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The Highs and Lows of Blood Pressure Targets in Elderly Adults and Other High-Risk Populations

“The greatest obstacle to discovery is not ignorance—it is the illusion of knowledge.” —Daniel Boorstin, 12th Librarian of the U.S. Congress

Despite major public health efforts to reduce the prevalence and severity of hypertension, high blood pressure (BP) remains a pervasive and important risk factor for cardiovascular and related diseases, especially in elderly adults and racial and ethnic minorities.^{1,2} One of the major challenges for providers is the inconsistency of recommendations in the major clinical guidelines. The recent recommendations for the management of high BP by the panel members appointed to the Eighth Joint National Committee (JNC8) included raising the JNC7 recommended therapeutic target BP goal for persons aged 60 and older from 140/90 mmHg¹ to 150/90 mmHg.³ Although many randomized controlled clinical trials have been conducted in older populations, differences in study design (e.g., inclusion and exclusion criteria), outcomes (e.g., differing BP goals and achieved BP levels), medications, and participant characteristics make the creation of clinical guidelines using these heterogeneous studies an art rather than a science and complicating the application of the guidelines to a given person. A truly evidence-based recommendation generalizable to broader and more-specific populations is much more difficult than is generally appreciated.

An example of the challenge has been that most randomized controlled trials examining BP since the 1980s have compared the clinical outcomes of different pharmacological therapies and not different BP targets. These studies usually targeted JNC6 or JNC7 BP recommendations of 140/90 mmHg (or even lower targets in the presence of diabetes mellitus or chronic kidney disease) for each arm of differing pharmacological intervention.^{1,4} One recent example to better understand the role of BP levels in high-risk older persons was a post hoc analysis⁵ performed on the International Verapamil SR Trandolapril (INVEST) study⁶ cohort, which enrolled 8,354 individuals aged 60 and older (11.6% black, 39.6% Hispanic) with hypertension and coronary artery disease and baseline systolic BP (SBP) of 150 mmHg or greater to atenolol with hydrochlorothiazide or verapamil sustained release (SR) with trandolapril. The INVEST study found similar mortality and morbidity in high-risk persons treated with calcium channel blockers or beta-blockers treated to JNC6 BP levels.⁶ The post hoc analysis found a significantly

greater graded risk for the unadjusted pooled occurrence of all-cause death, nonfatal myocardial infarction (MI), and nonfatal stroke with increasing levels of achieved BP (SBP <140 vs 140–149 vs ≥150 mmHg).⁵ Moreover, in the multiple propensity score-adjusted model, achieving the current 2014 JNC8 panel-recommended SBP target of 140 to 149 mmHg was associated with a greater risk of cardiovascular mortality ($P = .04$), total stroke ($P = .002$), and nonfatal stroke ($P = .03$) than with with SBP less than 140 mmHg.⁵ Although this was a secondary analysis, it provides some limited evidence in the absence of randomized trials designed to answer that specific question.

Another major concern for older persons treated to a more-aggressive BP target is the risk of falls, but again, the data are conflicting. In one study of 406 participants aged 60–86, a higher BP medication dose was associated with more falls;⁷ a similar association was observed in 4,961 community-living adults with hypertension aged 70 and older.⁸ By contrast, another study found no difference in falls and fractures in a study of intensive BP control (SBP <120 vs < 140 mmHg) that included more than 3,000 individuals aged 40 to 79 with type 2 diabetes mellitus.⁹ Finally, two recent metaanalyses found no greater risk of falls in persons aged 60 and older taking antihypertensive medication.^{10,11}

In this issue of the *Journal of the American Geriatrics Society*, Still and colleagues¹² provide an excellent review of current guidelines and recent trials for hypertension treatment in older adults, with a focus on African Americans, a population at especially high risk.¹³ Their analysis finds a consistent pattern of BP guideline recommendations from national and international hypertension, cardiovascular, nephrology, and endocrinology associations to target a goal of less than 140/90 mmHg for persons younger than 80 and 150/90 mmHg for those aged 80 and older, paying attention to symptoms or other factors that may mitigate aggressive BP lowering in a given individual aged 60–80. They conclude that there is insufficient evidence to raise the SBP goal from its current level of less than 140 mmHg, particularly in African Americans or those with cardiovascular disease or multiple cardiovascular risk factors.

The debate over a target BP of less than 140/90 mmHg versus one of 150/90 mmHg at age 60–79 focuses in large part on interpretation of data from different trials that various experts in the field may weigh differently, but the real question seems to be not so much the difference in clinical outcomes, because there appears to

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be little information on outcome differences in elderly adults between the goals of 140/90 and 150/90 mmHg, as the question of sending a message of importance to providers and patients and achieving adequate BP control at a population level balanced with minimizing the risk of hypotensive complications. Still and colleagues¹² posit that the new JNC8 panel recommendations may increase the risk of poor BP control and subsequent adverse cardiovascular events, particularly in high-risk populations, such as African Americans.³

There is even less evidence in large hypertension trials in elderly adults of participant characteristics and associated lower BP level at which the rate of cardiovascular events or adverse outcomes increase. What should be the lower BP level and how might that differ according to subgroup? Although there are no randomized controlled trials designed to answer this question specifically, it is likely that there are many trials with data that can be included in secondary analyses that would be highly informative and build a stronger base of evidence in this important but understudied area. Such data could provide a critical framework for population-level modeling of target upper and lower BP goals across a range for which there is conflicting evidence.

The members of the JNC8 panel are clearly dedicated to endorsing the highest quality of evidence-based care and accurately opined that there was not enough evidence to support the lower BP target of 140/90 mmHg that prior JNC panels recommended, but others have raised excellent points^{14,15} to question the corollary (that there is evidence to support raising the target). Given the many years since the first reports of hypertension treatment in elderly adults,^{16,17} and the subsequent evidence documenting a marked reduction in cardiovascular events attributed in large part to BP control over the last 30 years (primarily targeting 140/90 mmHg),^{1,2} it seems a more-prudent approach might be to accrue more-convincing evidence for a new target before making new clinical guideline recommendations. Older African Americans are one of the groups at highest risk, and evidence of new randomized clinical trials of older African Americans comparing the efficacy of a BP target of less than 150/90 mmHg with one of less than 140/90 mmHg has yet to be gathered.

In summary, Still and colleagues¹² present a compelling rebuttal to the recent recommendation of the JNC8 panel members to raise the target BP of 140/90 mmHg to 150/90 mmHg in persons aged 60 to 79, especially in high-risk subgroups such as African Americans, emphasizing the point that no direct trials have found a target BP of 150/90 mmHg to be superior to a target BP of 140/90 mmHg. Their suggestion to keep the original BP target recommendation is further grounded in the importance of maintaining consistency on an important public health message that has led to dramatic improvements in cardiovascular outcomes in the United States,^{1,2} but these new recommendations give the field of hypertension a reason to pause and reflect, because understanding of the evidence for optimal BP targets must periodically be revisited, especially as there has been a shift from an agrarian society to a digital society. Lifestyle habits, risk factors, exposures, and the clinical management of comorbid conditions such as hyperlipidemia and

diabetes mellitus have changed over time, as no doubt will the BP level at which the risk of cardiovascular events outweighs the risk of treatment and accepted targets for BP control in the presence of hypertension. Nevertheless, in the quest for excellence, the purity of evidence (which is still unclear) must not be allowed to overcome the prudence of reason in creating guidelines to help optimize outcomes for each individual treated. We await the results of trials that include sizeable numbers of diverse older adults, such as the Systolic Blood Pressure Intervention Trial, which has randomized more than 9,000 individuals to test the benefit of treating to a level of systolic BP of less than 140 mmHg, including many high-risk subgroups and persons aged 75 and older.¹⁸

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