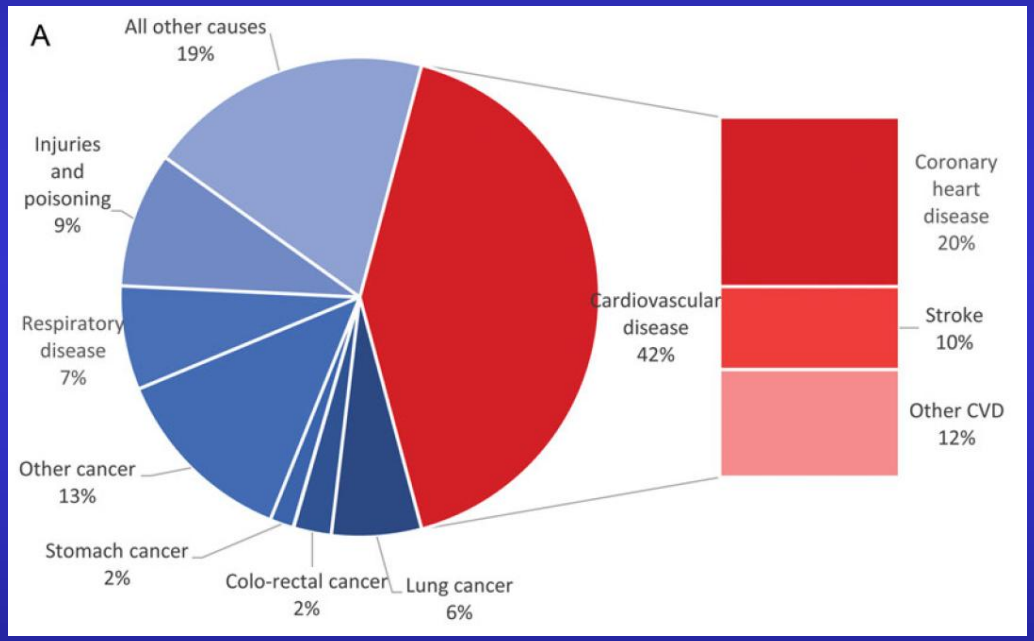
Cílové hodnoty u cévních mozkových příhod

Renata Cífková

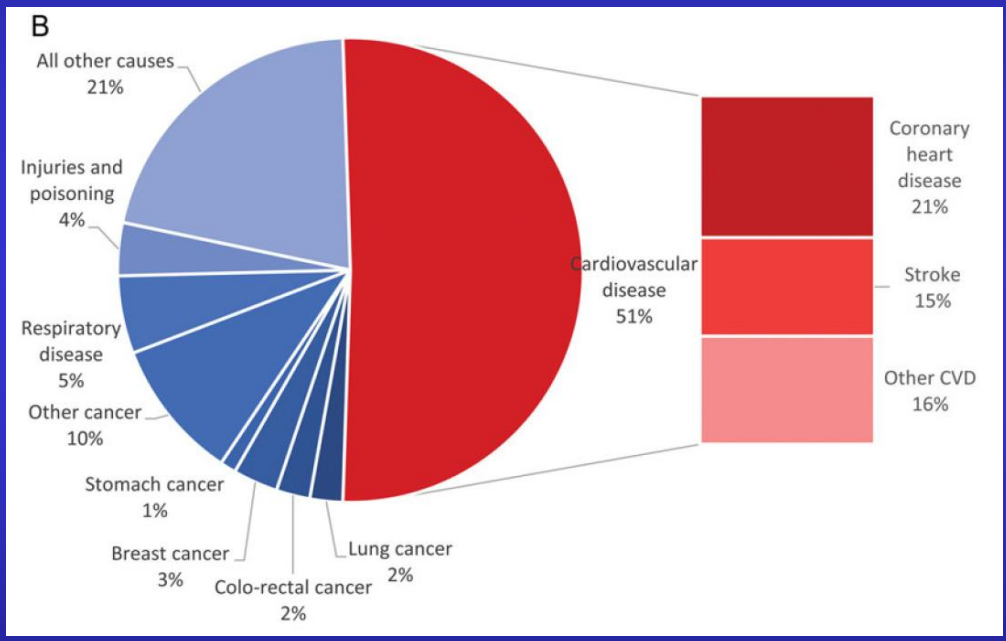
Centrum kardiovaskulární prevence 1. LF UK a TN,
II. interní klinika 1. LF UK a VFN,
Praha

Úmrtnost podle příčin, Evropa

Muži



Ženy



Eur Heart J 2014;35:2950-2959

Počty úmrtí podle příčin
Česká republika, 2013

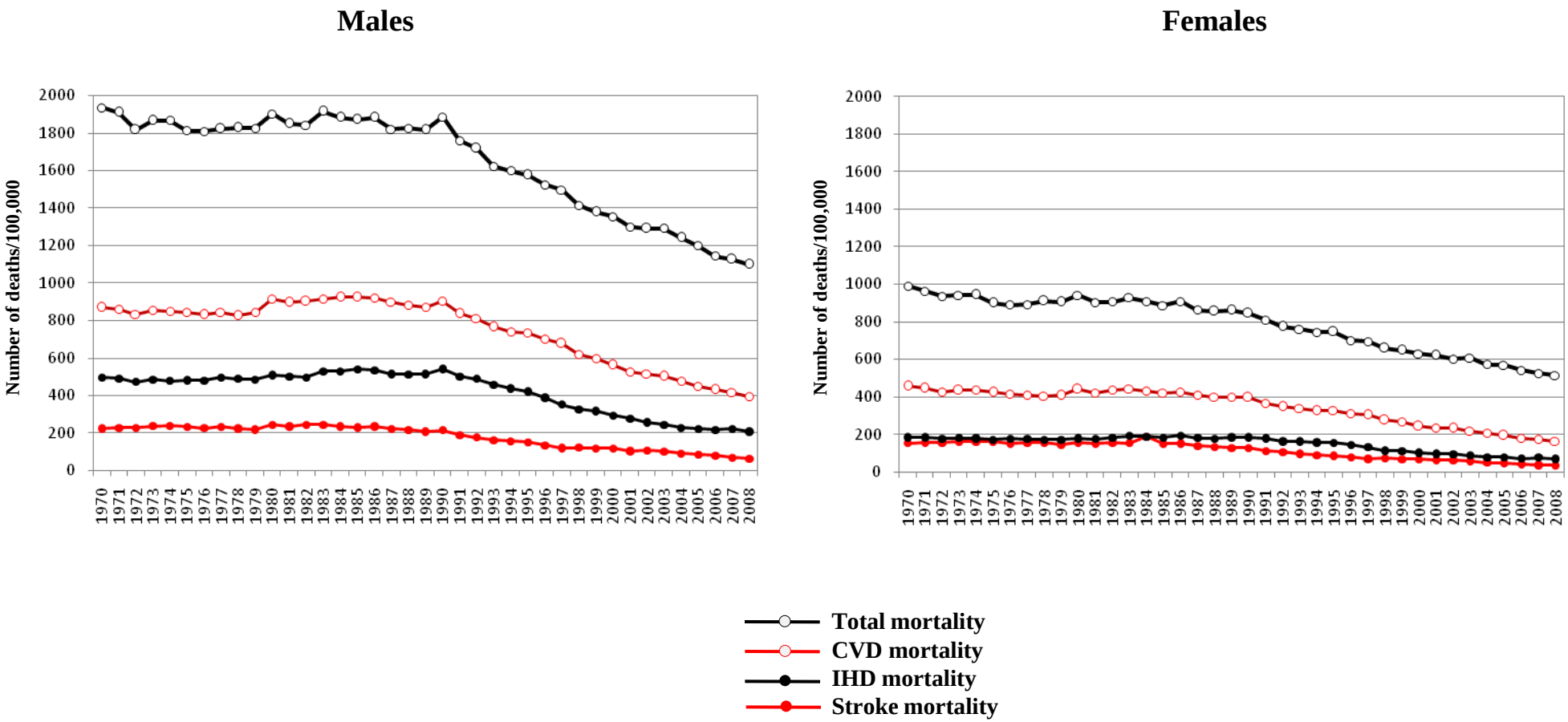
	Muži	*Ženy*
KVO	23 701	28 030
ICHS	13 412	14 524
CMP	4 249	6 067

ÚZIS 2014

Standardizovaná úmrtnost/100 000
Česká republika 1985 - 2013

Muži	1985	2013	△ %	p
- všechny příčiny	1581	892	- 43,6	< 0,001
- KVO	844	385	- 54,4	< 0,001
- ICHS	436	218	- 50,0	< 0,001
- CMP	250	69	- 72,4	< 0,001
Ženy				
- všechny příčiny	944	534	- 43,4	< 0,001
- KVO	548	251	- 54,2	< 0,001
- ICHS	223	128	- 42,6	< 0,001
- CMP	202	54	- 73,3	< 0,001

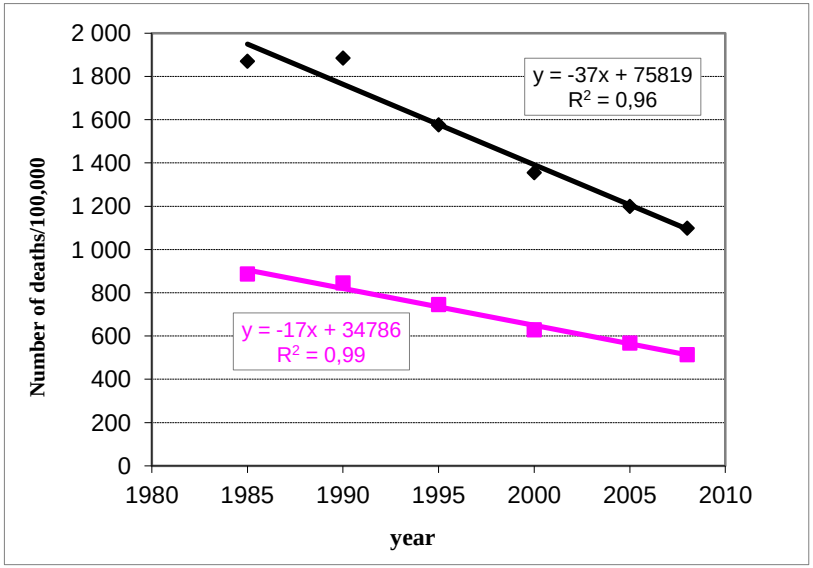
Age-stand. total, CVD, IHD, and stroke mortality (age group 35-74 yrs) Czech Republic 1970-2008



Cífková et al., J Hypertens 2010;28:2196-203

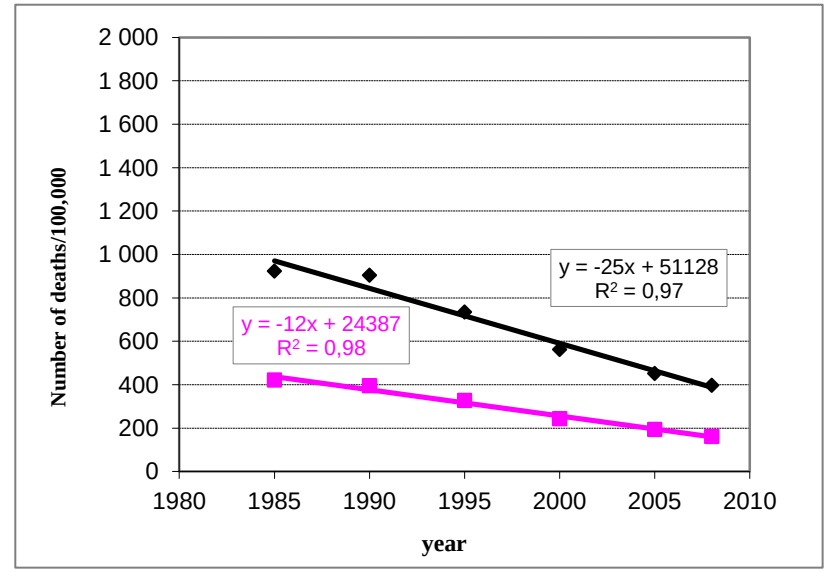
Total mortality, age 35-74 years

Males vs Females: p = 0,001



CVD mortality, age 35-74 years

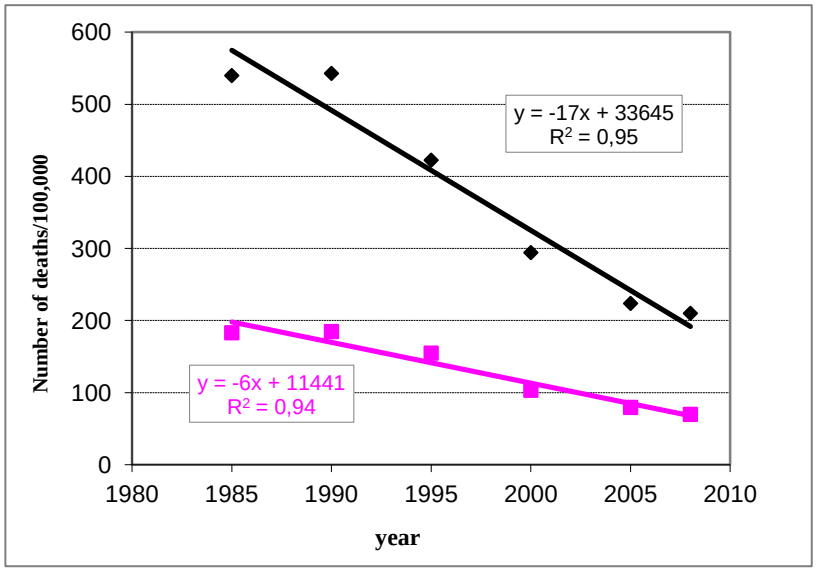
Males vs Females: p = 0,001



Males
Females

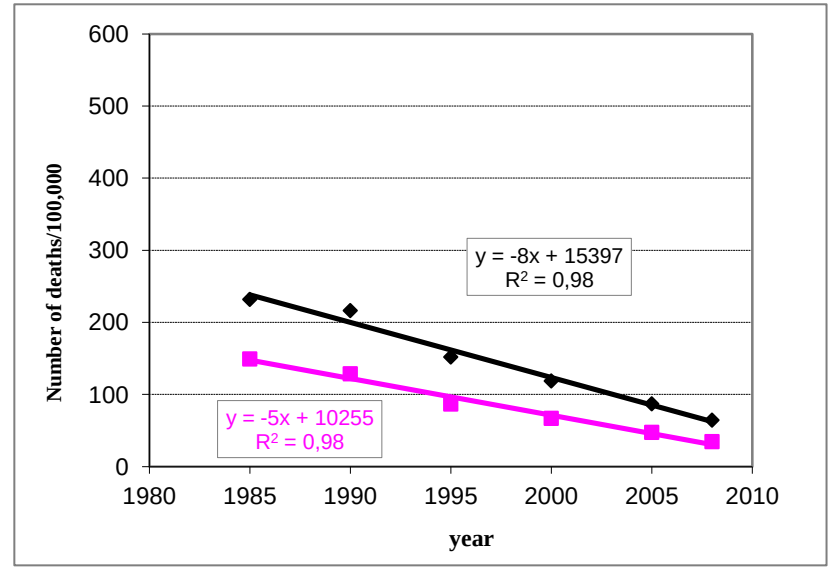
CAD mortality, age 35-74 years

Males vs Females: p = 0,001



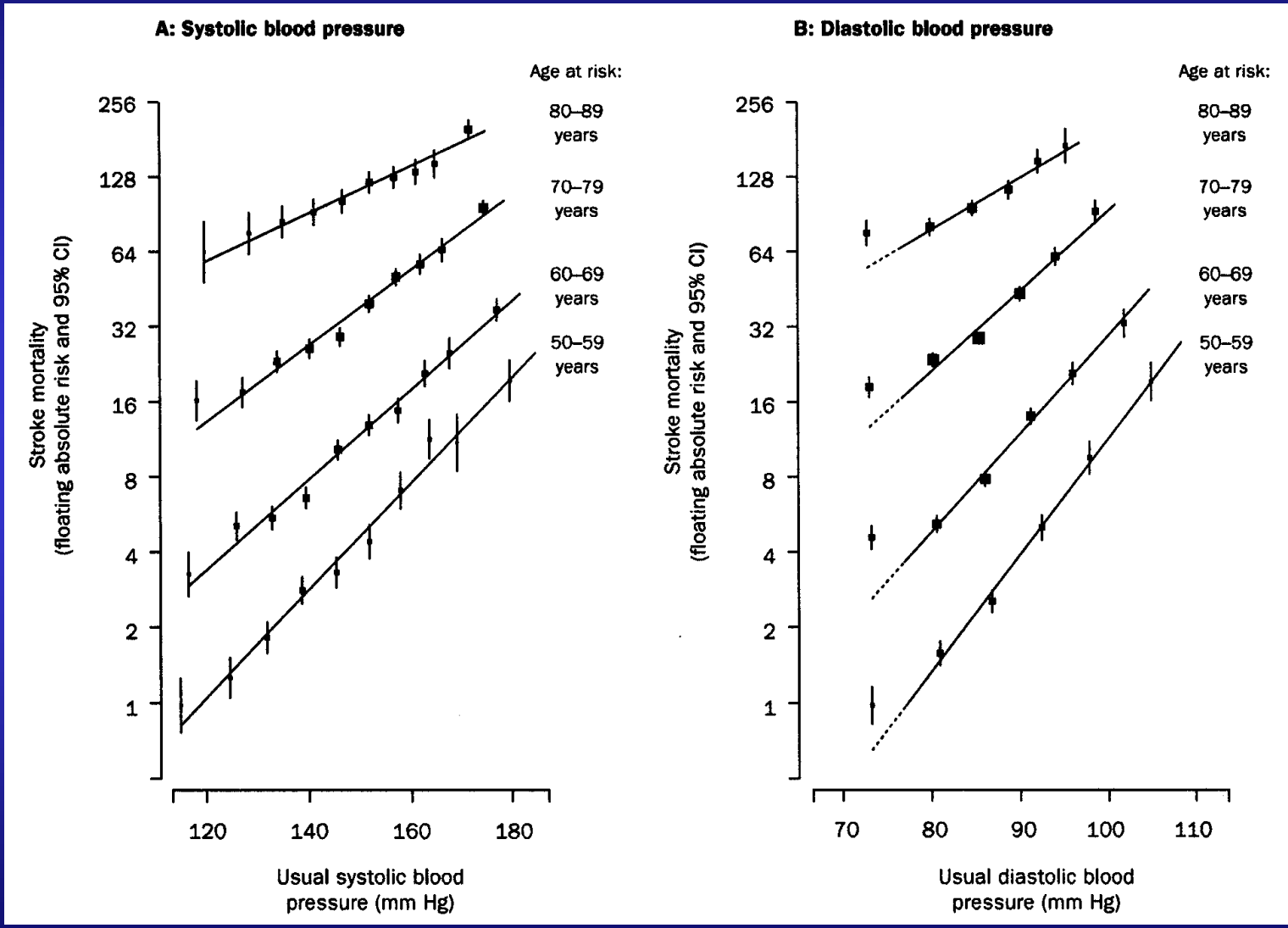
Stroke mortality, age 35-74 years

Males vs Females: p = 0,0041



Cífková et al., J Hypertens 2010;28:2196-203

Úmrtnost na CMP

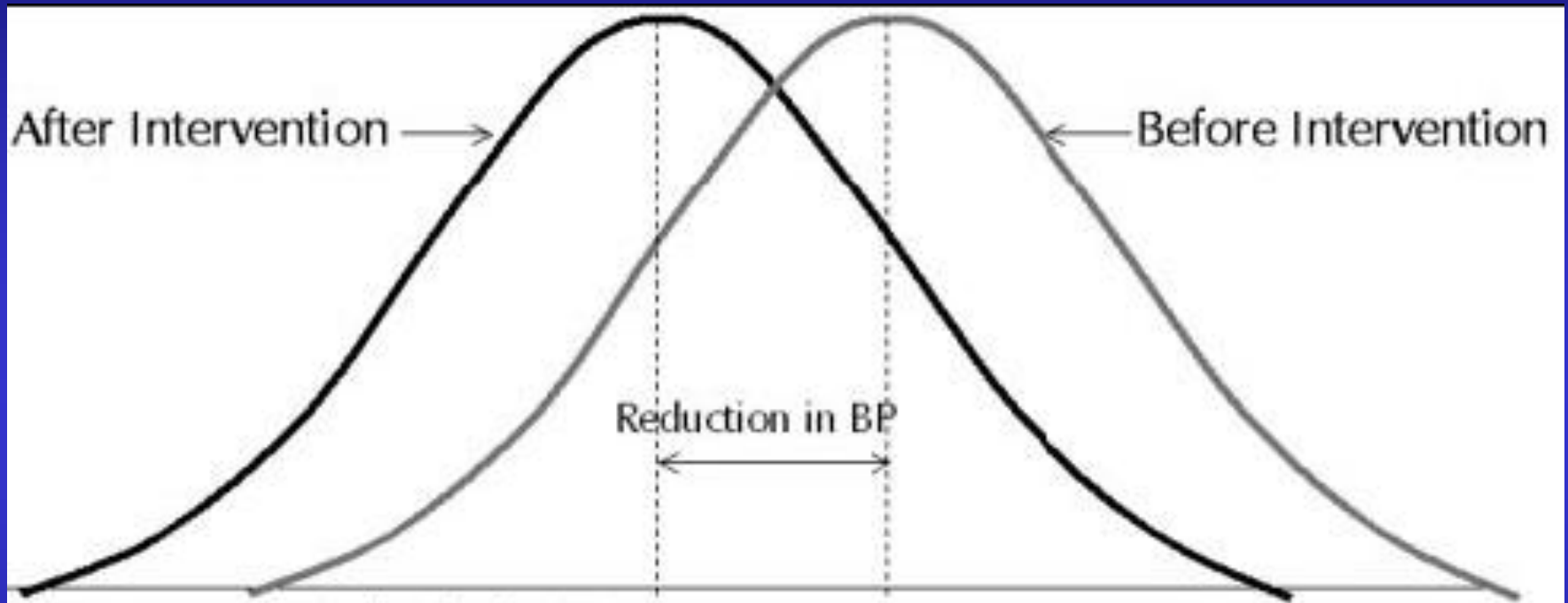


Lancet 2002;360:1903-13

- Snížení rizika CMP na úrovni populace
- TK v akutní fázi CMP
- Cílové hodnoty TK po CMP

Ovlivnění KV rizika na úrovni populace

Odhadovaný účinek snížení STK v populaci na snížení úmrtnosti



Reduction in BP mmHg	% Reduction in Mortality Stroke	CHD	Total
2	-6	-4	-3
3	-8	-5	-4
5	-14	-9	-7

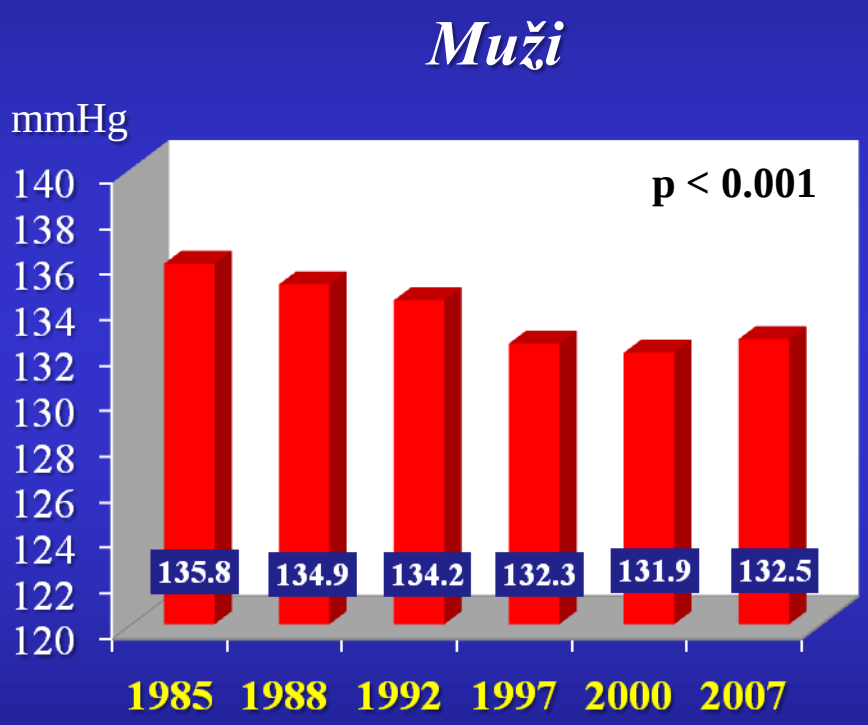
Arch Intern Med 1993;153:598-615

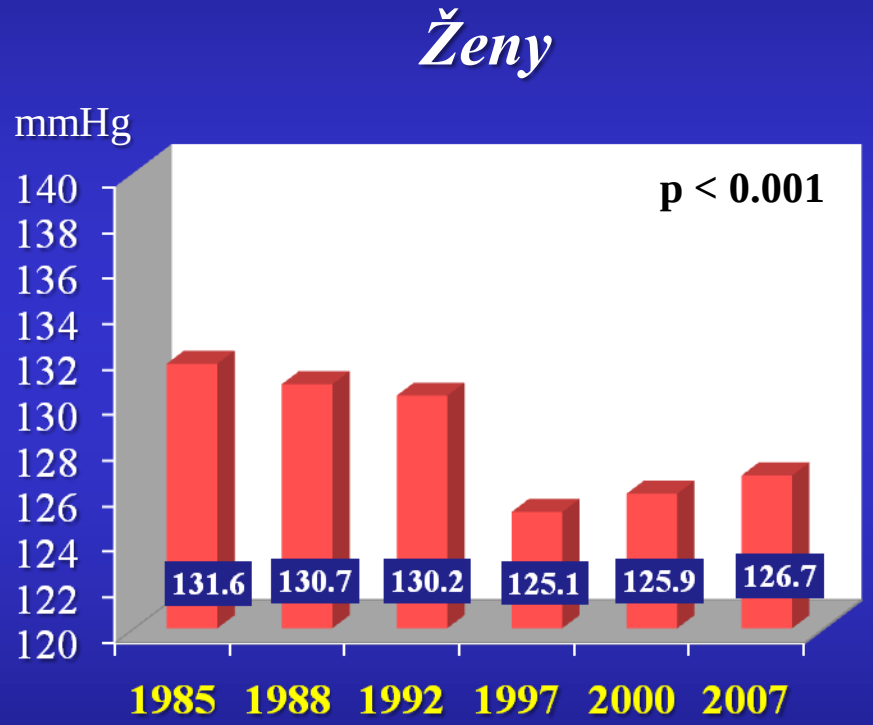
Malé snížení TK

na úrovni
celé populace

má výrazný protektivní účinek

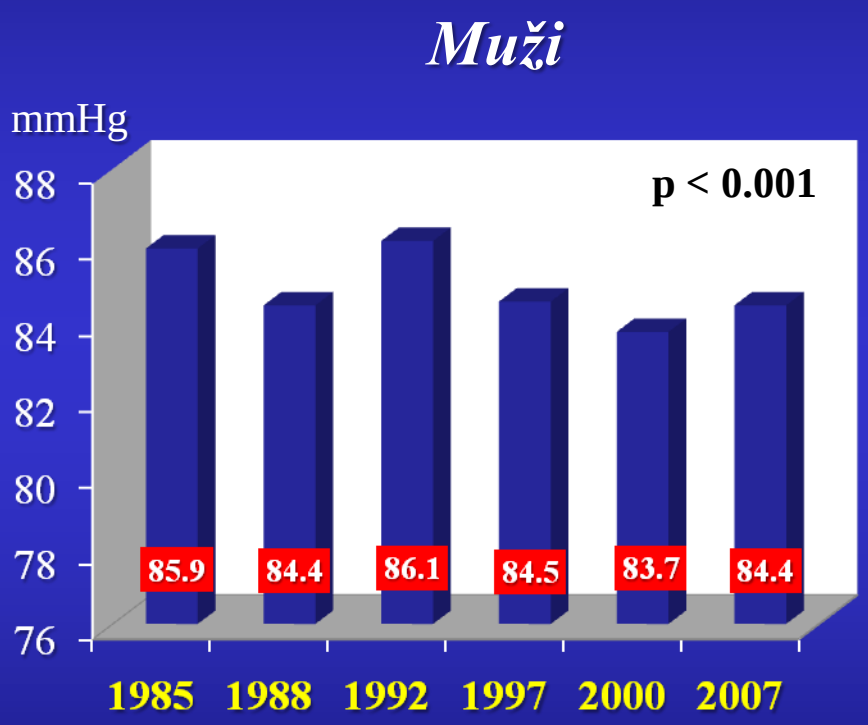
Systolický TK

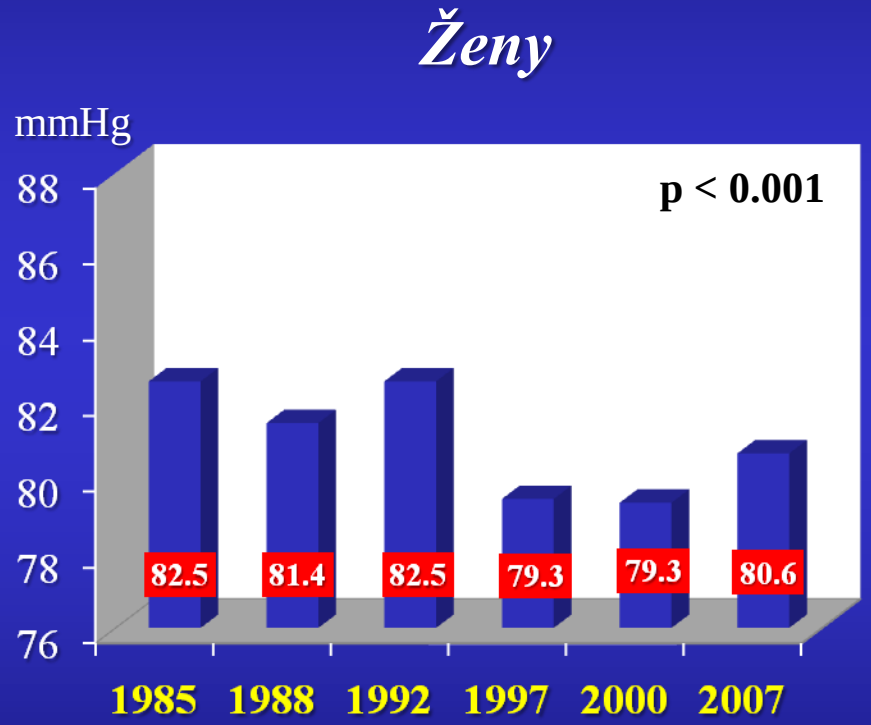




Atherosclerosis 2010; 211:676-681

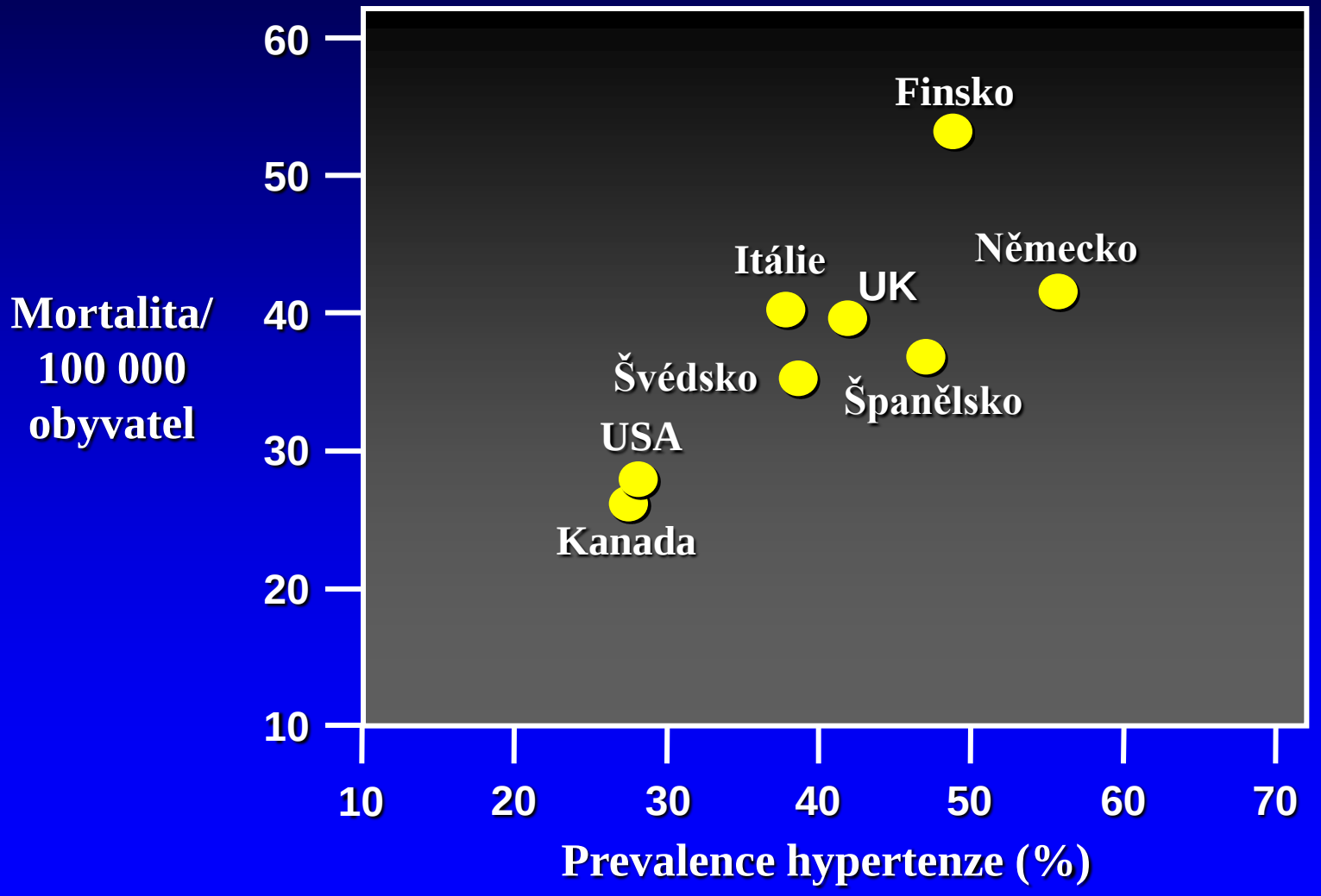
Diastolický TK





Atherosclerosis 2010; 211:676-681

Úmrtnost na CMP a prevalence hypertenze v Evropě a Americe

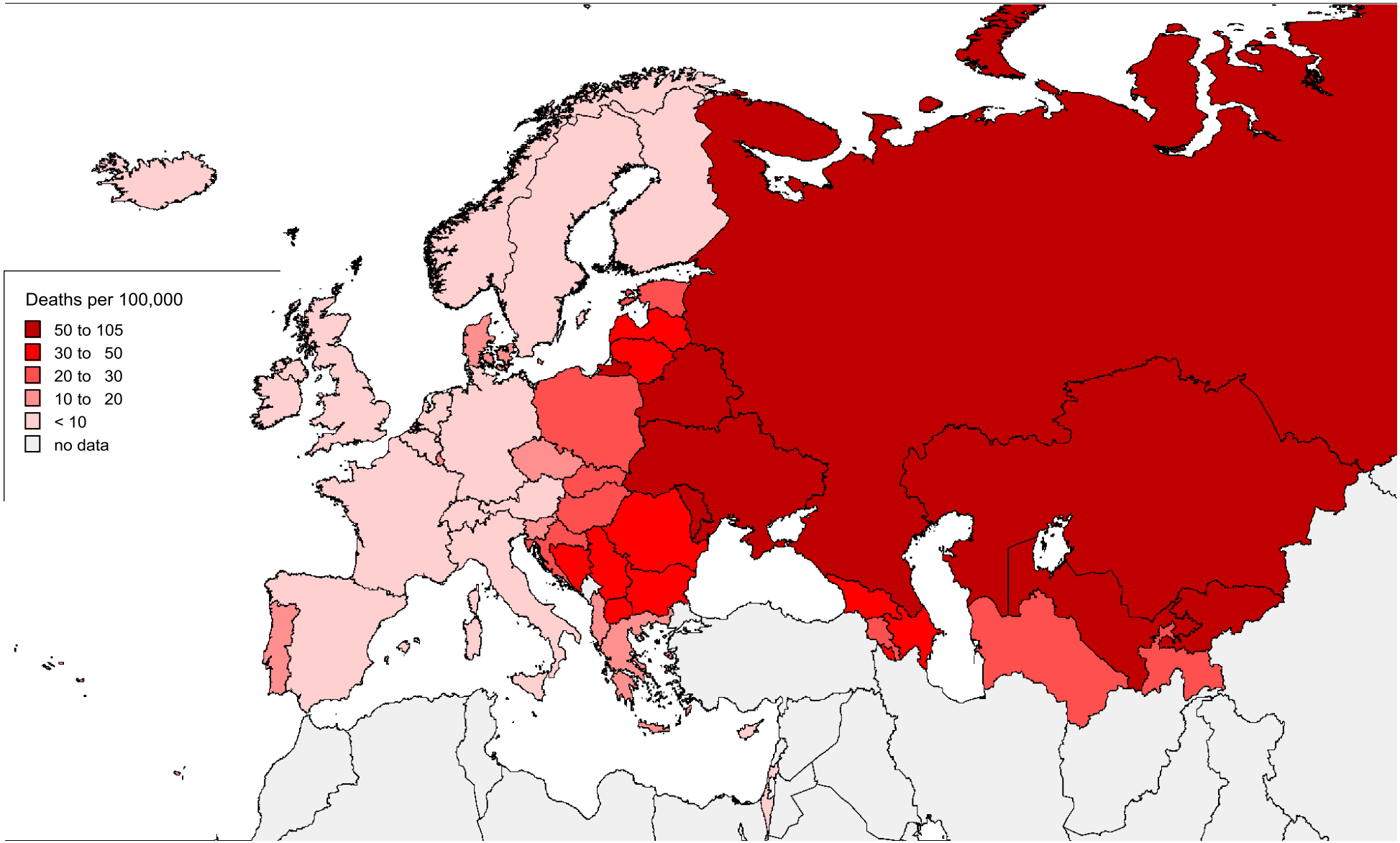


Wolf-Maier et al. JAMA 2003

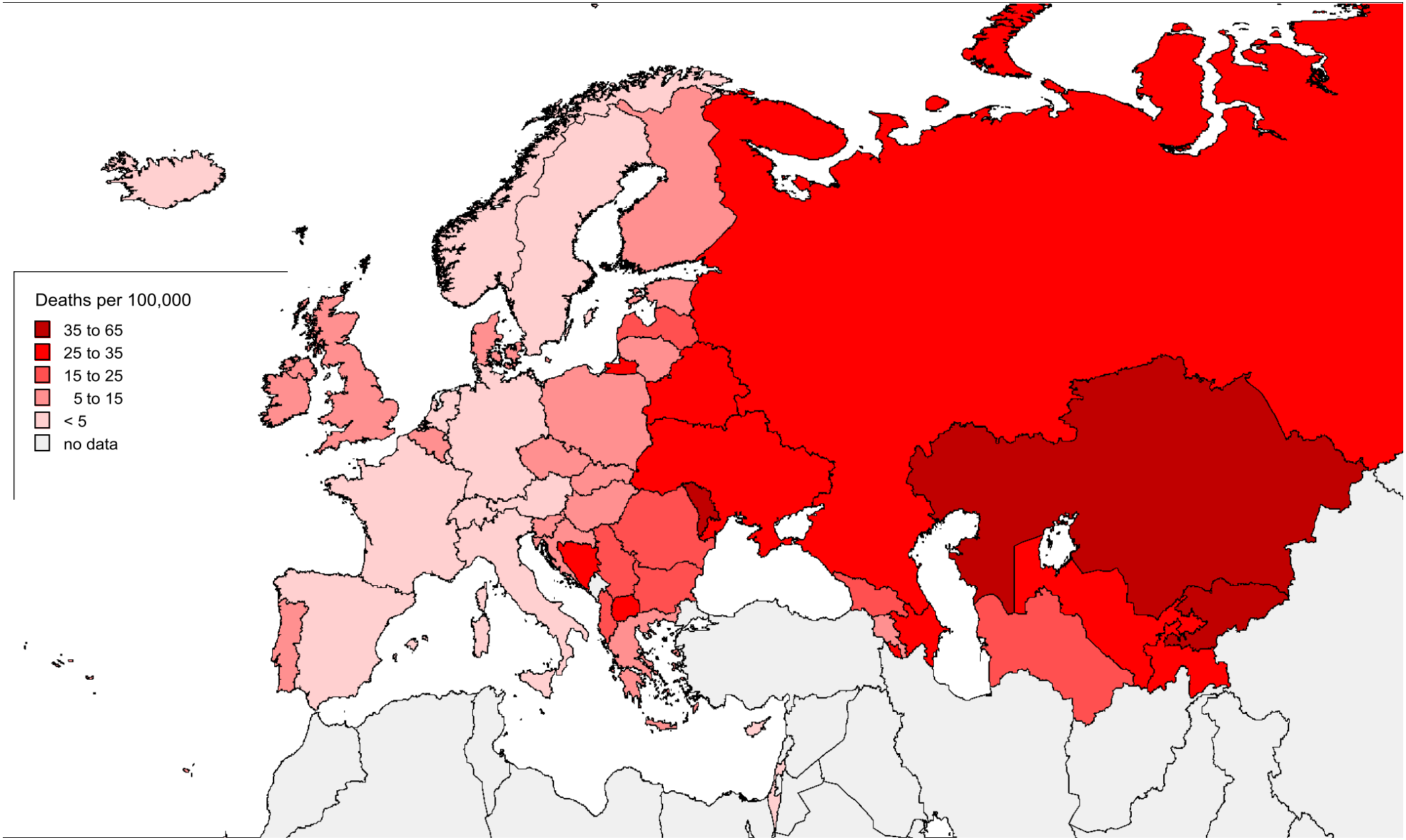
Úmrtnost na CMP a kontrola hypertenze

… úmrtnost na CMP může být použita jako indikátor kontroly hypertenze v populaci…

Age-standardized death rates from stroke, men aged 0 to 64 years, Europe

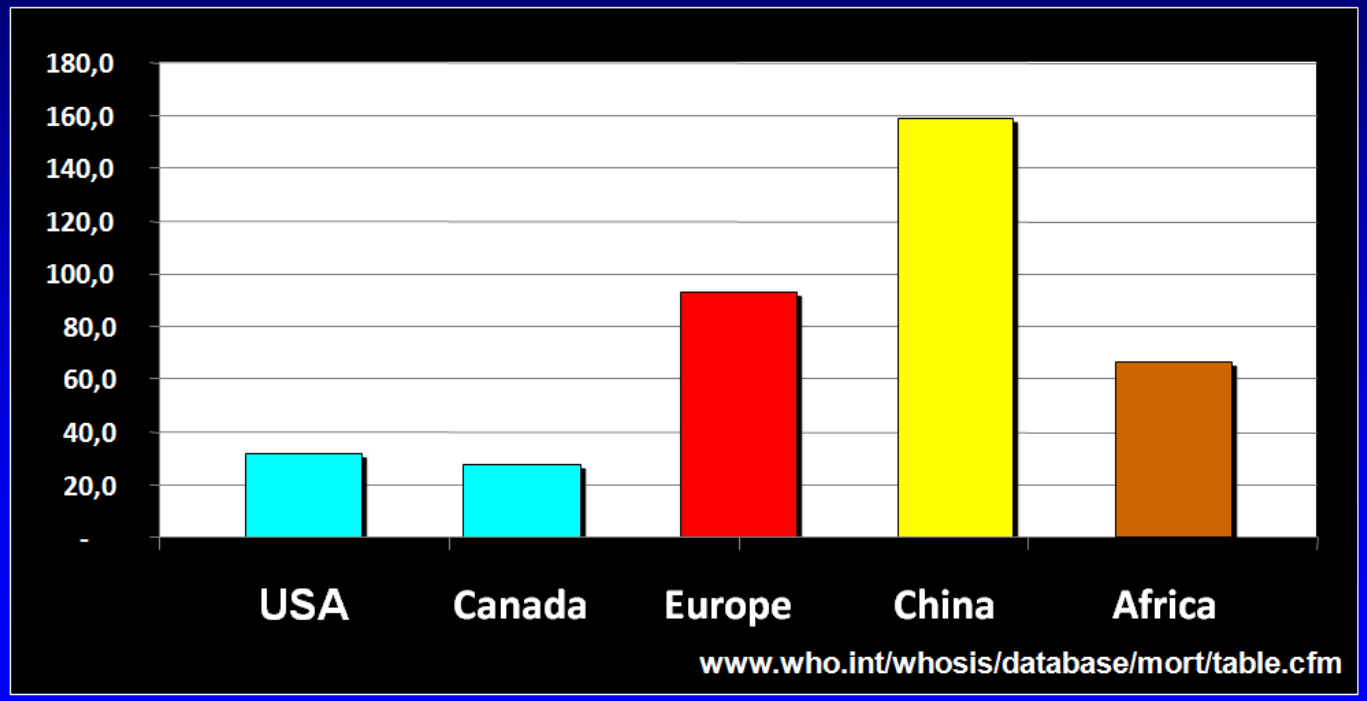


Age-standardized death rates from stroke, women aged 0 to 64 years, Europe



Stroke mortality in Europe, USA, Canada, China an Africa: WHO 2006

Yearly adjusted mortality rate by 100,000 inhabitants



Hospital Clínico. IDIBAPS
Universidad Barcelona

Redon J, et al Eur Heart J 2011 in press

25 % CMP jsou recidivující CMP

Riziko rekurence v 1. roce	**16 %**
v dalších letech	**4 %**

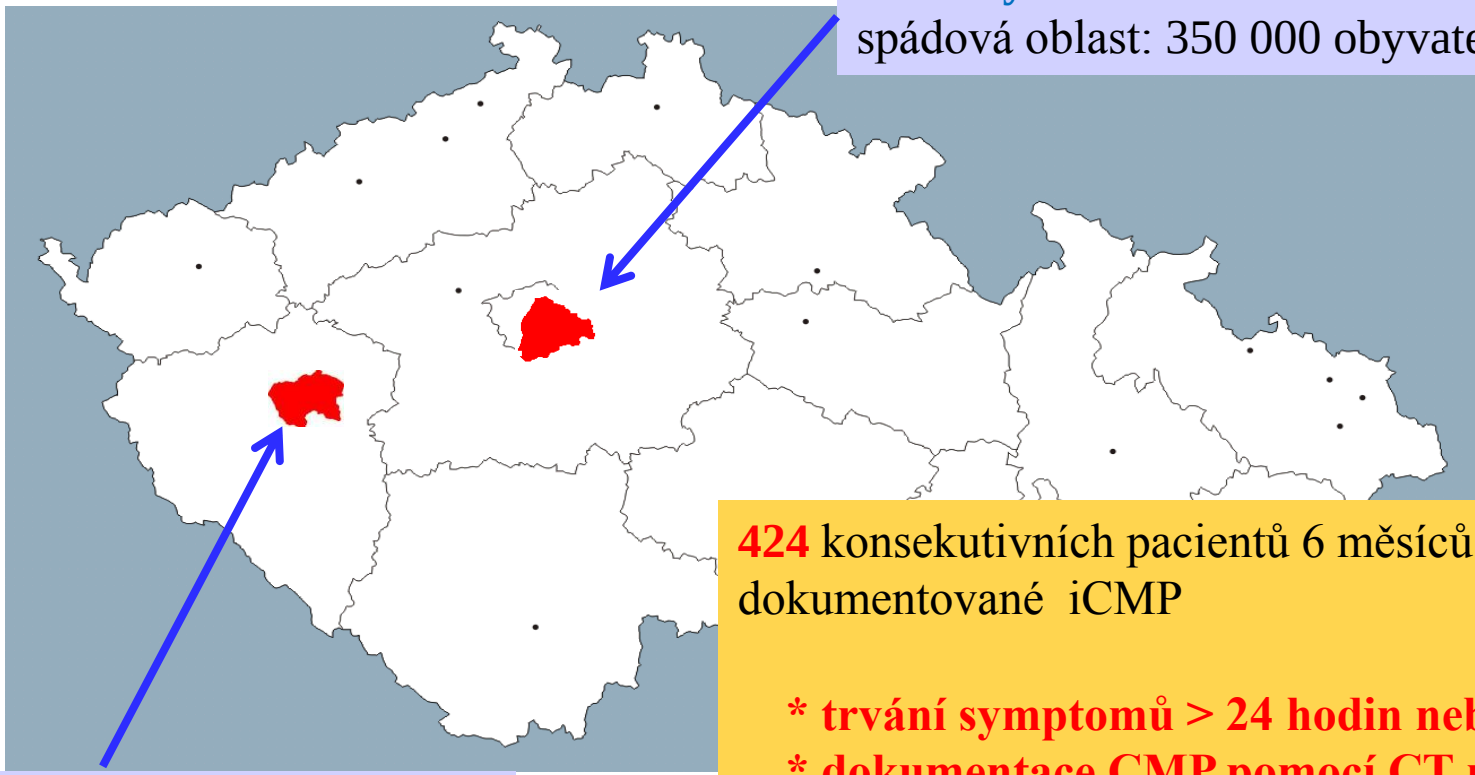
Stroke 2014; 45:315 – 353
Stroke 1999; 30:338 – 349

TK v akutní fázi CMP

Nemocní s první ischemickou CMP

736 pacientů přijatých do 2 regionálních iktových center (z celk. počtu 24) v období 2009-2012

Thomayerova nemocnice v Praze
spádová oblast: 350 000 obyvatel



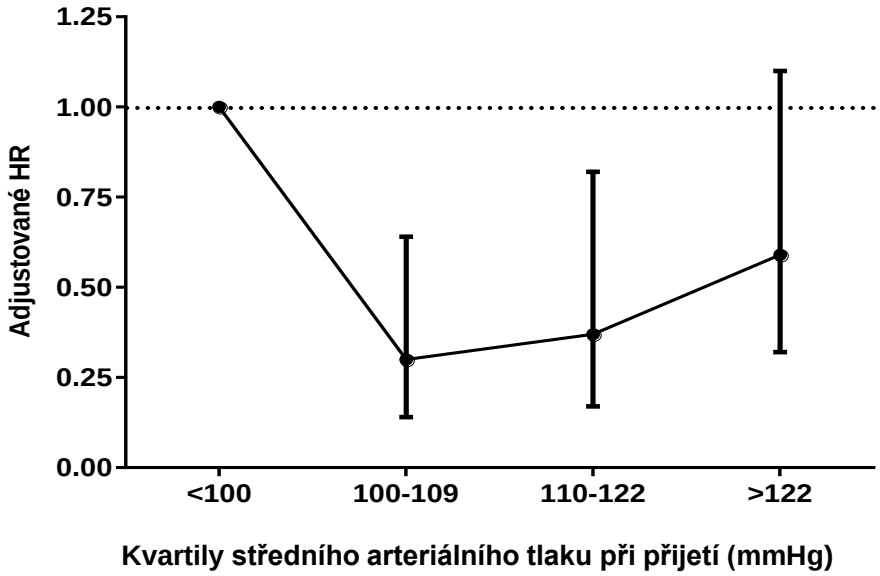
424 konsekutivních pacientů 6 měsíců – 3 roky po 1. dokumentované iCMP

*** trvání symptomů > 24 hodin nebo TL**
*** dokumentace CMP pomocí CT nebo MR**
*** věk 18-81 let**

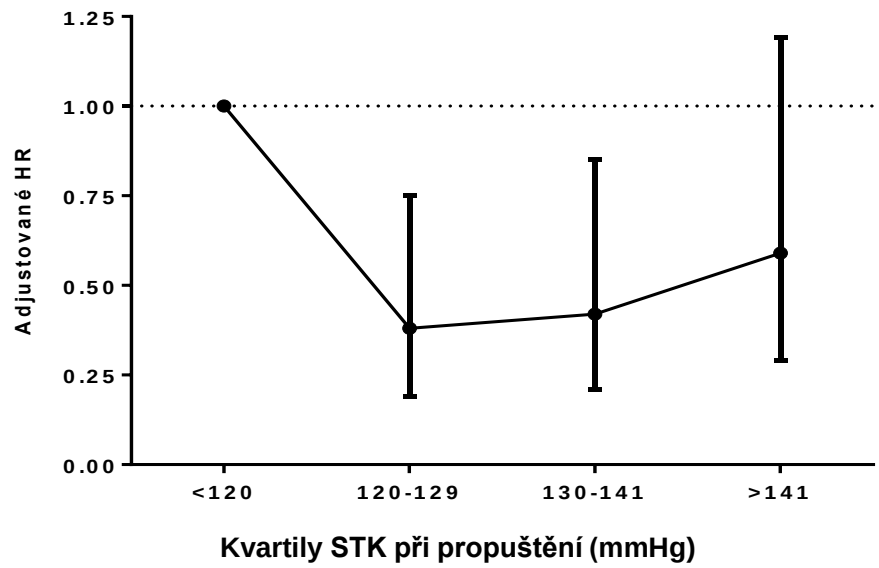
FN v Plzni
spádová oblast: 180 000 obyvatel

Krevní tlak v době příjmu a propuštění a riziko mortality po iCMP

Příjem



Propuštění



Adjustováno na věk, reperfuzní terapii, diabetes, závažnost iCMP, MTK v době příjmu a STK v době propuštění

J Hypertens 2015;33:339–345

Bezprostřední dopad výsledků na klinickou praxi

- Rutinní subtypizace iCMP
- Vysazování antihypertenzní medikace v akutní fázi iCMP u většiny pacientů

Interventions for deliberately altering blood pressure in acute stroke (Review)

Bath PMW, Krishnan K

THE COCHRANE COLLABORATION®

- **26 trials involving 17,011 participants**

Authors' conclusions

There is insufficient evidence that lowering blood pressure during the acute phase of stroke improves functional outcome.

Cochrane Database Syst Rev. 2014 Oct 28;10:CD000039.
doi: 10.1002/14651858.CD000039.pub3

Effects of antihypertensive treatment after acute stroke in the Continue Or Stop post-Stroke Antihypertensives Collaborative Study (COSSACS): a prospective, randomised, open, blinded-endpoint trial

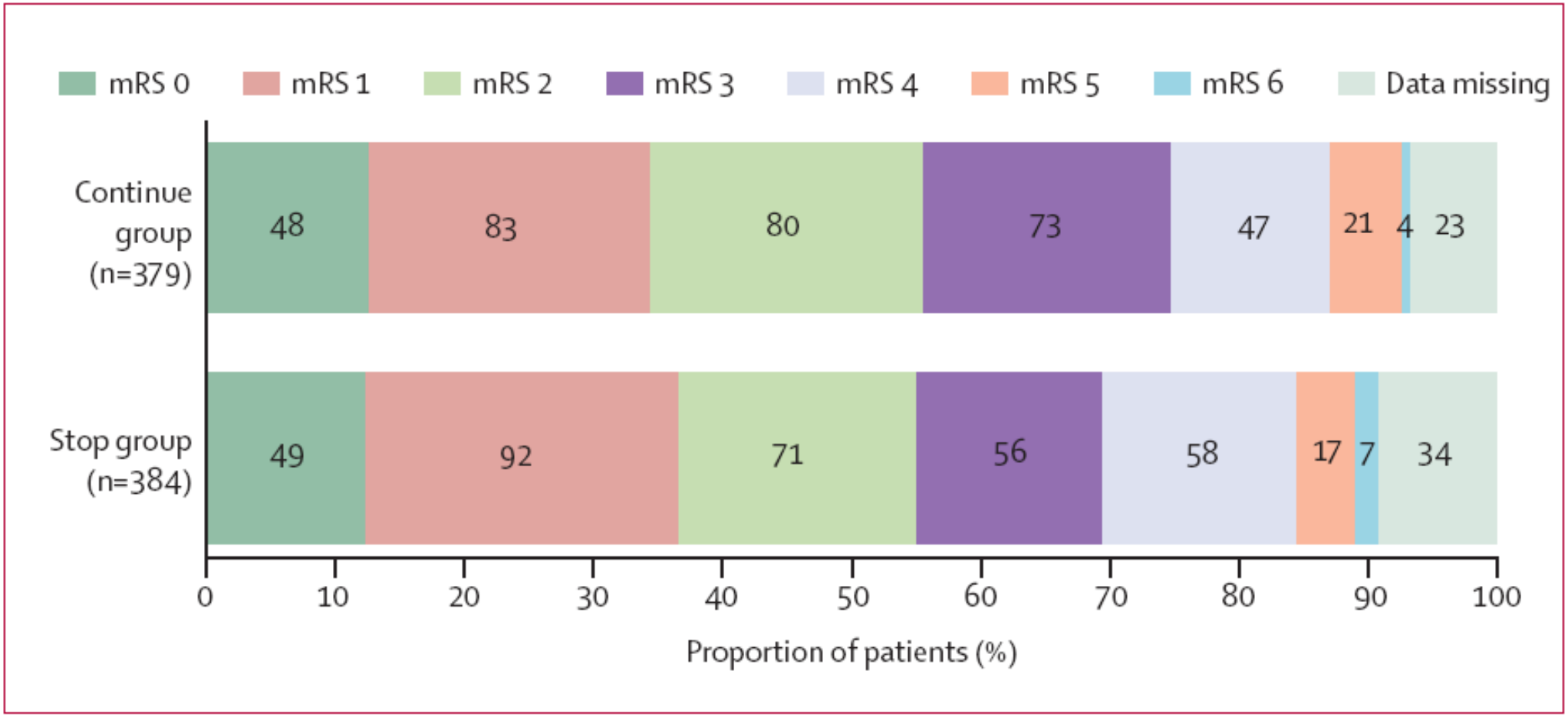
*Thompson G Robinson, John F Potter, Gary A Ford, Christopher J Bulpitt, Julia Chernova, Carol Jagger, Martin A James, Joanne Knight, Hugh S Markus, Amit K Mistri, Neil R Poulter, on behalf of the COSSACS Investigators**

Conclusions

Continuation of antihypertensive drugs did not reduce 2-week death or dependency, cardiovascular event rate, or mortality at 6 months. Lower blood pressure levels in those who continued antihypertensive treatment after acute mild stroke were not associated with an increase in adverse events

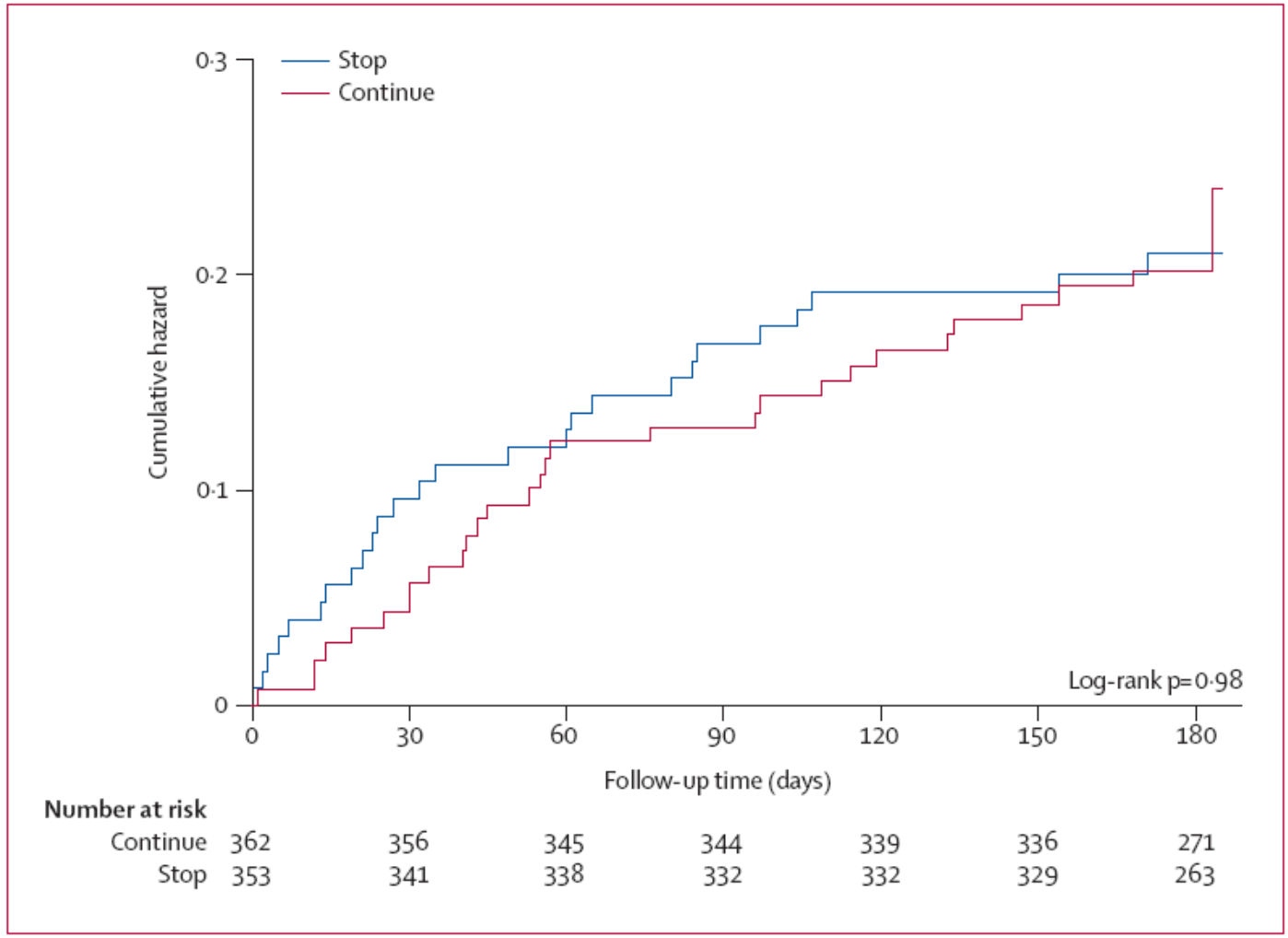
Lancet Neurol 2010; 9: 767–75

COSSACS



Lancet Neurol 2010; 9: 767–75

COSSACS



Lancet Neurol 2010; 9: 767–75

Original Investigation

Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke
The CATIS Randomized Clinical Trial

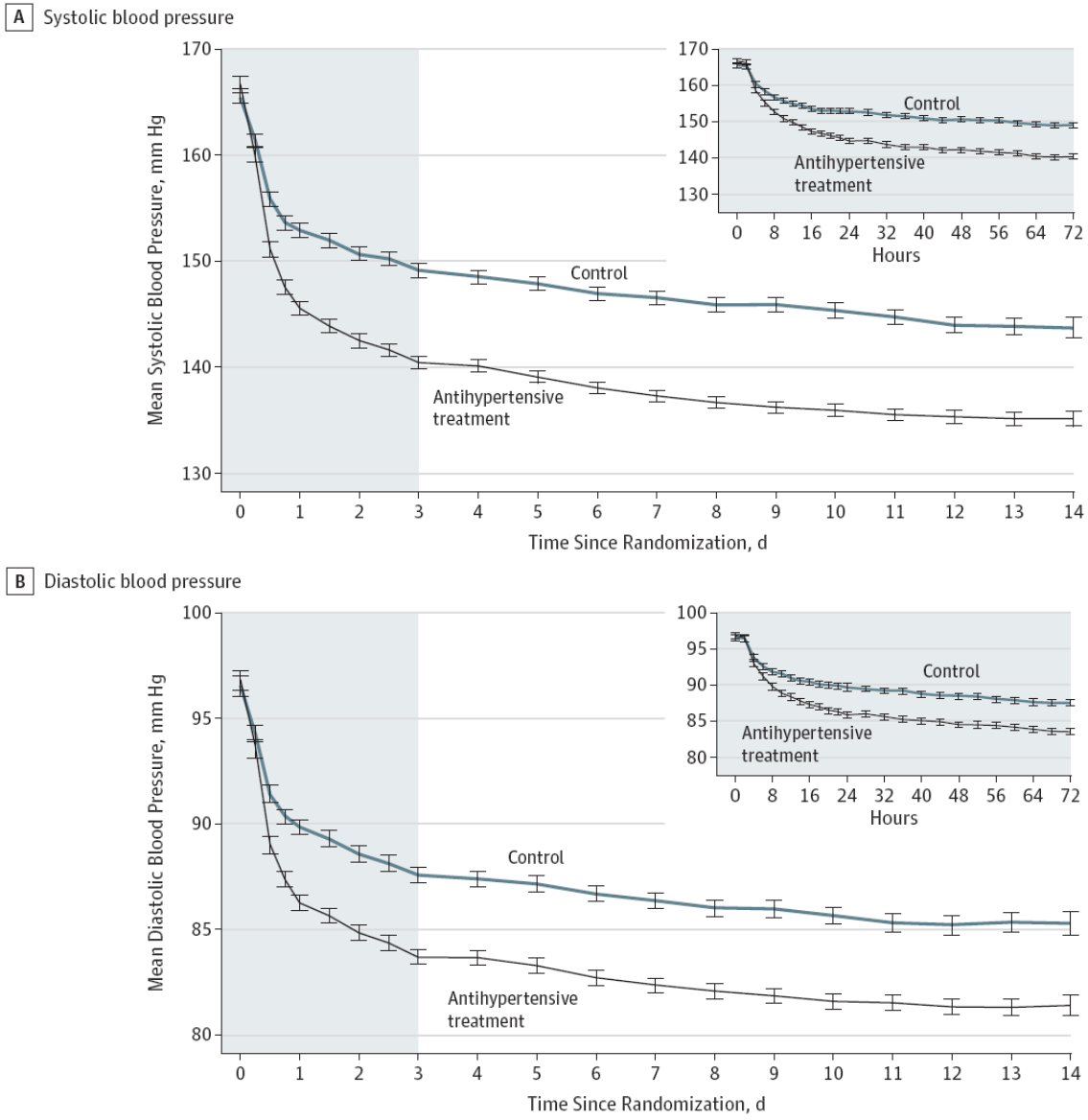
Jiang He, MD, PhD; Yonghong Zhang, MD, PhD; Tan Xu, MD, PhD; Qi Zhao, MD, PhD; Dali Wang, MD; Chung-Shiuan Chen, MS; Weijun Tong, MD; Changjie Liu, MD; Tian Xu, MD; Zhong Ju, MD; Yanbo Peng, MD; Hao Peng, MD; Qunwei Li, MD; Deqin Geng, MD; Jintao Zhang, MD; Dong Li, MD; Fengshan Zhang, MD; Libing Guo, MD; Yingxian Sun, MD; Xuemei Wang, MD; Yong Cui, MD; Yongqiu Li, MD ; Dihui Ma, MD; Guang Yang, MD; Yanjun Gao, MD; Xiaodong Yuan, MD; Lydia A. Bazzano, MD, PhD; Jing Chen, MD, MS; for the CATIS Investigators

CONCLUSIONS AND RELEVANCE

Among patients with acute ischemic stroke, blood pressure reduction with antihypertensive medications, compared with the absence of hypertensive medication, did not reduce the likelihood of death and major disability at 14 days or hospital discharge.

JAMA 2014;311:475-485

Mean Systolic and Diastolic Blood Pressure Since Randomization, by Treatment Group



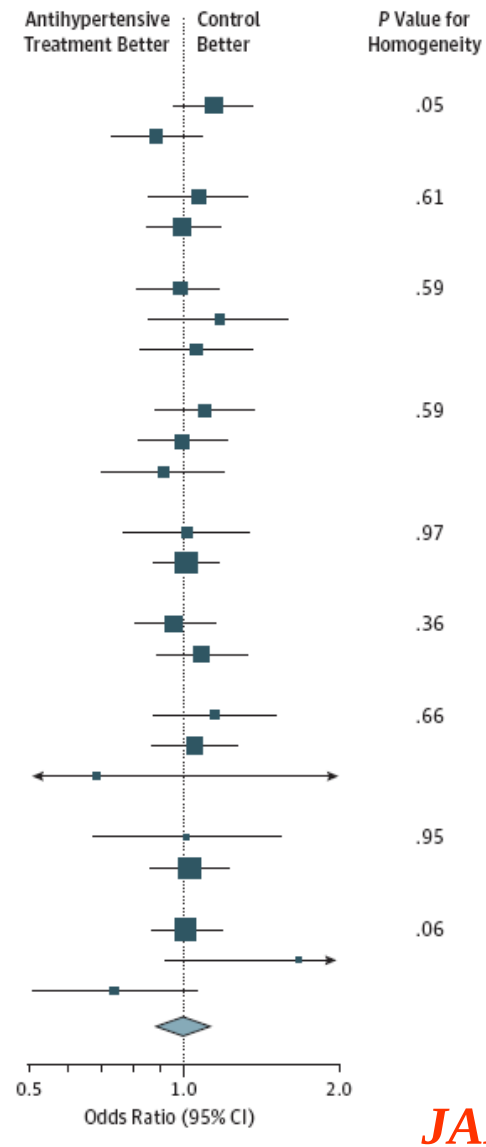
No. of participants

Antihypertensive treatment	2038	2017	1989	1945	1910	1883	1842	1764	1695	1602	1477	1351	1218	1079	856
Control	2033	2017	1998	1951	1927	1878	1828	1761	1654	1559	1456	1338	1224	1055	817

JAMA. 2014;311(5):479-489

Effect of Antihypertensive Treatment on Death or Major Disability at 14 Days or Hospital Discharge

Subgroup	Antihypertensive Treatment Total, No.	Antihypertensive Treatment Events, No. (%)	Control Total, No.	Control Events, No. (%)	Odds Ratio (95% CI)	P Value for Homogeneity
Age, y						
<65	1198	352 (29.4)	1203	325 (27.0)	1.12 (0.94-1.34)	.05
≥65	833	331 (39.7)	824	356 (43.2)	0.87 (0.71-1.05)	
Sex						
Women	715	267 (37.3)	743	269 (36.2)	1.05 (0.85-1.30)	.61
Men	1316	416 (31.6)	1284	412 (32.1)	0.98 (0.83-1.15)	
Time to randomization, h						
<12	1015	376 (37.0)	1082	412 (38.1)	0.96 (0.80-1.14)	.59
12-23	401	132 (32.9)	331	99 (29.9)	1.15 (0.84-1.57)	
≥24	609	172 (28.2)	609	167 (27.4)	1.04 (0.81-1.34)	
Baseline SBP, mm Hg						
<160	715	225 (31.5)	765	228 (29.8)	1.08 (0.87-1.35)	.59
160-179	838	288 (34.4)	851	297 (34.9)	0.98 (0.80-1.19)	
≥180	478	170 (35.6)	411	156 (38.0)	0.90 (0.69-1.19)	
History of hypertension						
No	428	150 (35.0)	430	151 (35.1)	1.00 (0.75-1.32)	.97
Yes	1603	533 (33.3)	1597	530 (33.2)	1.00 (0.87-1.16)	
Use of antihypertension medications						
No	1022	354 (33.8)	1045	366 (35.0)	0.95 (0.79-1.13)	.36
Yes	1009	338 (33.5)	982	315 (32.1)	1.07 (0.88-1.29)	
Baseline NIHSS score						
0-4	1065	134 (12.6)	1009	113 (11.2)	1.14 (0.87-1.49)	.66
5-15	871	460 (52.8)	923	479 (51.9)	1.04 (0.86-1.25)	
≥16	95	89 (93.7)	93	89 (95.7)	0.67 (0.18-2.44)	
Baseline Rankin score						
<3	914	47 (5.1)	900	46 (5.1)	1.01 (0.66-1.53)	.95
≥3	1117	636 (56.9)	1125	635 (56.4)	1.02 (0.86-1.21)	
Stroke subtype						
Thrombolic	1513	539 (35.6)	1540	544 (35.3)	1.01 (0.87-1.18)	.06
Embolic	93	60 (64.5)	92	48 (52.2)	1.67 (0.92-3.01)	
Lacunar	366	66 (18.0)	338	78 (23.1)	0.73 (0.51-1.06)	
Overall	2031	683 (33.6)	2027	681 (33.6)	1.00 (0.88-1.14)	



JAMA 2014;311(5):479-489

Efficacy of nitric oxide, with or without continuing antihypertensive treatment, for management of high blood pressure in acute stroke (ENOS): a partial-factorial randomised controlled trial

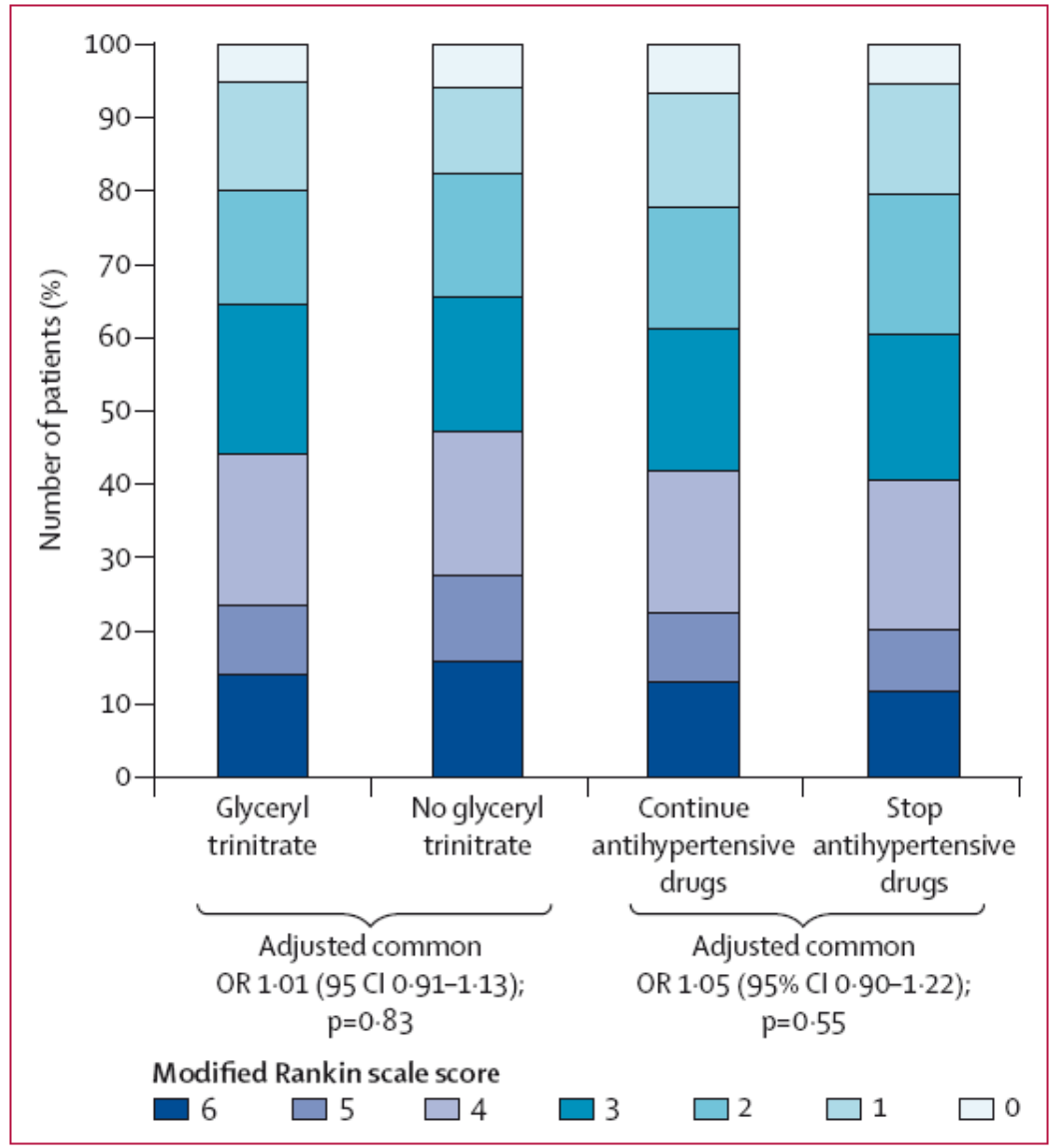
The ENOS Trial Investigators*

Conclusions

In patients with acute stroke and high blood pressure, transdermal glyceryl trinitrate lowered blood pressure and had acceptable safety but did not improve functional outcome. We show no evidence to support continuing prestroke antihypertensive drugs in patients in the fi rst few days after acute stroke.

Lancet 2015;385:617–28

Distribution of modifi ed Rankin Scale scores at 90 days



Lancet 2015; 385: 617–28

Medicine®

SYSTEMATIC REVIEW AND META-ANALYSIS

OPEN

Blood Pressure Reduction in the Acute Phase of an Ischemic Stroke Does Not Improve Short- or Long-Term Dependency or Mortality

A Meta-Analysis of Current Literature

Rong Zhao, MD, Feng-Di Liu, MD, Shuo Wang, MD, Jia-Li Peng, MD, Xiao-Xiao Tao, MD, Bo Zheng, MD, Qi-Ting Zhang, MD, Qian Yao, MD, Xiao-Lei Shen, MD, Wen-Ting Li, MD, Ying Zhao, MD, Yi-Sheng Liu, MD, Jing-Jing Su, MD, PhD, Liang Shu, MD, Min Zhang, MD, and Jian-Ren Liu, MD, PhD

- **22 studies**
- **Conclusions: Antihypertensive agents effectively reduce BP during the acute phase of an ischemic stroke, but provide no benefit with respect to short- and long-term dependency and mortality.**

Medicine 94(23):e896

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Edward C. Jauch, Jeffrey L. Saver, Harold P. Adams, Jr, Askiel Bruno, J.J. (Buddy) Connors, Bart M. Demaerschalk, Pooja Khatri, Paul W. McMullan, Jr, Adnan I. Qureshi, Kenneth Rosenfield, Phillip A. Scott, Debbie R. Summers, David Z. Wang, Max Wintermark and Howard Yonas

Stroke. published online January 31, 2013;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

2. Patients who have elevated blood pressure and are otherwise eligible for treatment with intravenous rtPA should have their blood pressure carefully lowered (Table 9) so that their systolic blood pressure is <185 mm Hg and their diastolic blood pressure is <110 mm Hg *(Class I; Level of Evidence B)* before fibrinolytic therapy is initiated. If medications are given to lower blood pressure, the clinician should be

Trombolýza: TK <185/110

7. In patients with markedly elevated blood pressure who do not receive fibrinolysis, a reasonable goal is to lower blood pressure by 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is not known, but consensus exists that medications should be withheld unless the systolic blood pressure is >220 mm Hg or the diastolic blood pressure is >120 mm Hg *(Class I; Level of Evidence C)*. (Revised from the previous guideline[13])

Ostatní:

- **TK <220/120** - vysadit anti-HT medikaci
- **TK >220/120 –** snížit TK o 15% za 24h

TK u pacientů po CMP

Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial

*The SPS3 Study Group**

Summary

Background Lowering of blood pressure prevents stroke but optimum target levels to prevent recurrent stroke are unknown. We investigated the effects of different blood-pressure targets on the rate of recurrent stroke in patients with recent lacunar stroke.

Methods In this randomised open-label trial, eligible patients lived in North America, Latin America, and Spain and had recent, MRI-defined symptomatic lacunar infarctions. Patients were recruited between March, 2003, and April, 2011, and randomly assigned, according to a two-by-two multifactorial design, to a systolic-blood-pressure target of 130–149 mm Hg or less than 130 mm Hg. The primary endpoint was reduction in all stroke (including ischaemic strokes and intracranial haemorrhages). Analysis was done by intention to treat. This study is registered with ClinicalTrials.gov, number NCT 00059306.

Findings 3020 enrolled patients, 1519 in the higher-target group and 1501 in the lower-target group, were followed up for a mean of 3·7 (SD 2·0) years. Mean age was 63 (SD 11) years. After 1 year, mean systolic blood pressure was 138 mm Hg (95% CI 137–139) in the higher-target group and 127 mm Hg (95% CI 126–128) in the lower-target group. Non-significant rate reductions were seen for all stroke (hazard ratio 0·81, 95% CI 0·64–1·03, p=0·08), disabling or fatal stroke (0·81, 0·53–1·23, p=0·32), and the composite outcome of myocardial infarction or vascular death (0·84, 0·68–1·04, p=0·32) with the lower target. The rate of intracerebral haemorrhage was reduced significantly (0·37, 0·15–0·95, p=0·03). Treatment-related serious adverse events were infrequent.

Interpretation Although the reduction in stroke was not significant, our results support that in patients with recent lacunar stroke, the use of a systolic-blood-pressure target of less than 130 mm Hg is likely to be beneficial.

Lancet 2013; 382: 507–15

Published Online
May 29, 2013
http://dx.doi.org/10.1016/S0140-6736(13)60852-1

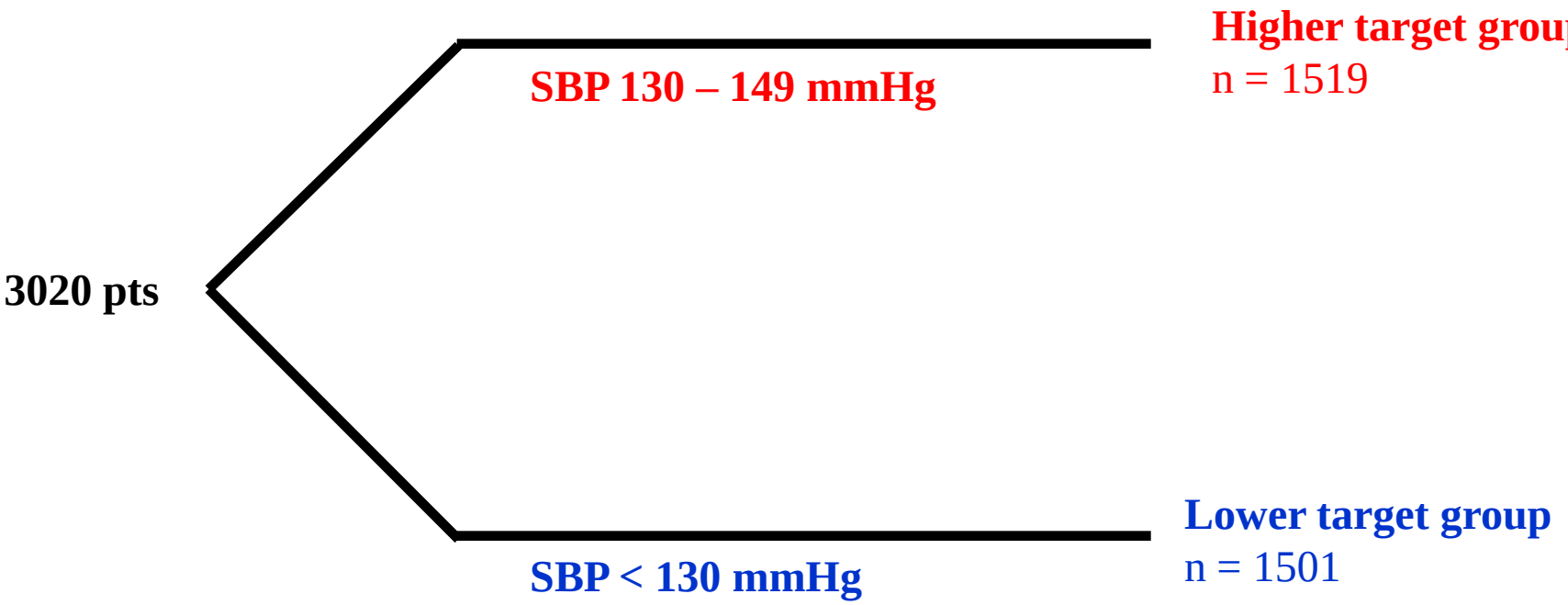
This online publication has been corrected. The corrected version first appeared at thelancet.com on August 9, 2013

See **Comment** page 482

*Members listed at end of paper

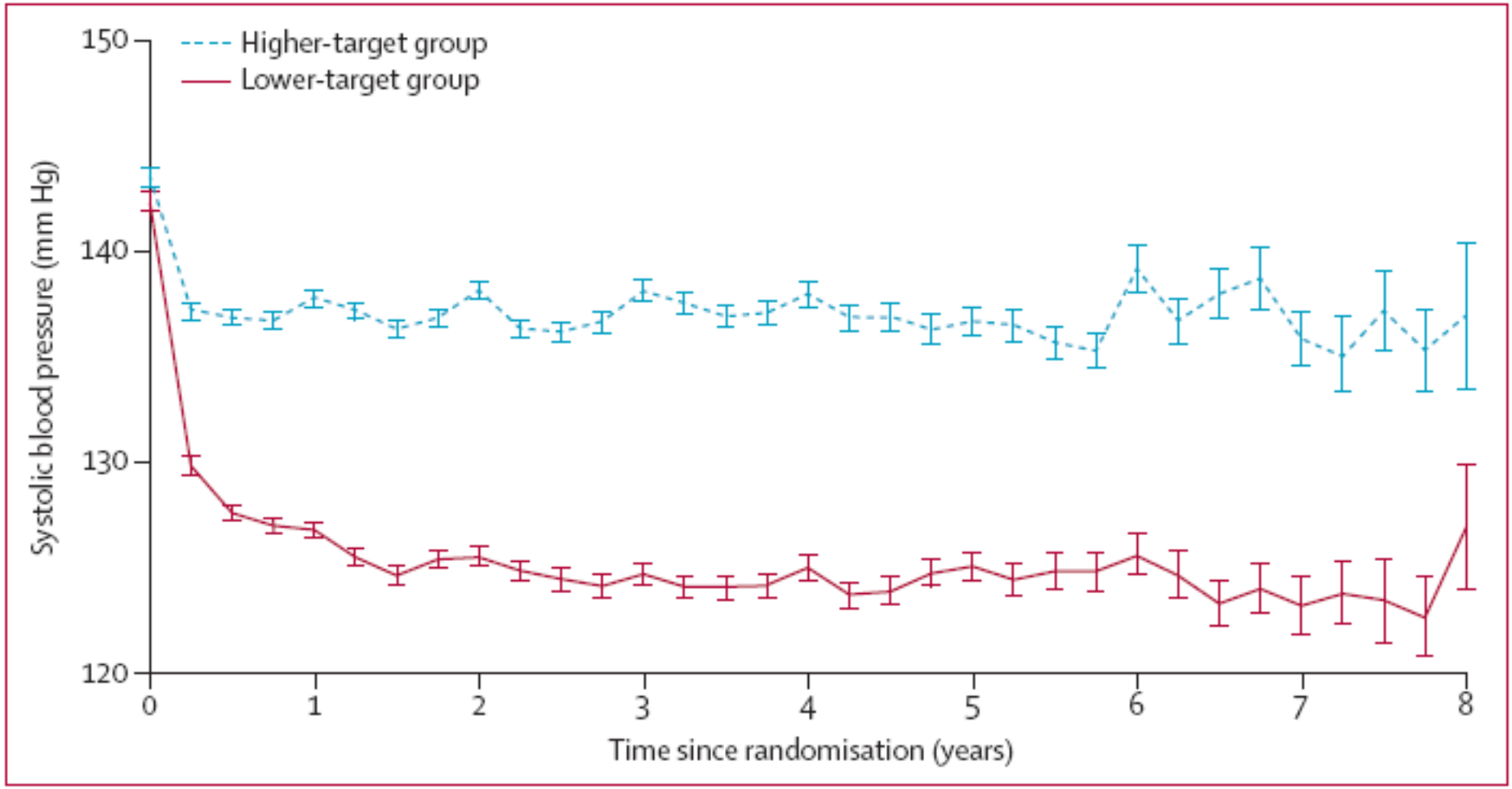
Correspondence to:
Prof Oscar R Benavente, Department of Medicine, Division of Neurology, Brain Research Centre, University of British Columbia, S169-2211 Wesbrook Mall, Vancouver, BC V6T 2B5, Canada
oscar.benavente@ubc.ca

SPS3 randomised trial
Study design



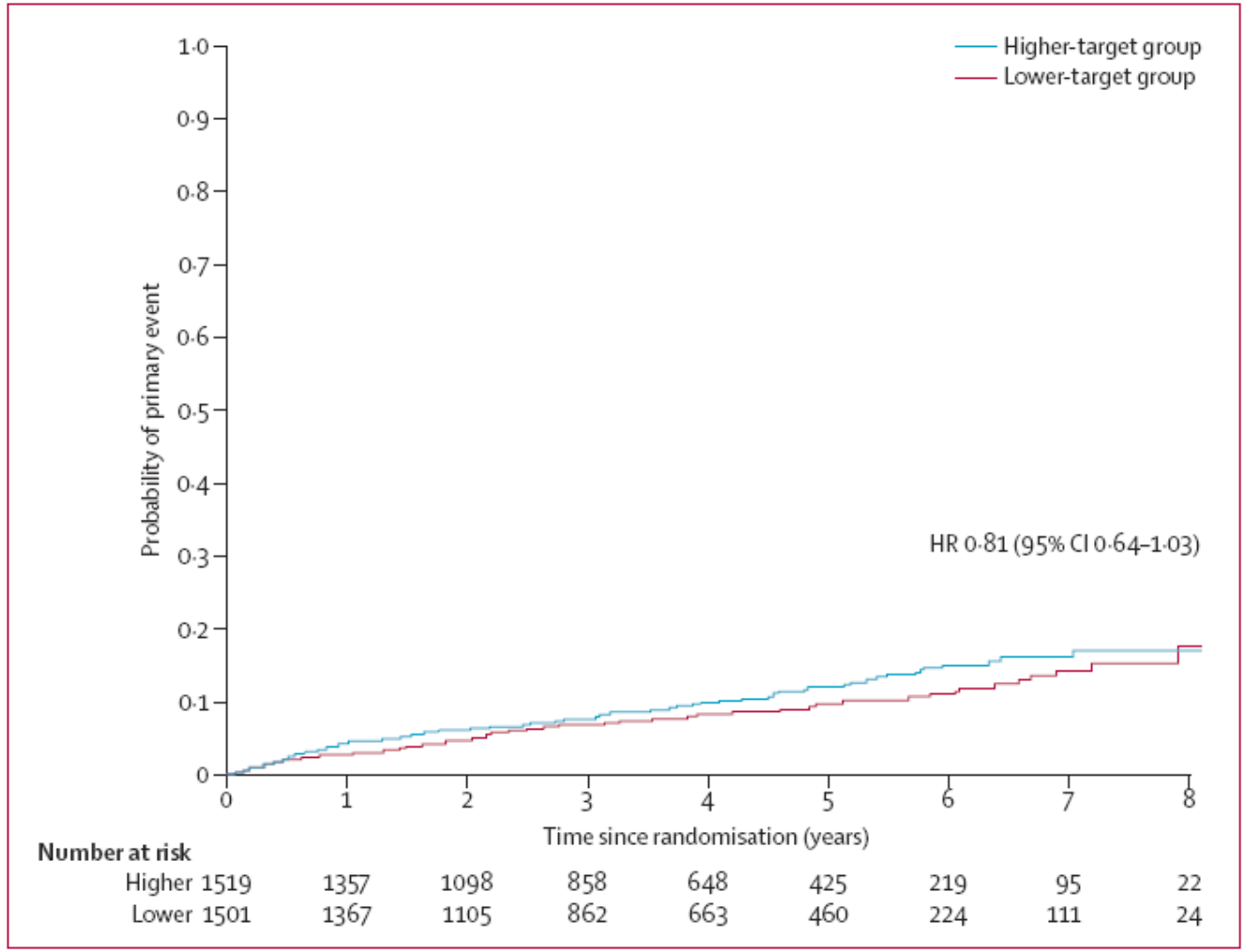
Lancet 2013; 382: 507 – 515

SPS3 randomised trial
SBP



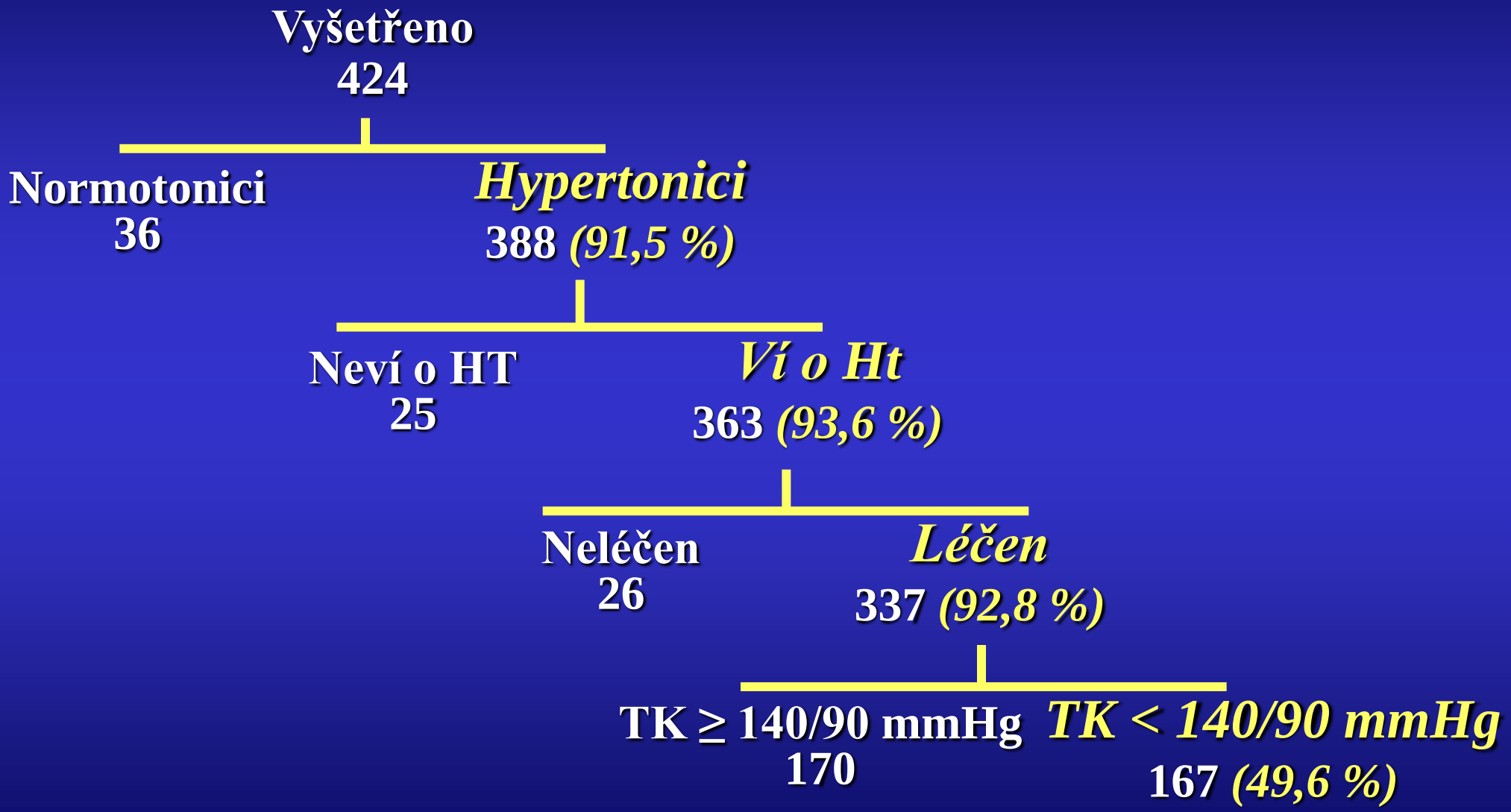
Lancet 2013; 382: 507 – 515

SPS3 randomised trial
Primary event

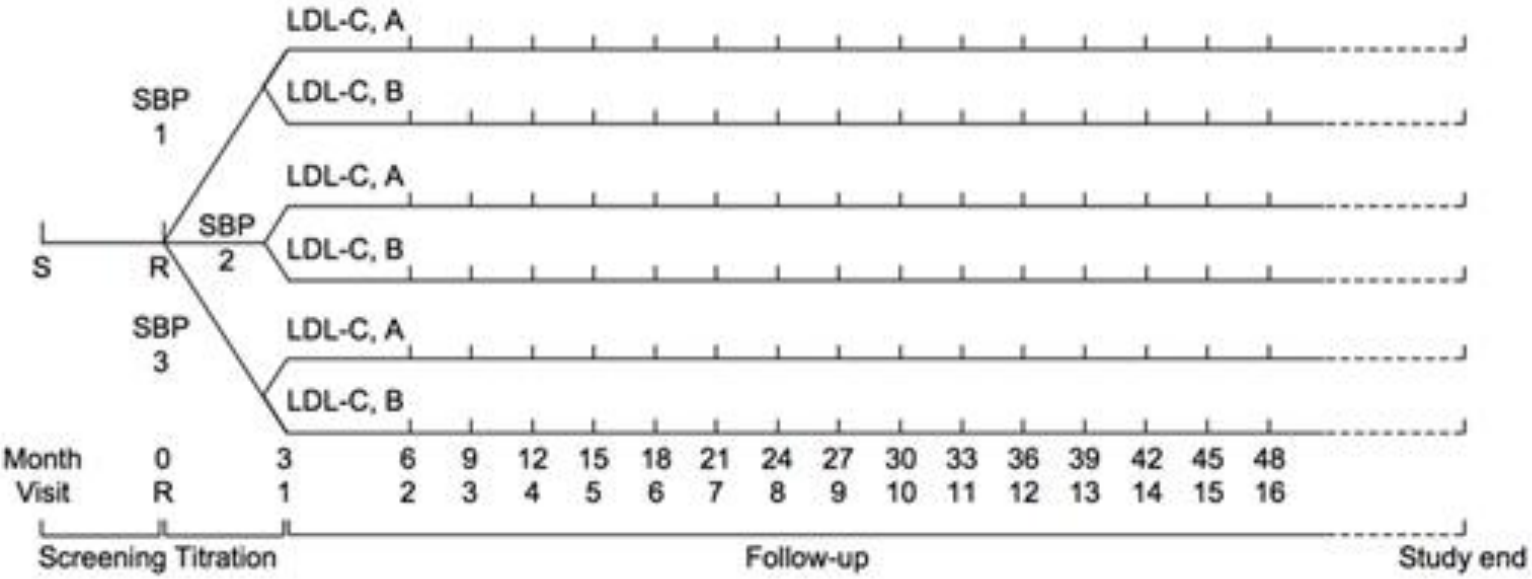


Lancet 2013; 382: 507 – 515

Nemocní po první ischemické CMP



ESH-CHL-SHOT Flow Chart



BP	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x		x
ABP	x								x				x				x			x		x
LDL-C	x		x	x	x		x		x		x		x		x		x		x	x		x
Blood	x								x				x				x			x		x
Microalbuminuria	x								x				x				x			x		x
ECG	x								x								x					x
Echocard, PWV	[x]								[x]													[x]
Carotid US	x								[x]													[x]
Disability	x								x				x				x					x
Cognition	x								x											x		x
Depression	x								x													x
Brain MR / CT	x																					x

ESH-CHL-SHOT

Goal SBP

- < 145-135 mmHg
- < 135-125 mmHg
- < 125 mmHg

Goal LDL-cholesterol

- 2.8-1.8 mmol/l
- < 1.8 mmol/l

Zdůvodnění pokračování ESH-CHL-SHOT po publikaci studie SPRINT

Pacienti zařazovaní do studie SHOT se liší od pacientů ve studii SPRINT

SHOT zařazuje pacienty, kteří byli ze studie SPRINT vyloučeni

- **starší pacienti po CMP**

Jediná dosud provedená studie testující 2 různé hodnoty STK u pacientů po CMP (SPS3 trial) neprokázala přínos z nižších hodnot TK

Pacienti ve studii SPRINT nebyli ve zvláště vysokém KV riziku

- incidence závažných KV příhod > 2 %/rok
- KV mortalita 0,43 %/rok (cca 25 % celkové mortality oproti očekávaným 50%), způsobeno pravděpodobně nízkou prevalencí KVO při vstupu do studie
- pokles koronárních příhod a CMP nebyl signifikantní
- předčasné ukončení studie SPRINT snížilo statistickou sílu studie

Zdůvodnění pokračování ESH-CHL-SHOT po publikaci studie SPRINT

- Ve studii SPRINT bylo nejvíce sníženo srdeční selhání (50 %)
- Významně byla snížena náhlá smrt, která se vyskytuje zejména u pacientů se srdečním selháním.

- Snížení srdečního selhání je ovlivněno snížením TK a také skupinou antihypertenziv

Diuretika a RAS blokátory jsou výrazně účinnější v prevenci srdečního selhání než blokátory kalciových kanálů (jejich užívání bylo o 50 % vyšší než standardní léčba)

Velké rozdíly v STK mezi intenzivně a standardně léčenou skupinou ve studii SPRINT

Velký výskyt NÚ

Therapeutic strategies in hypertensive patients with cerebrovascular disease

Recommendations	Class[a]	Level[b]
It is not recommended to intervene with BP-lowering therapy during the first week after acute stroke irrespective of BP level, although clinical judgement should be used in the face of very high SBP values.	III	B
Antihypertensive treatment is recommended in hypertensive patients with a history of stroke or TIA, even when initial SBP is in the 140–159 mmHg range.	I	B
In hypertensive patients with a history of stroke or TIA, a SBP goal of <140 mmHg should be considered.	IIa	B
In elderly hypertensives with previous stroke or TIA, SBP values for intervention and goal may be considered to be somewhat higher.	IIb	B
All drug regimens are recommended for stroke prevention, provided that BP is effectively reduced.	I	A

J Hypertens 2013; 31: 1281-1357

Závěry

- Primární prevence: TK < 120/80 mm Hg u zdravé populace je spojen s minimálním rizikem úmrtí na CMP
- V prvním týdnu po CMP se nedoporučuje podávat antihypertenziva s výjimkou ovlivnění velmi vysokých hodnot STK
- Léčba hypertenze je doporučena hypertonikům s anamnézou CMP/TIA s hodnotami STK 140–159 mm Hg

Závěry pokrač.

- Cílová hodnota STK pro hypertoniky po CMP nebo TIA:

  < 140 mm Hg; event. vyšší pro starší hypertoniky

- Pro prevenci CMP je možno užít všechna antihypertenziva, pokud účinně snižují TK