

ORIGINAL RESEARCH & CONTRIBUTIONS

Special Report

2014 Hypertension Guideline: Recommendation for a Change in Goal Systolic Blood Pressure

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Editor's note: A copy of the August 2014 Kaiser Permanente Adult Hypertension National Guideline follows this article.

ABSTRACT

The 2014 Kaiser Permanente Care Management Institute National Hypertension Guideline was developed to assist primary care physicians and other health care professionals in the outpatient treatment of uncomplicated hypertension in adult men and nonpregnant women aged 18 years and older. The new guideline reflects general acceptance, with minor modifications, of the "Evidence-Based Guideline" report by the panel members appointed to the National Heart, Lung, and Blood Institute 8th Joint National Committee. A major practice change is the recommendation for goal systolic blood pressure less than 150 mmHg in patients aged 60 years and older who are treated for hypertension in the absence of diabetes or chronic kidney disease. This article describes the reasons for, evidence for, and consequences of the change, and is followed by the National Guidelines handout.

INTRODUCTION

The 2014 Kaiser Permanente (KP) Care Management Institute National Hypertension Guideline was developed to assist primary care physicians and other health care professionals in the outpatient treatment of uncomplicated hypertension in adult men and nonpregnant women aged 18 years and older. The new guideline reflects general acceptance of the "Evidence-Based Guideline" report by the panel members appointed to the National Heart, Lung, and Blood Institute (NHLBI) 8th Joint National Committee (JNC 8).¹ A major practice change is the recommendation for goal systolic blood pressure less than 150 mmHg in patients aged 60 years and older who are treated for hypertension in the absence of diabetes or chronic kidney disease (CKD) compared with the previous standard less than 140 mmHg. This change has major consequences for the routine primary care management of patients with hypertension.

How Large Is the Affected Population and How Strong Is the New Recommendation?

Using the results of the National Health and Nutrition Examination Survey between 2005 and 2010, it has been estimated that the US treatment-eligible adult hypertension population would decrease from 20.3% to 19.2% compared

with that of the 7th Joint National Committee guideline, and the population with treatment-eligible hypertension who are aged 60 years and older would decline from 68.9% to 61.2%.² As of October 2014, with an 85% hypertension control rate less than 140/90 mmHg, there are 18,690 patients aged 60 years and older without diabetes or CKD in the KP Southern California hypertension registry who have systolic blood pressures of 140 to 149 mmHg and are affected by the new recommendation. These patients represent 2.5% of the total KP Southern California adult hypertension registry of 740,003 individuals.

Evidentiary support for this recommendation was strong, according to the Care Management Institute Grading of Recommendations Assessment, Development and Evaluation standard for grading the quality of evidence scale, and it received a strong rating using principles evaluating the strength of the body of evidence and degree of certainty developed by the NHLBI before it convened the first JNC 8 panel meeting in August 2008. This recommendation was a segue from the relevant Evidence Statements, which evaluated randomized clinical trials passing scrutiny from a 14-category evidence assessment scale used by a trained and independent methodology team collaborating with those experts appointed to the JNC 8 panel. These Evidence Statements are available in the full online Evidence-Based Guideline report.¹

What is the Basis of the Supportive Evidence?

The age 60 years threshold for the systolic blood pressure target was decided on the basis of the Systolic Hypertension in the Elderly Program (SHEP) trial findings and the Systolic Hypertension in Europe (Syst-Eur) trial results.^{3,4} In these highly rated randomized controlled trials, stroke, the primary endpoint, was reduced by 36% and 42%, respectively, and major cardiovascular events were reduced by 32% and 31%, respectively. These two large trials containing representative population samples fulfill the NHLBI strong evidence requirement for multiple supportive randomized controlled trials. The JNC 8 Evidence Statements 1 to 3 for Clinical Question 2 describe the evidence, and a strong recommendation is the logical result.^{1p82-3}

There is no evidence from a randomized controlled clinical trial to support the opinion that a systolic blood pressure goal less than 140 mmHg in the elderly hypertensive population is superior to a systolic goal less than 150 mmHg. The absence

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of evidence for a lower blood pressure target does not equal benefit. One opinion properly criticizes the strength of the Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients⁵ and Valsartan in Elderly Isolated Hypertension Study⁶ results demonstrating equivalency of goal systolic pressure less than 140 mmHg compared with goal systolic pressures less than 150 mmHg and less than 160 mmHg, because these were short-term trials.⁷ However, that critique does not offer additional information to the previously published Evidence-Based Guideline Clinical Question 2: Evidence Statement 6, which attached low-quality evidence to these trials.^{1p84-5}

PROBLEMS WITH USE OF ACHIEVED BLOOD PRESSURE TRIALS

Achieved blood pressure trials are those in which the intervention is to introduce antihypertensive medication to examine the effect of medication on cardiovascular risk reduction rather than to examine outcomes achieving a prespecified goal blood pressure. These trial results should not be used to inform blood pressure targets because they ask a different question. Retrospective analyses correlating achieved blood pressures to outcome measures are inherently biased.

The NHLBI process followed by the panel appointed to JNC 8 is in agreement with The Cochrane Collaboration methodologists who independently decided the following:

*The cohort of patients with low blood pressure as identified by achieved blood pressure selects for patients who did not have sustained elevated blood pressure in the first place ... , for patients in whom the blood pressure is most easily reduced with low doses of antihypertensive drugs, for patients with the lowest baseline blood pressure, and for patients who are most compliant with drug and non-drug therapy to lower blood pressure All of these factors are also most likely associated with a lower risk of having an adverse cardiovascular event. The approach is thus heavily biased for finding [fewer] cardiovascular events in the patients with lower blood pressure, and thus must not be encouraged.*⁸

These limitations of analyses based on post hoc achieved blood pressures were confirmed in an analysis of the African American Study of Kidney Disease and Hypertension, which concluded that the retrospective use of achieved blood pressures would have erroneously led to the opposite conclusion of the intention-to-treat goal blood pressure analysis in this landmark study.⁹

The Felodipine Event Reduction study,¹⁰ the Perindopril Protection against Recurrent Stroke trial,¹¹ and Blood Pressure Trialists' Collaboration reports¹²⁻¹⁴ purport to show that additional blood pressure lowering is beneficial. These are examples of clinical trials and meta-analyses representing on-treatment achieved blood pressure results rather than intention-to-treat goal blood pressure outcomes and were rejected by the NHLBI methodology team because of bias. Notably, reference to mean achieved systolic blood pressures in the SHEP and Syst-Eur trials of 142 mmHg and 144 mmHg,

respectively, fails to mention the mean achieved systolic blood pressure in Syst-Eur, which was 151 mmHg.⁴

The argument to use "totality of evidence" does not constitute sufficient rationale for inclusion of clinical trials and meta-analyses containing inherent bias.

Where Does the Lower-is-Better Blood Pressure Hypothesis Originate, and Has It been Validated?

Much of the "lower is better" paradigm is based on strong prospective observational data of more than 1 million patients in 61 prospective studies¹⁵ as well as on many retrospective analyses of achieved blood pressures in the clinical trials. However, the retrospective findings are mixed. A more recent population-based retrospective cohort study revealed no difference between systolic intensification thresholds of 130 mmHg to 150 mmHg across a broad spectrum of baseline cardiovascular risk.¹⁶ Analyses of large numbers of hypertensive KP patients with hypertension, as well as US military veterans with hypertension and CKD, suggest increased mortality and end-stage kidney disease associated with lower attained blood pressures.^{17,18}

Does the treatment of blood pressure to lower blood pressure targets, as opposed to higher blood pressure targets, reverse cardiovascular risk? Seven randomized clinical trials have investigated this hypothesis in high-risk patients with CKD, diabetes, older age, and a personal history of stroke. None has shown significant benefit for meeting the primary endpoint with more intense antihypertensive therapy that seeks a lower blood pressure goal.^{5,6,19-23}

WHAT IS THE RISK OF REVERSING POPULATION GAINS IN CARDIOVASCULAR BENEFIT?

How can we be sure that a higher systolic goal will not reverse gains already made in stroke and cardiovascular disease reduction? Gains in cardiovascular disease reduction have been associated with hypertension control, widespread use of high-potency statins, and improved secondary prevention in patients with known coronary artery disease and stroke.^{24,25} Because patients are receiving better overall care, power calculations for recent hypertension treatment trials on the basis of adverse rates of cardiovascular events for historic cohorts often fall short of forecasts, leading to underpowering.^{19,20} Given the success of population care strategies achieving very high rates of blood pressure control and eliminating racial performance gaps in large diverse populations,²⁶⁻²⁹ we need to ensure that we use the highest evidence base to define blood pressure targets. Implementation difficulties and problems with clinical inertia are independent issues and should not be used to justify inappropriately low blood pressure goals.

What are the Risks of Overtreatment?

Overtreatment needs to be a concern. In the KP Southern California adult hypertension registry in which nearly 90% of patients attained blood pressure control less than 140/90 mmHg, the mean systolic pressure is 127 mmHg, and almost 10% of patients receiving antihypertensive therapy have a most recent systolic pressure less than 110 mmHg. The

disadvantages of overtreatment include: 1) exposure to side effects of unnecessary medications and excessive medication doses; 2) polypharmacy in the elderly³⁰; 3) reduced medication adherence associated with a large number of medications³¹; 4) a possible increase in falls with serious injury³²; 5) possibly a J- or U-curve increase in cardiovascular risk¹⁷; and 6) unnecessary use of limited health care resources, including office visits, population care outreach, medication prescriptions, and laboratory testing. A general review of 16 treatment trials indicated the potential for harm with more aggressive antihypertensive therapy in the absence of benefit.³³

Is There a Risk of Changing Goal Blood Pressure in the Presence of Uncertainty?

How can we be certain that the systolic blood pressure target less than 150 mmHg for patients with hypertension aged 60 years and older is accurate? The purpose of guideline development is to gather evidence with the least chance of bias, and this sort of evidence is best obtained from higher-quality randomized controlled clinical trials. All the panelists appointed to JNC 8 concurred with the NHLBI evidence review process, and, following several straw votes during more than one year, the final recorded vote at a face-to-face meeting conducted in Bethesda, MD, at the National Institutes of Health on February 27-28, 2013, on Recommendation 1 was 15 in favor and 2 against. The final recorded vote on the 3 evidence statements supporting Recommendation 1 was unanimously in favor. The SHEP and Syst-Eur trial results^{3,4} provide strong evidence to support the Evidence-Based Guideline's recommended goal blood pressure in elderly patients. In contrast, there are no known clinical trials that address goal blood pressure that have examined the 18- to 59-year age stratum, and therefore recommendation for less than 140/90 mmHg for this population is based on expert opinion.

There is a need for additional clinical trials examining the question of goal blood pressure for various populations of hypertensive individuals. Those trials should include examination of important health outcomes at a goal systolic pressure less than 150 mmHg compared with less than 130 mmHg in elderly patients with diabetes and CKD. There is good evidence to justify such a randomized clinical trial in patients with diabetes,^{3,4,34} including Evidence Statement 18 for Clinical Question 2 in James et al.¹ If the ongoing Systolic Blood Pressure Intervention Trial does not find a significant outcome difference treating to goal systolic pressure less than 140 mmHg compared with less than 120 mmHg in patients with CKD, a future trial comparing less than 150 mmHg with less than 130 mmHg would be justified in this population as well.

IS THE EVIDENCE-BASED GUIDELINE RECOMMENDATION FOR GOAL SYSTOLIC PRESSURE LESS THAN 150 MMHG FOR AGE 60 AND OLDER AN OUTLIER COMPARED WITH OTHER GUIDELINES?

Recommendations from the 2013 European Society of Hypertension/European College of Cardiology for blood

pressure goals in the treatment of hypertension in elderly patients include a few “may consider,” “if treatment is well tolerated” recommendations along with a top “solid evidence” recommendation.³⁵ That single, solid-evidence recommendation targets a goal systolic blood pressure 140 mmHg to 150 mmHg “in the elderly.” In the SHEP and Syst-Eur trials, “elderly” enrollment began at age 60 years. In an e-mail from Giuseppe Mancia, MD, co-chair of the European Society of Hypertension/European College of Cardiology guideline, which was circulated to panel members appointed to JNC 8, *elderly* was defined as beginning at age 65 years (G Mancia, MD; personal communication, 2013 Dec).² In a letter to the European Society of Hypertension/European College of Cardiology guideline authors in the December 2013 issue of the *Journal of Hypertension*, a writer expressed concern regarding the new blood pressure goal stating that it was “rational” but worried about the impact on clinical inertia. In their letter of reply, Mancia et al³⁶ stated, “Clinical inertia has to be fought ... by other means than by recommending inappropriately low [blood pressure] targets.”

Therefore, there is fair concordance in the age group targeted for a systolic blood pressure goal target less than 150 mmHg in hypertension guidelines submitted by hypertension experts on both sides of the Atlantic.

Why Not Make the Threshold for the less than 150 mmHg Goal Recommendation Age 80 Rather than Age 60?

Given the findings of the SHEP and Syst-Eur trials,^{3,4} there is greater certainty defining the age group 60 years and older, rather than age 80 years and older, for goal systolic pressure less than 150 mmHg. Only a single trial, the Hypertension in the Very Elderly Trial, has established goal systolic blood pressure in the age 80 years and older population less than 150 mmHg, a population described as the “very elderly.”³⁷

A single randomized clinical trial does not constitute sufficient evidence to merit a strong recommendation at this age level in the presence of multiple randomized clinical trials in support of the age 60 threshold.

Does the less than 150 mmHg Goal Recommendation Include Higher Risk Groups?

Epidemiologic data have defined higher cardiovascular risk strata in the general population, but randomized controlled clinical trials demonstrating statistically significant reversal of risk with lower blood pressure goals in higher-risk groups have been notably absent.^{5,6,19-23}

SHEP and Syst-Eur enrolled patient populations that were representative of a broad spectrum of cardiovascular risk. Increasing age alone is a dominant cardiovascular disease risk factor.¹⁵ Additionally, the SHEP trial population included 14% African-American patients compared with 12.6% in the US population. Both SHEP and Syst-Eur also included patients with a history of myocardial infarction and stroke.^{1,3} Sixty-one percent of patients in SHEP had a baseline electrocardiographic abnormality. Thirty percent of patients in Syst-Eur had a prior “cardiovascular complication.” The

... there is greater certainty defining the age group 60 years and older, rather than age 80 years and older, for goal systolic pressure less than 150 mmHg.

Hypertension in the Very Elderly Trial included patients with myocardial infarction, stroke, and heart failure.³⁶

Attention has been drawn to the Secondary Prevention of Small Subcortical Strokes trial comparing goal systolic pressure less than 150 mmHg to less than 130 mmHg in patients with a personal history of lacunar stroke.²⁰ Although the primary endpoint of recurrent stroke was non-significant ($p = 0.08$), confidence intervals (0.64 to 1.03) did not preclude benefit of the lower goal. Furthermore, the subgroup of intracerebral hemorrhage was significantly reduced ($p = 0.03$).⁶ However, “there was no heterogeneity in treatment effect on the primary outcome in any of the demographic or clinical subgroups,” the annual primary stroke rate in the control group was only 2.77% vs 7% predicted, and intracerebral hemorrhage comprised fewer than 10% of total strokes.²⁰ The nonstatistically significant separation of total stroke in the more intensively treated group compared with the less intensively treated group in the Secondary Prevention of Small Subcortical Strokes trial was only 0.5% events per year. Therefore, the evidence favoring a goal systolic pressure lower than 150 mmHg in hypertensive individuals aged 60 years and older with a personal history of stroke is speculative.

ENDORSEMENTS OF THE EVIDENCE-BASED GUIDELINE

The American Association of Family Practitioners, representing more than 100,000 primary care physicians, has endorsed the Evidence-Based Guideline. That approval is important because nearly all hypertensive patients receive hypertension care from primary care physicians. Additionally, the National Quality Committee for Quality Assurance has adopted the new reform, and goal systolic blood pressure less than 150 mmHg in the absence of diabetes is a 2014 performance measure for the Healthcare Effectiveness Data and Information Set. The Veteran's Administration and Department of Defense patient care systems have adopted goal systolic blood pressure less than 150 mmHg for general population hypertension patients age 60 and over.³⁸

It will be difficult to reproduce the methodologic rigor and independent sponsorship of the Evidence-Based Guideline now that the NHLBI has unfortunately decided to remove itself from stewardship of future hypertension guidelines, and will not approve any guideline. The level of evidence-based medicine used to develop this hypertension guideline, on the basis of Institute of Medicine principles, is unsurpassed.

An essential point is that blood pressure goals for patients with hypertension must be based on a high degree of evidence, and bias is best removed by reliance on the randomized controlled clinical trials to make this determination. A common rationale for recommending blood pressure goals lower than those that are evidence based is to combat clinical inertia. However, implementation is a separate issue, and high-performing systems of health care have addressed clinical inertia successfully.^{26-29,39} ❖

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Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Normal

If we possessed instruments delicate enough we might be able to determine what the normal arterial pressure of a given individual was, and to note any variation from it We are ... driven to depend upon the most treacherous of all methods, the impressions conveyed to our minds through the sensory nerves of the fingers By constant practice and study, each physician makes for himself a standard of atrial pressure which he recognizes as normal.

— *The Study of the Pulse*, Sir James Mackenzie, MD, 1853-1925,
Scottish cardiologist and pioneer in the study of cardiac arrhythmias