Unpacking Recent Hypertension Guidelines

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August 21, 2014

Disclosures: Member of Panel Appointed to the Eighth Joint National Committee (JNC 8)

Why is the debate about blood pressure goals important?

Number of Avoidable Deaths from CVD deaths – United States, 2001 -2010

Age Groups	CVD Deaths in 2001	CVD Deaths in 2010	Percent Decline in Death Rate ($p < .05$)
35-54	46,426	43,884	**-6%**
55-64	61,105	65,680	**-27%**
65-74	117,662	87,741	**-37%**

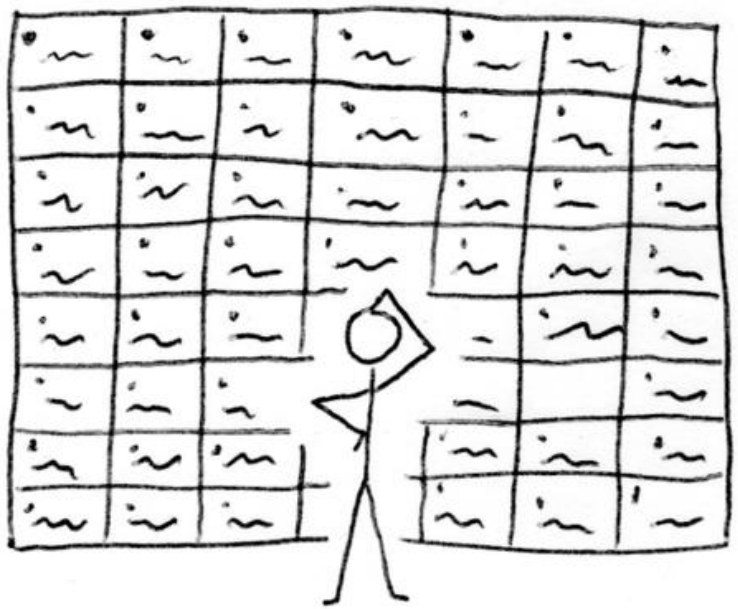
 MMWR 9/26/2013 Schieb LJ

Rates of Avoidable Deaths Data Illustrates Murray's **Eight Americas: new perspectives on U.S. health disparities.**

Race/Ethnicity and sex	2001 Rates per 100,000	2010 (% Decline over 10 years p < .05)
Asian Females	36	22 (-39%) Asian men 47
White Men	112	81 (-28%)
Hispanic Men	93	63 (-28%)
Black Men	200	143 (-28%)

MMWR 9/6/2013 Schieb

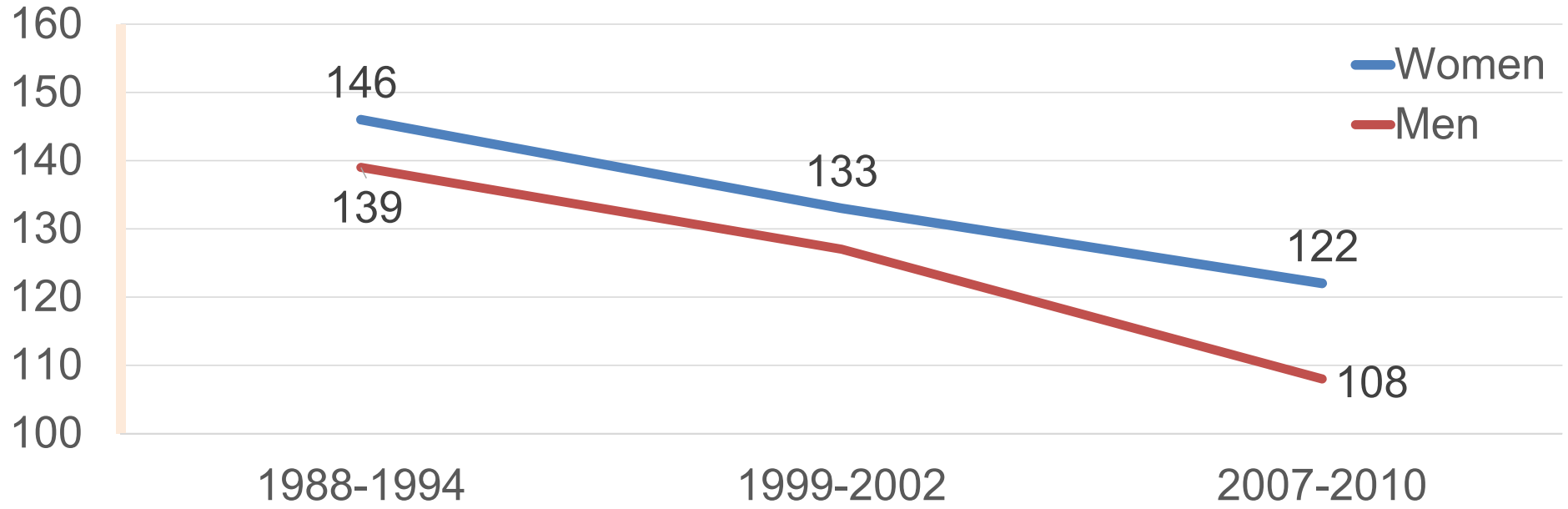
Disentangling Complexity is Challenging – Why did CVD decrease and how can we make additional progress ?



http://www.smallmanart.com/2012/07/05/disentangling-complexity.html - © Stefano Masini 2012

A Partial Answer: Trends in LDL 1988-2010

Age Specific LDL mg/dL in Adults 60-69. Carroll et al. 2012 JAMA



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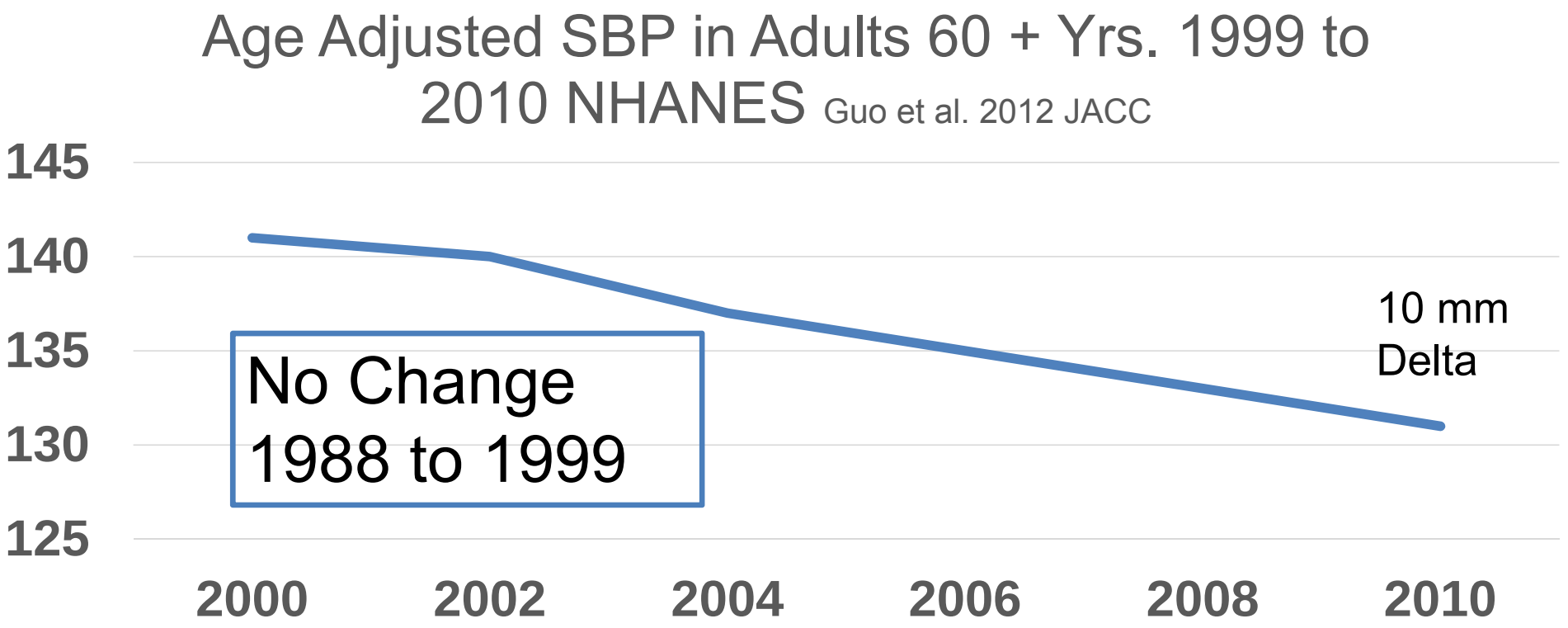
Another Contributor with a Different Secular Pattern



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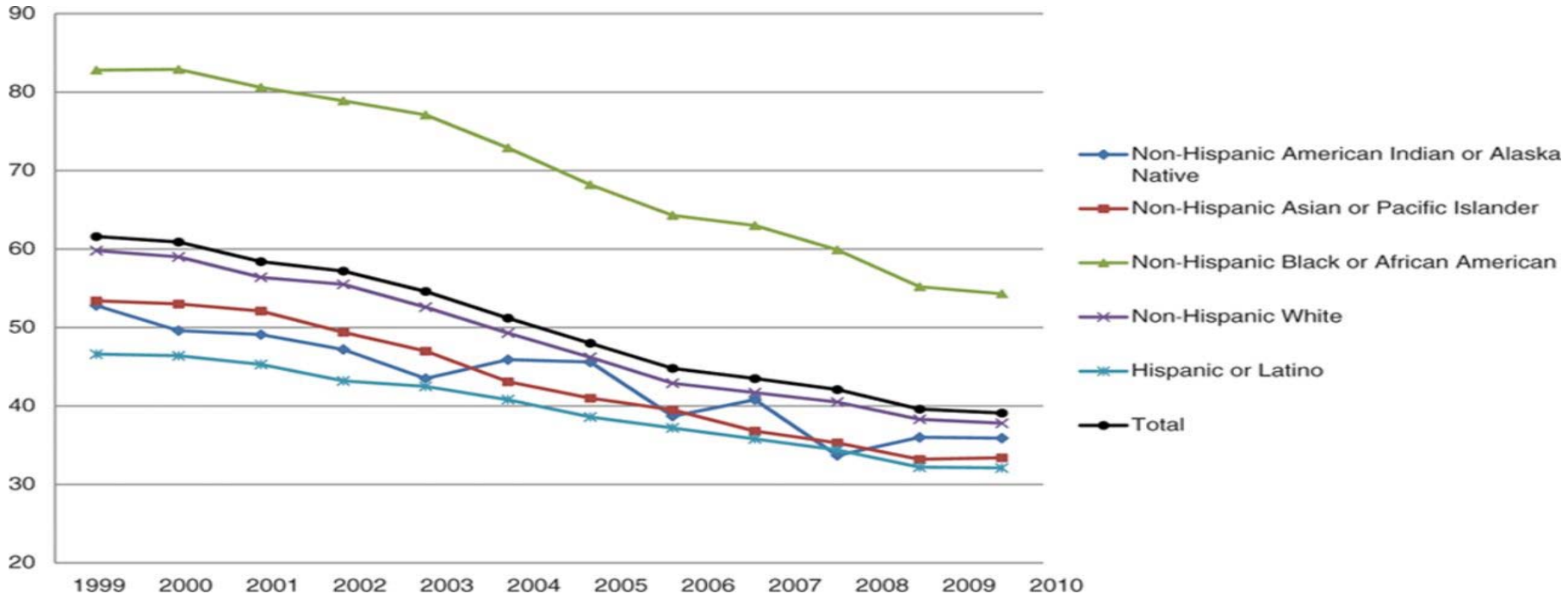
Stroke is very important in this debate

- Why
  - Relationship is strongest between hypertension as a cause of stroke and “ a fall in stroke rates would therefore be expected to into a decreased risk of dementia” Walter Koroshetz – Acting Director NINDS Nature 510 June 26 2014

Age-adjusted death rates for cerebrovascular disease by race and by year: United States, 1999 to 2010.



Lackland D T et al. Stroke. 2014;45:315-353

American Heart Association.

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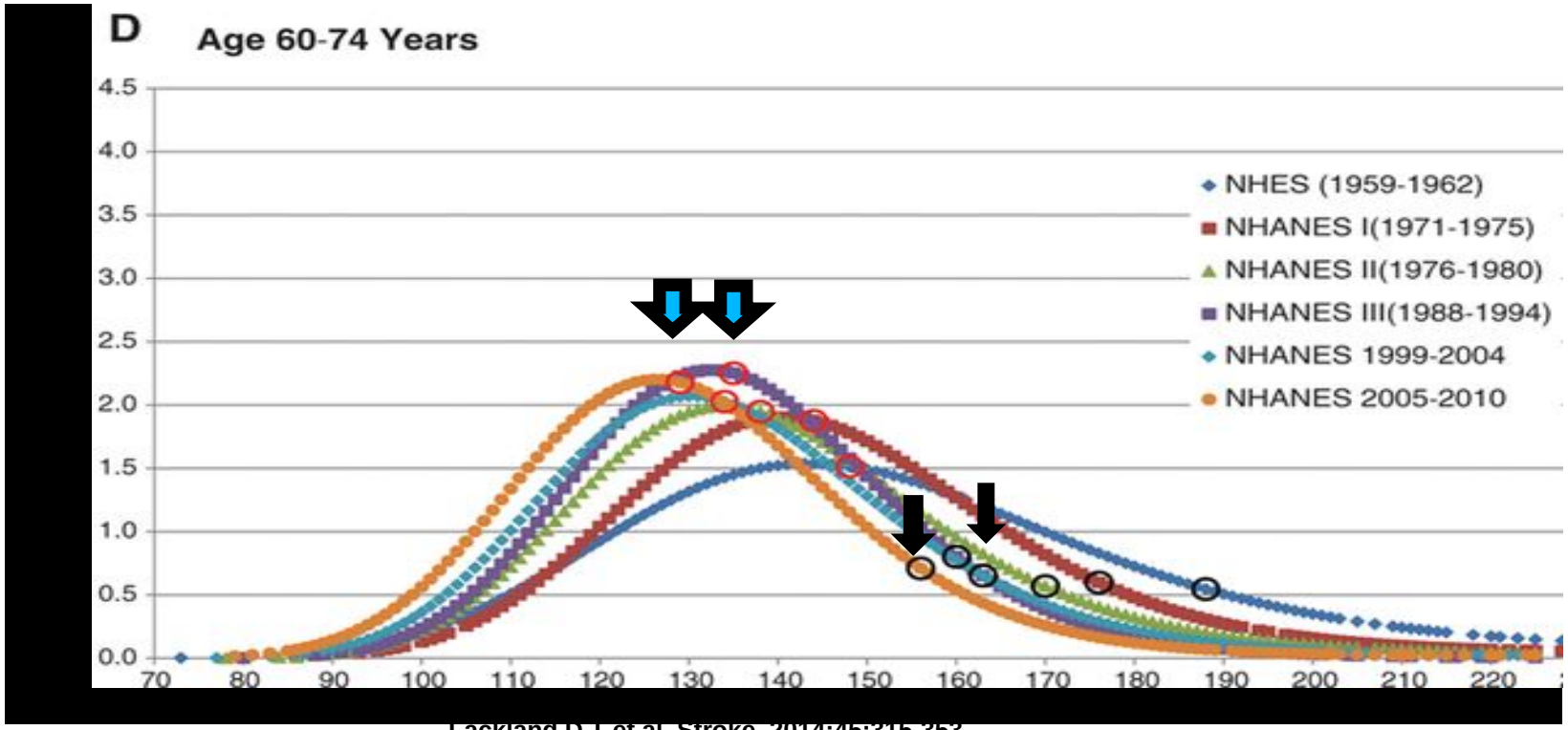
US CVD Death Rates for Individuals < and > than 65 years

Condition (Cause of death by underlying Cause)	Age < 65 or ≥ 65 years	1999-2010 Yearly Average Death Rate per 100,000	1989-1998 Average annual % change in age-adjusted death rates	1999-2010 Average annual % change in age-adjusted death rates
Coronary Disease	< 65	30	-3.6	-3.4
Coronary Disease	≥ 65	1038	-2.7	-5.6
Stroke	< 65	7	-1.3	-2.3
Stroke	≥ 65	356	-0.9	-5.3

Smoothed weighted frequency distribution, median, and 90th percentile of systolic blood pressure: United States, 1959 to 2010.



Lackland D T et al. Stroke. 2014;45:315-353

American Heart Association.

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Factors Influencing the Decline in Stroke Mortality

by Daniel T. Lackland, Edward J. Roccella, Anne F. Deutsch, Myriam Fornage, Mary G. George, George Howard, Brett M. Kissela, Steven J. Kittner, Judith H. Lichtman, Lynda D. Lisabeth, Lee H. Schwamm, Eric E. Smith, and Amytis Towfighi

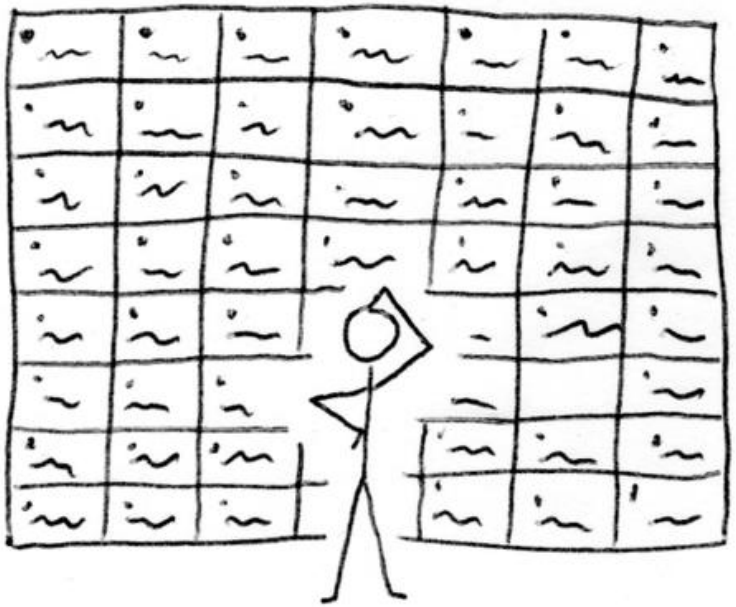
“Although it is difficult to calculate specific attribute risks estimates , efforts in hypertension control initiated in the 1970’s appear to have had the most substantial influence on the accelerated decline in stroke mortality. “

Stroke
Volume 45(1):315-353
December 23, 2013

American Heart Association.

NIH National Heart, Lung, and Blood Institute

Disentangling Complexity is Challenging – Many new guidelines?



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Four New Guidelines

- 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)
- American Society of Hypertension and the International Society of Hypertension Clinical Practice Guidelines for the Management of Hypertension in the Community
- 2013 European Society of Hypertension/European Society of Cardiology Guidelines

Four New Guidelines

- 2013 Canadian Hypertension Guidelines

- Each set of these guidelines was independently developed. They used different methodology and criteria for reaching their conclusions and varied in how comprehensive their recommendations were. All acknowledged that many keys questions remained unanswered and called for greater research

Systolic Blood Pressure Treatment Goals and Thresholds

- Areas of agreement 140/90 for both Goal and Threshold
  - Individuals younger than 60
  - Individuals with diabetes
  - Individuals with chronic kidney disease (CKD) without significant proteinuria

The JAMA Report in December 2013

- **2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)**
- Paul A. James, MD[1]; Suzanne Oparil, MD[2]; Barry L. Carter, PharmD[1]; William C. Cushman, MD[3]; Cheryl Dennison-Himmelfarb, RN, ANP, PhD[4]; Joel Handler, MD[5]; Daniel T. Lackland, DrPH[6]; Michael L. LeFevre, MD, MSPH[7]; Thomas D. MacKenzie, MD, MSPH[8]; Olugbenga Ogedegbe, MD, MPH, MS[9]; Sidney C. Smith Jr, MD[10]; Laura P. Svetkey, MD, MHS[11]; Sandra J. Taler, MD[12]; Raymond R. Townsend, MD[13]; Jackson T. Wright Jr, MD, PhD[14]; Andrew S. Narva, MD[15]; Eduardo Ortiz, MD, MPH[16,17]

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Table 6. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options
2014 Hypertension guideline	General ≥60 y	<150/90	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type diuretic or CCB
	General <60 y	<140/90	
	Diabetes	<140/90	Thiazide-type diuretic, ACEI, ARB, or CCB
	CKD	<140/90	ACEI or ARB

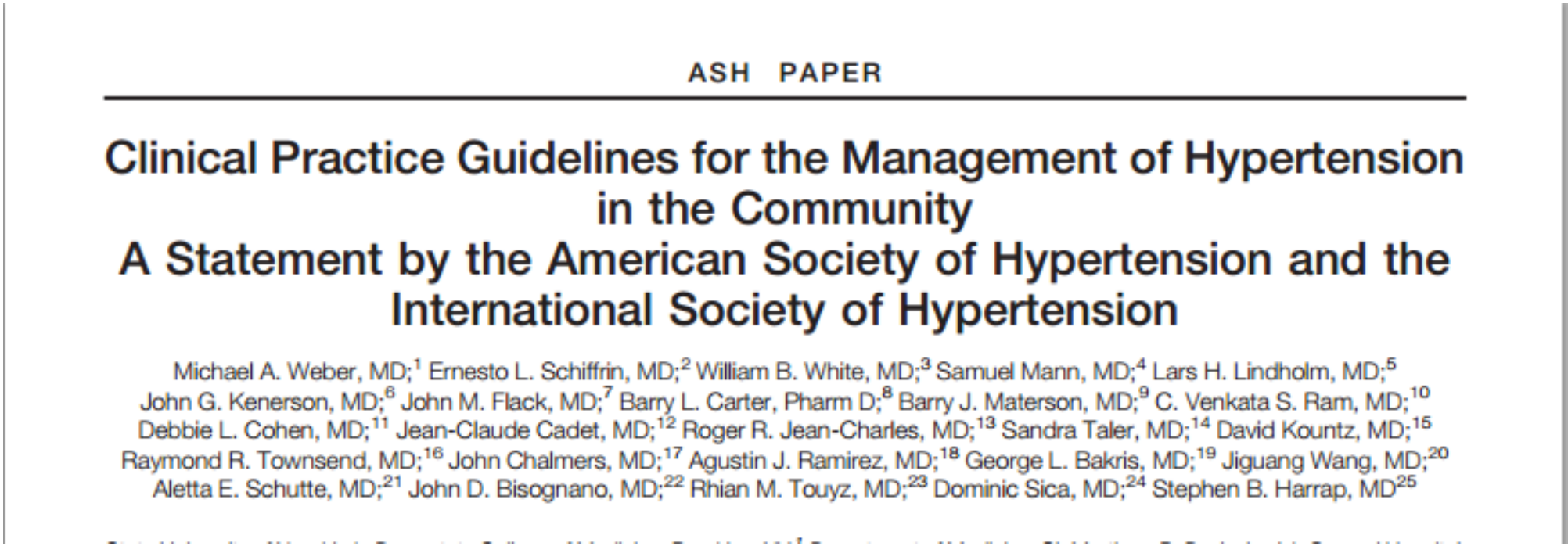
Guideline Goal BP and Initial Drug Therapy for Adults With Hypertension

JAMA. 2014;311(5):507-520. doi:10.1001/jama.2013.284427

Recommendation 1's Corollary Recommendation

- **Corollary Recommendation - …** if pharmacologic treatment for high BP results in lower achieved SBP (eg, <140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)

Other views



ASH PAPER

Clinical Practice Guidelines for the Management of Hypertension in the Community
A Statement by the American Society of Hypertension and the International Society of Hypertension

Michael A. Weber, MD;[1] Ernesto L. Schiffrin, MD;[2] William B. White, MD;[3] Samuel Mann, MD;[4] Lars H. Lindholm, MD;[5] John G. Kenerson, MD;[6] John M. Flack, MD;[7] Barry L. Carter, Pharm D;[8] Barry J. Materson, MD;[9] C. Venkata S. Ram, MD;[10] Debbie L. Cohen, MD;[11] Jean-Claude Cadet, MD;[12] Roger R. Jean-Charles, MD;[13] Sandra Taler, MD;[14] David Kountz, MD;[15] Raymond R. Townsend, MD;[16] John Chalmers, MD;[17] Agustin J. Ramirez, MD;[18] George L. Bakris, MD;[19] Jiguang Wang, MD;[20] Aletta E. Schutte, MD;[21] John D. Bisognano, MD;[22] Rhian M. Touyz, MD;[23] Dominic Sica, MD;[24] Stephen B. Harrap, MD[25]

http://www.ash- us.org/documents/ASH_ISH-Guidelines_2013.pdf

Where do ASH and the JAMA JNC 8 diverge on SBP Thresholds and goals?

- For patients older than 80 years, the suggested threshold for starting treatment is at levels ≥150/90 mm Hg. Thus, the target of treatment should be <140/90 mm Hg for most patients but <150/90 mm Hg for older patients (unless these patients have chronic kidney disease or diabetes, when <140/90 mm Hg can be considered).

http://www.ash- us.org/documents/ASH_ISH-Guidelines_2013.pdf

Minority View from JNC 8 Panel members on only one recommendation

Annals of Internal Medicine | SPECIAL ARTICLE

Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View

Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, PhD; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP

- Wright was frank: "This article is not intended as an attack on the 2014 hypertension guidelines. . . . The purpose of this *Annals* commentary was to clarify the rationale behind the defense of keeping the 140-mm-Hg target, rather than raising it to 150 mm Hg".
- Lot of dialogue and mutual respect on the Panel

Treatment Goals and Thresholds in Older individuals

- Biggest area of diversion is between 60 and 79 years old
- There is more general agreement for those for individuals 80 and over, particularly if they are fragile, that the treatment goal should be seriously considered 150/90 rather than 140/90

After the JAMA publication and again this week American Heart Association and ACC rise concerns

"

It (recent study in JACC 8/16/2014) underscores ongoing concerns about adopting the unofficial 2013 targets as proposed by the panel originally appointed to write JNC 8. The ACC and AHA, working with the NHLBI, are in the process of assembling the writing panel that will evaluate evidence from a variety of sources and provide a comprehensive update of the hypertension guideline."

Statement by the president's of AHA and ACC 8/16/204

These differing perspectives were reflected within the Appointed JNC 8 Panel

Majority Perspective

- “ No. 2, I do think a lot of physicians who take care of the elderly have been concerned over the years about the potential for causing harm by overtreating blood pressure." It's certainly not uncommon for elderly patients to become dizzy on standing because of the antihypertensive medication or medications they take. Such patients, James noted, are at an increased risk for falls and their sequelae”.

Minority Perspective

- What is the trial evidence of increase risk of serious adverse events with treatment to < 140 mg Hg.
- JATOS, VALISH, and SPS3 all concluded that lower goal was safe.

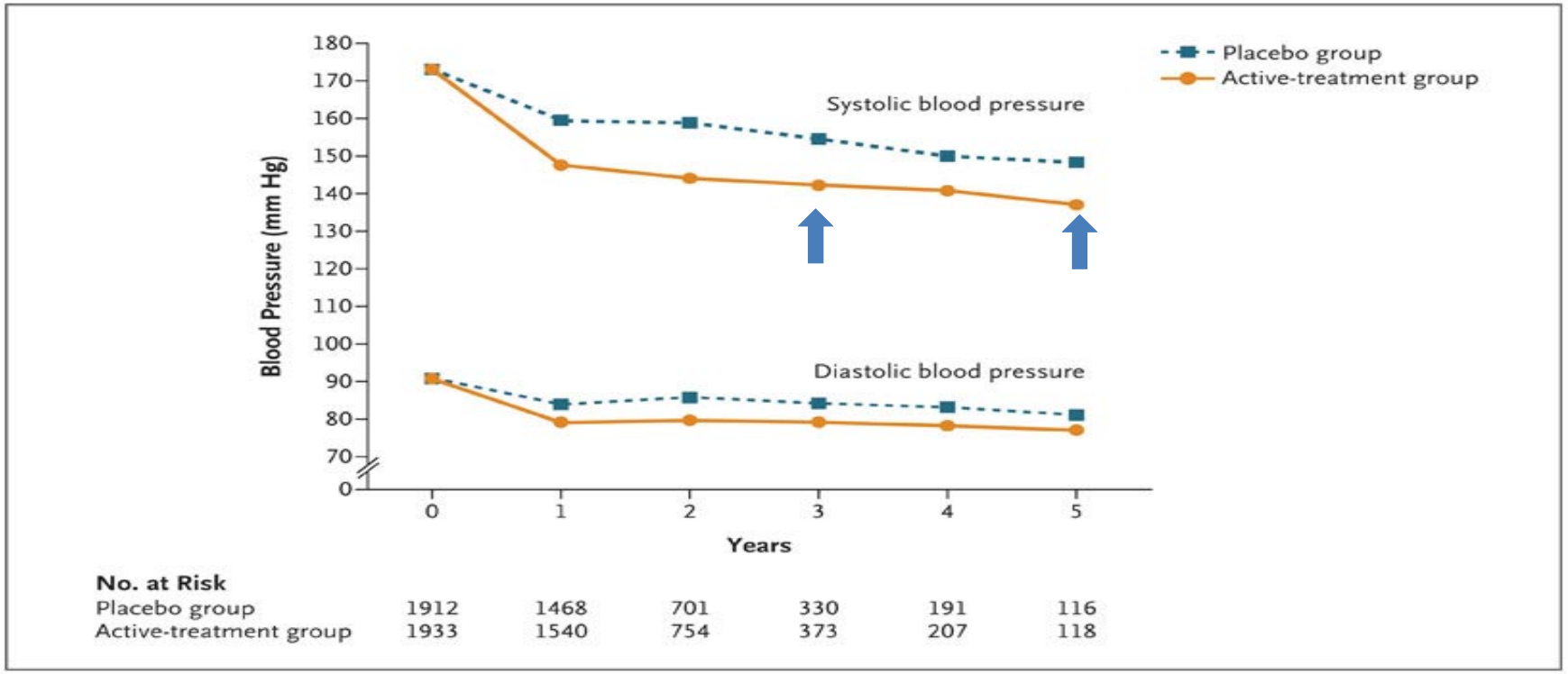
One of the Reasons for Differing Conclusions

Table 2 Trials Comparing SBP < 140 mmHg vs. Higher SBP Goal

Trial (N)	Total Endpts	Composite CVD	Stroke
JATOS(21) (n=4,418)	N= 172	Rate per 1000 py: 22.6 vs 22.7 P=0.99	Rate per 1000 py: 13.7 vs. 12.9 P=0.77
VALISH(17) (N = 3,260)	N= 99	HR: 0.89 p = 0.383	HR: 0.68 p = 0.237
FEVER(16) (n=9,711)	N = 575	HR: 0.73 P = 0.0002	HR: 0.73 P=.0019

- There is mixed epidemiological evidence of some harm with hypertension treatment.
- Is there relevant trial evidence of harm?

HYVET - Blood Pressure, Measured by Study Group

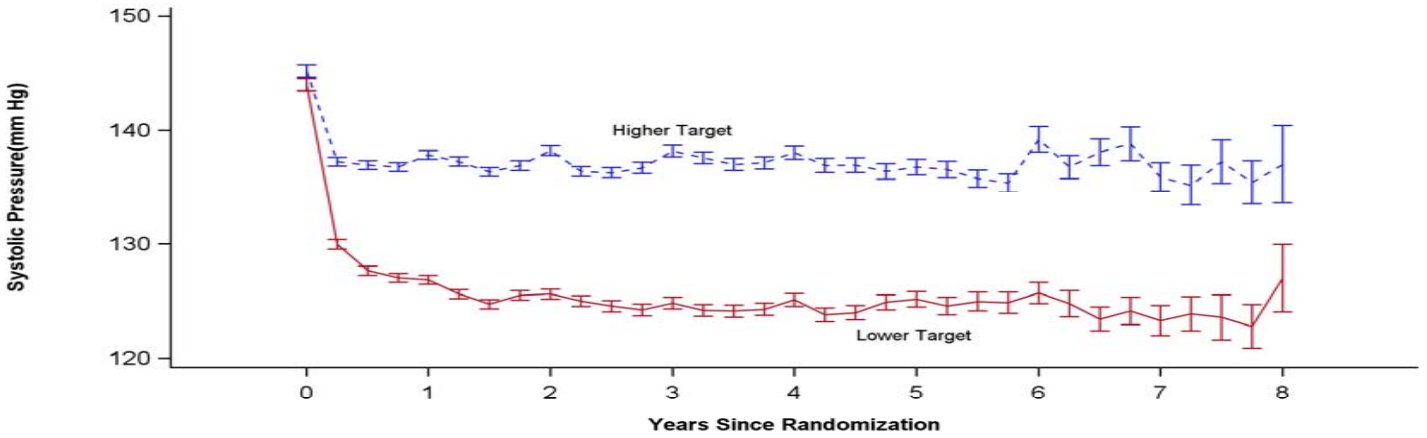


Adverse Effects of Diuretic and ACEI Combination in HYVET

P=0.30). The number of serious adverse events reported was 448 in the placebo group and 358 in the active-treatment group (P=0.001). Only five of these events (three in the placebo group and two in the active-treatment group) were classified by the local investigator as possibly having been due to the trial medication.

SPS3

Systolic Blood Pressure by Treatment Groups



Mean No. of Medications									
Prescribed									
Lower Target	1.7	2.4	2.5	2.5	2.6	2.6	2.8	2.6	2.5
Higher Target	1.7	1.8	1.8	1.8	1.9	1.9	2.2	2.3	2.5
No. of Patients									
Lower Target	1501	1333	1091	859	652	478	231	118	28
Higher Target	1519	1366	1095	841	635	456	224	115	29
Mean SBP(SE)									
Lower Target	144.0(0.54)	126.9(0.38)	125.6(0.46)	124.8(0.51)	125.1(0.58)	125.1(0.68)	125.7(0.95)	123.3(1.31)	127.0(2.97)
Higher Target	145.2(0.54)	137.8(0.39)	138.2(0.43)	138.2(0.52)	138.0(0.58)	136.8(0.67)	139.2(1.14)	135.9(1.26)	137.0(3.41)

- **At 1 yr follow-up average SBPs were 138 vs. 127 mm Hg**
- **Last observed visit, average SBP difference between groups was 11 mm Hg**

SPS 3 Serious adverse related to hypotension

	Higher-target group (n=1519)		Lower-target group (n=1501)		Hazard ratio (95% CI)	p value
	Number of patients	Rate (% per patient-year)	Number of patients	Rate (% per patient-year)		
All	15	0·26	23	0·40	1·53 (0·80–2·93)	0·20
Orthostatic syncope	5	0·09	11	0·19	2·18 (0·76–6·27)	0·14
Stroke associated with hypotension	1	0·02	2	0·03	2·00 (0·18–22·09)	0·57
Myocardial infarction	0	0	0	0	NA	NA
Fall with injury	0	0	3	0·052	NA	NA
Other	11	0·19	9	0·15	0·82 (0·34–1·97)	0·65

NA=not applicable.

Table 3: Serious adverse events related to hypotension

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SPS 3 Side effects potentially related to BP management

	Higher-target group (n=1519)	Lower-target group (n=1501)	Odds ratio (95% CI)	p value
Unsteadiness when standing	355 (24%)	375 (26%)	1·09 (0·92–1·29)	0·31
Blurred vision when standing	103 (7%)	85 (6%)	0·82 (0·61–1·11)	0·19
Dizziness when standing up	304 (21%)	324 (22%)	1·10 (0·92–1·31)	0·30
Light-headedness when standing	236 (16%)	222 (15%)	0·94 (0·77–1·15)	0·54
Palpitations when standing	24 (0·4%)	21 (0·4%)	0·86 (0·48–1·55)	0·62

Table 4: Side-effects potentially related to blood-pressure management

ACCORD Adverse Events

	Intensive N (%)	Standard N (%)	P
Serious AE	77 (3.3)	30 (1.3)	<0.0001
Hypotension	17 (0.7)	1 (0.04)	<0.0001
Syncope	12 (0.5)	5 (0.2)	0.10
Bradycardia or Arrhythmia	12 (0.5)	3 (0.1)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Renal Failure	5 (0.2)	1 (0.04)	0.12
eGFR ever <30 mL/min/1.73m^2	99 (4.2)	52 (2.2)	<0.001
Any Dialysis or ESRD	59 (2.5)	58 (2.4)	0.93
Dizziness on Standing†	217 (44)	188 (40)	0.36

† Symptom experienced over past 30 days from HRQL sample of N=969 participants assessed at 12, 36, and 48 months post-randomization

Margolis et al.: Intensive BP Control, Falls, and Fractures

Lowering BP in ACCORD (119 mm Hg vs. 134 mm Hg) "compared with standard treatment did not result in an increased rate of falls or fractures, and in fact showed possible trends towards fewer fractures in the intensively treated patients… However, the data reported here call into question whether the commonly cited concern about the long-term risk of falls and fractures should hinder the adoption of evidence-based guidelines for blood pressure treatment in older people and those with diabetes."

J Gen Intern Med August 16 2014

What will resolve the controversy ?

"More data"

Jackson Wright

"High-quality health care is often summarized as delivering the right care to the right patient every time"

Paul A. James

Some views since

- “Earlier this year guidelines… (JAMA)… recommend that physicians become less strict.. This is a perilous step” Walter J. Koroshetz – in Nature June 26 2014

Take Home Messages

- Within the US the consensus has been shattered
- It seems likely that some organizations will adopt the higher standard and some will not.
- Some of us fear the adverse impact of particularly on the rate of stroke among high risk groups.
- Some believe that average level of blood pressure is well below 140 mm Hg in some organizations like in Kaiser of Southern California and that raising the standard will do some good and no harm. Both views are sincerely held.

National Heart, Lung,
and Blood Institute

Thank You (Incomplete List) although what I said may not reflect their views.

Jackson Wright
Daniel Lackland
Gbenga Ogedeghe
Cheryl Dennison
Michael Mussolino
Joni Snyder
Paul Sorlie
Stefano Masini
Other Member of the JNC 8 Panel
Authors of the articles that I used.