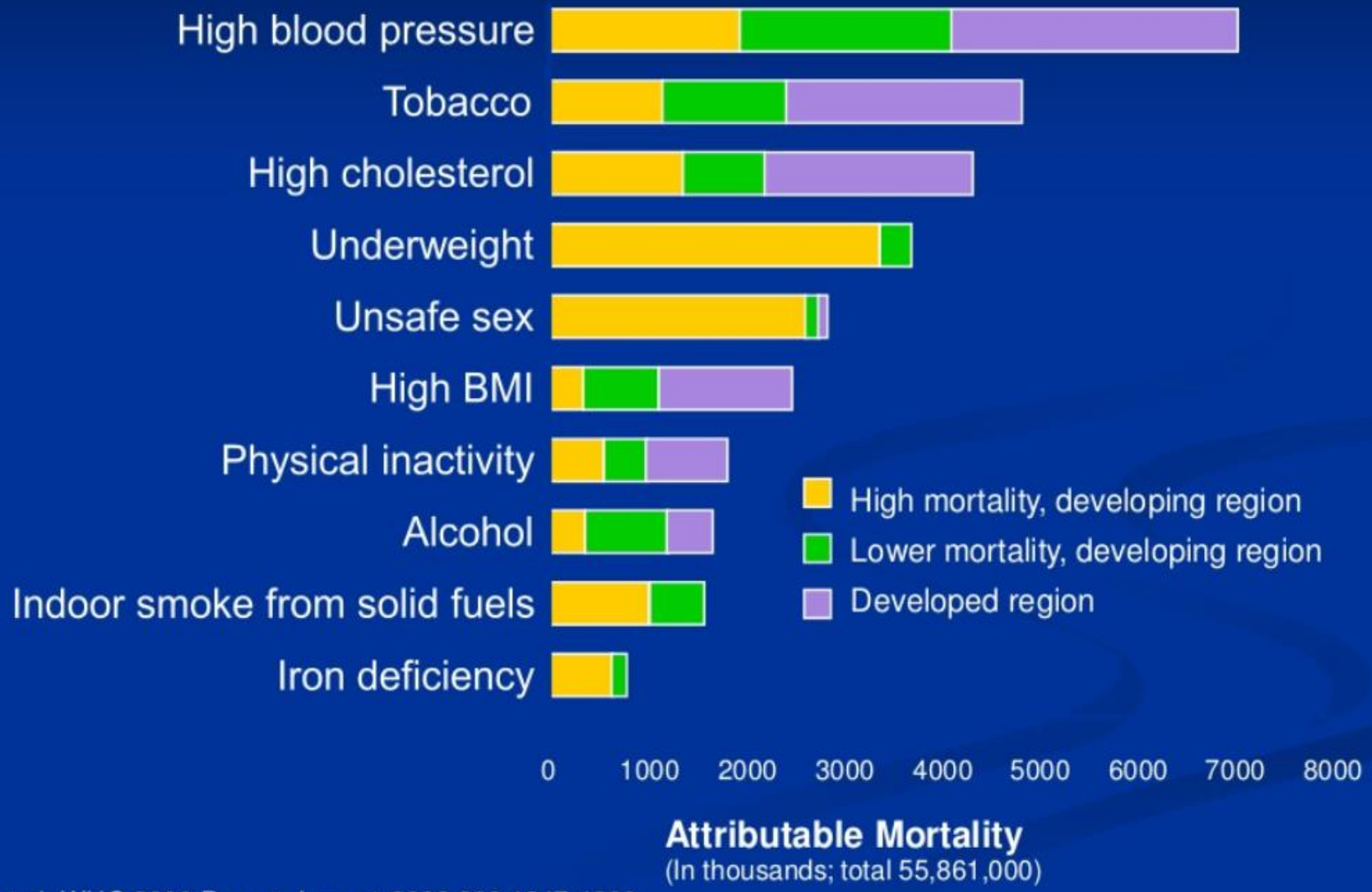
Missed Diagnosis of Masked Hypertension : Need to Treat!

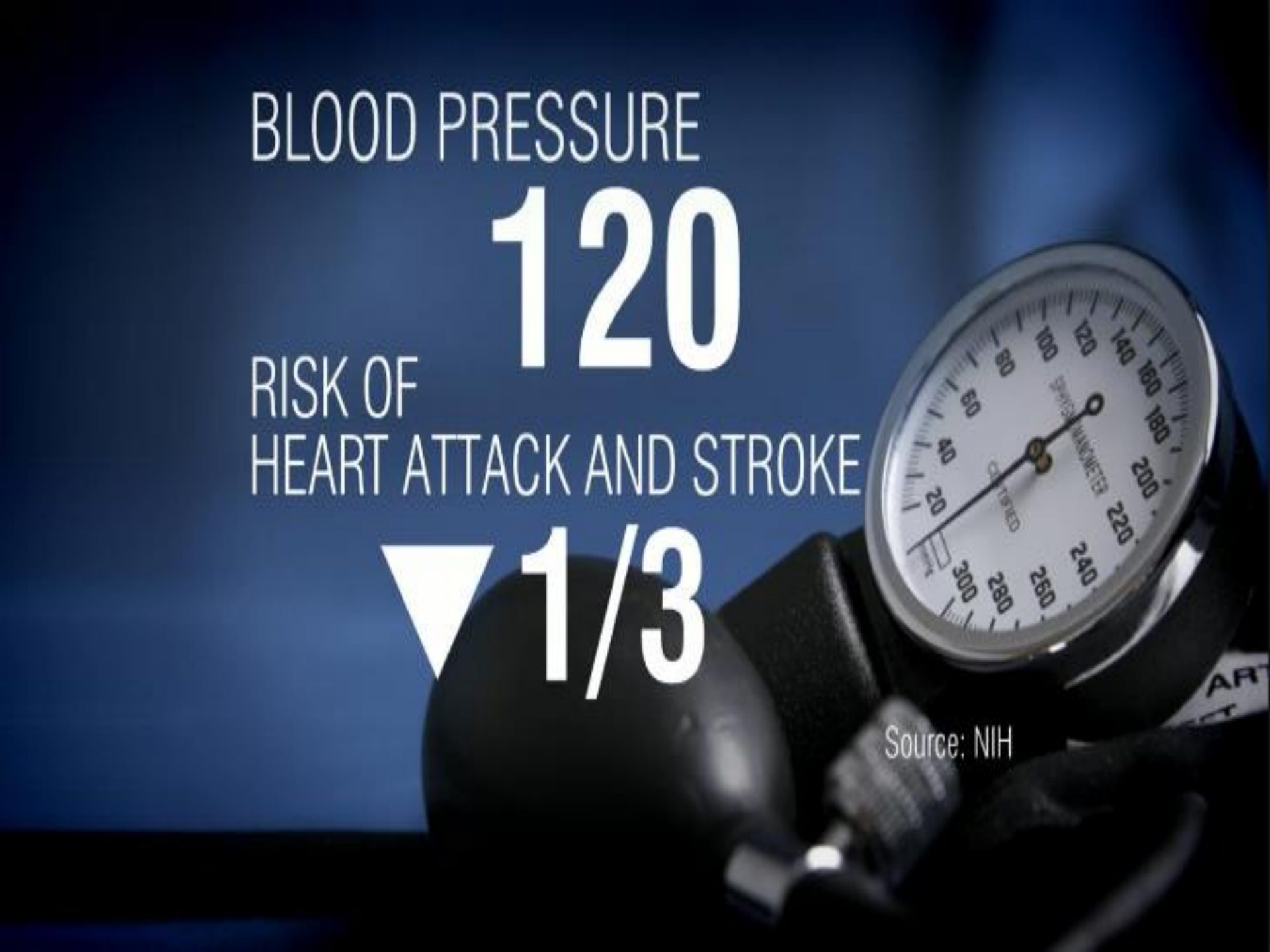
Kyoung-Im Cho

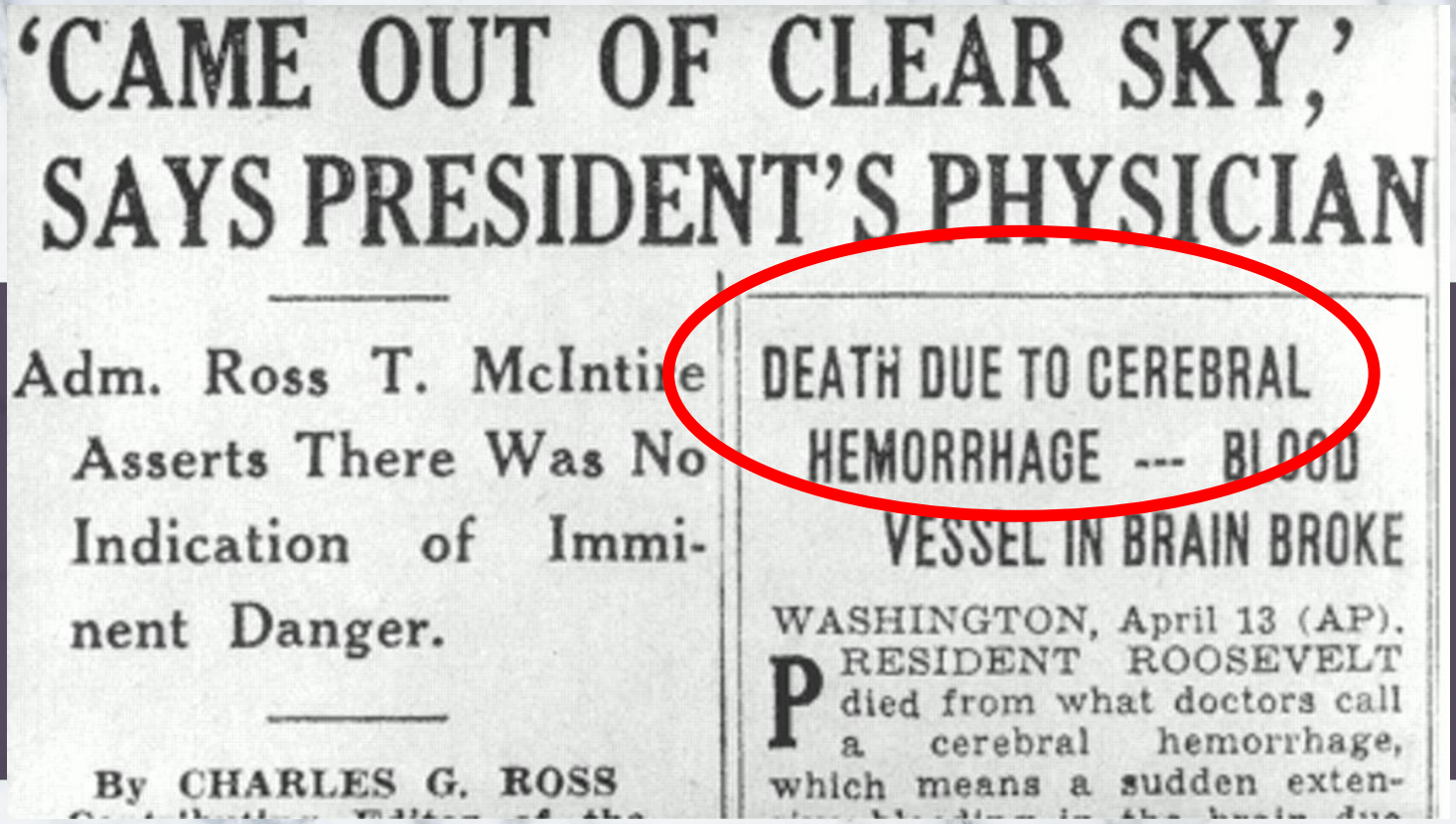
Kosin University Gospel Hospital

Proportion of deaths attributable to leading risk factors worldwide



Ezzati et al. WHO 2000 Report. *Lancet*. 2002;360:1347-1360


BLOOD PRESSURE
120
RISK OF
HEART ATTACK AND STROKE
▼1/3
Source: NIH



‘CAME OUT OF CLEAR SKY,’ SAYS PRESIDENT’S PHYSICIAN

Adm. Ross T. McIntire Asserts There Was No Indication of Imminent Danger.

By CHARLES G. ROSS

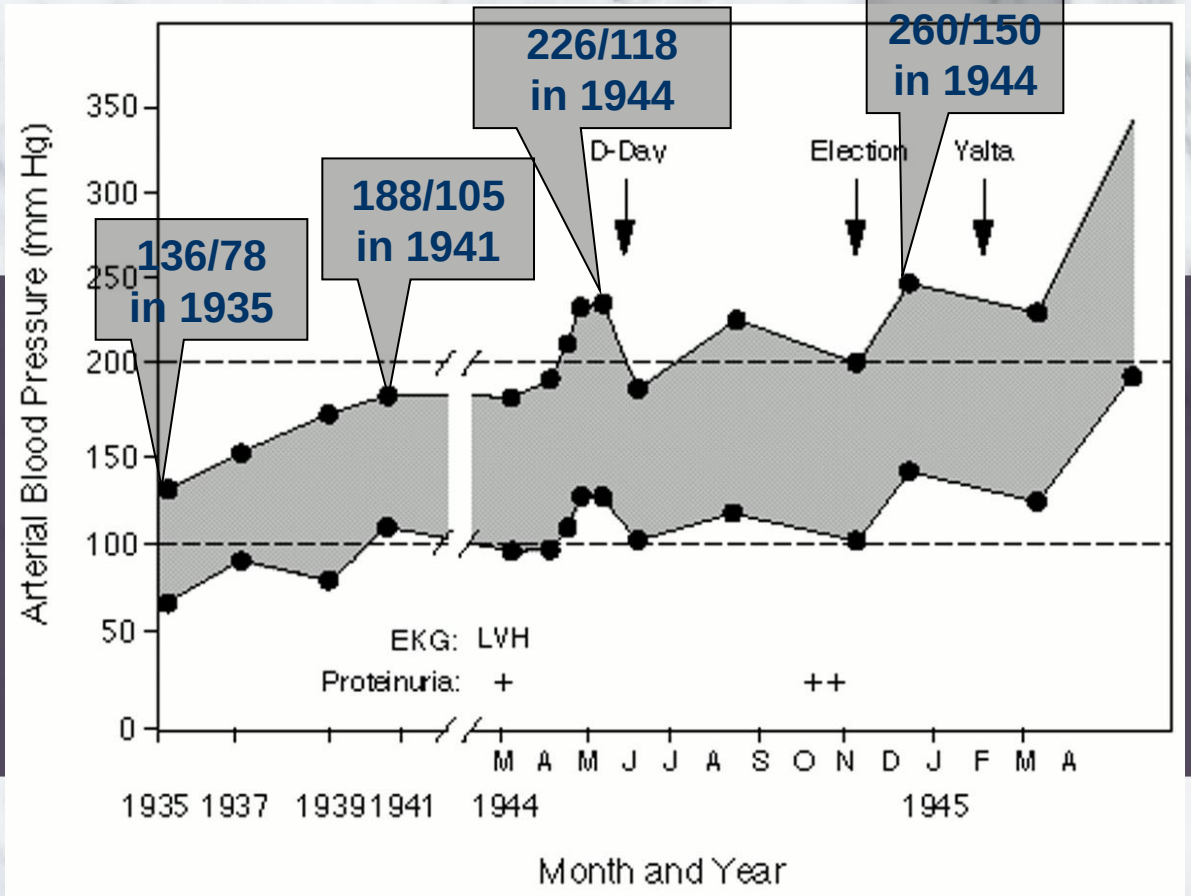
DEATH DUE TO CEREBRAL HEMORRHAGE --- BLOOD VESSEL IN BRAIN BROKE

WASHINGTON, April 13 (AP). PRESIDENT ROOSEVELT died from what doctors call a cerebral hemorrhage, which means a sudden exten-

Headlines of the *St. Louis Post-Dispatch,* April 13, **1945**

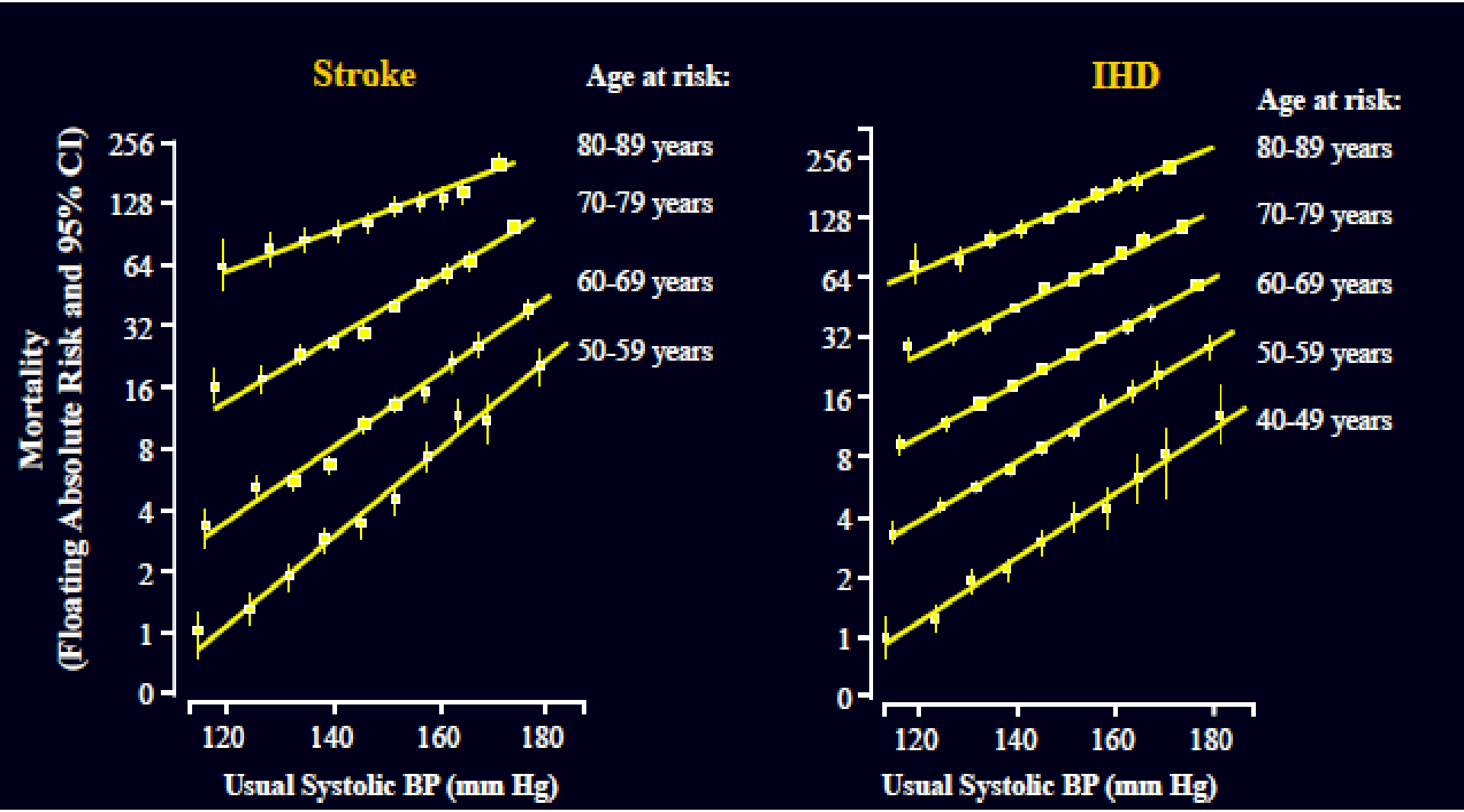
1882-1945
Thirty-Second President
(1933-1945)

Franklin D. Roosevelt



Messerli FH, *N Engl J Med.* 1995

Hypertension, Universal Findings

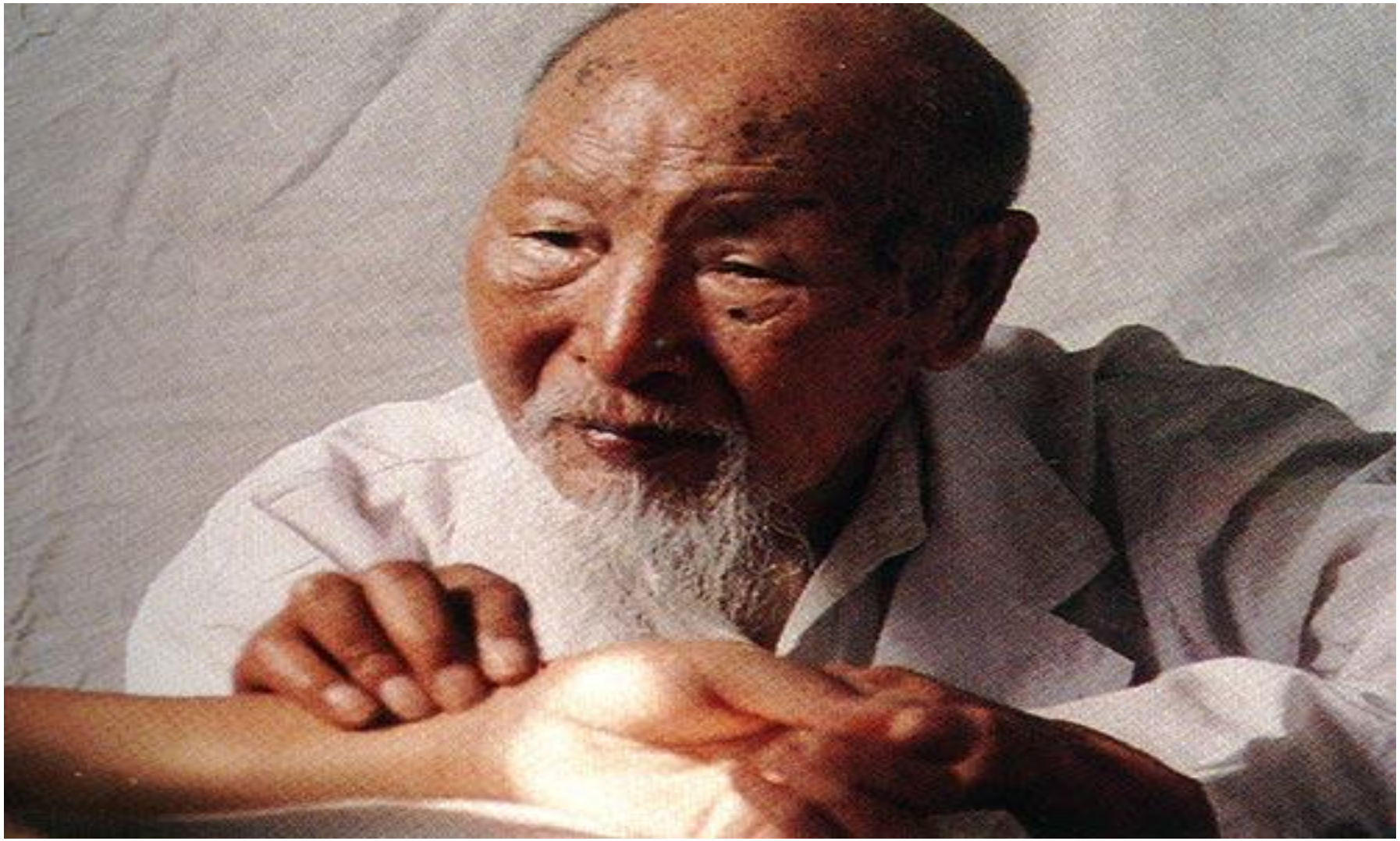


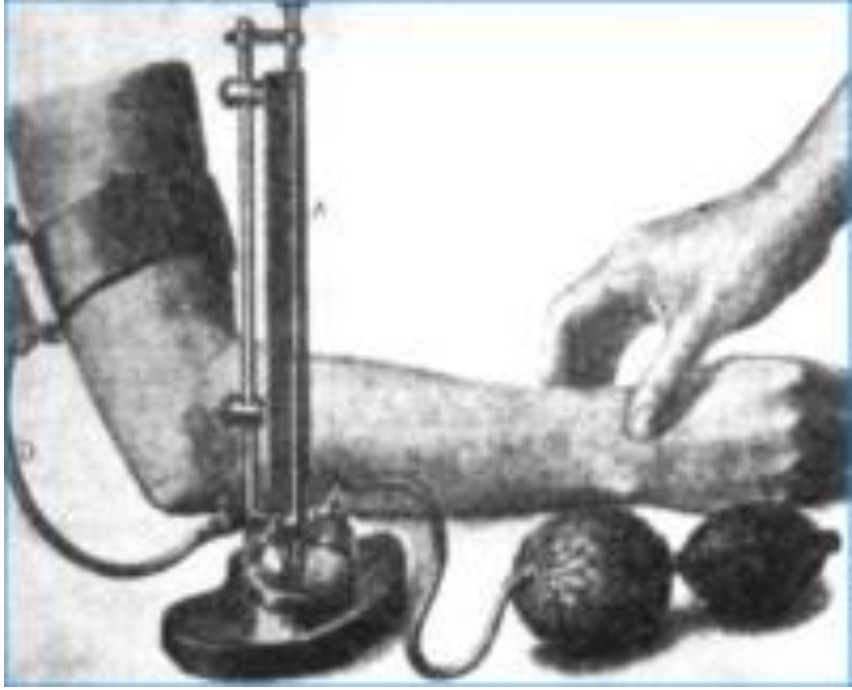
Lancet 2002;360:1903

Blood Pressure Measurement

Stephen Hales Measuring Horse‘s Blood Pressure (1733)

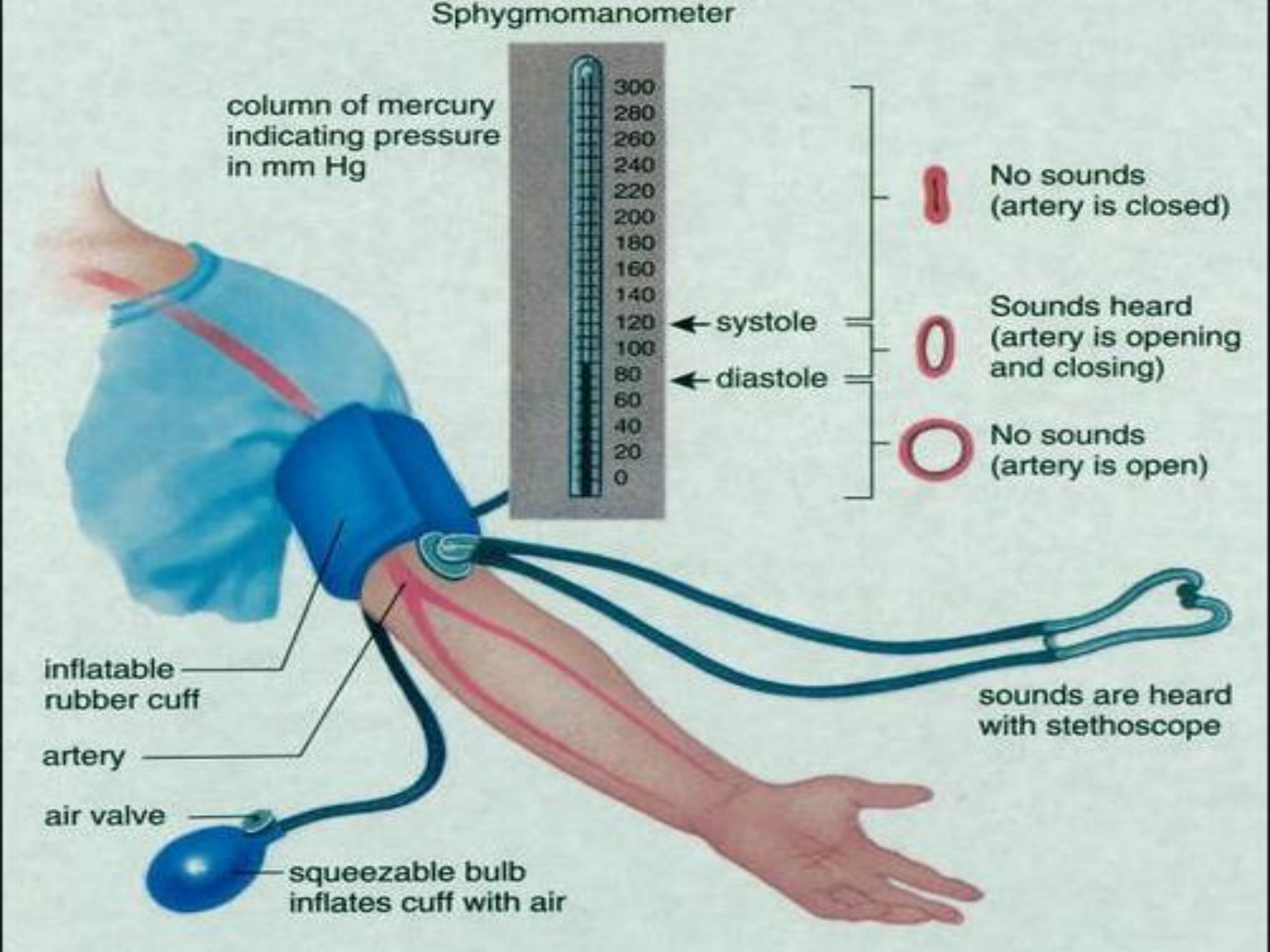
Pulse analysis was practiced in Chinese medicine thousands of years ago





Harvey Cushing used it.

Korotkoff introduced auscultation for diastolic pressure in 1905

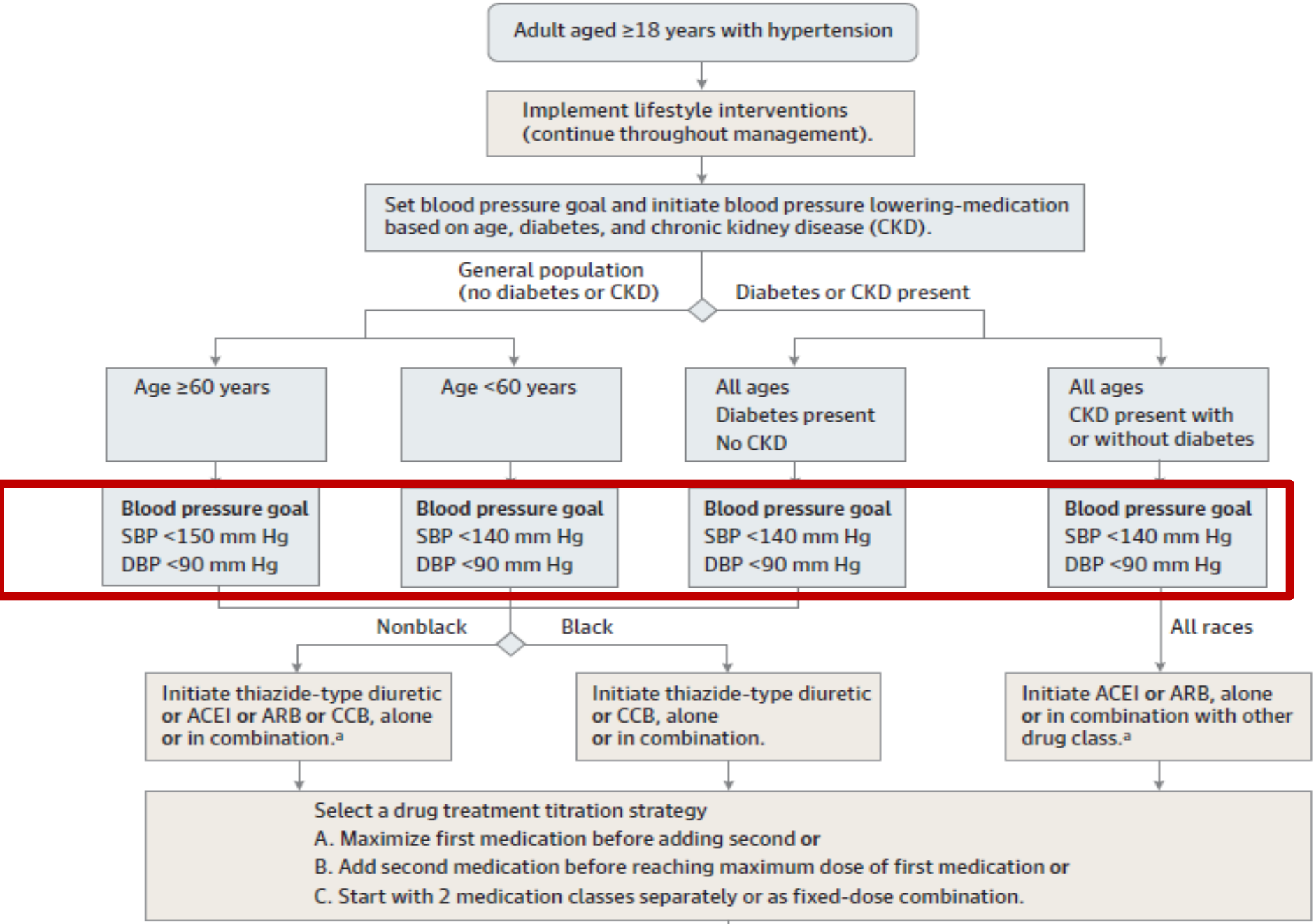

Sphygmomanometer
column of mercury indicating pressure in mm Hg
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
systole
diastole
No sounds (artery is closed)
Sounds heard (artery is opening and closing)
No sounds (artery is open)
inflatable rubber cuff
artery
air valve
squeezable bulb inflates cuff with air
sounds are heard with stethoscope

Clinical practice guidelines have traditionally recommended manual BP measurement in the office setting as the standard method for diagnosing hypertension

How should clinicians diagnose and stage hypertension?

- **When to diagnose hypertension:**
  - **≥2 readings obtained at 3 visits 2-4 wk apart**
  - **Average ≥140mmHg (systolic) or ≥90mmHg (diastolic)**
- Hypertension stages (JNC 7)
  - Normal blood pressure: ≤120/80 mm Hg
  - Prehypertensive: 120/80 to 139/89 mm Hg
  - Stage 1: 140/90 to 159/99 mm Hg
  - Stage 2: ≥160/100 mm Hg
- If >50y, systolic blood pressure >140 mmHg more important CVD risk factor than diastolic hypertension

JNC 8


Adult aged ≥18 years with hypertension
Implement lifestyle interventions (continue throughout management).
Set blood pressure goal and initiate blood pressure lowering-medication based on age, diabetes, and chronic kidney disease (CKD).
General population (no diabetes or CKD)
Diabetes or CKD present
Age ≥60 years
Age <60 years
All ages Diabetes present No CKD
All ages CKD present with or without diabetes
Blood pressure goal SBP <150 mm Hg DBP <90 mm Hg
Blood pressure goal SBP <140 mm Hg DBP <90 mm Hg
Blood pressure goal SBP <140 mm Hg DBP <90 mm Hg
Blood pressure goal SBP <140 mm Hg DBP <90 mm Hg
Nonblack
Black
All races
Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.a
Initiate thiazide-type diuretic or CCB, alone or in combination.
Initiate ACEI or ARB, alone or in combination with other drug class.a
Select a drug treatment titration strategy
A. Maximize first medication before adding second or
B. Add second medication before reaching maximum dose of first medication or
C. Start with 2 medication classes separately or as fixed-dose combination.

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

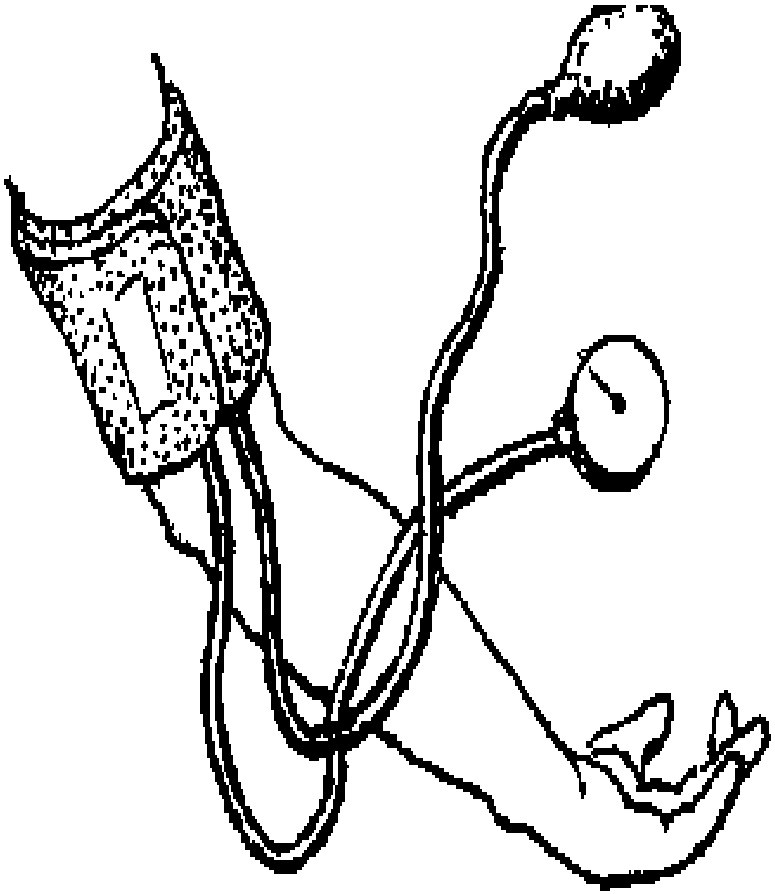
2013 ESH/ESC Guidelines for the management of arterial hypertension

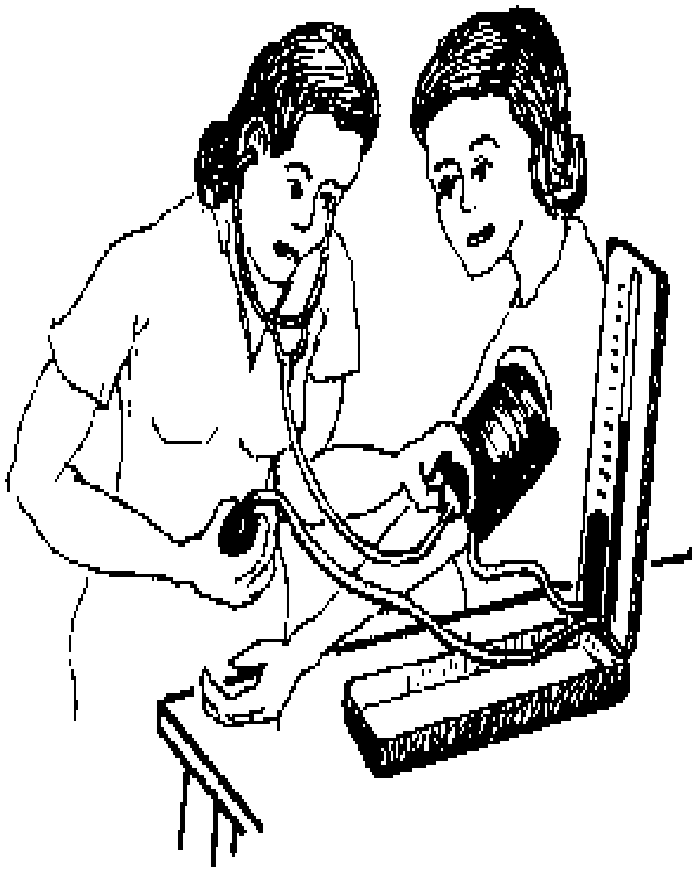
The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Manual BP: relatively inaccurate, over-diagnoses hypertension by provoking office-induced increases in BP and correlates poorly with both the awake ambulatory BP and target organ damage

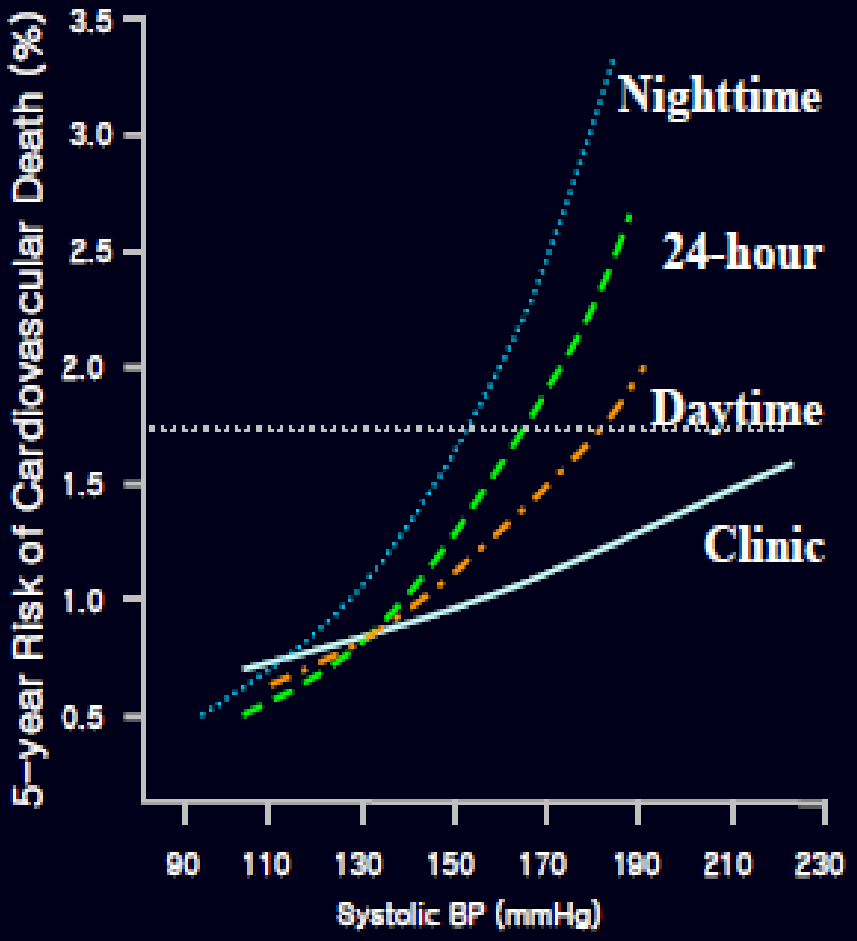


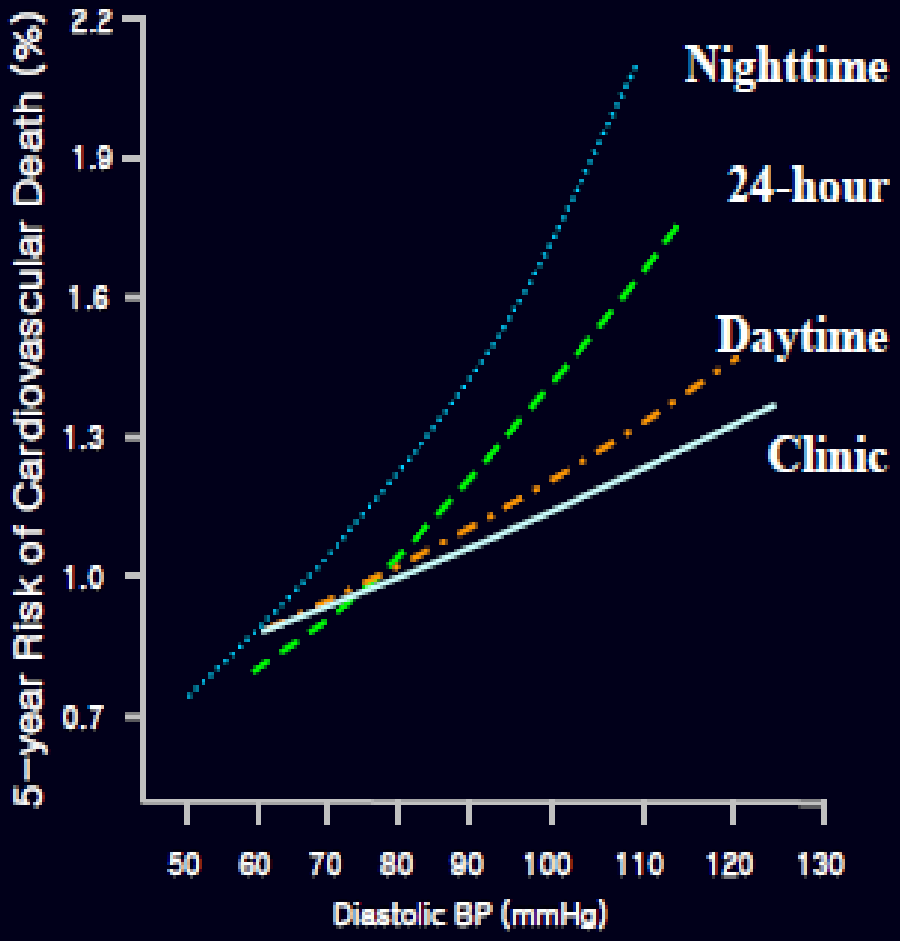


The most recent guidelines recommend 24-h ambulatory BP and home BP for diagnosing hypertension

Prognostive Value of ABPM

Dublin outcome study: 5292 subjects FU for 8.4years





Hypertens2005;46:156-161

Progressive disease
leading to organ damage!

BP Thresholds for Diagnosis
Ambulatory BP Monitoring

24-hour & night BP are known to be superior to mean clinic BP as predictors of CV outcomes or stroke.

Stage of Hypertension	Office BP (mmHg)	24hr. Daytime ABPM Average	Home ABPM Average
Stage 1 Hypertension	≥140 /90 but <160/100	≥135/85	≥135/85
Stage 2 Hypertension	≥160 / 100	≥150/95	≥150/95
Severe Hypertension	≥180/110		
Accelerated Hypertension	Usually ≥180/110 + retinal haemorrhages and/or papilloedema		

If office BP≥140/90mmHg, recommend ABPM.
If office BP ≥180/110mmHg, start antihypertensive drugs.

2기 전단계 고혈압의 특징

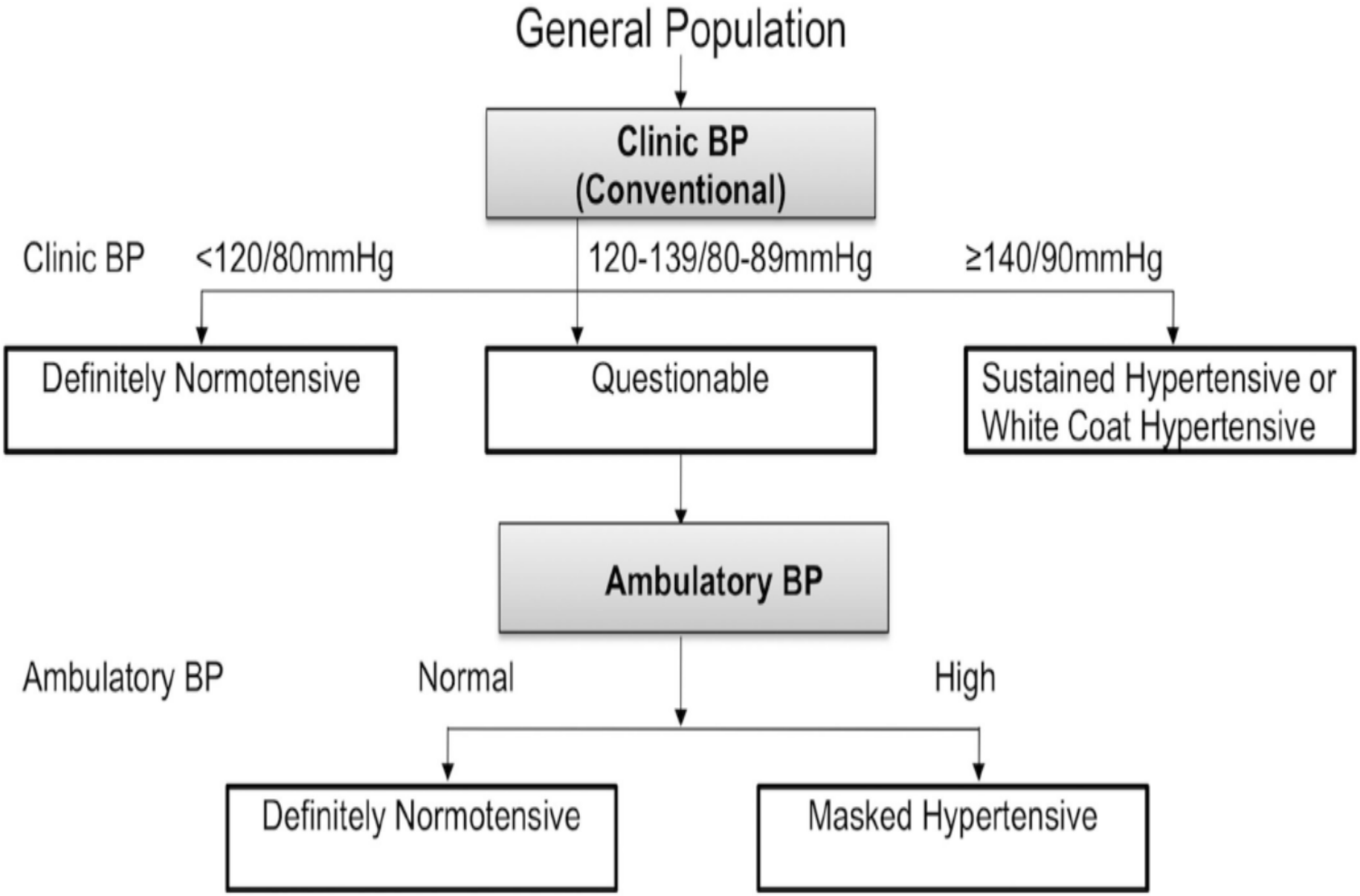
- 정상혈압에 비해 심혈관 예후가 나쁘다
- 고혈압으로 진행할 가능성이 높다
- 가면고혈압의 가능성이 있다
- 특정 상황에서 약물 치료가 필요하다

활동혈압을 이용한 혈압분류

Term	Definition
Home-clinic blood pressure difference	The difference between blood pressure measured with ABPM or at home (self-monitored) and blood pressure measured in the clinic.
White coat effect	A negative home-clinic blood pressure difference. Blood pressure measured with ABPM (or at home) is *lower* than the corresponding clinic blood pressure.
White coat hypertension	A negative home-clinic blood pressure difference. Blood pressure measured with ABPM (or at home) is <135/85 mm Hg but the corresponding clinic blood pressure is ≥140/90 mm Hg.
Masked effect	A positive home-clinic blood pressure difference. Blood pressure measured with ABPM (or at home) is *higher* than the corresponding clinic blood pressure.
Masked hypertension	A positive home-clinic blood pressure difference. Blood pressure measured with ABPM (or at home) is ≥135/85 mm Hg but the corresponding clinic blood pressure is <140/90 mm Hg.
Masked uncontrolled hypertension	A positive home-clinic blood pressure difference in patients with a previous diagnosis of hypertension. Blood pressure measured with ABPM (or at home) is ≥135/85 mm Hg but the corresponding clinic blood pressure is <140/90 mm Hg (incorrectly suggesting the patient is controlled).

When is ambulatory blood pressure monitoring indicated?

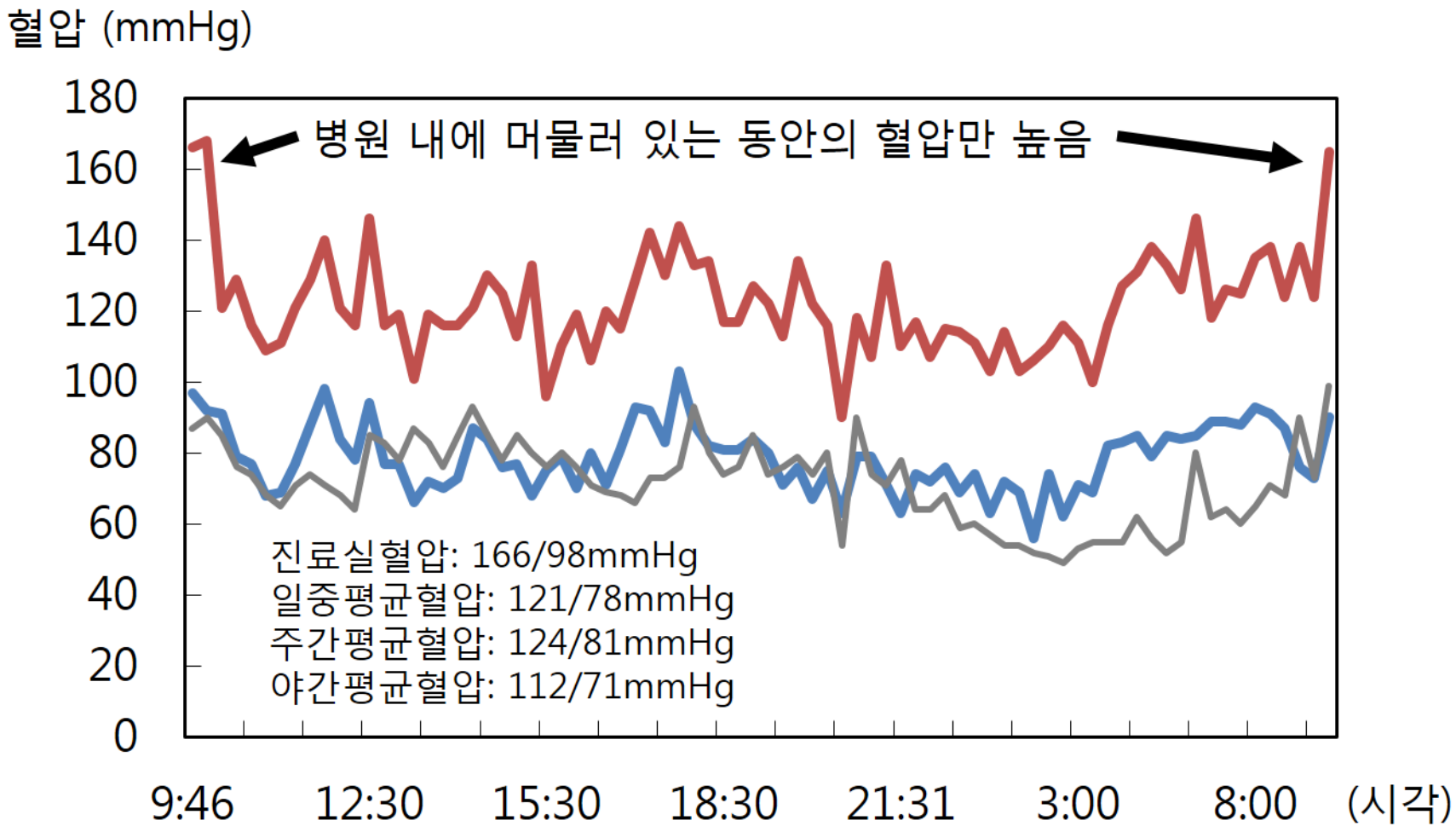
- **Possible white coat hypertension**
- Unusual variability of blood pressure
- Evaluation of nocturnal hypertension
- Evaluation of drug-resistant hypertension
- Determining the efficacy of drug treatment over 24h
- Diagnosis and treatment of hypertension in pregnancy
- Evaluation of symptomatic hypotension on various medications
- Evaluation of episodic hypertension or autonomic dysfunction
- **Possible masked hypertension**


General Population
Clinic BP (Conventional)
Clinic BP
<120/80mmHg
120-139/80-89mmHg
≥140/90mmHg
Definitely Normotensive
Questionable
Sustained Hypertensive or White Coat Hypertensive
Ambulatory BP
Ambulatory BP
Normal
High
Definitely Normotensive
Masked Hypertensive

What is white coat hypertension?

- Elevated blood pressure at the office
  - Lower blood pressure at home or with 24-h ambulatory blood pressure monitor
- Prevalence: 10% to 20%
- Poses elevated risk for overt hypertension and CVD
  - Lifestyle modifications and regular follow-up recommended
  - Pharmacologic treatment not recommended

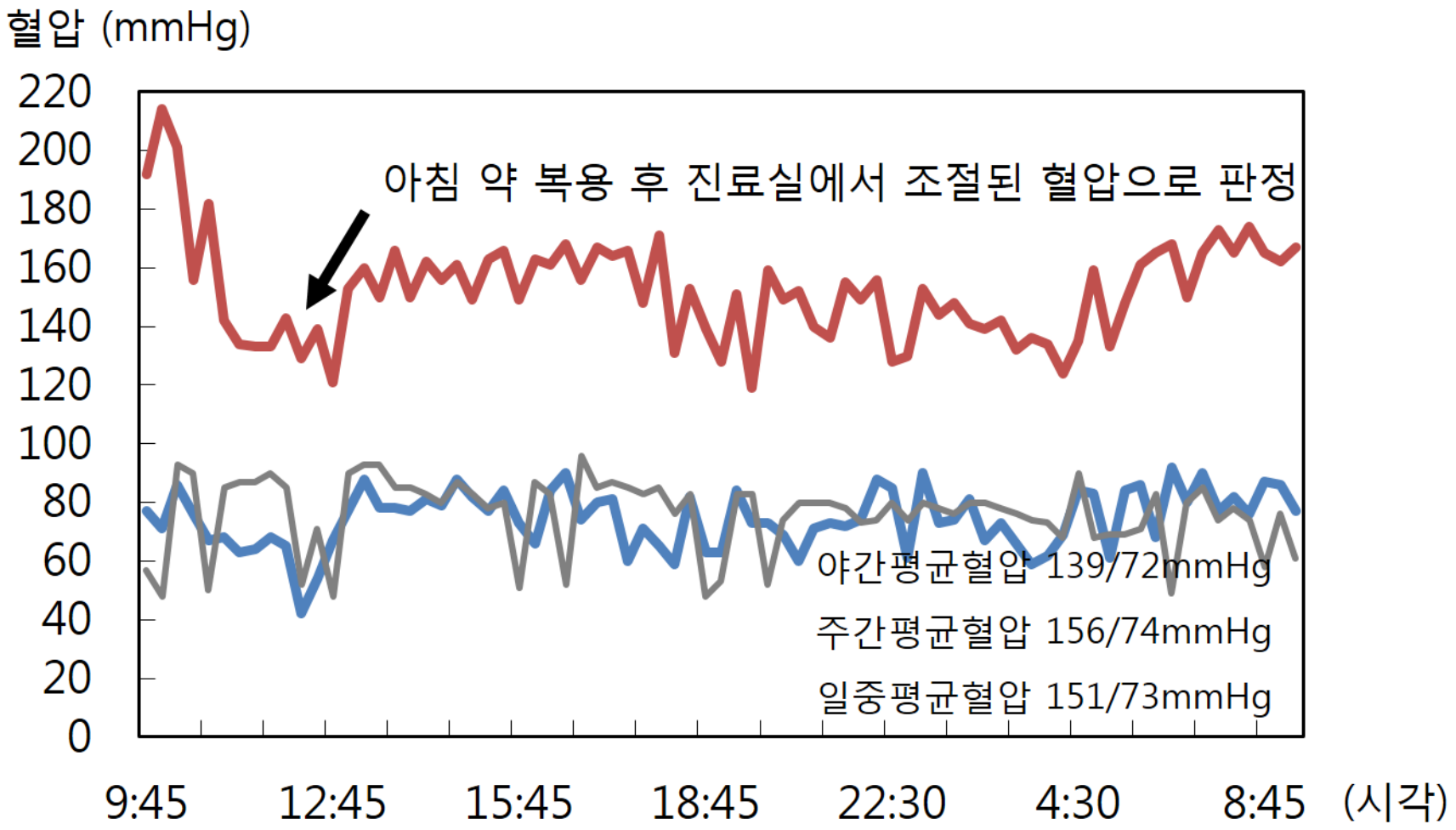
백의고혈압 (White-coat HTN)



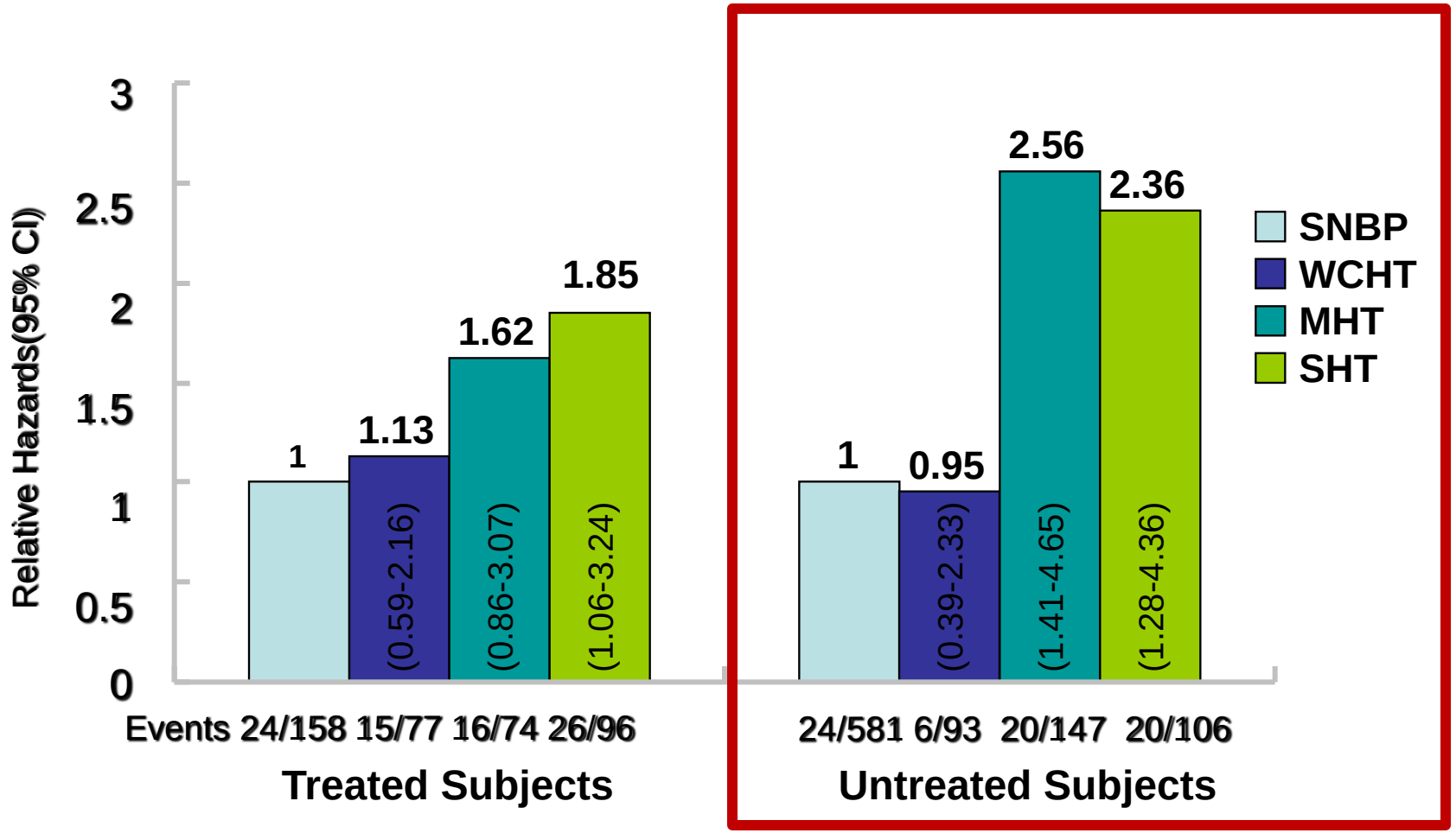
What is masked hypertension?

- Normotensive in the office but elevated blood pressure out of the office
  - Prevalence: 10% to 40%
  - Increases sustained hypertension and CV death risk
- Screen for suspected masked hypertension
  - Home readings
  - Ambulatory blood pressure monitoring

가면고혈압 (Masked HTN)



진료실 혈압은 정상인데 활동혈압이 높은 가면고혈압의 예후는 지속적 고혈압만큼 위험도가 높다. 가면고혈압은 치료받기 어렵고 비치료군에서 가면 고혈압은 지속적 고혈압과 동일하게 위험하다.



sustained normal blood pressure (SNBP), white-coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT)

J Am Coll Cardiol 2005;46:508-515

Important questions that remain unanswered in the area of masked hypertension

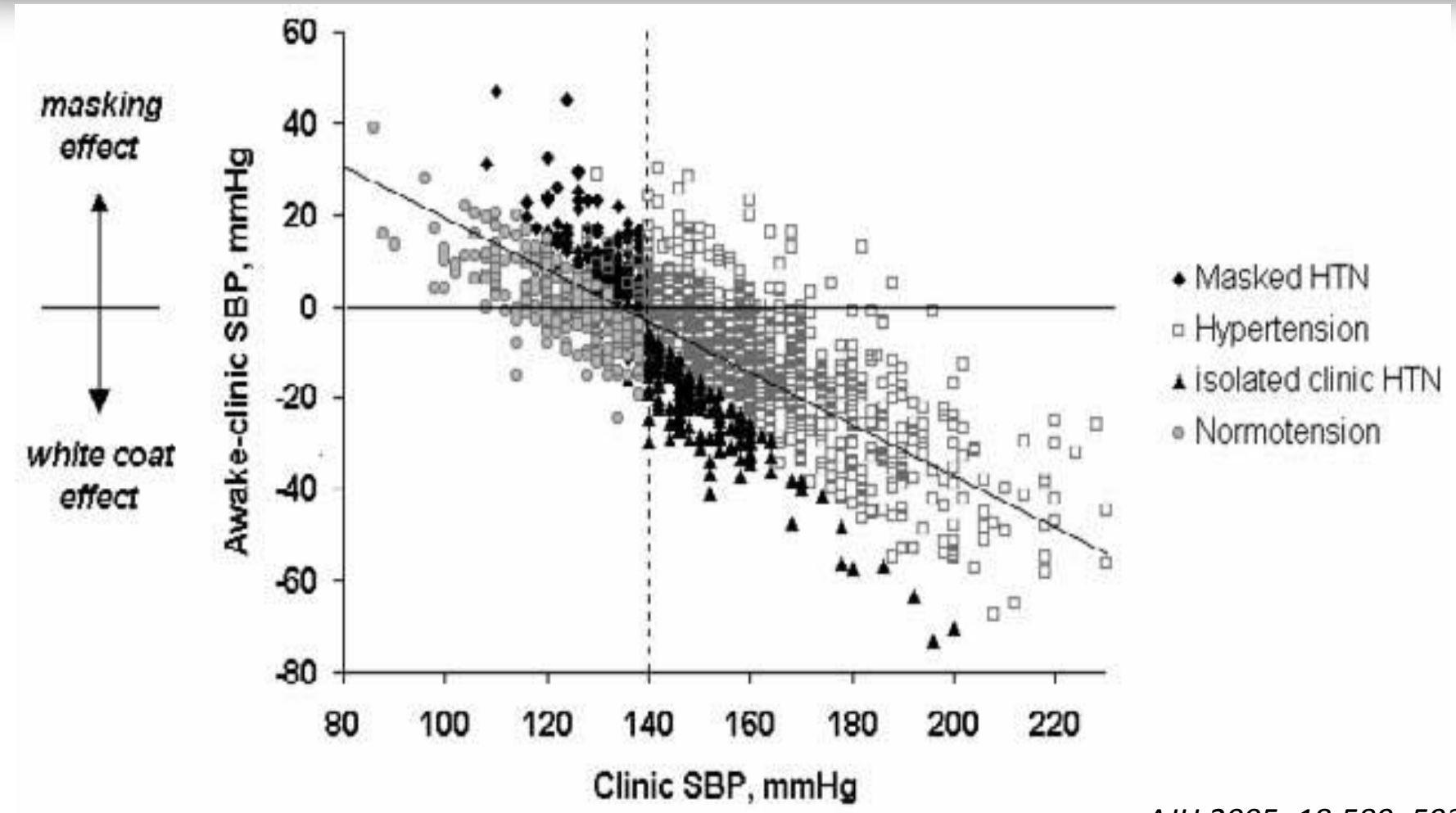
1. What **ambulatory BP cutpoint** should be used in the definition of masked hypertension?
2. **How many clinic (and over how many visits) and ambulatory readings** should be obtained for the diagnosis of masked hypertension?
3. **Which ambulatory BP monitoring time frame** (daytime, nighttime, or 24 hours) should be used in the definition of masked hypertension?
4. **Should manual or automated devices be used for** clinic BP assessment for the diagnosis of masked hypertension?
5. **What diagnostic strategy is most accurate and cost-effective** for the detection of masked hypertension?

Important questions that remain unanswered in the area of masked hypertension

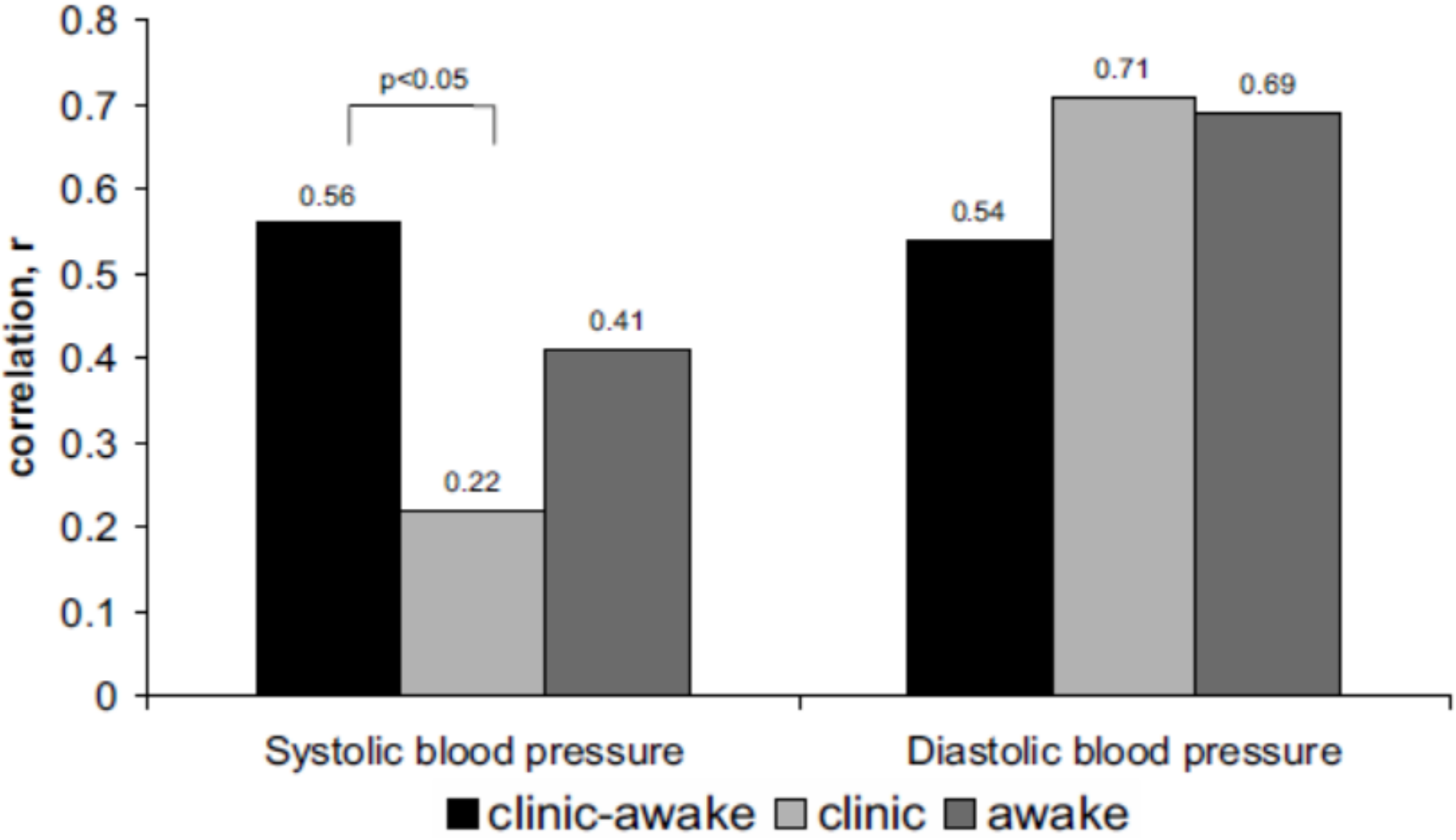
6. **Should home BP monitoring be used** to diagnose masked hypertension?
7. **Does treatment of masked hypertension improve clinical outcomes?**
8. Do patients with **masked (uncontrolled) hypertension taking antihypertensive medications have the same prognosis as patients with masked hypertension on no antihypertensive medications?**
9. Does treatment of these groups have similar **benefits in reducing end-organ damage and adverse clinical outcomes**?
10. What are the **mechanisms that underlie masked hypertension**?

In Clinical Practice, Masked Hypertension Is as Common as Isolated Clinic Hypertension: Predominance of Younger Men

Iddo Z. Ben-Dov, Liora Ben-Arie, Judith Mekler, and Michael Bursztyn



AJH 2005; 18:589–593



AJH 2005; 18:589–593

Review

Masked Hypertension: A Review

Thomas G. PICKERING[1)], Kazuo EGUCHI[1),2)], and Kazuomi KARIO[2)]

Table 1. Prevalence of Masked Hypertension in Various Studies

Author	Population	*N*	ABP criterion	Prevalence (%)
Imai *et al.* (*47*)	Population Ohasama	969	133/78	10
Sega *et al.* (*39*)	Population PAMELA	3,200	125/79	9
Björklund *et al.* (*48*)	Population 70-year-old men	578	135/85	14
Liu *et al.* (*9*)	Healthy volunteers	234	135/85	21
Selenta *et al.* (*33*)	Healthy volunteers	319	135/85	23

ABP, ambulatory blood pressure.

Hypertens Res 2007; 30: 479–488

Possible characteristics of individuals with masked hypertension

- relatively young age
- male sex
- stress or increased physical activity during the daytime
- smoking or drinking habits.
- treated hypertensive patients (in whom the prognosis is worse than predicted from the clinic pressure)
- children, in whom it may be a precursor of sustained hypertension

ORIGINAL ARTICLE

Predictors of the Home-Clinic Blood Pressure Difference: A Systematic Review and Meta-Analysis

James P. Sheppard,[1] Ben Fletcher,[1] Paramjit Gill,[2] Una Martin,[3] Nia Roberts,[4] and Richard J. McManus[1]

BACKGROUND
Patients may have lower (white coat hypertension) or higher (masked hypertension) blood pressure (BP) at home compared to the clinic, resulting in misdiagnosis and suboptimal management of hypertension. This study aimed to systematically review the literature and establish the most important predictors of the home-clinic BP difference.

METHODS
A systematic review was conducted using a MEDLINE search strategy, adapted for use in 6 literature databases. Studies examining factors that predict the home-clinic BP difference were included in the review. Odds ratios (ORs) describing the association between patient characteristics and white coat or masked hypertension were extracted and entered into a random-effects meta-analysis.

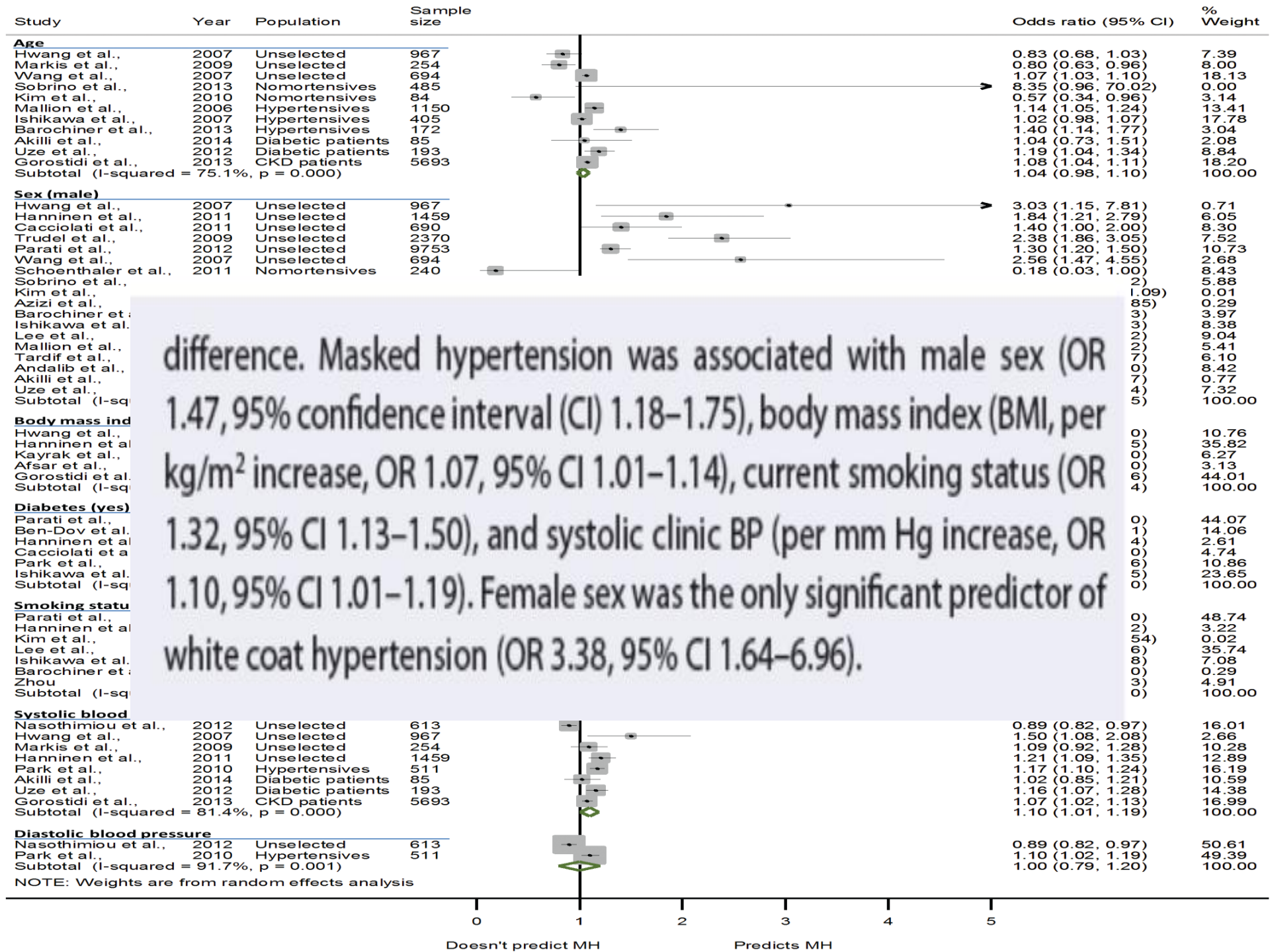
RESULTS
The search strategy identified 3,743 articles of which 70 were eligible for this review. Studies examined a total of 86,167 patients (47% female) and reported a total of 60 significant predictors of the home-clinic BP difference. Masked hypertension was associated with male sex (OR 1.47, 95% confidence interval (CI) 1.18–1.75), body mass index (BMI, per kg/m^2 increase, OR 1.07, 95% CI 1.01–1.14), current smoking status (OR 1.32, 95% CI 1.13–1.50), and systolic clinic BP (per mm Hg increase, OR 1.10, 95% CI 1.01–1.19). Female sex was the only significant predictor of white coat hypertension (OR 3.38, 95% CI 1.64–6.96).

CONCLUSIONS
There are a number of common patient characteristics that predict the home-clinic BP difference, in particular for people with masked hypertension. There is scope to incorporate such predictors into a clinical prediction tool which could be used to identify those patients displaying a significant masked or white coat effect in routine clinical practice.

Keywords: ambulatory blood pressure monitoring; hypertension; masked hypertension; primary care; white coat hypertension.

doi:10.1093/ajh/hpv157

American Journal of Hypertension 29(5) May 2016

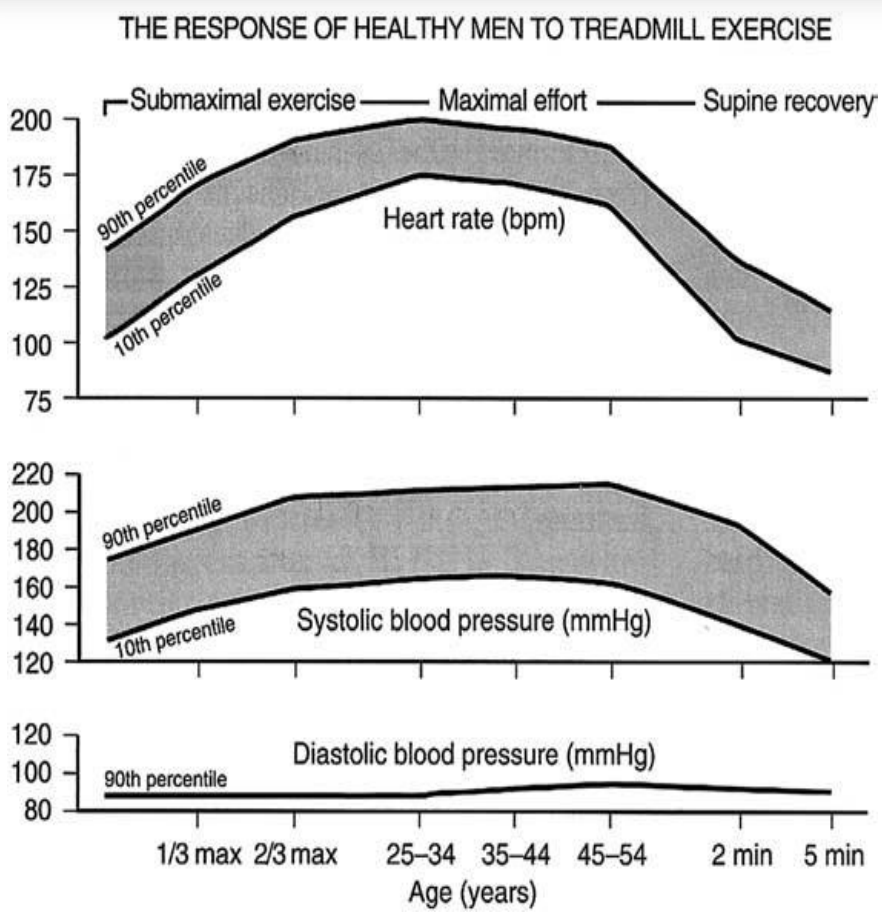


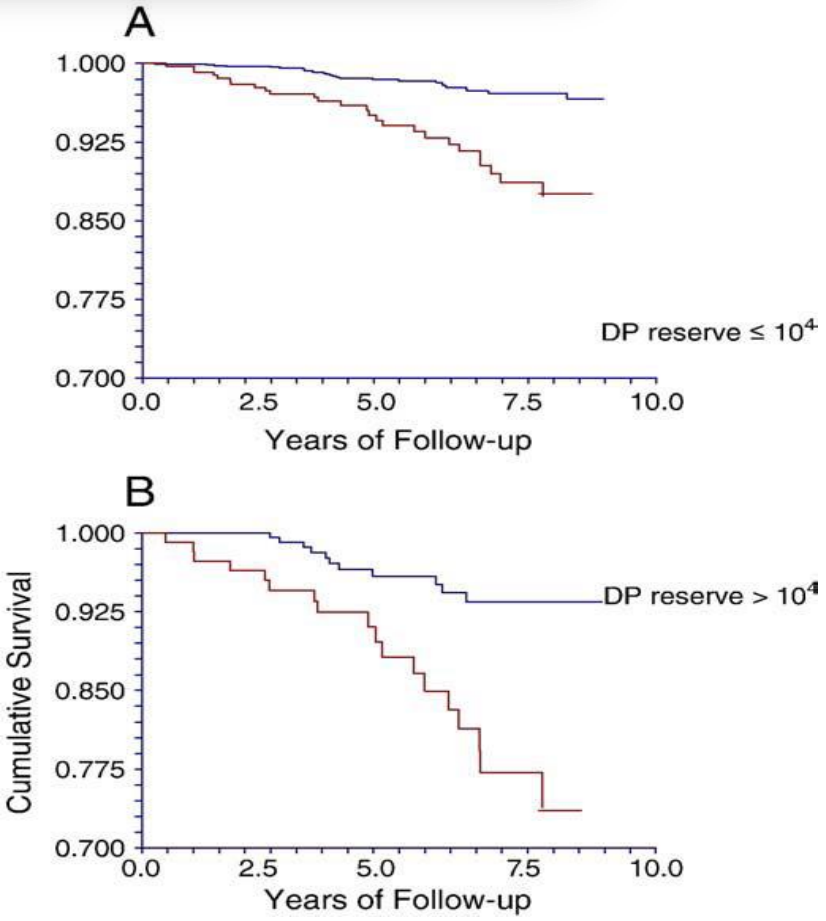
difference. Masked hypertension was associated with male sex (OR 1.47, 95% confidence interval (CI) 1.18–1.75), body mass index (BMI, per kg/m^2 increase, OR 1.07, 95% CI 1.01–1.14), current smoking status (OR 1.32, 95% CI 1.13–1.50), and systolic clinic BP (per mm Hg increase, OR 1.10, 95% CI 1.01–1.19). Female sex was the only significant predictor of white coat hypertension (OR 3.38, 95% CI 1.64–6.96).

Author	Population	N	Follow-up	Anti-hypertensive meds (%)	Out-of-clinic BP measure	Cutpoint for Ambulatory HTN*	Prevalence †	Outcome	Adjusted HR (95% CI)‡
Bjorklund et al (2003)[15]	70 years, men and women from Sweden (ULSAM)	578	5.9 yrs (mean)	No	Daytime ABPM	≥135/85 mmHg	12.0% (30.4%)	Death from CHD, stroke, and PVD, and nonfatal CHD and stroke	2.77 (1.15 to 6.68) for MHT, 2.94 (1.49 to 5.82) for SHT
Ohkubo et al (2005)[9]	≥40 years, Japanese men and women from Ohasama, Japan	1332	10.2 yrs (mean)	Yes (30%)	Awake ABPM	≥135/85 mmHg	16.6% (23.0%)	CV mortality and stroke morbidity CV mortality Stroke morbidity	2.13 (1.38–2.29) for MHT, 2.26 (1.49–3.41) for SHT. 1.88 (0.95–3.72) for MHT, 1.94 (1.04–3.61) for SHT. 2.17 (1.31–3.60) for MHT, 2.83 (1.77–4.54) for SHT.
Mancia et al (2006)[4]	25–74 years, Italian men and women from Monza (PAMELA study)	2024	12.3 yrs (average)	Yes (not stated)	24-hr ABPM and HBPM	≥125/79 mmHg (ABP) ≥135/83 mmHg (home)	8.5% (14.7%)	CV death All-cause mortality	Linear trend from WCT, MHT to SHT (P=0.0142) using ABPM. Linear trend from WCT, MHT to SHT (P=0.0084) using HBPM. Linear trend from WCT, MHT to SHT (P=0.1332) using ABPM. Linear trend from WCT, MHT to SHT (P=0.0560) using HBPM.
Hansen et al (2006)[7]	41–72 years, Danish men and women (MONICA 1 survey)	1700	9.5 yrs (mean)	Yes (9%)	Daytime ABPM	≥135/85	12.4% (19.7%)	CV mortality, ischemic heart disease, and stroke	1.52 (0.91–2.54) for MHT, 2.10 (1.45–3.06) for SHT
Hanninen et al (2012)[46]	44–74 years, Finnish men and women (Health 2000 study)	2046	7.5 yrs (mean)	Yes (23%)	HBPM	≥135/85	9.2% (17.9%)	CV events All-cause mortality	1.00 (0.60–1.67) for MHT, 1.88 (1.32–2.68) for SHT 1.28 (0.72–2.29) for MHT, 1.39 (0.90–2.16) for SHT

The Blood Pressure Response to Dynamic Exercise Testing: A Systematic Review

Vy-Van Le, Teferi Mitiku, Gannon Sungar, Jonathan Myers and Victor Froelicher





Journal of the American College of Cardiology
© 2000 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 36, No. 5, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(00)00903-7

Hypertension

Exercise BP Response in Subjects With High-Normal BP

Exaggerated Blood Pressure Response to Exercise and Risk of Future Hypertension in Subjects With High-Normal Blood Pressure

Nobuyuki Miyai, PHD,* Mikio Arita, MD, FACC,† Ikuharu Morioka, MD,* Kazuhisa Miyashita, MD,* Ichiro Nishio, MD,‡ Shintaro Takeda, MD†

Wakayama, Japan

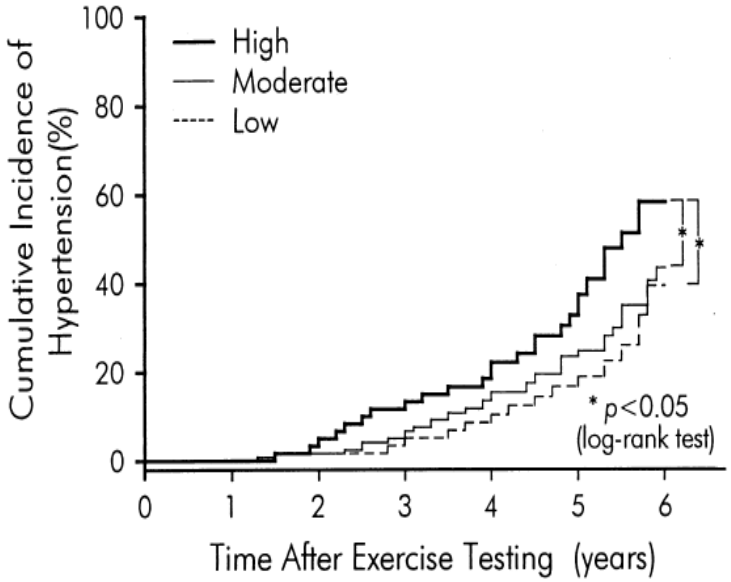


Figure 1. Cumulative incidence of hypertension in subjects with high-normal blood pressure as a function of three categories of systolic blood pressure change during ergometric exercise at baseline. Three categories are upper (high, n = 60), middle two (moderate, n = 120) and lower quartiles (low, n = 59). The subjects in the high category showed significantly higher incidence of hypertension compared with those in moderate and low categories over six years of follow-up.

J Clin Epidemiol Vol. 51, No. 1, pp. 29–35, 1998
Copyright © 1998 Elsevier Science Inc. All rights reserved.

ELSEVIER

0895-4356/98/$19.00
PII S0895-4356(97)00223-0

Exaggerated Blood Pressure Response to Dynamic Exercise and Risk of Future Hypertension

Charles E. Matthews,[1] Russell R. Pate,[1,] Kirby L. Jackson,[1] Dianne S. Ward,[1] Caroline A. Macera,[1] Harold W. Kohl,[2] and Steven N. Blair[2]*

[1]School of Public Health, University of South Carolina, Columbia, South Carolina; and [2]Cooper Institute for Aerobics Research, Dallas, Texas

an exaggerated rise by absolute numbers, **with values 210 mm Hg or greater for men and 190 mm Hg or greater for women**

European Journal of Internal Medicine 20 (2009) 366–368

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

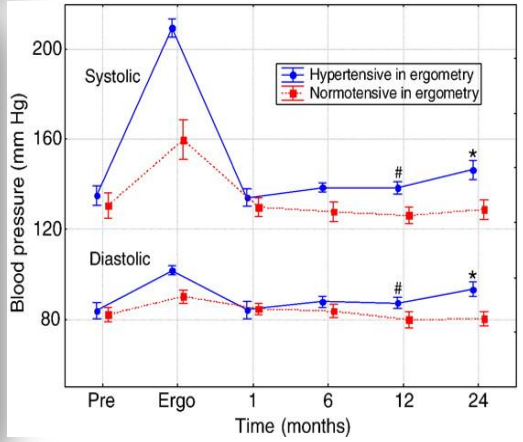
ELSEVIER

Original article

High blood pressure response to stress ergometry could predict future hypertension

Raymond Farah [a,*], Revital Shurtz-Swirski [b], Makhoul Nicola [c]

[a] Department of Internal Medicine B, Ziv Medical Center, Safed, Israel
[b] Eliachar Research Laboratory, Western Galilee Hospital, 22100, Nahariya, Israel
[c] Intensive Care Medicine, Western Galilee Hospital, 22100, Nahariya, Israel



Journal
Clinical and Experimental Hypertension ›
Volume 32, 2011 - Issue 8

Enter keywords, authors, DOI etc.

Submit an article | Back to journal

131 Views
0 CrossRef citations
0 Altmetric

Research Article

Exaggerated Blood Pressure Response to Exercise – A New Portent of Masked Hypertension

Mehmet Kayrak, **Ahmet Bacaksiz**, Mehmet Akif Vatankulu, Selim S. Ayhan, Zeynettin Kaya, Hatem Ari, ...Show all

Pages 560-568 | Received 25 Nov 2009, Accepted 29 Mar 2010, Published online: 23 Nov 2010

Download citation | http://dx.doi.org/10.3109/10641963.2010.503298

Masked hypertension

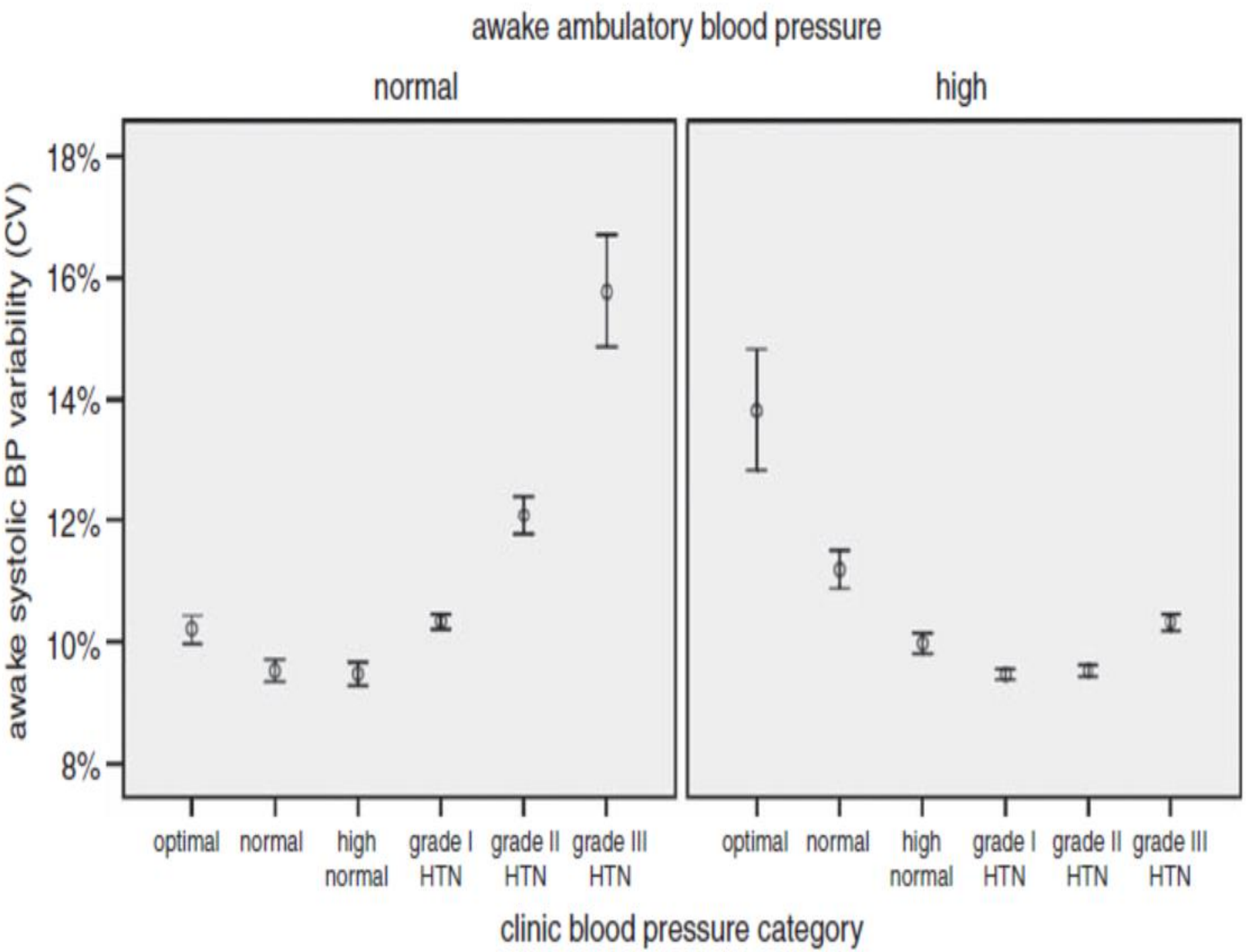
ORIGINAL ARTICLE

The role of blood pressure variability in misdiagnosed clinic hypertension

Amos Cahan[1], Iddo Z Ben-Dov[2], Judith Mekler[1] and Michael Bursztyn[1]

1. **Greater ambulatory BP variability carried increased risk for both false diagnosis of hypertension (OR: 2.09, 95% CI: 1.58–2.76), and missed clinic diagnosis of hypertension (OR: 1.86, 95% CI: 1.48–2.33).**
2. **The former was more striking in women, in whom high variability carried greater odds for false diagnosis of hypertension (OR: 2.76, 95% CI: 1.96–3.89).**
3. **Women with high BP variability are more susceptible to hypertension misdiagnosis.**
4. **It is possible that high BP variability contributes to the increased CV risk related to both masked hypertension and white coat hypertension**

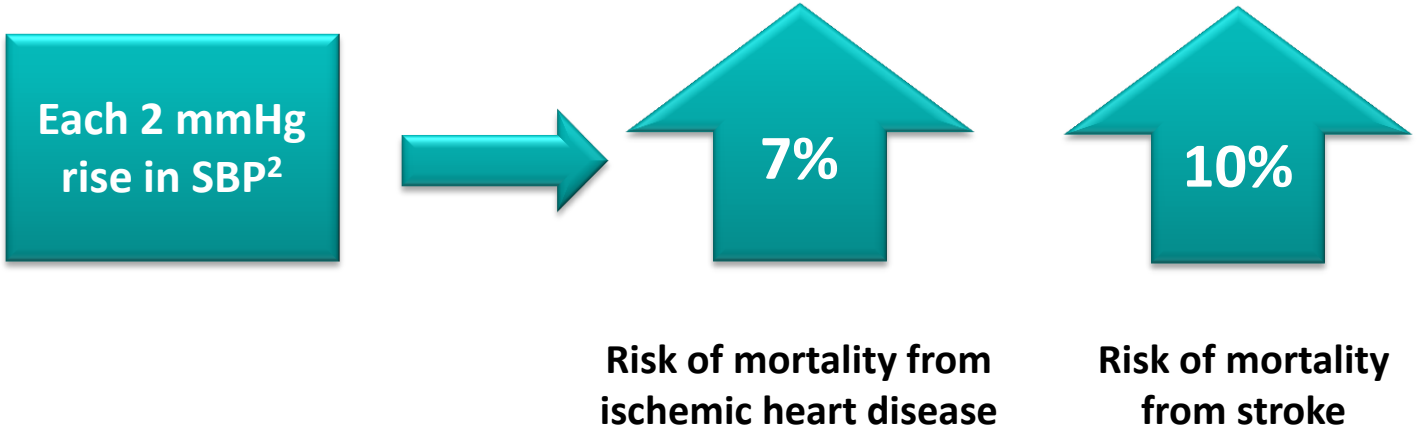
Hypertension Research (2011) **34**, 187–192; doi:10.1038/hr.2010.190; published online 11 November 2010


awake ambulatory blood pressure
normal
high
awake systolic BP variability (CV)
18%
16%
14%
12%
10%
8%
optimal
normal
high normal
grade I HTN
grade II HTN
grade III HTN
optimal
normal
high normal
grade I HTN
grade II HTN
grade III HTN
clinic blood pressure category

Fluctuation: Does Blood Pressure Variability (BPV) Matter?

Reducing BP prevents CV outcomes in patients with hypertension

- There is an undoubted and well-proven benefit in reducing mean BP in patients with hypertension to prevent CV events[1-3]



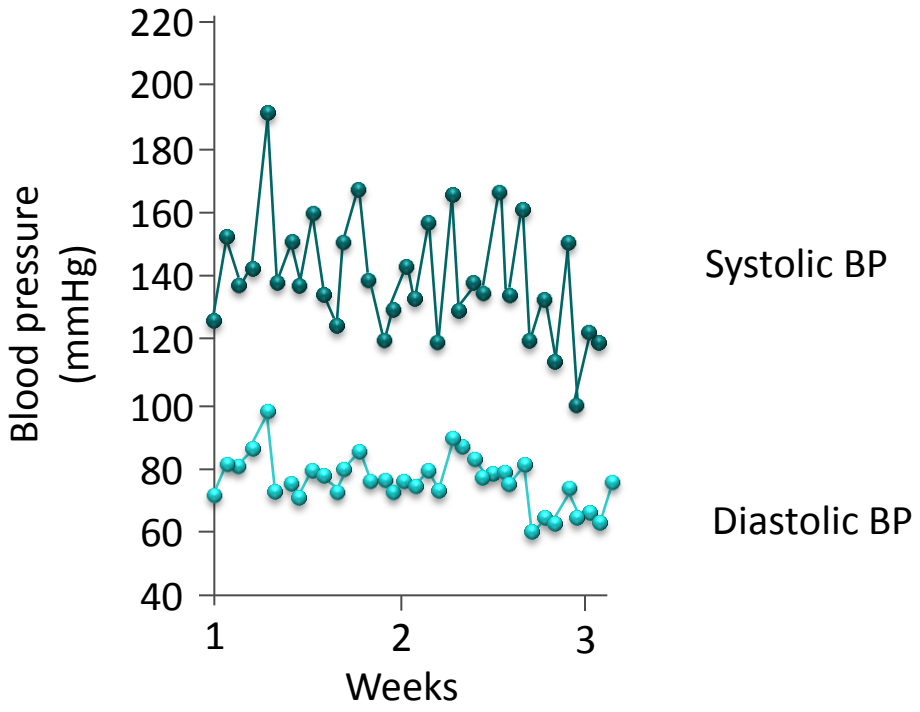
- BP goals for patients with hypertension with or without added CV risk are well established in the hypertension guidelines[1-3]

1. Mancia G, et al. *Eur Heart J*. 2007;28:1462-1536.
2. NICE Hypertension guidelines 2011 http://publications.nice.org.uk/hypertension-cg127.
3. Chobanian AV, et al. *JAMA*. 2003;289:2560-2572.

Recent evidence suggests that reducing BPV also prevents vascular outcomes

- How BP reduction is achieved and sustained is clinically important
- Reducing BP fluctuation over time as well as mean BP has recently been recognized as a potential target for improved management of hypertension to prevent vascular outcomes, particularly stroke[1,2]

Aim to reduce both BP and BPV



1. Muntner P et al. *Hypertension*. 2011;57:160-166.
2. Rothwell PM. *Lancet*. 2010;375:938-948.

What is BPV?

- BP normally fluctuates during the day and can vary from day to day in response to environmental challenges, eg, stress, activity, carrying out tasks, etc [1]

- Pronounced fluctuations in BP can occur over short- and long-term observation periods

- Episodic hypertension is common[2]
  - In a cohort of patients with previous TIAs, only 12% had stable hypertension, but **69% had episodic hypertension** (some systolic BP readings ≤140 mmHg, and some >140 mmHg)

1. Schillaci G, et al. *Hypertension*. 2011;58:133-135.
2. Rothwell PM. *Lancet*. 2010;375:938-948.

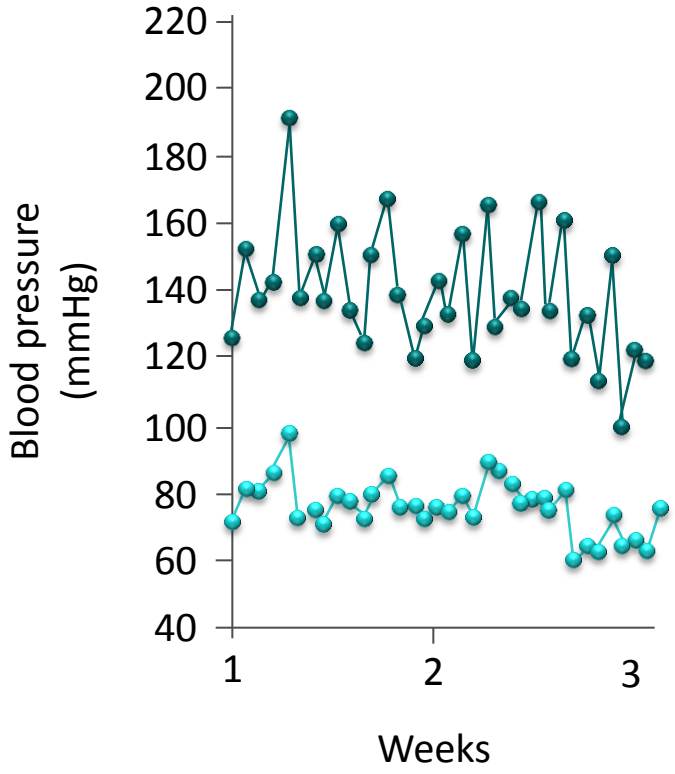
Measurement of BPV

1. over a 24-48 hour period with ABPM showing **hour-to-hour variability**

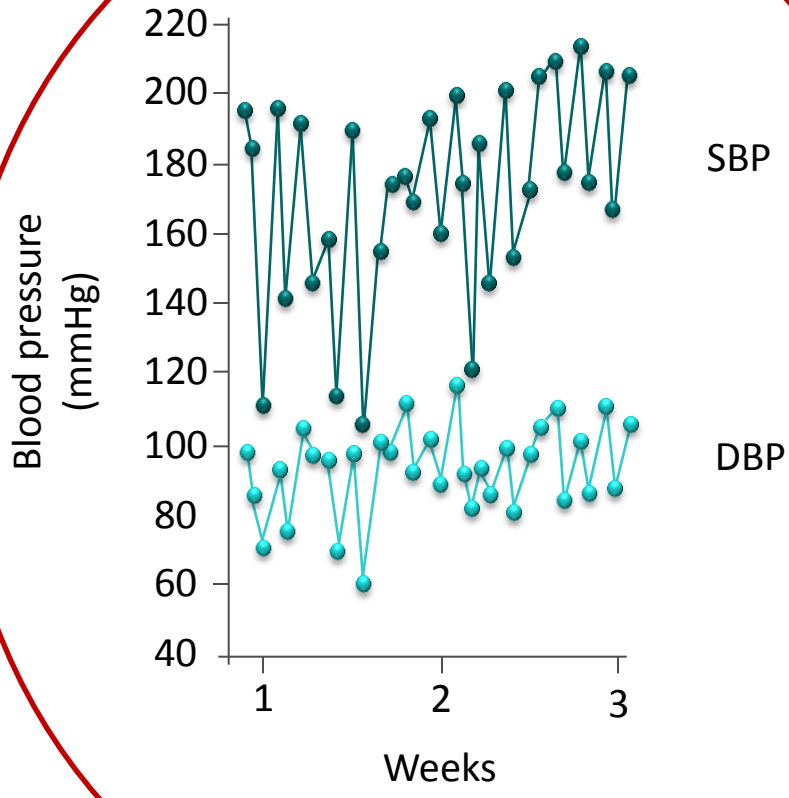
2. between clinic visits (**visit-to-visit variability)** in the short and long term

3. Home monitoring: **interday variation**

Within-individual BPV over time varies from one patient to another



Patient 1 with lower BPV



Patient 2 with higher BPV

Rothwell PM. *Lancet*. 2010;375:938-948.

Major determinants of increased BPV

24-hour ABPM BPV

Patients with hypertension, N = 577[1]
Baseline ABPM

- Age
- Systolic BP
- Heart rate variability

Visit-to-visit BPV

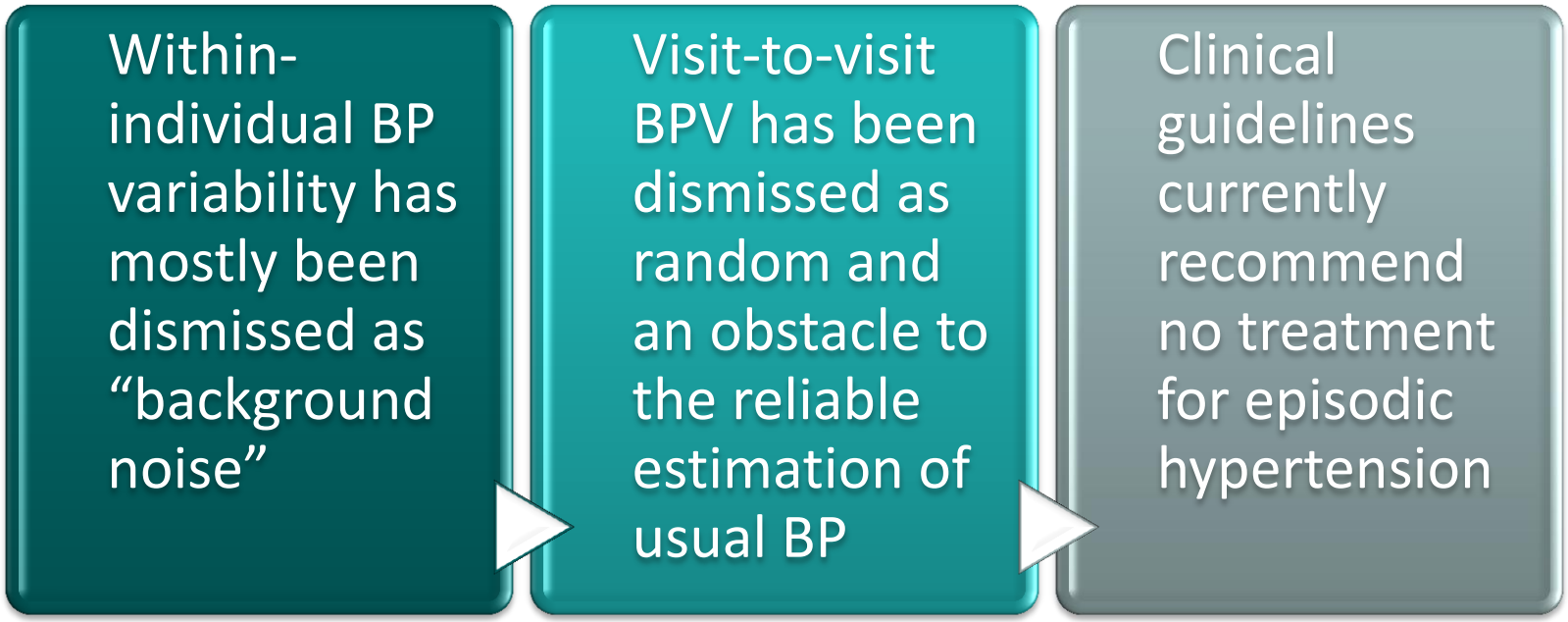
NHANES III population survey, N = 956[2]
Over 3 visits

- Age
- Female gender
- Systolic BP
- Pulse pressure
- History of myocardial infarction
- Use of ACEI

1. Zhang Y, et al. *Hypertension*. 2011;58:155-160.
2. Muntner P, et al. *Hypertension*. 2011; 57:160-166.

ABPM, ambulatory BP monitoring; ACEI, angiotensin-converting enzyme inhibitor; BP, blood pressure; BPV, BP variability.

BPV has been largely dismissed in the past



BP, blood pressure; BPV, BP variability.

Rothwell PM. *Lancet*. 2010;375:938-948.

Need to Treat : masked hypertension

1. It is important because it is not diagnosed by routine medical examinations, but carries **an adverse prognosis, both in terms of increased target organ damage and cardiovascular events.**
2. It is a true continuum of **sustained hypertension** rather than an aberrant measurement artifact.
3. an important role of **psychosocial factors** as a potential mechanism for the development
4. explained as a conditioned response to **anxiety** in office settings, and highlighted the role that diagnostic labeling plays in its development.

BPV can be monitored in the short term and in the long term

Beat-to-beat BPV	Second-to-second BPV	Minute-to-minute BPV	Hour-to-hour BPV	Day-to-day BPV	Visit-to-visit BPV
Computer analysis of BP tracing			24-hour ABPM Less commonly through home and clinic BP measurements	Home BP monitoring Less commonly through 24-hour ABPM or clinic measurements	Clinic BP measurements Less commonly through 24-hour ABPM and home BP measurements

- Level of assessment within a treatment group
  - **Within-individual variability**: multiple readings within each subject available
  - **Inter/between-individual variability**: single readings for each subject available


Blood pressure variability: A new target to slow
the progression of vascular damage

Increased 24-hour BPV has been associated with cardiovascular damage

- **In patients with mild to moderate hypertension, 24-hour BPV has been related to the rate and severity of target organ damage (TOD)**[1](108 patients, *P* <0.05)

- **Increased awake systolic BPV over a 24-hour period correlates with subclinical TOD**
  - Carotid IMT and LV mass index progressively increased across tertiles of awake systolic BPV over a 24-hour period (180 patients, *P* for trend 0.001 and 0.003, respectively)
  - Awake systolic BPV was identified as an independent predictor for these endpoints[2]

1. Parati G, et al. *J Hypertens*. 1987;5:93-98.
2. Tatasciore A, et al. *Hypertension*. 2007;50:325-332.

BP, blood pressure; BPV, BP variability; TOD, target organ damage.

Day-to-day BPV is an independent predictor of CV risk

- The Ohasama observational study of 2455 Japanese residents concluded that day-to-day BPV is an independent predictor of CV and stroke mortality after adjustment for mean BP
  - Home BP and heart rate were measured once every morning for 26 days
  - Median follow-up period of 11.9 years

	*HR	*P*-value
Prognostic effect of increase in systolic BPV of +1 between-subject SD		
CV mortality	1.27	0.002
Stroke mortality	1.41	0.0009
Cardiac mortality	1.13	NS

*Adjusted for sex, age, obesity, smoking and drinking, history of CV disease, diabetes mellitus, hyperlipidemia and treatment with antihypertensive drugs, systolic BP, and heart rate.

Kikuya M, et al. *Hypertension*. 2008;52:1045-1050.

Atherosclerosis 233 (2014) 19–26

Contents lists available at ScienceDirect

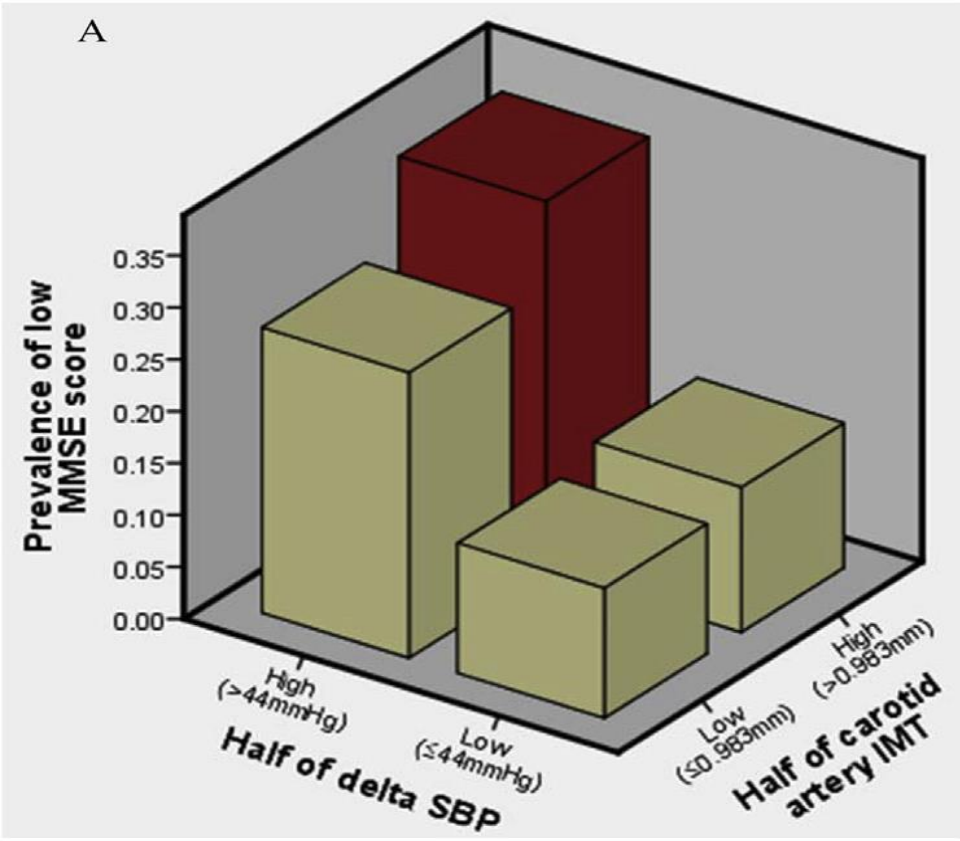
Atherosclerosis

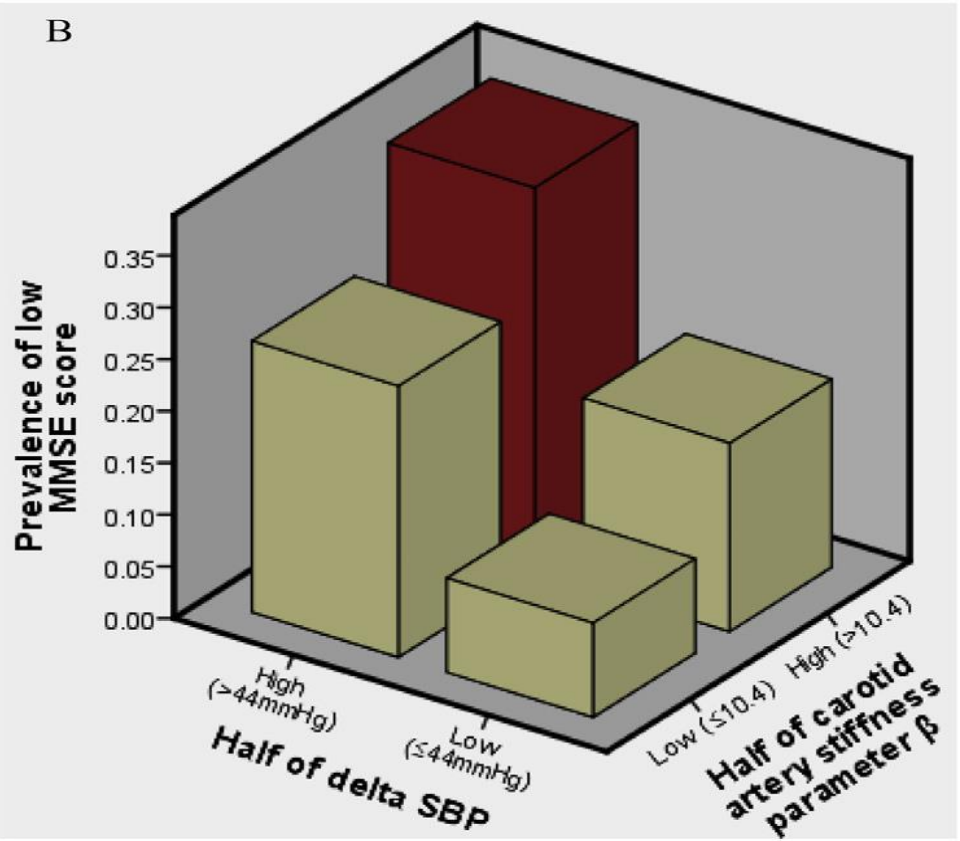
journal homepage: www.elsevier.com/locate/atherosclerosis

Visit-to-visit blood pressure variability in the elderly: Associations with cognitive impairment and carotid artery remodeling

Michiaki Nagai, Satoshi Hoshide, Mami Nishikawa, Shimpo Masahisa, Kazuomi Kario*

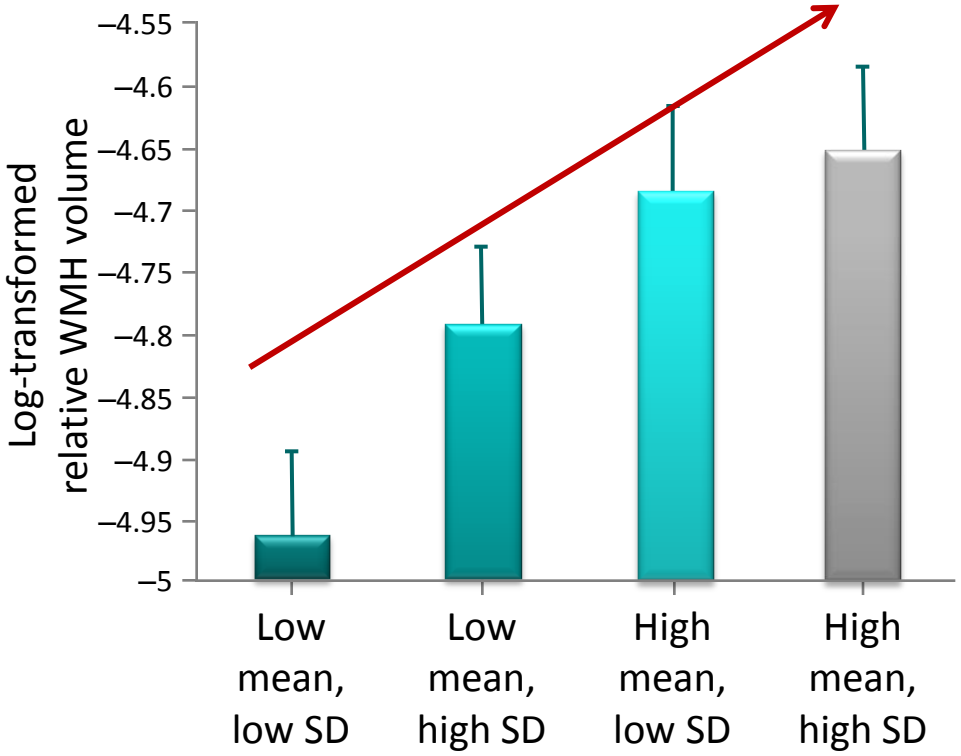
Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, Yakushiji 3311-1, Shimotsuke, Tochigi 329-0498, Japan

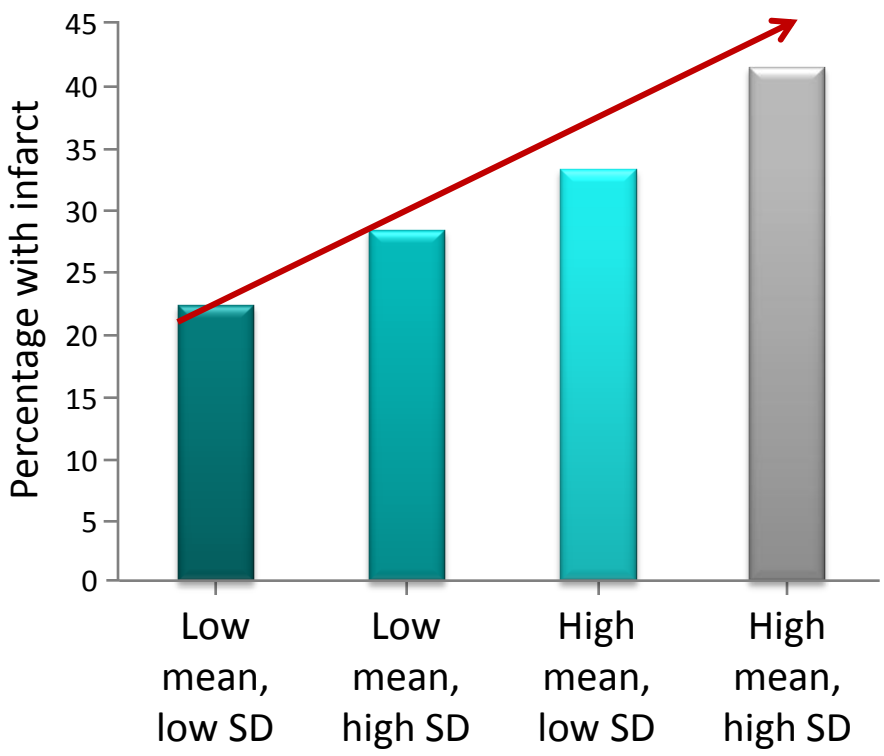




Increased risk of cerebrovascular disease with increased BP and BPV

- In the WHICAP study, cerebral WMH increased across 4 groups in a linear fashion – ie, the higher the mean/SD, the higher the WMH
- Increased mean BP and BPV were associated with increased risk of infarction





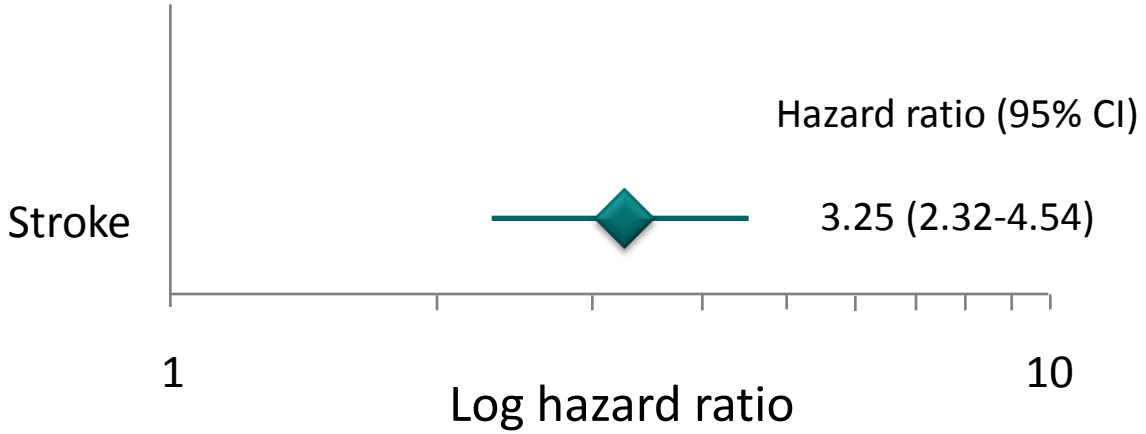
BP, blood pressure; BPV, BP variability; WMH, white matter hyperintensity.

Brickman AM, et al. *Arch Neurol*. 2010;67:564-569.

Visit-to-visit systolic BPV is a predictor for stroke in patients with hypertension

- ASCOT-BPLA trial of 19,257 patients aged 40 to 79 years with hypertension and at least 3 other CV risk factors
  - ***Visit-to-visit systolic BPV on-treatment* was a strong predictor of stroke and coronary events, independent of mean systolic BP in-clinic or on ABPM***

Patients in top-decile of BPV compared with first decile



*Atenolol and amlodipine treatment groups.

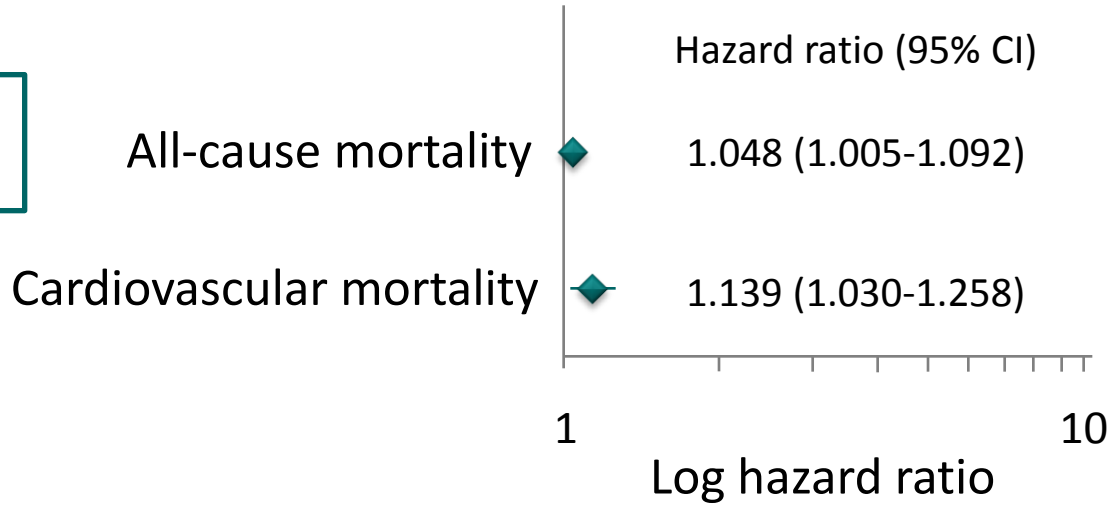
Rothwell PM, et al. *Lancet* .2010;375:895-905.

Visit-to-visit BPV predicts CV mortality in patients with type 2 diabetes

- Cohort study of 2161 patients with type 2 diabetes with follow-up period of 5.5 years

Prognostic significance of systolic BPV

Prognostic significance of pulse pressure variability

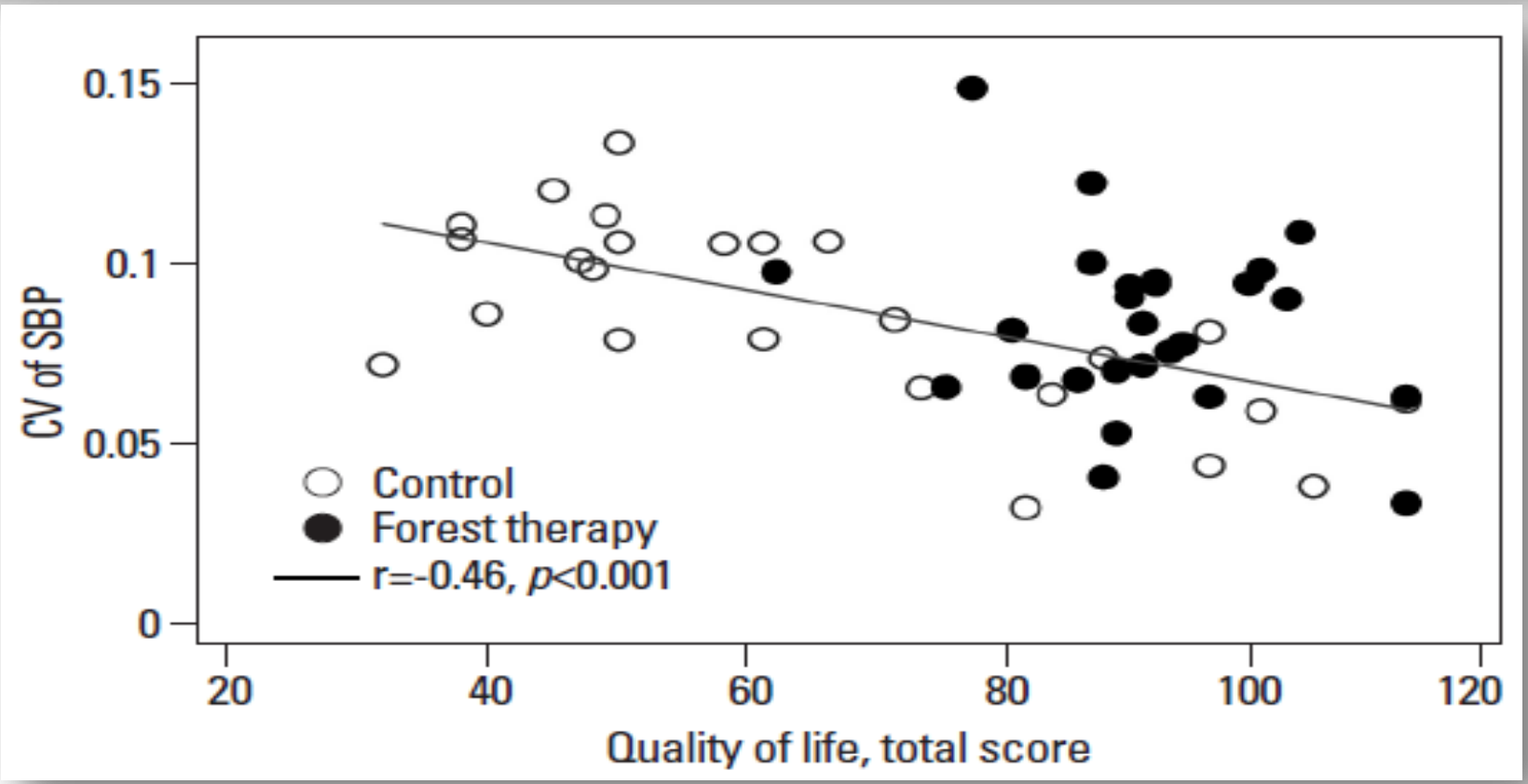


Hsieh Y-T, et al. *Eur J Clin Invest*. 2012;42:245-253.

Original Article | http://dx.doi.org/10.3349/ymj.2014.55.2.374 pISSN: 0513-5796, eISSN: 1976-2437 | Yonsei Med J 55(2):374-378, 2014

Relationship between Blood Pressure Variability and the Quality of Life

Jidong Sung,[1,2] Jong-Min Woo,[3,4] Won Kim,[3,4] Seoung-Kyeon Lim,[5] and Ahn-Soo Chung[4]

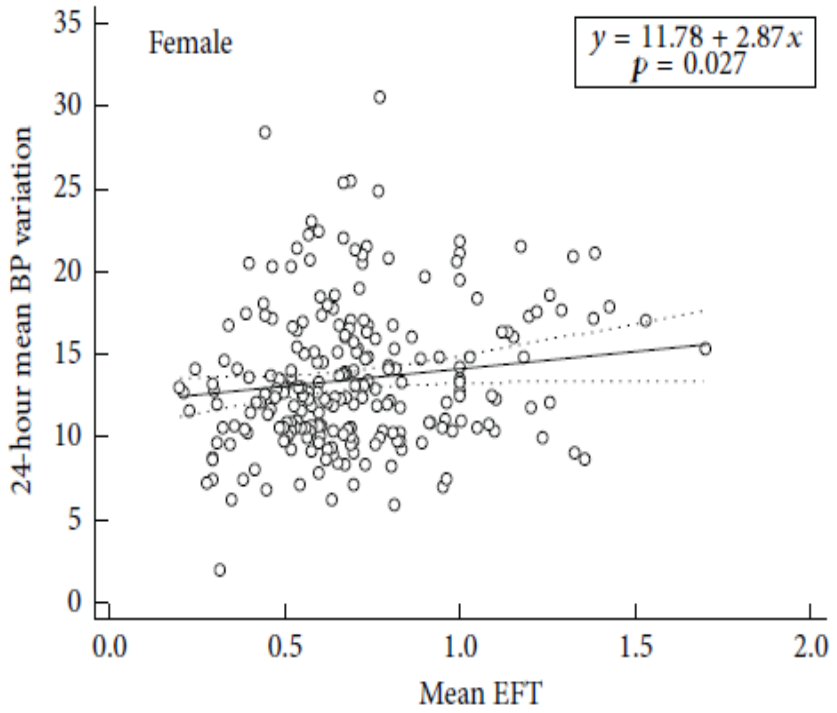


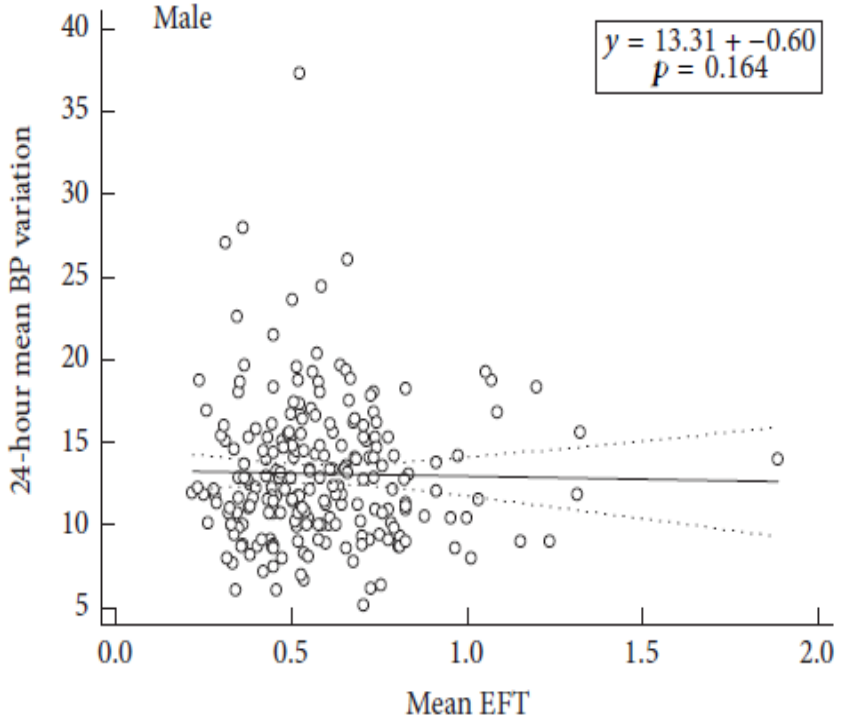
Hindawi Publishing Corporation
Journal of Diabetes Research
Volume 2015, Article ID 924539, 10 pages
http://dx.doi.org/10.1155/2015/924539

Research Article

Impact of Gender on the Association of Epicardial Fat Thickness, Obesity, and Circadian Blood Pressure Pattern in Hypertensive Patients

In Kyoung Shim, Kyoung-Im Cho, Hyun-Su Kim, Jung-Ho Heo, and Tae Joon Cha





nature publishing group

ORIGINAL CONTRIBUTIONS

Masked Hypertension, Endothelial Dysfunction, and Arterial Stiffness in Type 2 Diabetes Mellitus: A Pilot Study

Kageumi Takeno[1], Tomoya Mita[1,2], Shiho Nakayama[1], Hiromasa Goto[1,2], Koji Komiya[1], Hiroko Abe[1], Fuki Ikeda[1], Tomoaki Shimizu[1], Akio Kanazawa[1], Takahisa Hirose[1,3], Ryuzo Kawamori[4] and Hirotaka Watada[1–5]

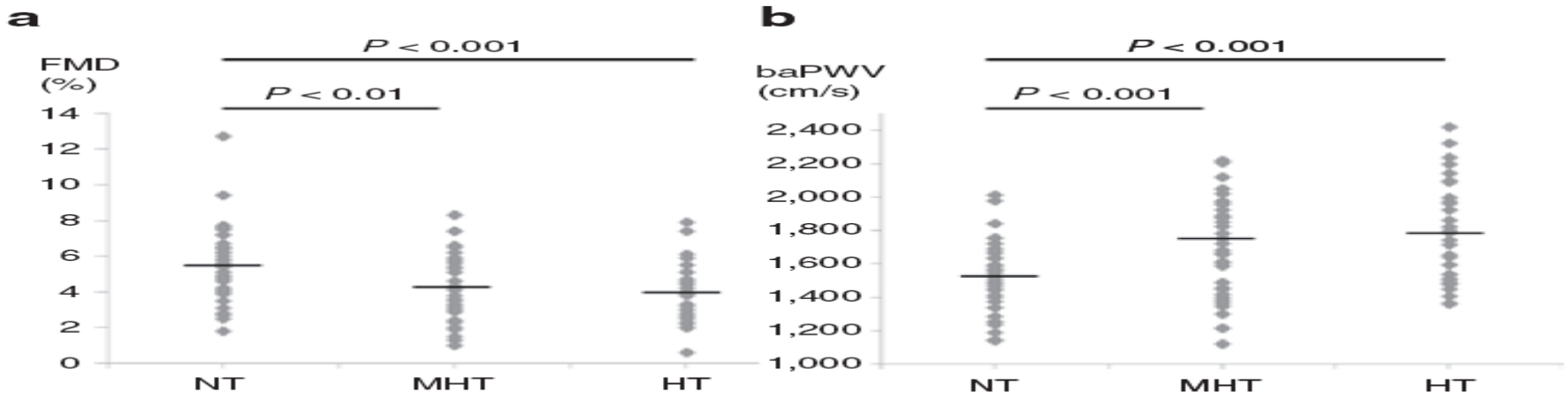


Figure 1 | FMD and baPWV in NT group, MHT group, and HT group. baPWV, brachial-ankle pulse wave velocity; FMD, flow-mediated dilatation; HT, hypertension; MHT, masked hypertension; NT, normotensive.

American Journal of Hypertension, 2012

Epidemiology/Population

Prognosis of White-Coat and Masked Hypertension

International Database of Home Blood Pressure in Relation to Cardiovascular Outcome

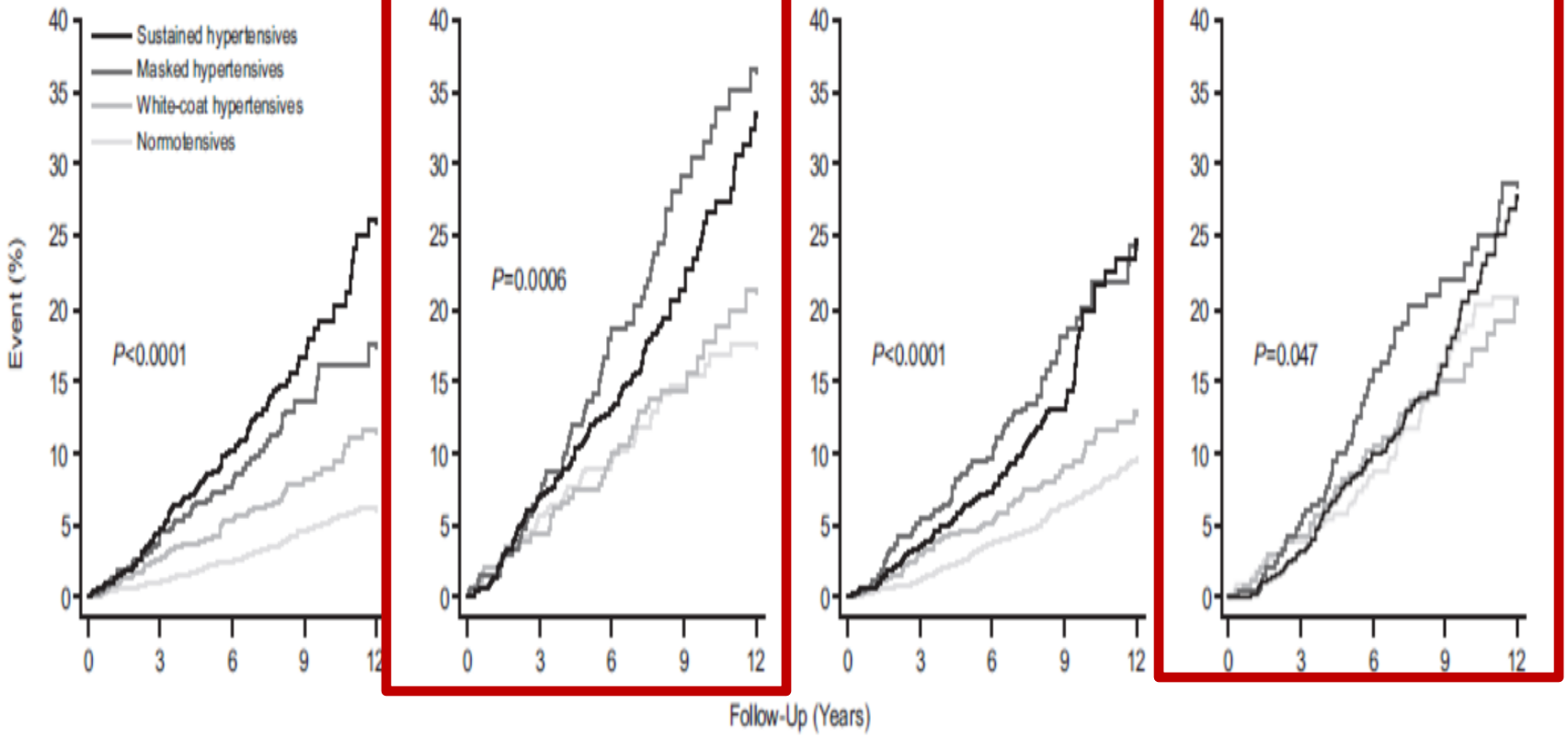
George S. Stergiou, Kei Asayama, Lutgarde Thijs, Anastasios Kollias, Teemu J. Niiranen, Atsushi Hozawa, José Boggia, Jouni K. Johansson, Takayoshi Ohkubo, Ichiro Tsuji, Antti M. Jula, Yutaka Imai, Jan A. Staessen;
on behalf of the International Database on HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO) Investigators

…..treated subjects with masked hypertension (low office and high home BP; 1.76; 95% CI [1.23–2.53]; P=0.002) and uncontrolled hypertension (high office and home BP; 1.40; 95% CI [1.02–1.94]; P=0.04) had higher CV risk than treated controlled patients.

In conclusion, white-coat hypertension assessed by home measurements is a CV risk factor in untreated but not in treated subjects probably because the latter receive effective treatment on the basis of their elevated office BP.

In contrast**, masked uncontrolled hypertension is associated with increased CV risk in both untreated and treated patients, who are probably undertreated because of their low office BP.**

Hypertension. 2014;63:675-682.



N° at risk																				
Sustained HT	924	860	627	142	60	661	600	382	117	62	924	888	678	161	67	661	636	421	133	77
Masked HT	404	368	305	128	56	232	210	138	61	42	404	381	319	139	61	232	220	150	73	53
White-coat HT	695	657	568	263	122	230	214	170	80	50	695	667	586	273	130	230	220	179	86	57
NT	2984	2904	2642	1302	665	328	301	237	134	98	2984	2926	2687	1340	686	328	311	247	144	103

Hypertension. 2014;63:675-682.

Home and ambulatory BP are not interchangeable but probably complementary methods

Novelty and Significance

What Is New?

- Most of the evidence on the prognostic relevance of white-coat and masked hypertension is based on ambulatory BP monitoring. This article based on a database including 6458 participants from 5 population studies provides evidence on the prognostic significance of these conditions detected by home BP measurements.
- The database allowed separate powered analyses of the prognostic relevance in untreated and treated subjects.

What Is Relevant?

- The prognostic relevance of white-coat and masked hypertension detected by home measurements differs in untreated and treated subjects.
- Masked hypertension is associated with increased cardiovascular risk in both untreated and treated subjects.
- In contrast, white-coat hypertension is a cardiovascular risk factor in untreated but not in treated subjects. This finding is in the same direction with published data with ambulatory BP monitoring, although the latter did not reach significant difference compared with normotension.

Summary

Masked hypertension detected by home BP measurements is associated with increased cardiovascular risk in both untreated and treated subjects. However, white-coat hypertension is a cardiovascular risk factor in untreated but not in treated subjects.

Home BP monitoring might not be interchangeable with ambulatory monitoring for the detection and prognosis of white-coat hypertension in untreated subjects.

Hypertension. 2014;63:675-682.

Need to Treat : masked hypertension

1. **Out-of-clinic monitoring of BP** would apply particularly to **smokers and those with BP in the prehypertensive range**.
2. Because masked hypertension might be that of a continuum from **prehypertension (based on office BP measurement) to masked hypertension (based on ambulatory BP)** and finally to **sustained hypertension (based on both office and ambulatory BP**), prehypertensive patients may progress to masked hypertension.
3. **Subsequently, patients who are prehypertensive should be screened for masked hypertension and treated**.

Take Home Message

- Masked hypertension is associated with an increased risk of CV morbidity and mortality compared to sustained normotension.
- The prevalence of masked hypertension ranges from 15 to 30% with non-elevated clinic BP, who may be at increased risk for heart disease and stroke due to masked hypertension.
- One practical point is that we should continue to follow such people rather than dismissing them, and encourage out-of-clinic monitoring of BP.
- This would apply particularly to smokers and those with BP in the prehypertensive range.

Take Home Message

- Fundamental issues that need to be addressed include standardizing the definition for diagnosis, comparing the **cost-effectiveness of strategies for screening and detection, gaining further insight into the mechanisms that underlie masked hypertension, and determining the optimal treatment strategy** for treating masked hypertension.

- Until these issues are addressed, masked hypertension will likely remain outside mainstream clinical care, and this public health concern will be largely unaddressed

T H A N K Y O U

Home BP monitoring

- 진료실혈압보다 심혈관질환의 발생을 더 정확히 예측함
- 고혈압의 진단 뿐만 아니라 고혈압의 관리에 중요함
- 환자의 순응도와 치료의 적극성을 높일 수 있음
- 표준화된 측정으로 활동혈압측정을 대체할 수 있음

Home BP monitoring

- **표준적인 방법으로 측정하도록 교육해야 함:**
  http://www.koreanhypertension.org/board/list.html?code=notice&num=398
- **정확성이 검증된 위팔 자동혈압계를 사용함.**
- **특히 처음 고혈압을 진단할 때 환자 교육이 중요함.**
- **측정 시각: 아침:** 기상 후 1시간 이내, 소변 본 후, 고혈압약 복용 전

  저녁: 잠자리 들기 전

  이외 측정이 필요하다고 판단된 경우
- **측정 빈도**: 측정당 2회 이상
- **측정 기간** : 처음 진단 할 때는 적어도 1주일 동안,

  치료 결과 평가 시 적어도 외래방문 직전 5-7일간