Many of Us Are Not Quite in Agreement with the New U.S. Hypertension Recommendations

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CME Objectives

- To advise clinicians about recent changes in practice recommendations hypertension management.
- To increase awareness of potential problems associated with these new recommendations.
- To discuss possible solutions for these and hypertension treatment related issues.

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The Problem

- In 2014 new Hypertension "Recommendations"

were published from "some" members appointed to the 8th Joint National Committee (JNC-8).

- Raised numerous questions/concerns:

  Elderly Population in general, and

  Black (AA) and Female Populations,

  CAD patients, Implementation Science,

  Omissions, etc., etc., etc.

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Details of the Problem

The report has garnered much attention due to major change in recommendations for HTN treatment among patients in the *general population ≥60 yo*, their *threshold for drug treatment,* and their *treatment goal*.

In response, multiple expert groups have opposed the recommendation to ***initiate drug treatment to lower BP at systolic BP ≥150 mm Hg*** (vs 140) and treat to a ***goal systolic BP of <150 mm Hg*** (vs 140) in those ***age ≥60 years.***

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Recommended BP Treatment Thresholds and Goals

- ASH/ISH, ESH/ESC, France, NICE, Canada -general BP goal adults:
  - <80 yo <140/90 mmHg
  - ≥80 yo <150/90 mmHg

- Panel members appointed to 8th JNC, opined –"lack of sufficient evidence from RCTs to support lowering SBP <140 mm Hg in people ≥60 yo. and recommended a threshold BP of ≥150/90 mmHg for initiating treatment and a BP goal of <150/90 mmHg for the general population ≥60 yo, without mention of sex, race, or CAD considerations.

- Recent NHANES data document that most hypertensive Americans ≥60 yo are women, and ~50% of those women are AAs. Women and AAs are known to be at high risk for stroke and other organ damage related to high BP (MI, HF and CKD).

Talking Points

I will address 3 areas while outlining issues and concerns with this proposed new strategy.

Certain at-risk populations, namely ***women, the elderly***,
AAs and other high risk cohorts (CAD, HF, etc.)

I propose that maintaining current targets, will allow for optimal treatment for older women and AAs, helping to close sex and race/ethnicity gaps in CVD morbidity/mortality.

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The Issues

HTN Prevalence, Cardiovascular Risk, Sex and Aging:

- Of the ***population attributable risk factors*** for CVD mortality, ***high BP represents almost half (41%) of the overall CVD mortality risk.***
- One in every three US adults (or 78 million nationally) has HTN.
- In *women* HTN prevalence increases more with aging v men.
- *Among women >65 yo, HTN is present in 70-90%* of the population.

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The Issues

Sex, HTN and Cardiovascular Risk

- **Public knowledge of CVD being the leading cause of mortality in women has increased substantially over time** but ***HTN as the most prevalent, modifiable risk condition has not***. So redirecting focus to "new thresholds and goals" distorts the main issue.

- Overall, HTN prevalence and HTN-related morbidity (MI, HF, CKD, etc.) /mortality are significantly higher in:
  - ***women*** v men
  - ***AA women*** more than in Caucasian women

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The Issues

***Sex, HTN, and Cardiovascular Risk (Continued)*:**

- Exact mechanisms why women have more hypertension are unknown- (reduced estrogen levels-linked to increased RAAS activity, enhanced sympathetic outflow, endothelin production and oxidative stress have all been suggested).

- Furthermore***, post-menopausal women*** have a **tendency towards *more increased weigh***t, which in turn increases risks for both HTN and stroke.

- **Older women have higher prevalence of uncontrolled BP, interestingly, despite an overall increased awareness of HTN and compliance with antihypertensive treatment v younger women or age-matched men.**

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Stroke

- Both ***new and recurrent stroke***, the most disabling and costly adverse sequelae of HTN, occur more frequently in women v. men.
- Stroke rate increases significantly with age and there are many more older women then men in the USA
- **Importantly, *women also tend to have greater disability* after a stroke v. men.**
- While the incidence of first ischemic stroke, the most common stroke, has declined slightly in Caucasian women over recent years, ***ischemic stroke rate in AA women is almost double that among Caucasian*** women.

Other Issues

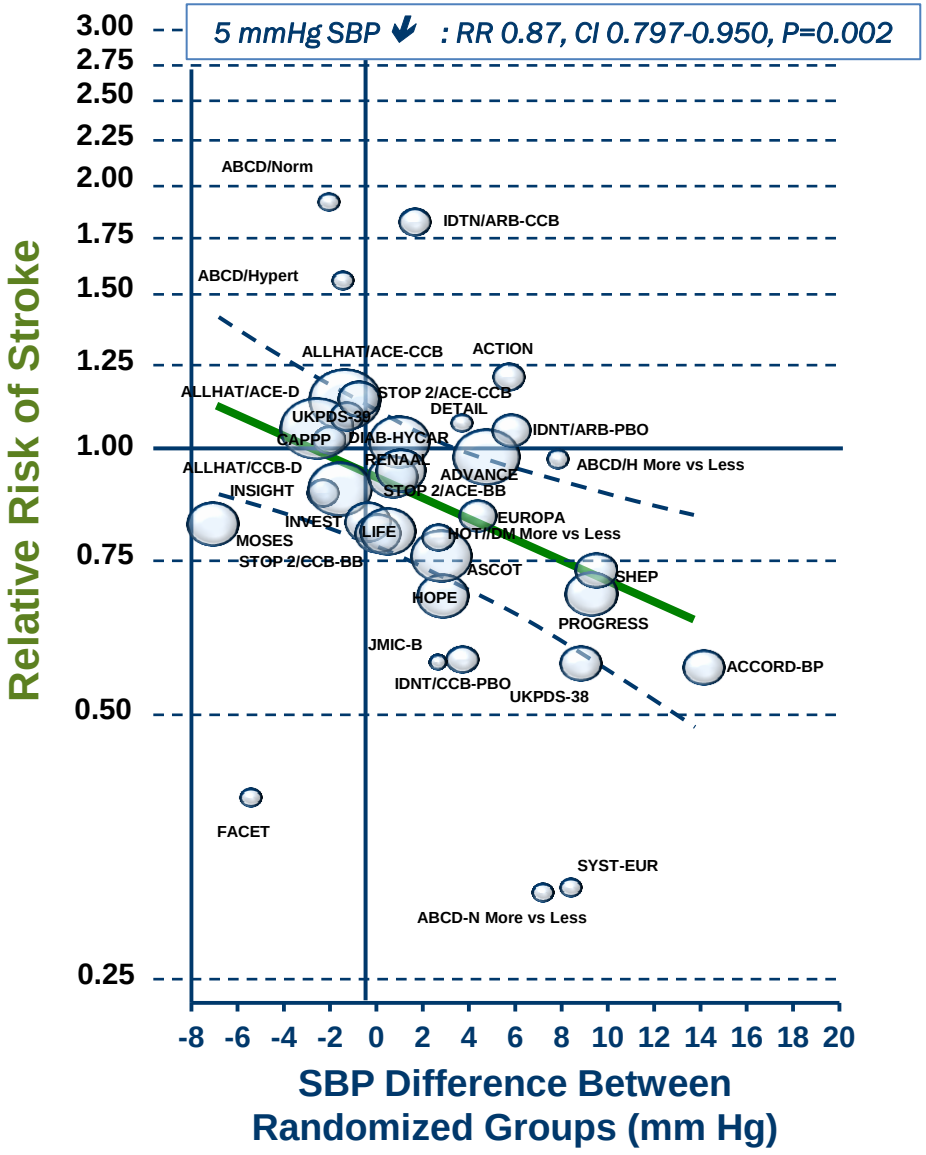
BP Control in Women:

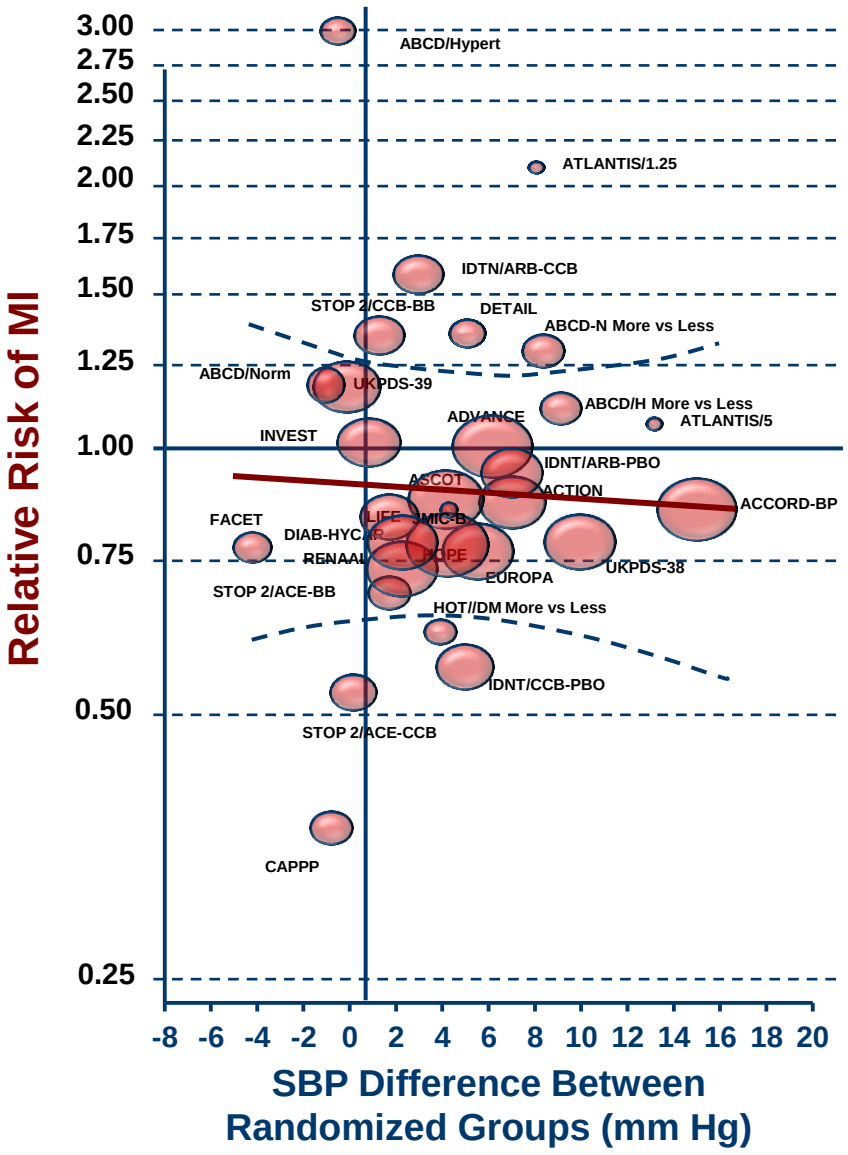
Benefits of BP control are well documented and include:

- Reduction in risk for stroke, MI, CAD, HF and death.
- A recent meta-analysis indicates that treatment of HTN in women >55 yo is associated with ~38% decrease in risk for fatal/nonfatal stroke.
- Yet, in the US, only ~half of those treated for HTN achieve control, based BP <140/90 mmHg.
- Even pre-HTN, SBP 120-139 or DBP 80-89 mm Hg, is associated with a significant 93% increase in risk of stroke among ***post-menopausal women*** v. normotensive women.

Relative Risk of Event Related to Difference in SBP: RCTs

Reboldi et al *J Hypertens* 2011;29:1253-69





Rethinking End Points in Clinical Trials: Insights From Patients and Trialists

Stoker JM et al *Circulation*. 2014; 130: 1254-61

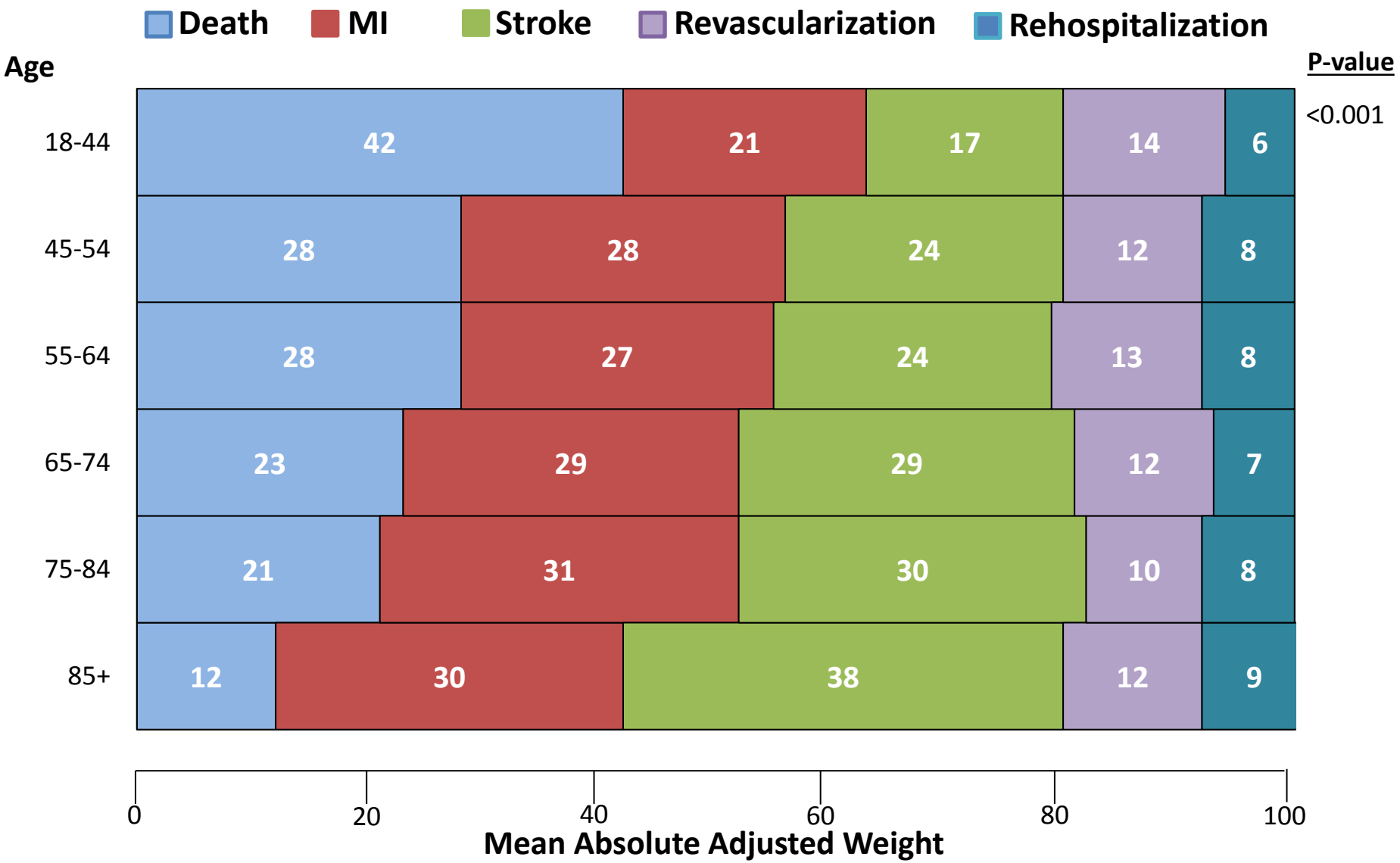
Comparison of End Point Weights By Patients and Trialists

		End Point Weight					End Point Ratio vs Death			
	n	Death	MI	Stroke	Revasc	Hosp	MI	Stroke	Revasc	Hosp
Respondent										
Patients*	785	**25** (12-40)	**28** (16-32)	**27** (16-32)	**12** (0-20)	**7** (0-20)	**1.12**	**1.08**	**0.48**	**0.28**
Trialists*	164	**40** (28-48)	**25** (18-28)	**21** (16-28)	**8** (4-12)	**5** (4-8)	**0.63**	**0.53**	**0.20**	**0.13**

Values are mean (interquartile range) on 100-point scale. Hosp, hospitalization for angina; MI, myocardial infarction; and Revasc, coronary revascularization. *P<0.001 comparison of the distribution of patients vs trialists weights.

Adjusted End Point Weights: Influence of Patient Age

Stoker JM et al *Circulation* 2014; 130:1254-61



Adjusted for race and annual income and rescaled to sum to 100. No differences observed relative to sex, HF, HTN, DM, marital status, education, prior MI, revasc, smoking, angina and ETOH use.

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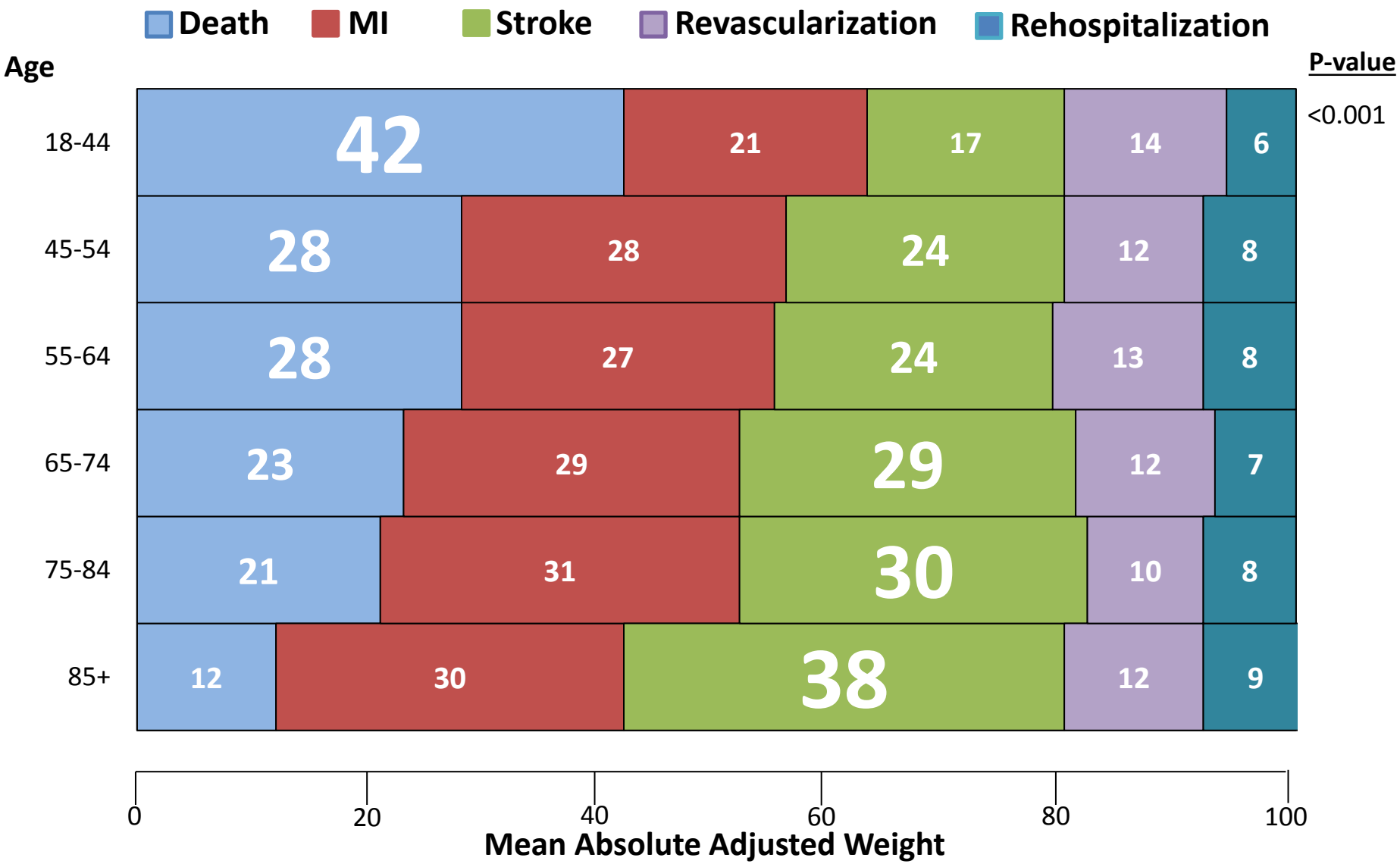

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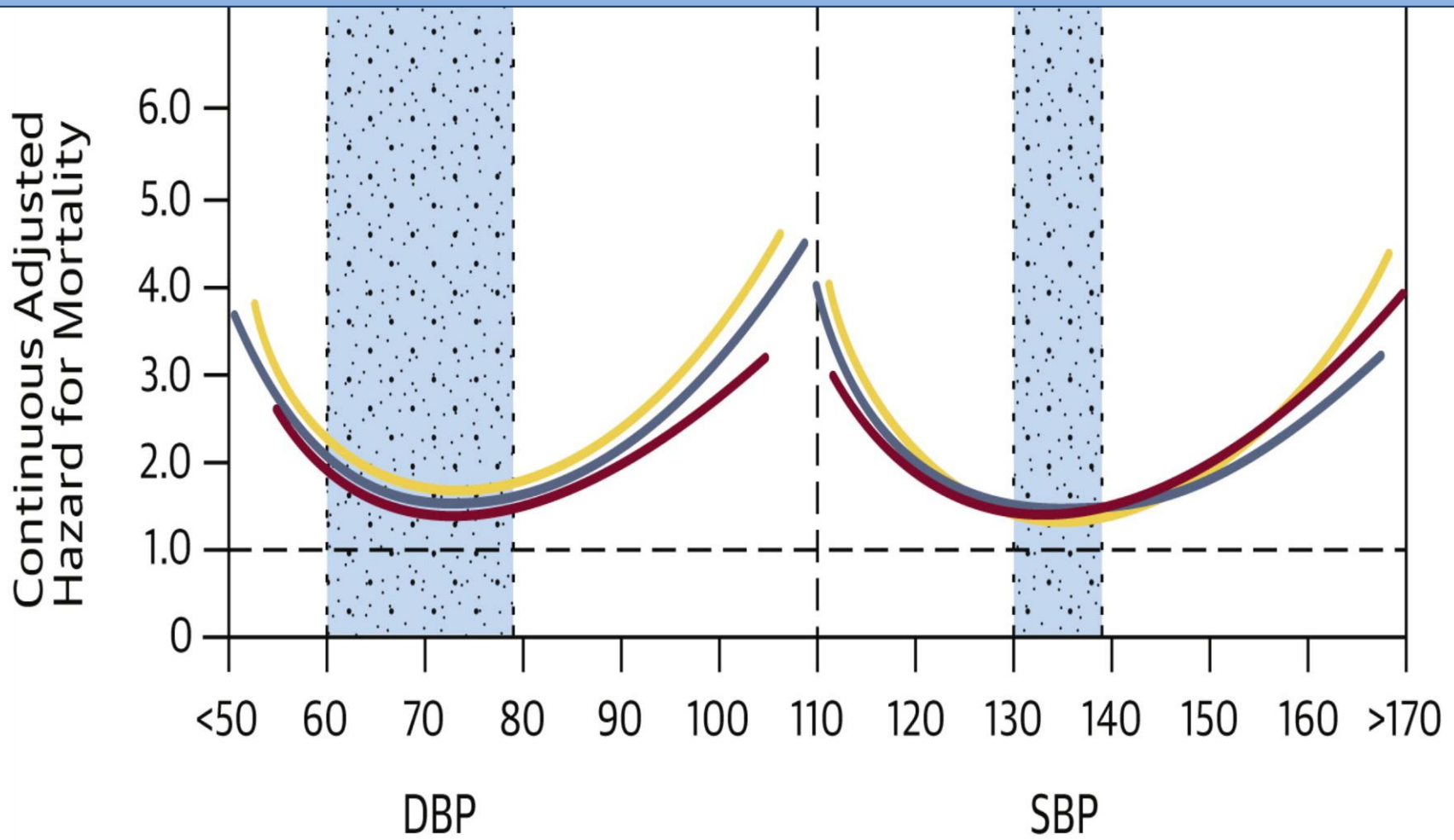
What Is the Ideal BP in Those Treated for Hypertension?

Data from a Large, Diverse Hypertension Population

J Am Coll Cardiol. 2014;64:588-97

N=398,419 treated hypertensive subjects, 30% with diabetes, Kaiser Permanente S CA



Achieved SBP 130-139 and DBP 60-79 mm Hg associated with best outcomes

Recommendations Questioned

- Some JNC 8 Panel members concluded “lack of evidence suggesting that setting a goal SBP of <140 mm Hg in those ≥60 yo provides additional benefit compared with a higher goal.

- They also had concerns that increased antihypertensive medications required to achieve lower BP goal would be associated with adverse events including falls and other risks.

- Yet, recent data suggest that risk for fall injuries and fractures is not increased in those treated with BP lowering agents (ACE-Is, ARBs, calcium antagonists and low dose thiazide diuretics).

Risk of Fall Injury for 20 Most Commonly Prescribed Drugs in the Elderly

Eur J Public Health 2014 Jul 31. pii: cku120. [Epub ahead of print]

Odds Ratios for Fall Injury by Medication Prescribed

Medication	ATC code	Expected effect[a]	Male $n = 110\,950$		Female $n = 211\,045$	
			OR (95% CI)		OR (95% CI)	
			Crude	Adjusted[b]	Crude	Adjusted[b]
Antithrombotic agents	B01A	–	1.63 (1.56–1.70)	1.17 (1.12–1.22)	1.56 (1.51–1.61)	1.17 (1.13–1.21)
Drugs for peptic ulcer and gastro-oesophageal reflux disease	A02B	–	2.05 (1.94–2.17)	1.21 (1.14–1.29)	1.74 (1.67–1.81)	1.13 (1.09–1.18)
Beta-blocking agents	C07A	–	0.98 (0.90–1.07)	0.77 (0.70–0.84)	1.05 (0.99–1.12)	0.89 (0.84–0.95)
High-ceiling diuretics	C03C	↑	1.94 (1.79–2.11)	1.32 (1.22–1.44)	1.52 (1.44–1.61)	1.14 (1.08–1.20)
Vitamin B12 and folic acid	B03B	–	2.03 (1.88–2.20)	1.54 (1.42–1.68)	1.65 (1.56–1.75)	1.30 (1.22–1.37)
Constipation drugs	A06A	↑	1.88 (1.73–2.05)	1.23 (1.13–1.34)	1.50 (1.41–1.59)	1.07 (1.00–1.13)
Calcium	A12A	↓	2.04 (1.77–1.36)	1.27 (1.09–1.47)	1.71 (1.62–1.80)	1.24 (1.18–1.31)
Glucose-lowering drugs	A10B	–	1.40 (1.28–1.53)	0.93 (0.85–1.01)	1.46 (1.37–1.57)	1.05 (0.98–1.13)
Hypnotics and sedatives	N05C	↑	2.32 (2.13–2.54)	1.76 (1.61–1.93)	1.47 (1.38–1.57)	1.21 (1.14–1.29)
Other analgesics and antipyretics	N02B	↑	2.45 (2.21–2.72)	1.74 (1.57–1.94)	1.56 (1.46–1.66)	1.22 (1.14–1.30)
Opioids	N02A	↑	3.54 (3.22–3.88)	2.30 (2.09–2.53)	2.73 (2.57–2.91)	2.00 (1.87–2.12)
NSAIDS	M01A	↑	1.22 (1.08–1.39)	0.99 (0.87–1.13)	1.37 (1.25–1.49)	1.14 (1.04–1.24)
ACE inhibitors	C09A	↑	0.98 (0.86–1.12)	0.77 (0.67–0.88)	1.04 (0.93–1.16)	0.87 (0.78–0.97)
Selective calcium channel blockers with mainly vascular effects	C08C	–	0.83 (0.72–0.97)	0.67 (0.57–0.78)	0.83 (0.75–0.92)	0.72 (0.65–0.80)
Thiazide/low-ceiling diuretics	C03A	↑	0.99 (0.83–1.18)	0.85 (0.71–1.02)	0.93 (0.84–1.03)	0.83 (0.75–0.91)
Antidepressants	N06A	↑	2.82 (2.44–3.25)	2.26 (1.95–2.62)	2.04 (1.87–2.23)	1.76 (1.61–1.93)
Oestrogens	G03C	–	n.a.	n.a.	0.85 (0.77–0.95)	0.70 (0.63–0.78)
Lipid-modifying agents	C10A	–	0.83 (0.71–0.98)	0.63 (0.54–0.75)	0.79 (0.77–0.95)	0.65 (0.57–0.74)
Thyroid preparations	H03A	↑	1.26 (0.98–1.63)	1.07 (0.83–1.40)	1.18 (1.06–1.31)	1.04 (0.94–1.16)
AT II antagonist	C09C	–	0.86 (0.69–1.07)	0.66 (0.53–0.83)	0.93 (0.80–1.07)	0.76 (0.65–0.87)

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Recommendations Questioned (Continued)

- A minority of panel members preferred to retain former threshold and treatment goals of 140/90 mmHg in the general population, except for those ≥80 yo.

- **Moreover, by not addressing various co-morbidities that are highly prevalent among the elderly, there is concern that new HTN recommendations have potential to further disadvantage the majority of older US hypertensive population (women and African Americans).**

- **This could negate much of the advances made in improving BP control and reducing their CVD-related adverse outcomes.**

- Additionally, for those with CAD, HF, prior stroke, PAD, etc. this "relaxed" treatment threshold and goal BP could have most important adverse consequences.

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“Scorecard” for the 9 JNC-8 Recommendations

- STRONG RECOMMENDATION: GRADE A 2
- MODERATE RECOMMENDATION: GRADE B 2
- WEAK RECOMMENDATION: GRADE C 1
- **‘EXPERT OPINION’** 6

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Where the "EXPERTS" Failed to Opine

- HOW TO BEST IMPLIMENT THE RECOMMENDATIONS? OMITTED
- WHERE, WHEN & HOW SHOULD WE MEASURE BP? OMITTED
  - CLINIC, OUT-OF-OFFICE, HOME, KIOSK, PHARMACY, etc. ?
  - DAYTIME, AM, NIGHTTIME, etc.?
- WHAT ABOUT CAD or HF PATIENTS? OMITTED
- SHOULD WE TREAT PREHYPERTENSIVE WITH DRUGS? OMITTED
- ARE BETA BLOCKERS 4TH LINE DRUGS FOR HTN? OMITTED
- COST CONSIDERATIONS? OMITTED
- RESISTANT HYPERTENSION DIAGNOSIS/TREATMENT? OMITTED
- WHAT IS THE ROLE OF DEVICES AND RENAL DENERVATION ? OMITTED
- HOW RAPIDLY SHOULD BP BE LOWERED? OMITTED
- WHAT ABOUT SODIUM, POTASSIUM, CALCIUM AND VITAMN D? OMITTED
- IS IT ONLY ABOUT BP OR MIGHT IT REALLY BE BEYOND BP? OMITTED

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Summary and Conclusions

- Although HTN guidelines available since 1977, ***BP control remains suboptimal***.

- Public health campaigns in the 1980's targeting HTN and its associated risk have contributed to improved BP control, but overall ***BP control remains far less than optimal***.

- Recent trends in some measures are encouraging, however significant further improvements in CVD risk factors are needed, particularly with ***BP control among high risk groups:*** women, the elderly, African Americans and those with co-morbidities.

- It is unlikely that these new recommendations will contribute to improving outcomes.

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