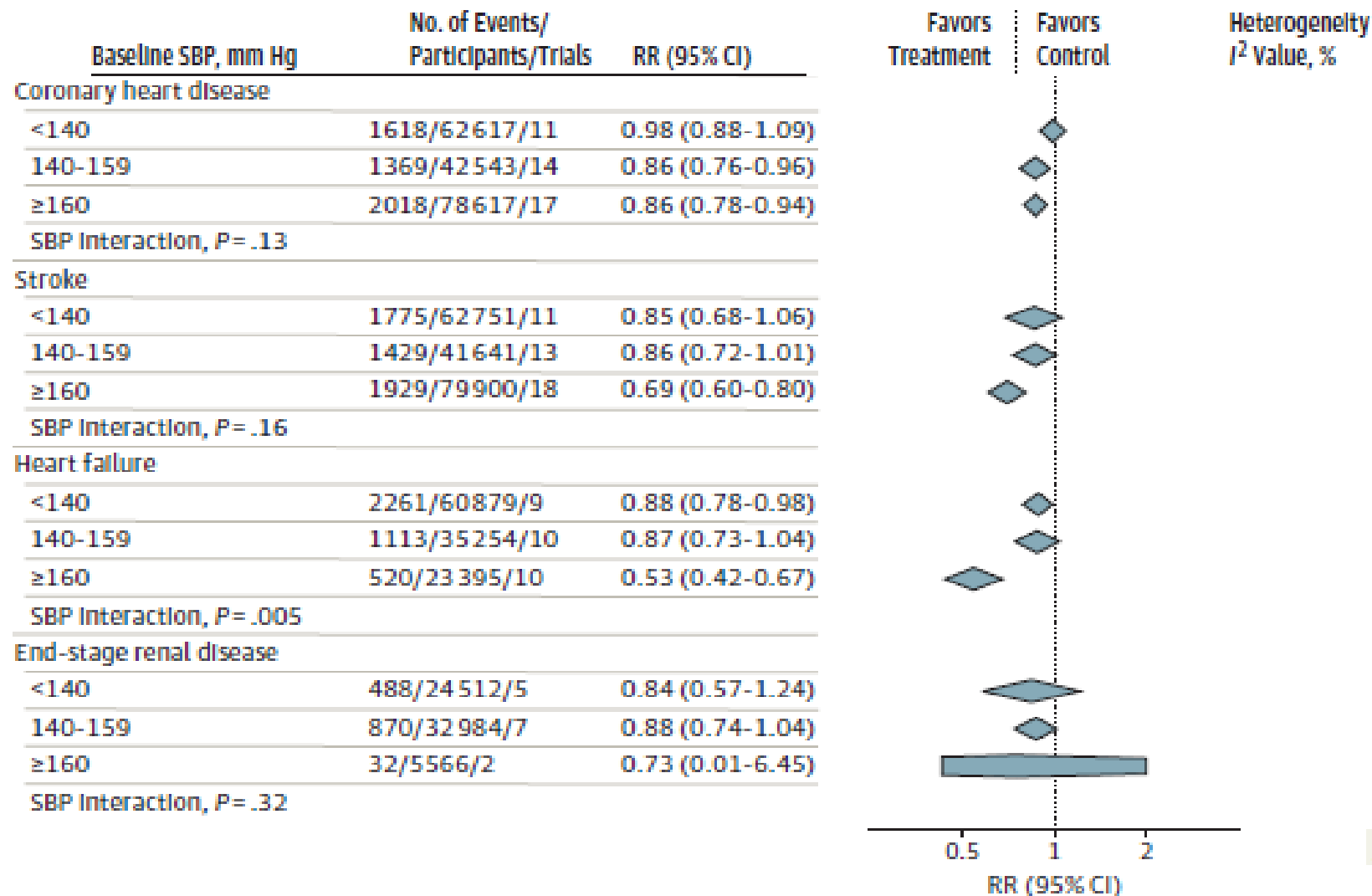
- Cible <140/90 mmHg
sauf chez > 80 ans et robuste: <150 mmHg
(plus bas possible si toléré debout).

Association of Blood Pressure Lowering With Mortality and Cardiovascular Disease Across Blood Pressure Levels

A Systematic Review and Meta-analysis

Mattias Brunström, MD; Bo Carlberg, MD, PhD

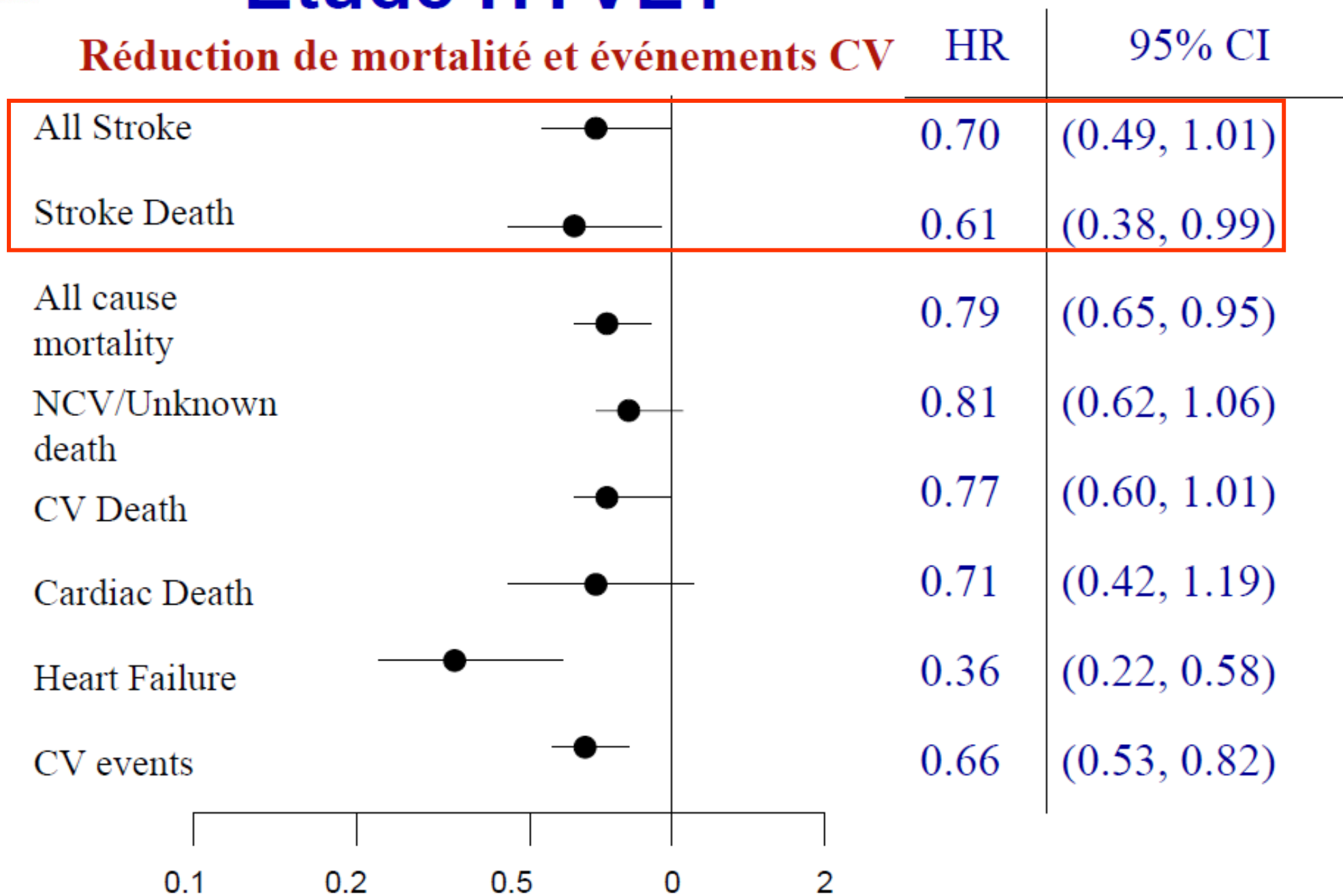
Figure 1. Effect of Treatment to Lower Blood Pressure (BP) at Different BP Levels in Primary Prevention



HYVET study

Beckett NS et al, N Engl J Med 2008 ; 358 : 1887-98

	<u>Design</u>	<u>Etude</u>
		1933 + 1912 patients
Age	≥ 80 ans	83,5 ans (60 % F)
TA inclusion	≥ 160 mm Hg	173/91 mm Hg
TA objectif	≤ 150 mm Hg	144/78 mm Hg vs. 161/84 mm Hg
Médicaments (vs. placebo)	Indapamide XL \pm Perindopril	Indapamide 26 % Combo 74 %



Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥ 75 Years

A Randomized Clinical Trial

OBJECTIVE To evaluate the effects of intensive (<120 mm Hg) compared with standard (<140 mm Hg) SBP targets in persons aged 75 years or older with hypertension but without diabetes.

DESIGN, SETTING, AND PARTICIPANTS A multicenter, randomized clinical trial of patients aged 75 years or older who participated in the Systolic Blood Pressure Intervention Trial (SPRINT). Recruitment began on October 20, 2010, and follow-up ended on August 20, 2015.

INTERVENTIONS Participants were randomized to an SBP target of less than 120 mm Hg (intensive treatment group, n = 1317) or an SBP target of less than 140 mm Hg (standard treatment group, n = 1319).

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

Table 1. Baseline Characteristics of Participants Aged 75 Years or Older

	Intensive Treatment (n = 1317)	Standard Treatment (n = 1319)
Female sex	499 (37.9)	501 (38.0)
Age, mean (SD), y	79.8 (3.9)	79.9 (4.1)
Race/ethnicity, No. (%)		
White	977 (74.2)	987 (74.8)
Seated blood pressure, mean (SD), mm Hg		
Systolic	141.6 (15.7)	141.6 (15.8)
Diastolic	71.5 (11.0)	70.9 (11.0)
Orthostatic hypotension, No. (%)	127 (9.6)	124 (9.4)
Serum creatinine, median (IQR), mg/dL	1.1 (0.9-1.3)	1.1 (0.9-1.3)
Estimated GFR ^a		
Mean (SD), mL/min/1.73 m ²	63.4 (18.2)	63.3 (18.3)
Frailty status, No. (%)		
Fit (frailty index ≤ 0.10)	159 (12.1)	190 (14.4)
Less fit (frailty index >0.10 to ≤ 0.21)	711 (54.0)	745 (56.5)
Frail (frailty index >0.21)	440 (33.4)	375 (28.4)

Table 3. Incidence of Cardiovascular, Renal, and Mortality Outcomes by Treatment Group

	Intensive Treatment		Standard Treatment		HR (95% CI) ^b	P Value
	No. With Outcome Events (n = 1317) ^a	% (95% CI) With Outcome Events/y	No. With Outcome Events (n = 1319) ^a	% (95% CI) With Outcome Events/y		
All participants						
Cardiovascular disease primary outcome ^c	102	2.59 (2.13-3.14)	148	3.85 (3.28-4.53)	0.66 (0.51-0.85)	.001
Myocardial infarction (MI) ^d	37	0.92 (0.67-1.27)	53	1.34 (1.02-1.75)	0.69 (0.45-1.05)	.09
ACS not resulting in MI ^d	17	0.42 (0.26-0.68)	17	0.42 (0.26-0.68)	1.03 (0.52-2.04)	.94
Stroke ^d	27	0.67 (0.46-0.97)	34	0.85 (0.61-1.19)	0.72 (0.43-1.21)	.22

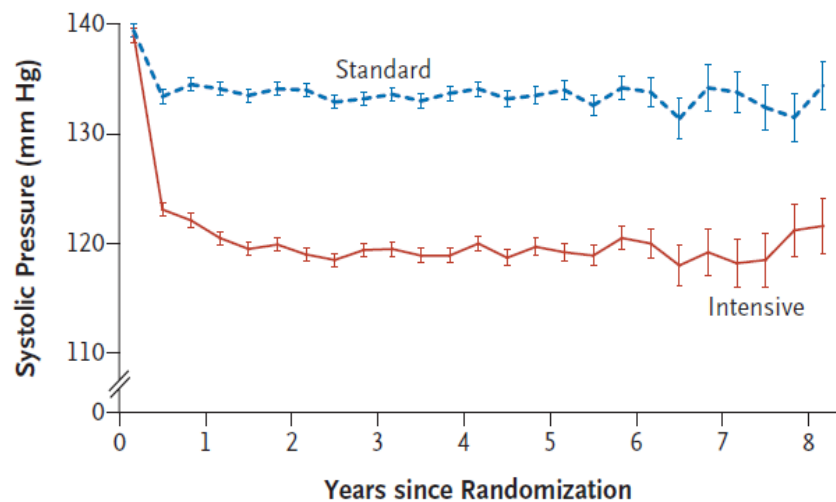


Table 3. Primary and Secondary Outcomes.

Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	no. of events	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03

Mean No. of Medications Prescribed

Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3

No. of Patients

Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

Figure 1. Mean Systolic Blood-Pressure Levels at Each Study Visit.

Un peu plus d'EI dans le groupe intensif:
hypotension, hypokaliémie

Systolic and Diastolic Blood Pressure Changes in Relation With Myocardial Infarction and Stroke in Patients With Coronary Artery Disease

Abstract—Excessively high and low achieved blood pressure (BP) may be associated with a bad outcome in patients with coronary artery disease, the J curve phenomenon. The effect of BP changes from baseline in relation with the subsequent risk of stroke and myocardial infarction (MI) is unknown. Of the 25 620 patients randomized in the Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) study, we selected 19 102 patients with coronary artery disease at baseline. BP at entry was 141/82 mmHg, and its average decrease during follow-up was 7/6 mmHg. BP entered the analysis as time-varying variable modeled with restricted cubic splines. After adjustment for several potential determinants of reverse causality, a change in BP from baseline by $-34/-21$ mmHg (10th percentile) was associated with a lesser risk of stroke without any significant increase in the risk of MI. A rise in systolic/diastolic BP from baseline by 20/10 mmHg (90th percentile) was associated with an increased risk of stroke, whereas the risk of MI increased with systolic BP and not with diastolic BP. In conclusion, in patients with coronary artery disease and initially free from congestive heart failure, a BP reduction from baseline over the examined BP range had little effect on the risk of MI and predicted a lower risk of stroke. An increase in systolic BP from baseline increased the risk of stroke and MI. The relationships of BP with risk were much steeper for stroke than for MI. A treatment-induced BP reduction over the explored range seems to be safe in patients with coronary artery disease.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00153101. (*Hypertension*. 2015;65:108-

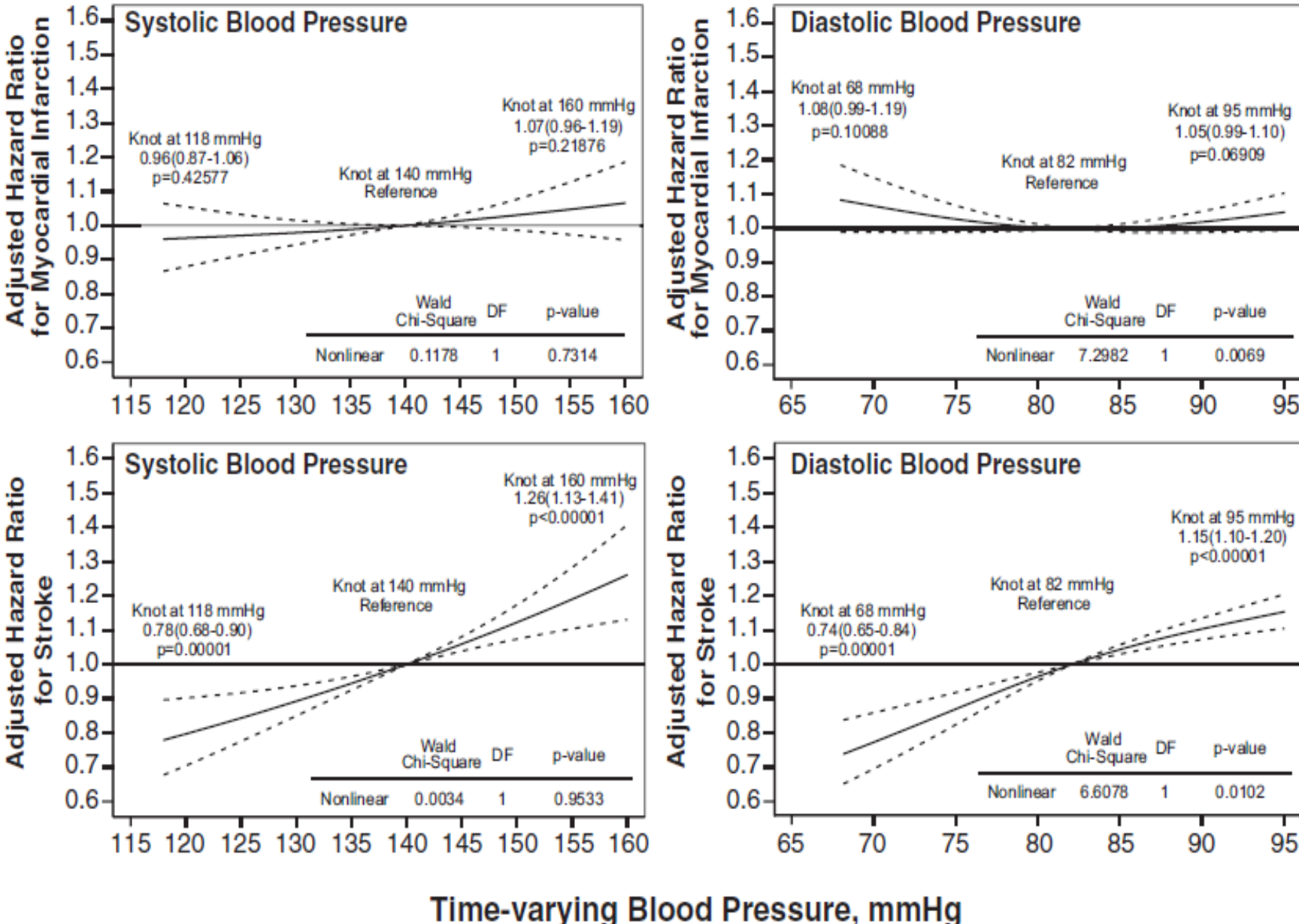


Figure 2. Myocardial infarction and stroke. Adjusted hazard ratio for achieved systolic and diastolic blood pressure

Findings From the CSPPT (China Stroke Primary Prevention Trial)

Characteristics	Total (n=17 720)
Age, y	59.9 (7.5)
Male, N (%)	7307 (41.2)
Body mass index, kg/m ²	24.8 (3.7)
Current smoking, N (%)	4268 (24.1)
Treatment group, N (%)	
Enalapril	8859 (50)
Enalapril–folic acid	8861 (50)
Baseline blood pressure, mm Hg	
Systolic	166.5 (20.2)
Diastolic	94.1 (11.8)

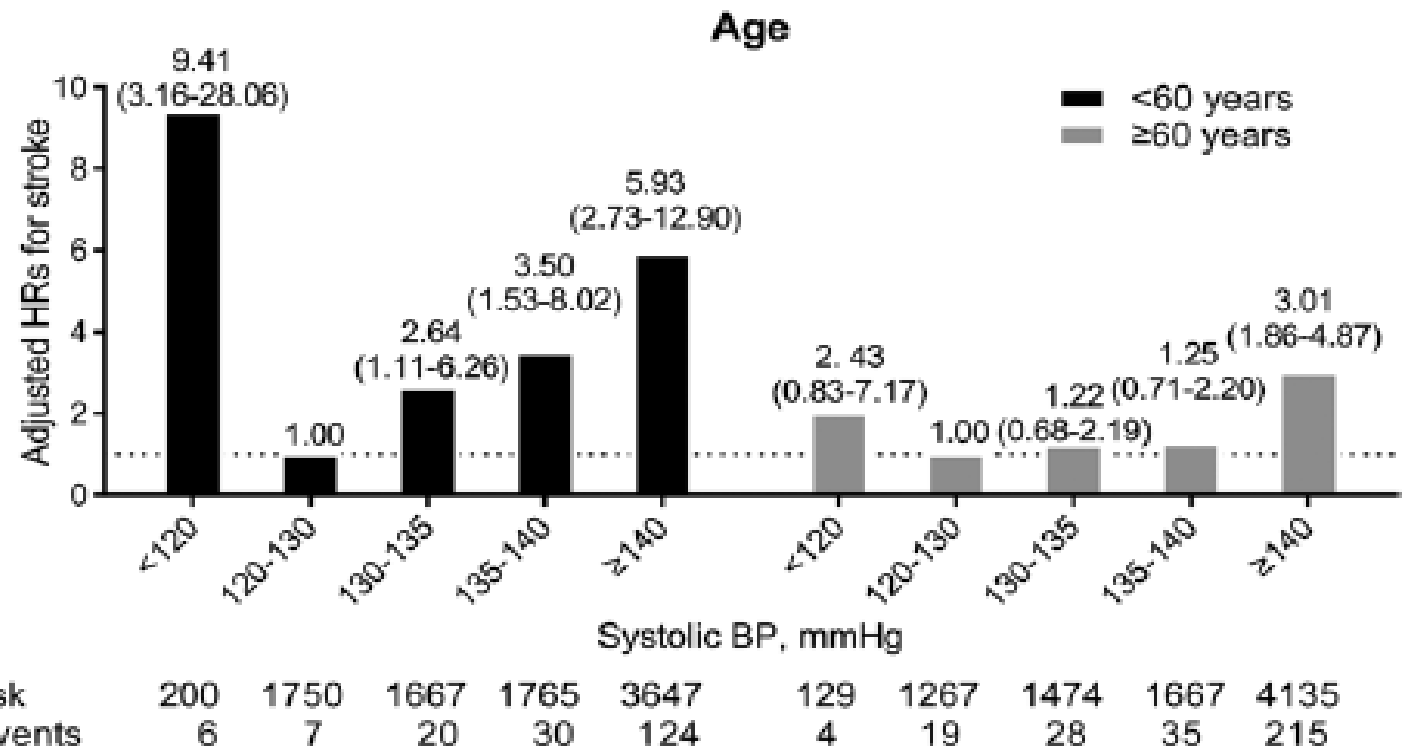


Figure 2. Comparisons of first stroke by time-averaged on-treatment systolic blood pressure (SBP) categories in different subgroups. HR indicates hazard ratio.

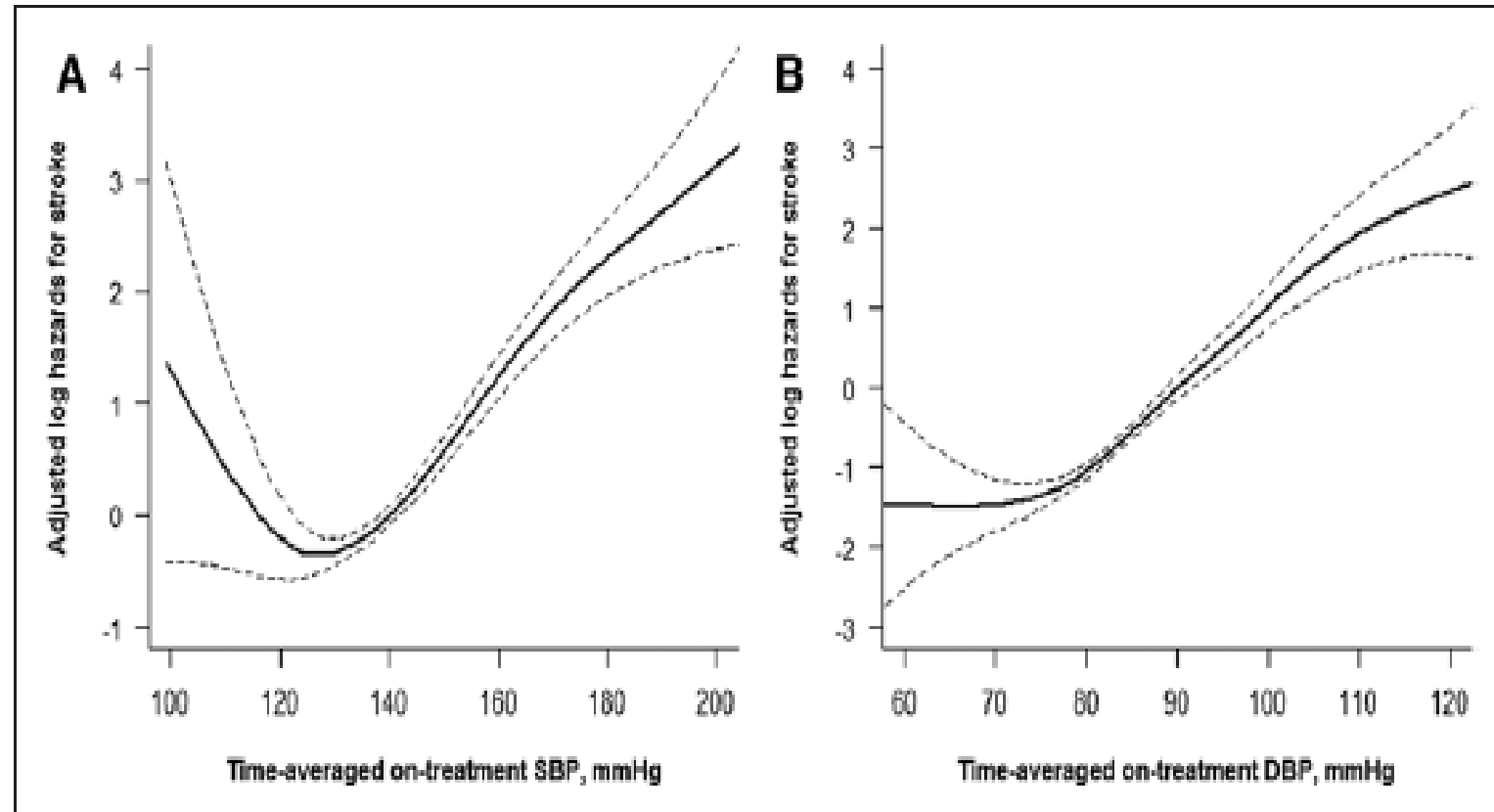


Figure 1. The association between time-averaged on-treatment systolic blood pressure (SBP) or diastolic blood pressure (DBP) and risk for first stroke.

Cible de PA prévention 1^{re} AVC:
120-130/70-80 mmHg si <60 ans

Table 23. BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General Prévention 1aire AVC		
Clinical CVD or 10-year ASCVD risk $\geq 10\%$	$\geq 130/80$	$< 130/80$
No clinical CVD and 10-year ASCVD risk $< 10\%$	$\geq 140/90$	$< 130/80$
Older persons (≥ 65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥ 130 (SBP)	< 130 (SBP)

Niveau de la tension artérielle et incidence d'AVC secondaire

Contexte épidémiologique

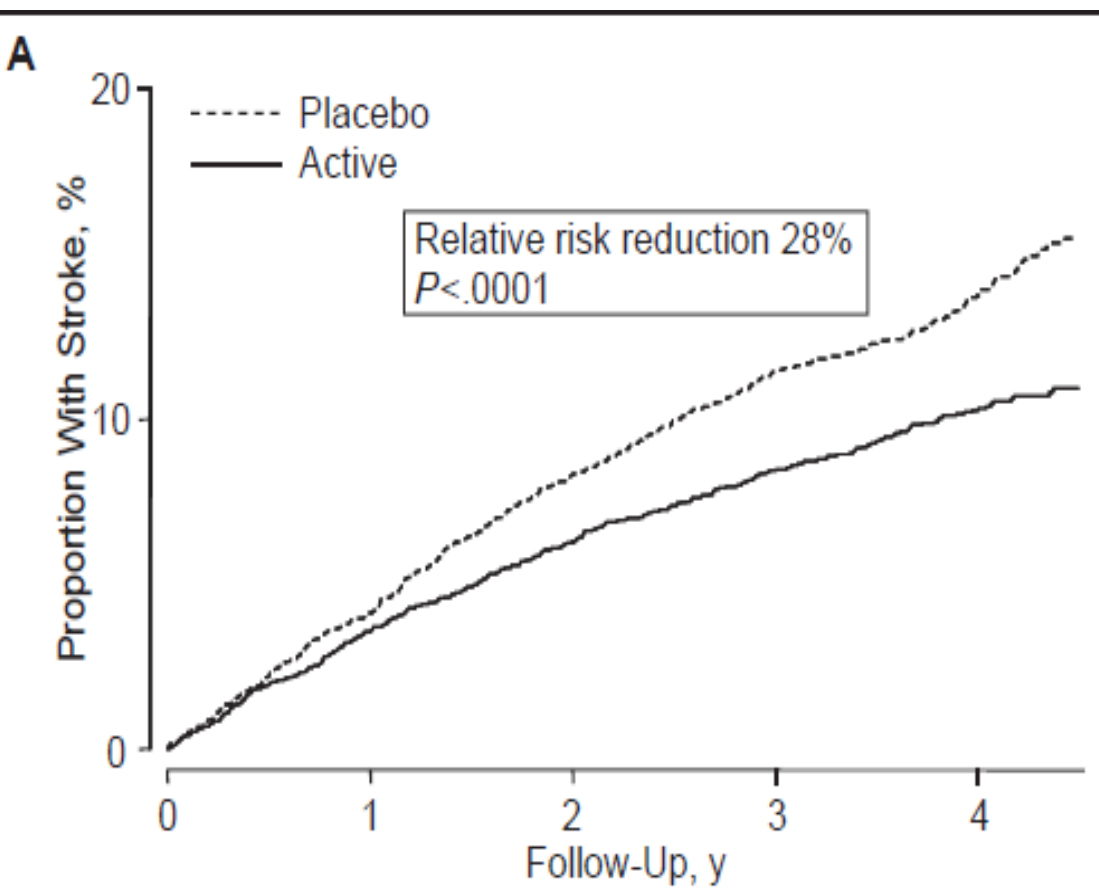
- La tension artérielle est liée directement au risque d'AVC secondaire chez des patients avec des antécédents de maladie cérébrovasculaire
- Fréquence
 - **15% des patients ayant survécu à un premier AVC font une récurrence d'AVC dans les 5 ans qui suivent le premier**
- **Risque plus élevé (8,8%) dans les 6 premiers mois après le premier AVC**
- Pronostic
 - **25% de toutes les récurrences d'AVC sont fatales dans les 28 jours**
 - **Mortalité plus élevée en cas de récurrence qu'en cas de 'first-ever stroke'**

Cible de la PA après stabilisation d'un AVC?

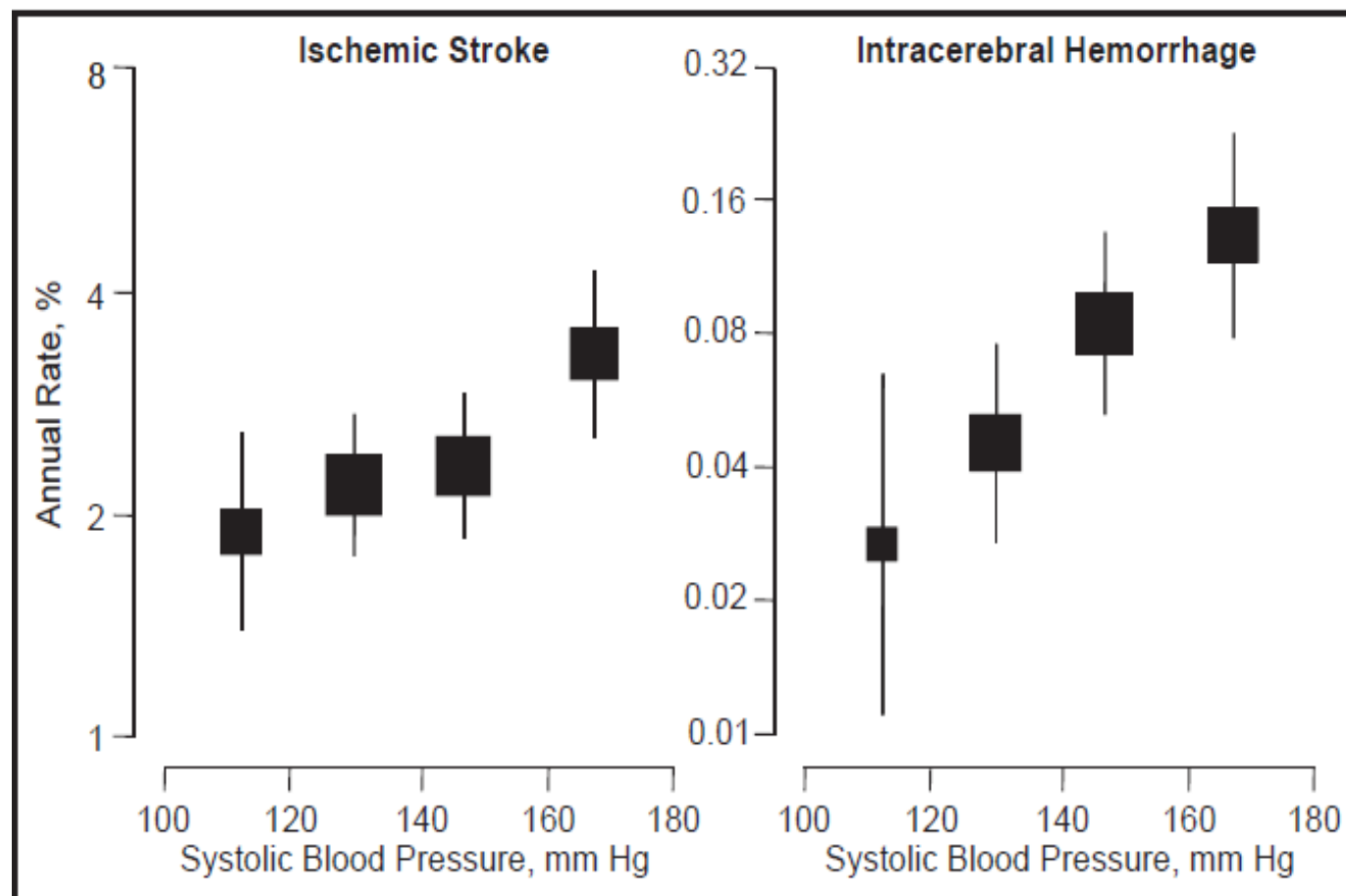
AVC stabilisés

Annual rates of ischemic stroke and intracerebral hemorrhage according to achieved follow-up systolic blood pressure levels.

Cumulative incidence of stroke



Lancet 2001



Lower systolic blood pressure is associated with poorer survival in long-term survivors of stroke

Journal of Hypertension 2014, 32:904–911

TABLE 2. Adjusted Cox regression analysis for outcome of composite endpoint or all-cause death at 10 years after stroke in 5-year survivors of stroke

<i>n</i> = 483	Composite endpoint			All-cause death		
	HR	95% CI	<i>P</i> -value	HR	95% CI	<i>P</i> -value
SBP ^a						
92–120 mmHg (<i>n</i> = 128)	1.61	1.08–2.41	0.019	1.54	1.04–2.31	0.033
121–130 mmHg (<i>n</i> = 118)	1.16	0.76–1.78	0.491	1.17	0.76–1.79	0.475
131–141 mmHg (<i>n</i> = 120)	1.00	–		1.00	–	
142–210 mmHg (<i>n</i> = 117)	1.25	0.81–1.91	0.313	1.16	0.75–1.78	0.503

Lower systolic blood pressure is associated with poorer survival in long-term survivors of stroke

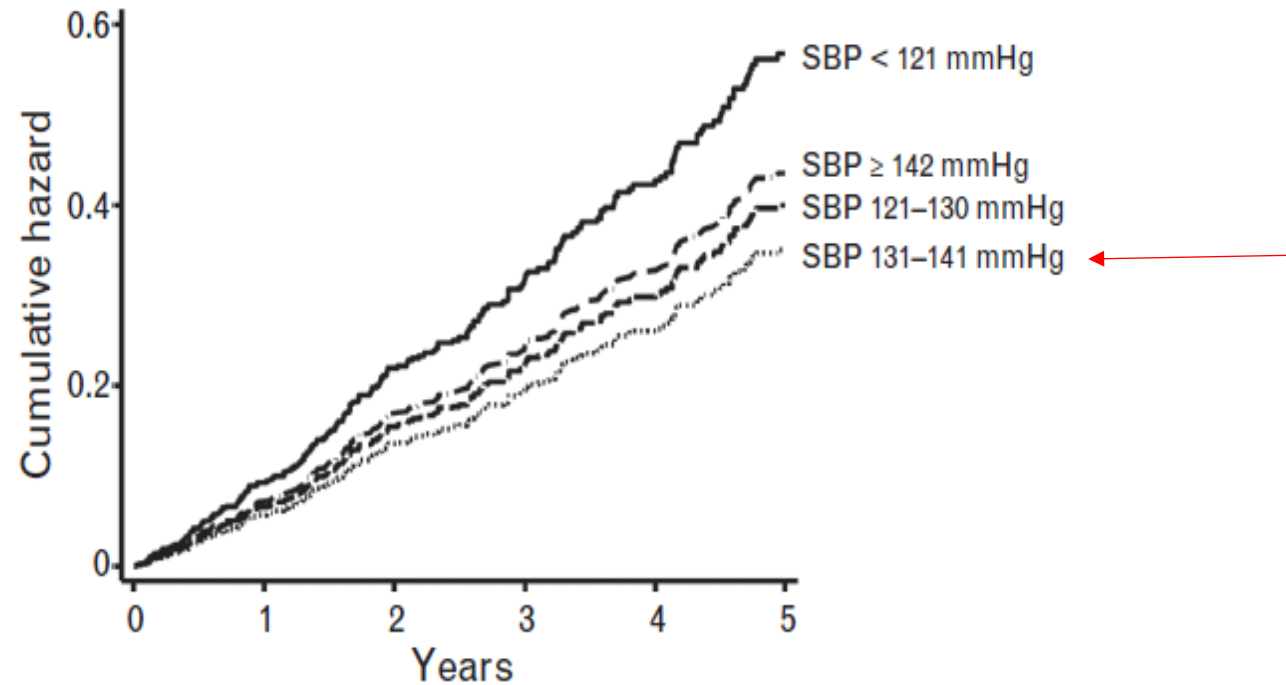


FIGURE 2 Cumulative hazard of composite endpoint of death or nonfatal vascular event after 5 years after NEMESIS entry. Adjusted for age, sex, socioeconomic status, history of high cholesterol, disability and domicile. Years refer to the number of years between 5 and 10 years after stroke. NEMESIS, North East Melbourne Stroke Incidence Study.

Conclusion: There was a greater risk of poor outcome in long-term survivors of stroke with low SBP. This is further evidence that low SBP may result in poor prognosis. Ideal blood pressure levels for long-term survivors of stroke may need to be reassessed.

Achieved Blood Pressure and Outcomes in the Secondary Prevention of Small Subcortical Strokes Trial

Michelle C. Odden, Leslie A. McClure, B. Peter Sawaya, Carole L. White, Carmen A. Peralta, Thalia S. Field, Robert G. Hart, Oscar R. Benavente, Pablo E. Pergola

Abstract—Studies suggest a J-shaped association between blood pressure and cardiovascular events in the setting of intensive systolic blood pressure control; whether there is a similar association with stroke remains less well established. The Secondary Prevention of Small Subcortical Strokes was a randomized trial to evaluate higher (130–149 mmHg) versus lower (<130 mmHg) systolic blood pressure targets in participants with recent lacunar infarcts. We evaluated the association of mean achieved blood pressure, 6 months after randomization, and recurrent stroke, major vascular events, and all-cause mortality. After a mean follow up of 3.7 years, there was a J-shaped association between achieved blood pressure and outcomes; the lowest risk was at ≈ 124 and 67 mmHg systolic and diastolic blood pressure, respectively. For example, above a systolic blood pressure of 124 mmHg, 1 standard deviation higher (11.1 mmHg) was associated with increased mortality (adjusted hazard ratio: 1.9; 95% confidence interval: 1.4, 2.7), whereas below this level, this relationship was inverted (0.29; 0.10, 0.79), $P < 0.001$ for interaction. Above a diastolic blood pressure of 67 mmHg, a 1 standard deviation higher (8.2 mmHg) was associated with an increased risk of stroke (2.2; 1.4, 3.6), whereas below this level, the association was in the opposite direction (0.34; 0.13, 0.89), $P = 0.02$ for interaction. The lowest risk of all events occurred at a nadir of ≈ 120 to 128 mmHg systolic blood pressure and 65 to 70 mmHg diastolic blood pressure. Future studies should evaluate the impact of excessive blood pressure reduction, especially in older populations with preexisting vascular disease.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00059306.

(*Hypertension*. 2016;67:63-69. DOI: 10.1161/HYPERTENSIONAHA.115.06480.)

Achieved Blood Pressure and Outcomes in the Secondary Prevention of Small Subcortical Strokes Trial

Secondary Prevention of Small Subcortical Strokes was a randomized trial to evaluate higher (130–149 mmHg) versus lower (<130 mmHg) systolic blood pressure targets in participants with recent lacunar infarcts. We evaluated the association of mean achieved blood pressure, 6 months after randomization, and recurrent stroke, major vascular events, and all-cause mortality. After a mean follow up of 3.7 years, there was a J-shaped association between achieved blood pressure and outcomes: **the lowest risk was at ≈ 124 and 67 mmHg** systolic and diastolic blood pressure, respectively.

Hypertension January 2016

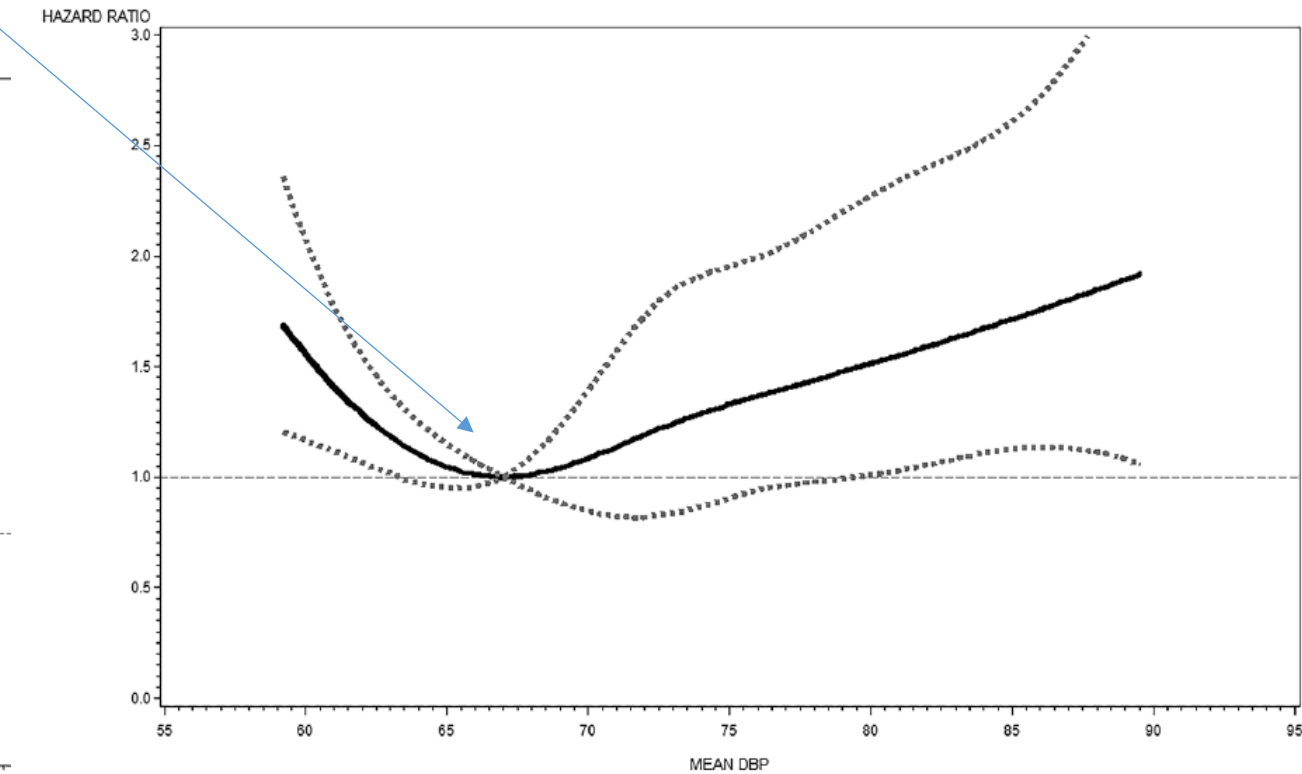
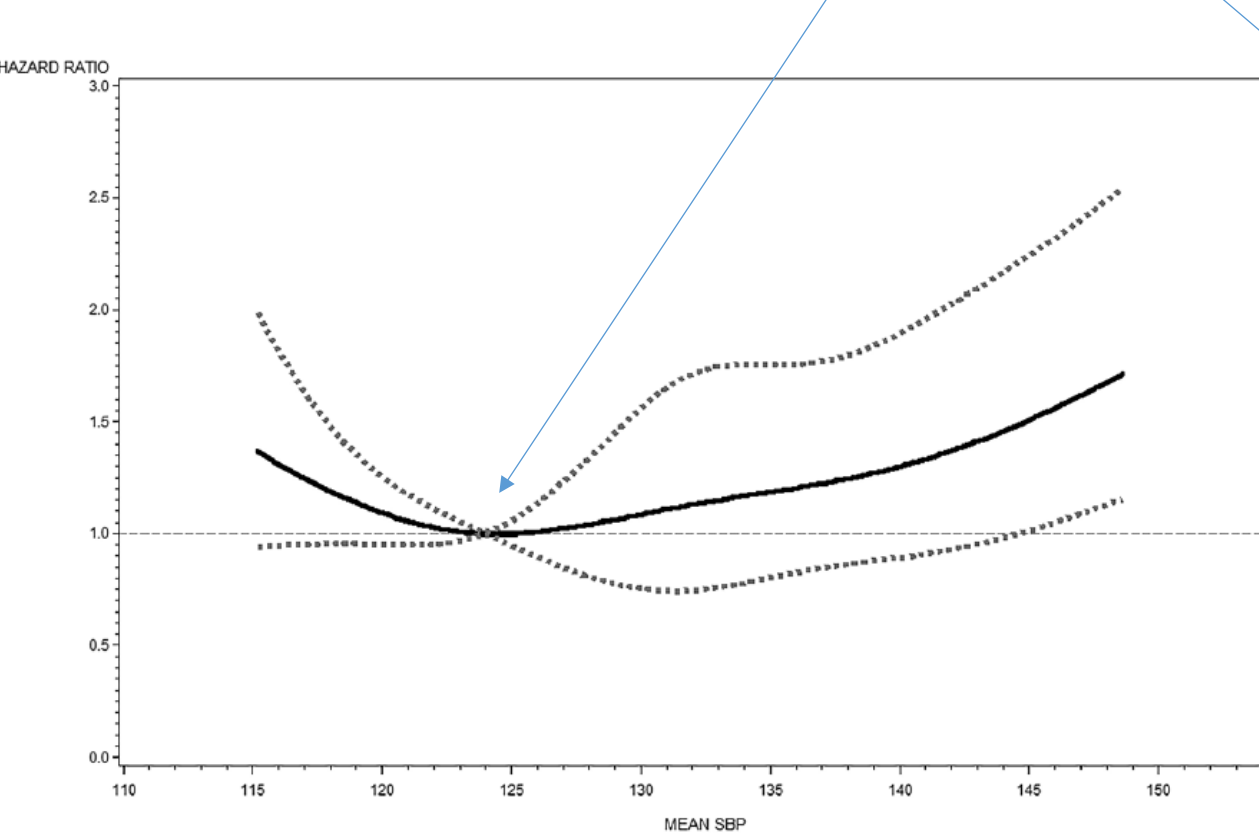


Figure 1. Nonlinear association between mean achieved systolic blood pressure (SBP; top) and diastolic blood pressure (DBP; bottom) and all stroke; dotted lines =95% confidence interval.

Blood Pressure Reduction and Secondary Stroke Prevention

A Systematic Review and Metaregression Analysis of Randomized Clinical Trials

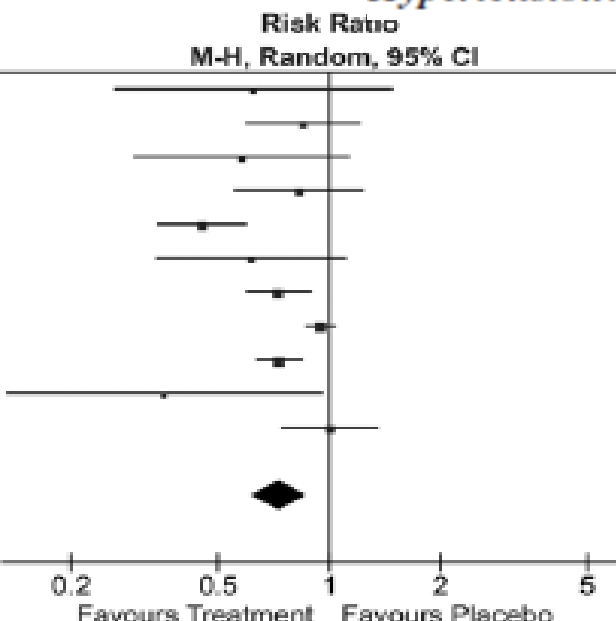
Hypertension. 2017;

Table 1. Baseline Characteristics of Included Studies

Study Name	Country	Year	Antihypertensive Treatment	Stroke Definition	Patients, n	ICH as Index Event, %
Carter ¹⁶	United Kingdom	1970	Guanethidine	>48 h	97	0
Dutch TIA ¹⁷	Netherlands	1993	Atenolol	>24 h	1473	0
TEST ¹⁸	Sweden	1995	Atenolol	>24 h	720	6.1
HOPE ¹⁹	Multicenter	2000	Ramipril	>24 h	1013	0
HSCSG ²⁰	United States	1974	Deserpidine/methyclothiazide	>24 h	452	0
Liu et al ²¹	China	2005	Perindopril/indapamide	>24 h	1520	17.7
Martí Massó and Lozano ²²	Spain	1990	Nicardipine	>24 h	264	0
MOSES ²³	Germany/Austria	2005	Eprosartan vs nitrendipine	>24 h/+neuroimaging	1352	5.4
PAST-BP ²⁴	United Kingdom	2016	NR	>24 h/+neuroimaging	529	0
PATS ²⁵	China	1995	Indapamide	+neuroimaging	5665	15.8
PRoFESS ²⁶	Multicenter	2008	Telmisartan	>24 h+neuroimaging	20 332	0
PROGRESS ²⁷	Multicenter	2001	Perindopril/indapamide	>24 h	6105	11
SCOPE ²⁸	Multicenter	1999	Candesartan	...	194	...
SPS3 ²⁹	Multicenter	2013	NR	+neuroimaging	3020	0

A

Study or Subgroup	Treatment		Placebo		Weight	Risk Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Carter et al	7	49	11	48	3.1%	0.62	[0.26, 1.47]
Dutch TIA	52	732	62	741	9.5%	0.85	[0.60, 1.21]
HOPE	13	500	23	513	4.5%	0.58	[0.30, 1.13]
HSCSG	37	233	42	219	8.5%	0.83	[0.55, 1.24]
Liu et al	67	762	147	758	11.5%	0.45	[0.35, 0.59]
Martí Massó and Lozano	20	170	18	94	5.5%	0.61	[0.34, 1.10]
PATS	159	2841	217	2824	13.4%	0.73	[0.60, 0.89]
PRoFESS	880	10146	934	10186	15.8%	0.95	[0.87, 1.03]
PROGRESS	307	3051	420	3054	14.8%	0.73	[0.64, 0.84]
SCOPE	5	97	14	97	2.5%	0.36	[0.13, 0.95]
TEST	74	372	69	348	10.9%	1.00	[0.75, 1.35]
Total (95% CI)		18953		18882	100.0%	0.73	[0.62, 0.87]
Total events	1621		1957				
Heterogeneity: Tau ² = 0.04; Chi ² = 39.47, df = 10 (P < 0.0001); I ² = 75%							
Test for overall effect: Z = 3.64 (P = 0.0003)							



B

Study or Subgroup	Treatment		Placebo		Weight	Risk Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Carter et al	10	49	16	48	3.2%	0.61	[0.31, 1.21]
Dutch TIA	41	732	33	741	7.1%	1.26	[0.80, 1.97]
HSCSG	15	233	19	219	3.5%	0.74	[0.39, 1.42]
Liu et al	27	762	50	758	6.8%	0.54	[0.34, 0.85]
PATS	87	2841	101	2824	15.6%	0.86	[0.65, 1.14]
PRoFESS	223	10146	263	10186	30.0%	0.85	[0.71, 1.02]
PROGRESS	181	3051	198	3054	26.4%	0.92	[0.75, 1.11]
TEST	34	372	39	348	7.4%	0.82	[0.53, 1.26]
Total (95% CI)		18186		18178	100.0%	0.85	[0.75, 0.96]
Total events	618		719				
Heterogeneity: Tau ² = 0.01; Chi ² = 8.45, df = 7 (P = 0.29); I ² = 17%							
Test for overall effect: Z = 2.56 (P = 0.01)							

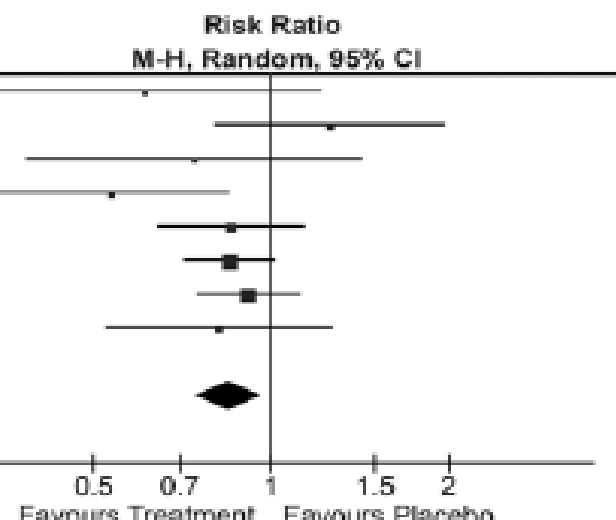


Figure 1. Forest plot on the risk of (A) recurrent stroke and (B) cardiovascular death between stroke patients randomized to antihypertensive treatment or placebo. CI indicates confidence interval.

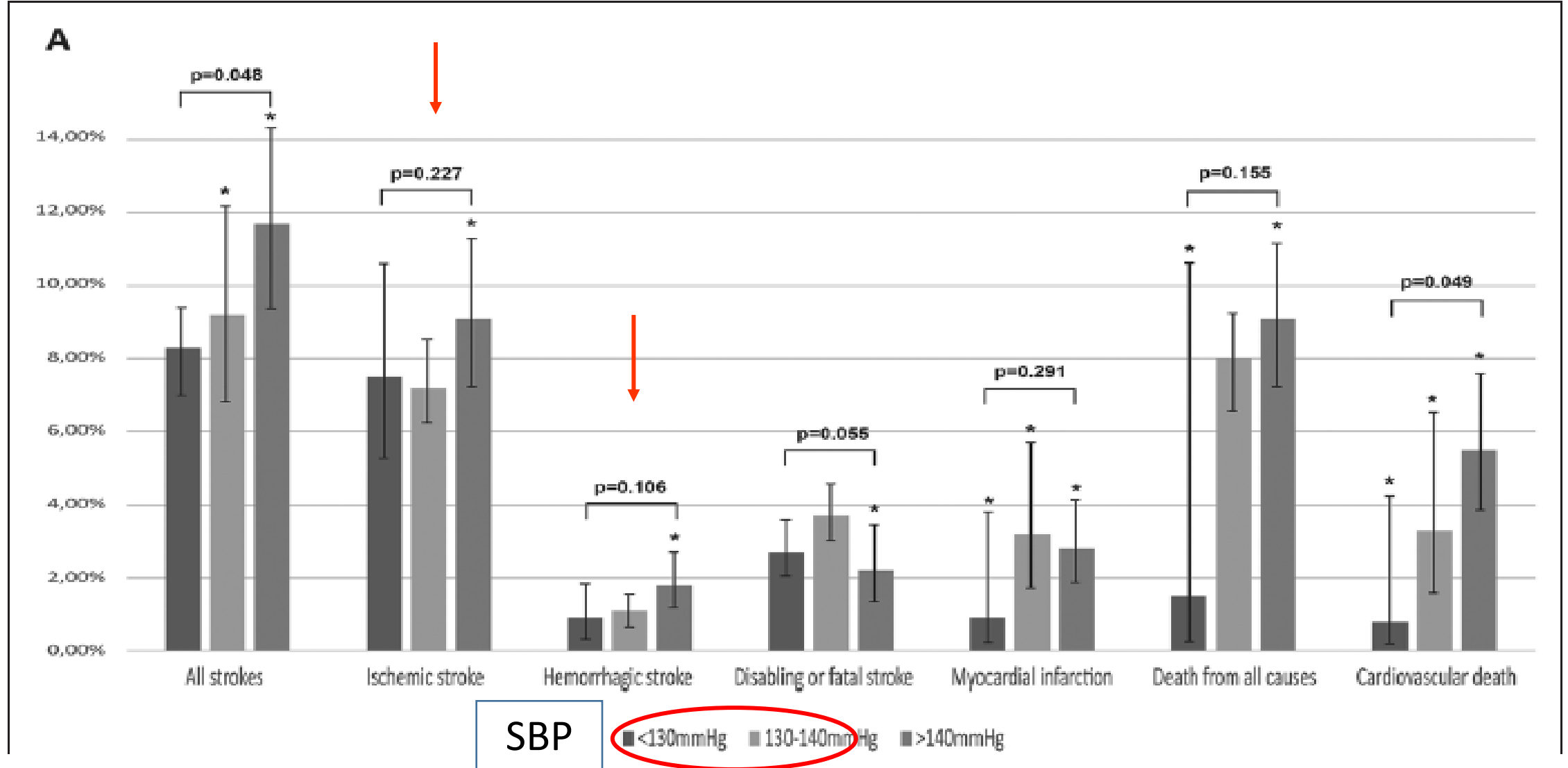


Figure 2. Overview of the subgroup analyses on the reported outcomes during follow-up according to the reported (A) achieved mean systolic blood pressure

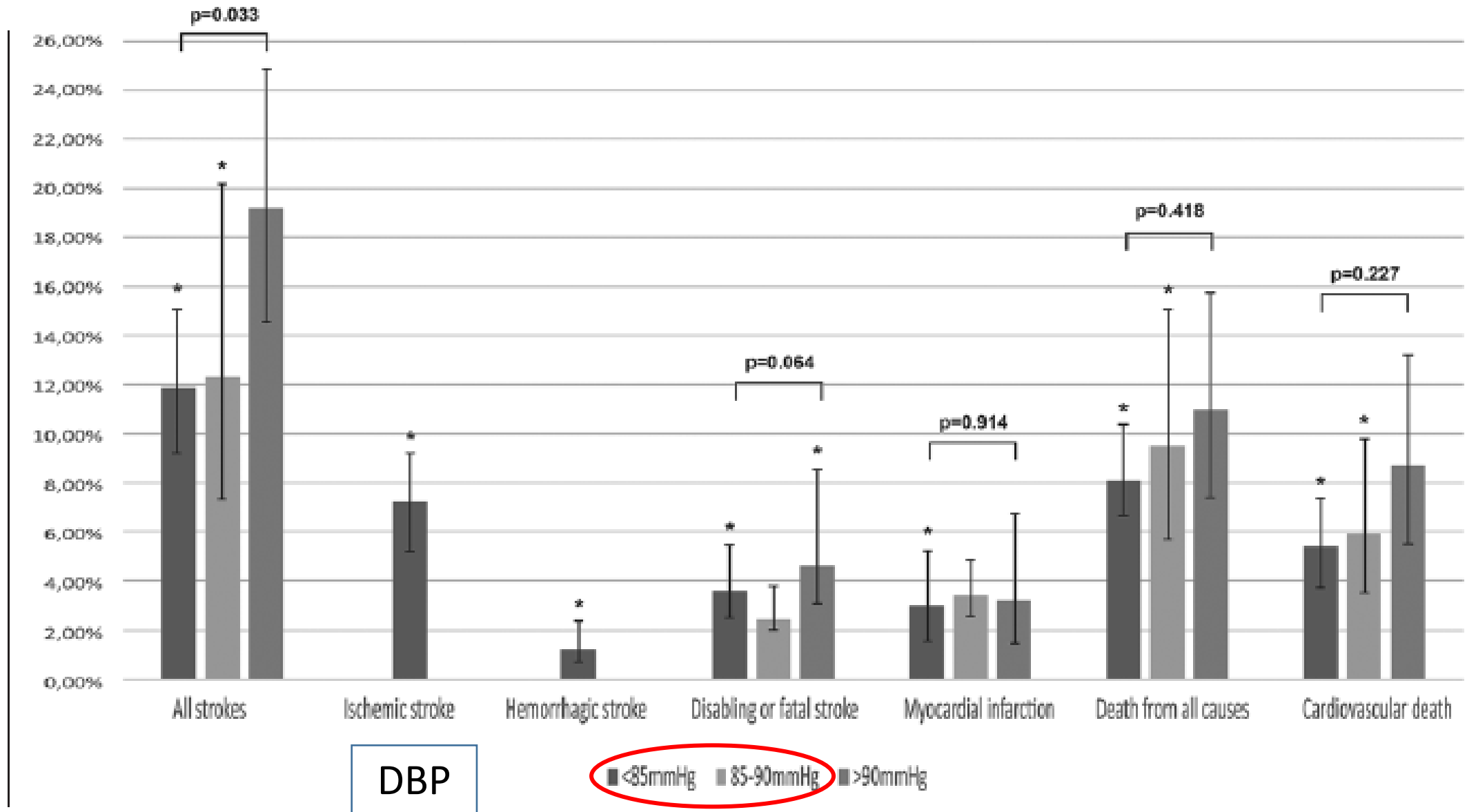


Figure 2. Overview of the subgroup analyses on the reported outcomes during follow-up according to the reported (B) achieved mean diastolic blood pressure in the patients' subgroups of included trials

Recommendations for Treatment of Hypertension for Secondary Stroke Prevention

References that support recommendations are summarized in Online Data Supplements 43 and 44.

COR	LOE	Recommendations
I	A	1. Adults with previously treated hypertension who experience a stroke or transient ischemic attack (TIA) should be restarted on antihypertensive treatment after the first few days of the index event to reduce the risk of recurrent stroke and other vascular events (1-3).
I	A	2. For adults who experience a stroke or TIA, treatment with a thiazide diuretic, ACE inhibitor, or ARB, or combination treatment consisting of a thiazide diuretic plus ACE inhibitor, is useful (1, 3-5).
I	B-R	3. Adults not previously treated for hypertension who experience a stroke or TIA and have an established BP of 140/90 mm Hg or higher should be prescribed antihypertensive treatment a few days after the index event to reduce the risk of recurrent stroke and other vascular events (1-3).
I	B-NR	4. For adults who experience a stroke or TIA, selection of specific drugs should be individualized on the basis of patient comorbidities and agent pharmacological class (6).
IIb	B-R	5. For adults who experience a stroke or TIA, a BP goal of less than 130/80 mm Hg may be reasonable (6, 7).
IIb	B-R	6. For adults with a lacunar stroke, a target SBP goal of less than 130 mm Hg may be reasonable (8).
IIb	C-LD	7. In adults previously untreated for hypertension who experience an ischemic stroke or TIA and have a SBP less than 140 mm Hg and a DBP less than 90 mm Hg, the usefulness of initiating antihypertensive treatment is not well established (9).

Aux USA

Gestion PA après AVC
(stabilisé):
Si HTA, cible de PA
<130/80 mmHg si pas
de C/I

Si pas d'HTA avant et
PA <140/90, pas de
traitement mais suivi

Choix Diurétique et/ou
ISRA si pas de C/I

HT in acute stroke : should it be treated ?

Hypertension in acute ischemic stroke : treat

JD Spence JD, Del Maestro RF
Arch Neurol 1985 ; 42 : 1000-02

Hypertension in acute ischemic stroke : not to treat

Yatsu FM, Zivin J
Arch Neurol 1985 ; 42 : 999-1000

HTA à la phase aiguë d'un AVC

- AVC ischémique : dans 77 % des cas avec HTA et dans 15% des cas une PA > 184 mmHg, surtout si HTA avant.
- Réaction hypertensive (SNA) en phase aiguë.
- PA diminue spontanément dès les 90 premières min après le déficit.
- Meilleur pronostic si PAS aux alentours de 130 mmHg.
- HTA sévère (>220 mmHg) ou hypotension (PAS < 110 mmHg), délétère!
- Dans 24 à 48 premières heures d'un AVC ischémique, ne pas traiter l'HTA sauf si raisons associées (DC, dissection aorte) ou fibrinolyse.

Blood Pressure Decrease During the Acute Phase of Ischemic Stroke Is Associated With Brain Injury and Poor Stroke Outcome

Stroke. 2004;35:520-527.

José Castillo, MD, PhD; Rogelio Leira, MD, PhD; María M. García, MD, PhD; Joaquín Serena, MD, PhD; Miguel Blanco, MD, PhD; Antoni Dávalos, MD, PhD

TABLE 2. Changes in Blood Pressure Between Admission and the First Day and Stroke Outcome*

	Systolic Blood Pressure				Diastolic Blood Pressure			
	Drop >20 mm Hg	Drop 0–20 mm Hg	Increase >0 mm Hg	<i>P</i> Value	Drop >20 mm Hg	Drop 0–20 mm Hg	Increase >0 mm Hg	<i>P</i> Value
Early neurological deterioration, %	54.4 (57)	13.6 (177)	30.3 (66)	<0.001	56.1 (50)	14.2 (197)	35.8 (53)	<0.001
Poor neurological outcome, %	90.2 (51)	49.0 (151)	57.4 (54)	<0.001	77.3 (44)	53.3 (167)	62.2 (45)	0.014
Mortality at 3 months, %	23.5 (51)	10.6 (151)	13.0 (54)	0.066	25.0 (44)	9.0 (167)	20.0 (45)	0.009
Volume of infarct, mean±SD, mL	133±66 (56)	77±60 (174)	108±73 (66)	<0.001	137±60 (49)	80±64 (195)	110±70 (52)	<0.001

Number of patients evaluated in each group is shown in parentheses.

*Changes in BP during the first day were not obtained in 2 patients who died within the first 24 hours.

Jo Leonardi-Bee, MSc; Philip M.W. Bath, FRCP; Stephen J. Phillips, FRCPC;
Peter A.G. Sandercock, FRCP; for the IST Collaborative Group

Methods—We included in the analysis 17 398 patients from IST with confirmed ischemic stroke. A single measurement of SBP was made immediately before randomization. Clinical events within 14 days of randomization were recorded:

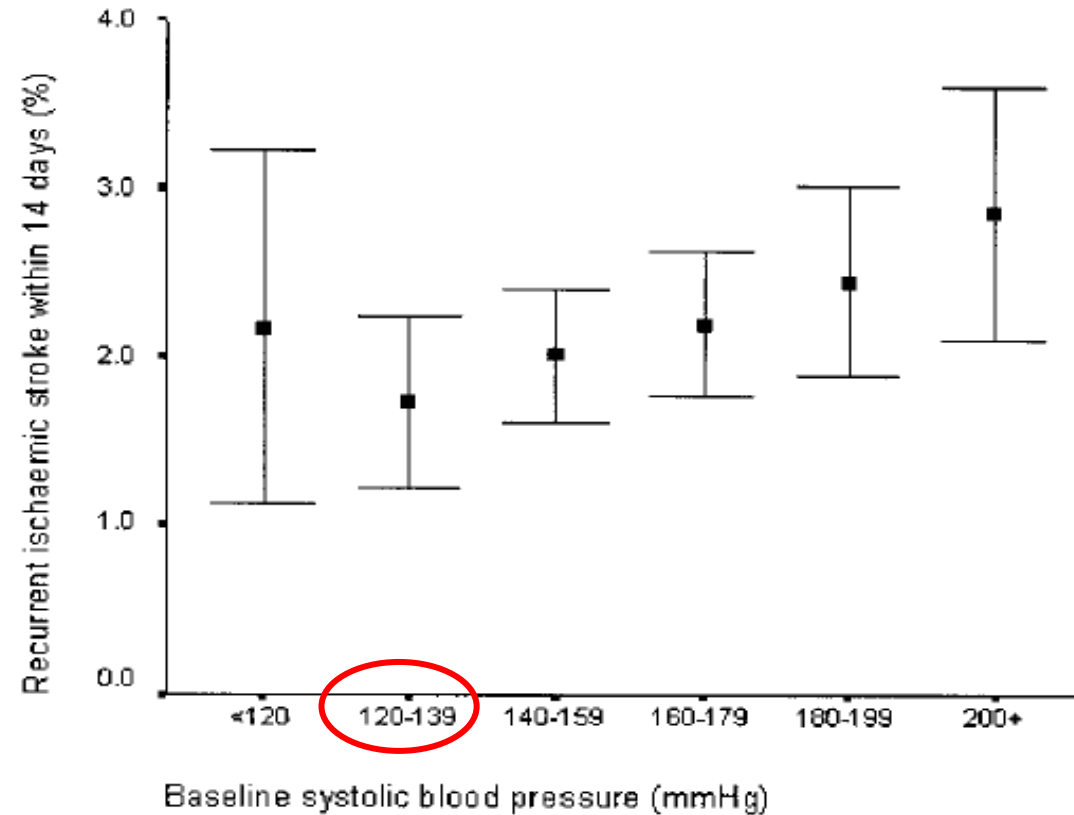
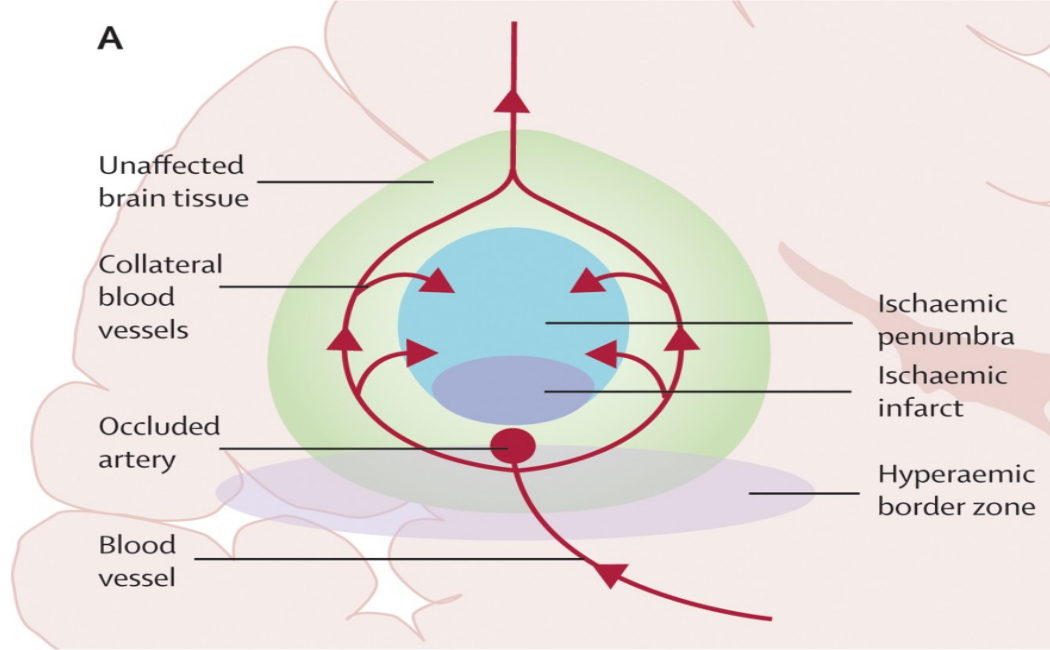
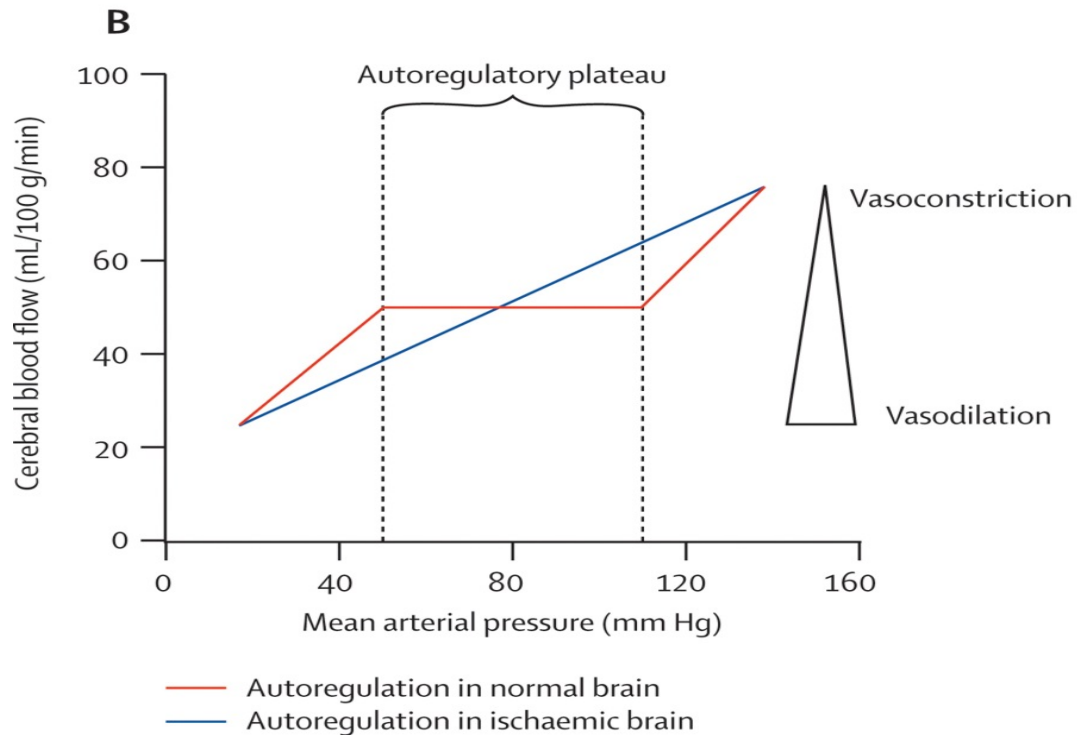


Figure 3. Frequency of recurrent ischemic stroke by SBP from 17 398 patients with confirmed acute ischemic stroke. Squares indicate mean within each SBP group; 95% CIs are represented by T bars.



Blood flow in ischemic and normal brain tissue



Tikhonoff V et al,
Lancet Neurol 2009

American Heart Association / American Stroke Association
Guidelines for the early management of patients with **acute ischemic stroke**
Stroke 2013 ; 44 : 870-947: **BP management**

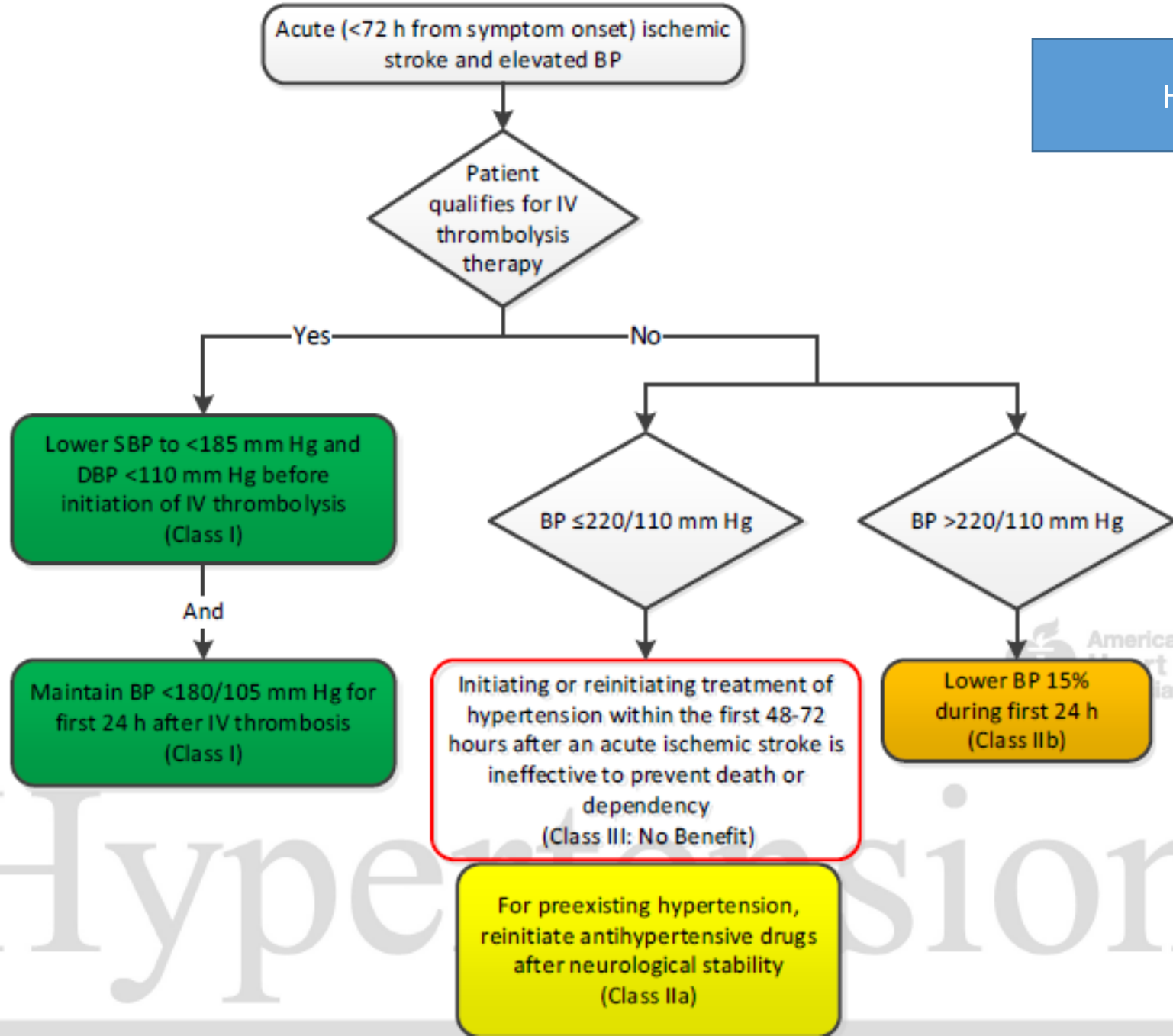
No fibrinolysis

... not to lower BP during the initial 24 h unless the BP is > 220/120 mm Hg or there is a concomitant specific condition that would benefit from BP reduction remains reasonable (2007 = IC).

Fibrinolysis

... gentle approach to bringing BP < 180/110 mm Hg to qualify for iv rtPA.

Once iv rtPA is given, the BP must be maintained < 180/105 mm Hg (2007 = IB).



Hypertension

Which drugs ? (fibrinolysis studies)

AHA/ASA Guidelines (Stroke 2013 ; 44 : 870-947)

Labetalol or nicardipine

Other agents may be considered :
hydralazine, enalaprilat, nitroprusside, ...

Table 6. Suggested Recommended Guidelines for Treating Elevated BP in Spontaneous ICH

**AVC
hémorragique**

1. If SBP is >200 mm Hg or MAP is >150 mm Hg, then consider aggressive reduction of BP with continuous intravenous infusion, with frequent BP monitoring every 5 min.
2. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is the possibility of elevated ICP, then consider monitoring ICP and reducing BP using intermittent or continuous intravenous medications while maintaining a cerebral perfusion pressure ≥ 60 mm Hg
3. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is not evidence of elevated ICP, then consider a modest reduction of BP (eg, MAP of 110 mm Hg or target BP of 160/90 mm Hg) using intermittent or continuous intravenous medications to control BP and clinically reexamine the patient every 15 min.

Note that these recommendations are Class C. SBP indicates systolic blood pressure; MAP, mean arterial pressure.

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

BACKGROUND

Whether rapid lowering of elevated blood pressure would improve the outcome in patients with intracerebral hemorrhage is not known.

METHODS

We randomly assigned 2839 patients who had had a spontaneous intracerebral hemorrhage within the previous 6 hours and who had elevated systolic blood pressure to receive intensive treatment to lower their blood pressure (with a target systolic level of <140 mm Hg within 1 hour) or guideline-recommended treatment (with a target systolic level of <180 mm Hg) with the use of agents of the physician's choosing.

The primary outcome was death or major disability, which was defined as a score of 3 to 6 on the modified Rankin scale (in which a score of 0 indicates no symptoms, a score of 5 indicates severe disability, and a score of 6 indicates death) at 90 days. A prespecified ordinal analysis of the modified Rankin score was also performed.

The rate of serious adverse events was compared between the two groups.

Cible PAS
<140 vs <180
à atteindre
en 1h

Table 1. Baseline Characteristics of the Participants.*

Characteristic	Intensive Blood-Pressure Lowering (N= 1399)	Guideline- Recommended Blood-Pressure Lowering (N= 1430)
Time from onset of ICH to randomization — hr		
Median	3.7	3.7
Interquartile range	2.8–4.8	2.9–4.7
Age — yr	63.0±13.1	64.1±12.6
Male sex — no. (%)	898 (64.2)	882 (61.7)
Recruited from China — no. (%)	947 (67.7)	973 (68.0)
Blood pressure — mm Hg		
Systolic	179±17	179±17
Diastolic	101±15	101±15
NIHSS score†		
Median	10	11
Interquartile range	6–15	6–16
GCS score‡		
Median	14	14
Interquartile range	12–15	12–15

Table 2. Treatment of Patients with Intracerebral Hemorrhage.

N Engl J Med 2013;368:2355-65.

Variable	Intensive Blood-Pressure Lowering (N = 1399)	Guideline-Recommended Blood-Pressure Lowering (N = 1430)	P Value
Time from ICH to start of treatment — hr			<0.001
Median	4.0	4.5	
Interquartile range	2.9–5.1	3.0–7.0	
Time from randomization to start of treatment — hr			<0.001
Median	0.1	0.3	
Interquartile range	0.0–0.39	0.0–2.8	
Blood-pressure-lowering treatment during first 24 hr — no. (%)			
Any intravenous treatment	1260 (90.1)	613 (42.9)	<0.001
Use of a single intravenous agent	849 (60.7)	421 (29.4)	<0.001
Type of intravenous agent used			
Alpha-adrenergic antagonist, such as urapidil	454 (32.5)	191 (13.4)	
Calcium-channel blocker, such as nicardipine or nimodipine	227 (16.2)	122 (8.5)	
Combined alpha- and beta-blocker, such as labetalol	202 (14.4)	83 (5.8)	
Nitroglycerin	209 (14.9)	59 (4.1)	
Diuretic, such as furosemide	174 (12.4)	94 (6.6)	
Nitroprusside	169 (12.1)	28 (2.0)	
Hydralazine	82 (5.9)	50 (3.5)	
Other	85 (6.1)	44 (3.1)	

INTERACT II

Anderson CS et al. N Engl J Med 2013 ; 368 : 2355-65

	< 140 mm Hg	< 180 mm Hg	P
Primary end-point	52 %	55.6 %	0,06
m Rankin Score	OR 0,87 (95 % CI 0.77 – 1.00)		0.04
Death	11.9 %	12 %	NS
Non-fatal SAE	23.3 %	23.6 %	NS
BP (1 h)	150 mm Hg	164 mm Hg	0.0001
BP (6 h)	139 mm Hg	153 mm Hg	0.0001

CONCLUSIONS

In patients with intracerebral hemorrhage, intensive lowering of blood pressure did not result in a significant reduction in the rate of the primary outcome of death or severe disability. An ordinal analysis of modified Rankin scores indicated improved functional outcomes with intensive lowering of blood pressure.

American Heart Association / American Stroke Association

Guidelines for the management of spontaneous intracerebral hemorrhage
Stroke 2015 ; 46 : 2032-2060

	Class	Level of evidence
If SBP 150-220 mmHg and no contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe.	I	A
And can be effective for improving functional outcome.	IIa	B
If SBP > 220 mm Hg, it may be reasonable to consider aggressive reduction of BP with a continuous iv infusion and frequent BP monitoring.	IIb	C

Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D.,
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Claudia S. Moy, Ph.D., Robert Silbergleit, M.D., Thorsten Steiner, M.D.,
Jose I. Suarez, M.D., Kazunori Toyoda, M.D., Ph.D., Yongjun Wang, M.D.,
Haruko Yamamoto, M.D., Ph.D., and Byung-Woo Yoon, M.D., Ph.D.,
for the **ATACH-2** Trial Investigators and the Neurological Emergency

Among 1000 participants with a mean (\pm SD) systolic blood pressure of 200.6 ± 27.0 mm Hg at baseline, 500 were assigned to intensive treatment and 500 to standard treatment. The mean age of the patients was 61.9 years, and 56.2%

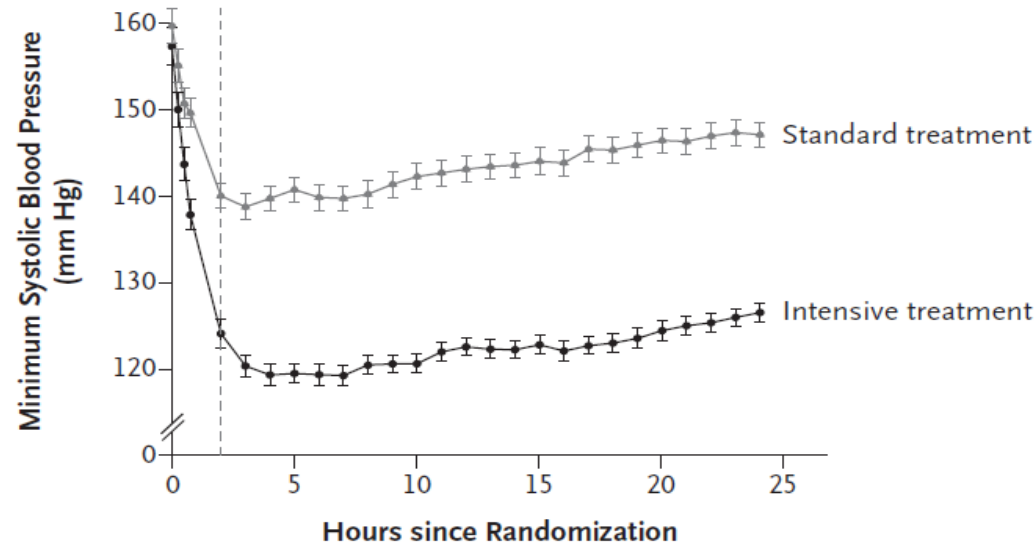


Figure 1. Mean Hourly Minimum Systolic Blood Pressure during the First 24 Hours after Randomization, According to Treatment Group.

Table 1. Demographic and Clinical Characteristics of the Participants, According to Treatment Group.*

Characteristic	Intensive Treatment (N = 500)	Standard Treatment (N = 500)
Age — yr	62±13.1	61.9±13.1
Male sex — no. (%)	304 (60.8)	316 (63.2)
Race — no. (%) [†]		
Asian	277 (55.4)	285 (57.0)
Black	73 (14.6)	58 (11.6)
White	142 (28.4)	145 (29.0)
Other or unknown	8 (1.6)	12 (2.4)
Hispanic ethnic group — no. (%) [†]	38 (7.6)	41 (8.2)
Recruited at site in Asia — no. (%)	264 (52.8)	273 (54.6)
Glasgow Coma Scale score — no. (%) [‡]		
3–11	73 (14.6)	74 (14.8)
12–14	152 (30.4)	142 (28.4)
15	275 (55.0)	284 (56.8)
Systolic blood pressure at presentation in emergency department — mm Hg [§]	200±27.1	201.1±26.9

Median NIHSS score (range) ¶	11 (0–40)	11 (0–40)
Intracerebral hematoma volume		
>30 cm ³ — no./total no. (%)	45/496 (9.1)	51/492 (10.4)
Median (range) — cm ³ †	10.3 (2.3–85.2)	10.2 (0.98–79.1)
Intraventricular hemorrhage — no./total no. (%)	122/496 (24.6)	142/492 (28.9)
Location of hemorrhage — no./total no. (%)		
Thalamus	193/496 (38.9)	180/492 (36.6)
Basal ganglia	255/496 (51.4)	251/492 (51.0)
Cerebral lobe	48/496 (9.7)	60/492 (12.2)
Cerebellum	0/496	1/492 (0.2)

* Plus–minus values are means \pm SD. There were no significant differences between the two groups at baseline.

† Race and ethnic group were self-reported. Asian race included patients enrolled in Asian countries and non-Asian countries.

‡ The Glasgow Coma Scale score (range, 3 to 15), a measure of level of consciousness, is a scale that quantifies response in three components, with a score of 3 indicating deep unconsciousness and higher scores indicating milder impairment of consciousness.

§ Data were missing for 1 patient in the standard-treatment group.

¶ The National Institutes of Health Stroke Scale (NIHSS), a serial measure of neurologic deficit, is a 42-point scale that quantifies neurologic deficits in 11 categories, with a score of 0 indicating normal function without neurologic deficit and higher scores indicating greater severity of deficit. Data were missing or were obtained outside the specified time window for 30 patients in the intensive-treatment group and for 41 in the standard-treatment group.

‖ Hematoma volume was measured by a central reader. The rapid assessment of the hematoma volume by the site investigator was used to determine eligibility.

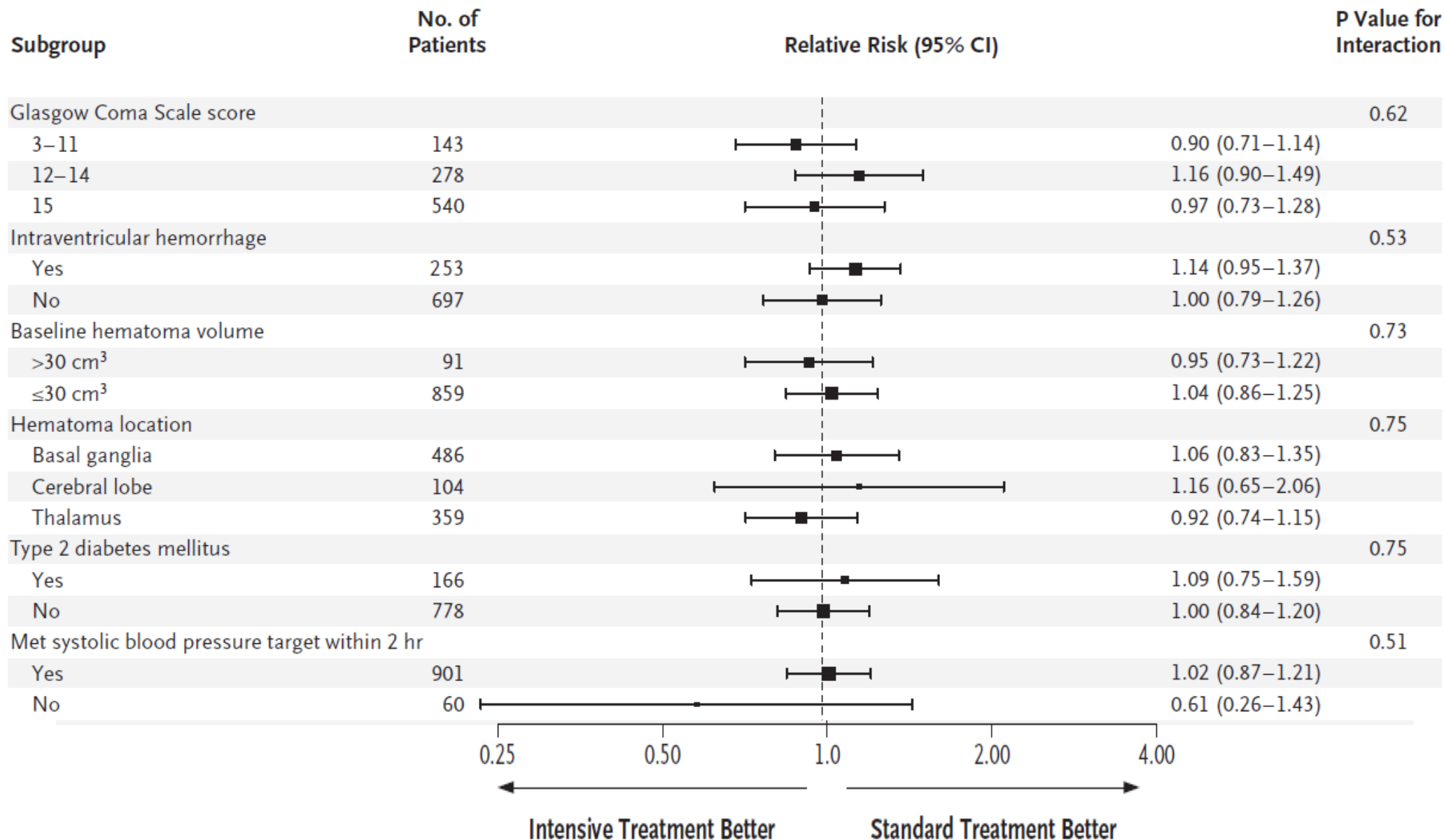


Figure 3. Unadjusted Relative Risk of Death or Disability at 3 Months, According to Subgroup.

ATACH-2: NS

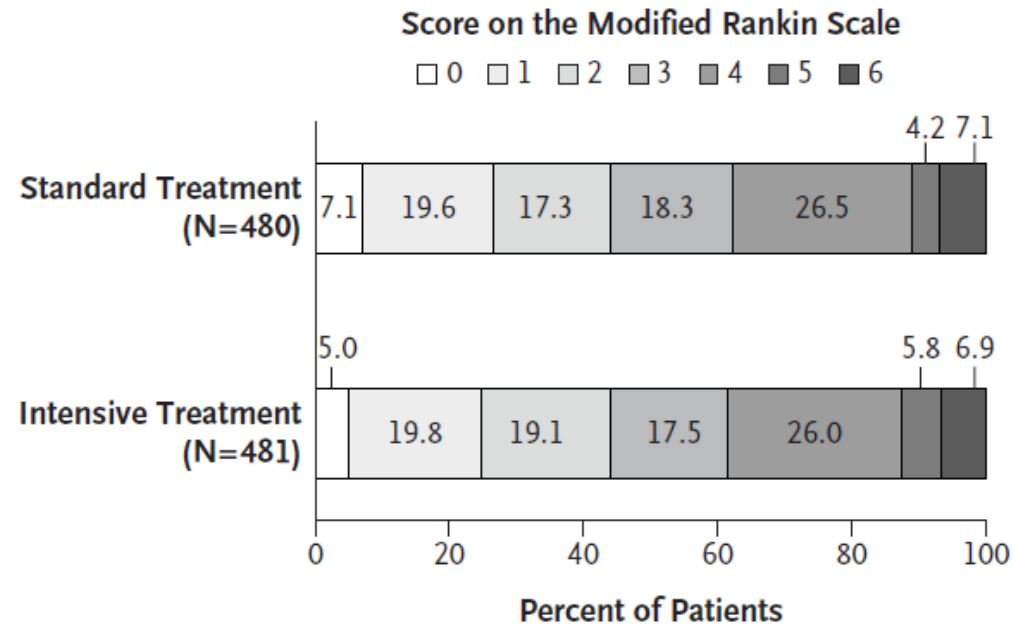


Figure 2. Distribution of Scores on the Modified Rankin Scale, According to Treatment Group.

The data are presented only for participants for whom a score on the modified Rankin scale score was obtained at 90 days. The percentage of participants with each score on the modified Rankin scale is shown in or above each cell. Scores range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability (able to carry out all usual activities, despite some symptoms), 2 slight disability (able to look after own affairs without assistance but unable to carry out all previous activities), 3 moderate disability (requires some help but able to walk unassisted), 4 moderately severe disability (unable to attend to bodily needs without assistance and unable to walk unassisted), 5 severe disability (requires constant nursing care and attention, bedridden, and incontinent), and 6 death. Percentages may not sum to exactly 100.0 owing to rounding.

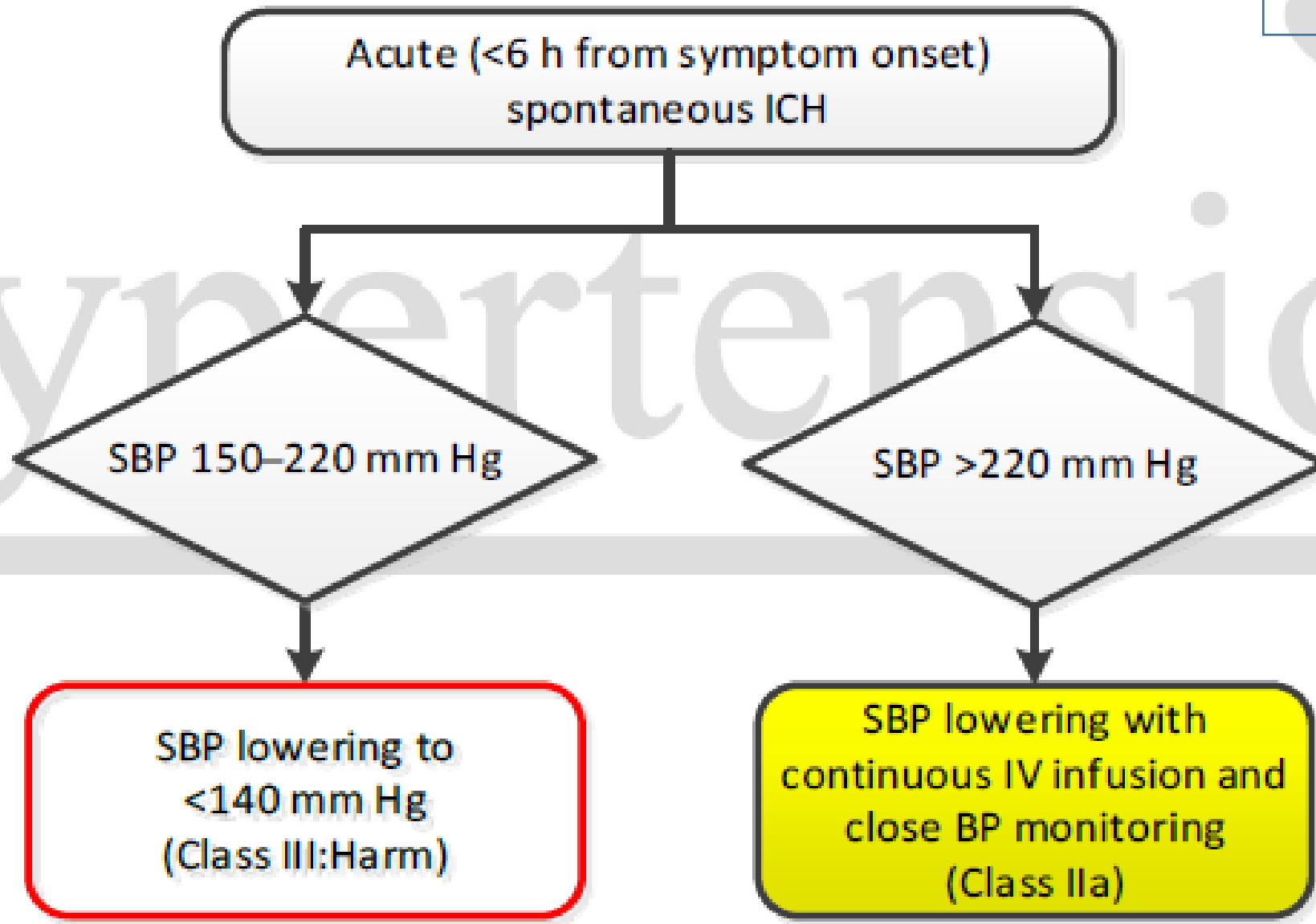
Par rapport à
INTERACT-2
ATACH-2
HTA plus sévère
Randomisation plus
précoce
Plus de patients à la
cible en 1h
Plus d'effets rénaux

CONCLUSIONS

The treatment of participants with intracerebral hemorrhage to achieve a target systolic blood pressure of 110 to 139 mm Hg did not result in a lower rate of death or disability than standard reduction to a target of 140 to 179 mm Hg. (Funded by the National Institute of Neurological Disorders and Stroke and the National Cerebral and Cardiovascular Center; ATACH-2 ClinicalTrials.gov number, NCT01176565.)

	Intensive treatment N (%)	Standard treatment N (%)	Unadjusted RR (95% CI) p=	Adjusted RR (95% CI)‡ p=
Serious renal AE within 7 days	4 (0.8%)	1 (0.2%)	4.00 (0.45, 35.79) p= 0.2150	4.50 (0.50, 40.65) p= 0.1804
Serious renal AE within 30 days	5 (1.0%)	4 (0.8%)	1.25 (0.34, 4.65) p= 0.7394	1.45 (0.38, 5.54) p= 0.5905
Serious renal AE greater than 30 days	1 (0.2%)	0 (0.0%)	NE*	NE*
Any renal AE within 7 days	45 (9.0%)	20 (4.0%)	2.25 (1.33, 3.81) p= 0.0025	2.32 (1.37, 3.94) p= 0.0018

Hypertension



Colors correspond to Class of Recommendation in Table 1.

BP indicates blood pressure; ICH, intracerebral hemorrhage; IV, intravenous; and SBP, systolic blood pressure.

Conclusions (1)

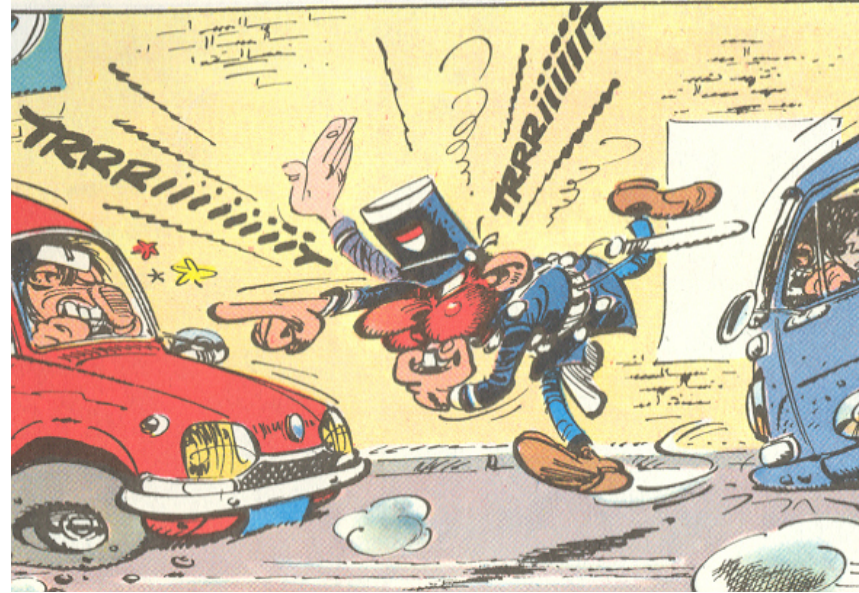
- Bien valider le niveau de PA et suivi de la PA à domicile
- Prévention **primaire** de l'AVC: cible PA chez l'HTA < 130/80 mmHg si risque CV > ou > 65 ans, sinon < 140/90 mmHg
- Prévention **secondaire**: cible PA < 130/80 mmHg si HT préalable
< 140/90 chez NT avant

Ne pas oublier d'agir sur tous les autres FRCV!

Conclusions (2)

En phase aiguë

- AVC **ischémique**: selon indication de thrombolyse
 - si oui, PA < 180/105 mmHg
 - si non, PA < 220/110 mmHg (pendant les premiers jours)
- AVC **hémorragique**:
 - baisser la PAS si >220 et la ramener doucement < 180 mmHg.
 - si PA < 220 mmHg, la maintenir < 180 mmHg, tenir compte de la PIC.
Pas d'avantage d'une PAS < 140 mmHg.



Merci de votre attention

Questions?

Table 9. Potential Approaches to Arterial Hypertension in Acute Ischemic Stroke Patients Who Are Candidates for Acute Reperfusion Therapy

Patient otherwise eligible for acute reperfusion therapy except that BP is $>185/110$ mm Hg:

Labetalol 10–20 mg IV over 1–2 minutes, may repeat 1 time; or

Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or

Other agents (hydralazine, enalaprilat, etc) may be considered when appropriate

If BP is not maintained at or below 185/110 mm Hg, do not administer rtPA

Management of BP during and after rtPA or other acute reperfusion therapy to maintain BP at or below 180/105 mm Hg:

Monitor BP every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours

If systolic BP >180 –230 mm Hg or diastolic BP >105 –120 mm Hg:

Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or

Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h

If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside

BP indicates blood pressure; IV, intravenously; and rtPA, recombinant tissue-type plasminogen activator.

Hypertension control in non-rt-PA candidates

For patients who are not candidates for thrombolysis with recombinant t-PA (rt-PA) and who have a systolic blood pressure of **less than 220 mm Hg** and a diastolic blood pressure of **less than 110 mm Hg** in the absence of evidence of end-organ involvement (ie, pulmonary edema, aortic dissection, hypertensive encephalopathy), **blood pressure should be monitored (without acute intervention)** and **stroke symptoms** and complications (eg, increased ICP, seizures) should be **treated**.

For patients with a **systolic blood pressure above 220 mm Hg** or a **diastolic blood pressure greater than 120 mm Hg**, **labetalol** (10-20 mg IV for 1-2 min) should be the initial drug of choice, unless a contraindication to its use exists. Dosing may be repeated or doubled every 10 minutes to a maximum dose of 300 mg.

Alternatively, **nicardipine** may be used for blood pressure control. Nicardipine is given intravenously at an initial rate of 5 mg/h and titrated to effect by increasing the infusion rate 2.5 mg/h every 5 minutes, to a maximum of 15 mg/h. Lastly, **nitroprusside** at 0.5 mcg/kg/min IV infusion may be used in the setting of continuous blood pressure monitoring. The goal of intervention is a reduction in blood pressure of 10-15%.

Table 3. Primary, Secondary, and Safety Outcomes at 90 Days.*

Variable	Intensive Blood-Pressure Lowering (N = 1399)	Guideline- Recommended Blood-Pressure Lowering (N = 1430)	Odds Ratio (95% CI)	P Value
Primary outcome: death or major disability — no./total no. (%)†	719/1382 (52.0)	785/1412 (55.6)	0.87 (0.75–1.01)	0.06
Secondary outcomes				
Score on the modified Rankin scale — no./total no. (%)‡			0.87 (0.77–1.00)	0.04
0: No symptoms at all	112/1382 (8.1)	107/1412 (7.6)		
1: No substantive disability despite symptoms	292/1382 (21.1)	254/1412 (18.0)		
2: Slight disability	259/1382 (18.7)	266/1412 (18.8)		
3: Moderate disability requiring some help	220/1382 (15.9)	234/1412 (16.6)		
4: Moderate–severe disability requiring assistance with daily living	250/1382 (18.1)	268/1412 (19.0)		
5: Severe disability, bed-bound and incontinent	83/1382 (6.0)	113/1412 (8.0)		
6: Death by 90 days	166/1382 (12.0)	170/1412 (12.0)		

Variable	Intensive Blood-Pressure Lowering (N = 1399)	Guideline- Recommended Blood-Pressure Lowering (N = 1430)	Odds Ratio (95% CI)	P Value
Safety outcomes — no./total no. (%)				
Neurologic deterioration in first 24 hr¶	198/1369 (14.5)	211/1395 (15.1)	0.95 (0.77–1.17)	0.62
Nonfatal serious adverse events	326/1399 (23.3)	338/1430 (23.6)		0.92
Any neurologic deterioration from intracerebral hemorrhage**	47/1399 (3.4)	55/1430 (3.8)		0.49
Recurrent intracerebral hemorrhage	4/1399 (0.3)	4/1430 (0.3)		
Ischemic or undifferentiated stroke	8/1399 (0.6)	8/1430 (0.6)		
Acute coronary event	5/1399 (0.4)	5/1430 (0.3)		
Other cardiovascular disease	22/1399 (1.6)	26/1430 (1.8)		
Noncardiovascular disease	160/1399 (11.4)	152/1430 (10.6)		0.49
Severe hypotension††	7/1399 (0.5)	8/1430 (0.6)		