Hypertension remains a growing problem in our aging population. Recent data from the National Health and Nutrition Examination Survey (NHANES) estimate that almost one-third of the adult population meets the criteria for hypertension (1). Furthermore, the prevalence increases with age; 65 percent of individuals over the age of 60 are hypertensive. Approximately three-quarters of the population with diagnoses of hypertension require some form of pharmacologic therapy, and the percentage is as high as 82 percent among individuals over the age of 60.

The Framingham Heart Study helped to elucidate the expected trajectory of blood pressure in normotensive and hypertensive individuals with aging. Initially, both systolic (SBP) and diastolic blood pressure (DBP) increase linearly with age. However, SBP and DBP diverge around the fifth to sixth decade, when DBP begins to decline whereas SBP continues to increase (2). Subsequent studies have shown the predominance of isolated systolic hypertension in individuals over the age of 50, have described it as a major predictor of cardiovascular events, and have suggested its importance as a modifiable target (3, 4).

Effects of treatment of hypertension on mortality and on cardiovascular and stroke outcomes

In 2000, a meta-analysis (5) of eight key randomized controlled trials (RCTs), including the Systolic Hypertension in the Elderly Program (SHEP) (6) and the Systolic Hypertension in Europe (Syst-Eur) trial (7), examined total mortality and cardiovascular outcomes in relation to SBP and also evaluated the benefit of antihypertensive therapy on these outcomes. The authors defined systolic hypertension as a value of 160 mm Hg or greater with a DBP of less than 95 mm Hg, excluding some trial participants with diastolic hypertension. In a pooled analysis, higher SBP was associated with higher total mortality (hazard ratio [HR] 1.26; 95 percent confidence interval [CI] 1.13–1.40; perm 10 mm Hg) and stroke risk (HR 1.22; 95 percent CI 1.04–1.40; per 10 mm Hg). By contrast, higher DBP was associated with a lower risk of all-cause mortality.

With regard to treatment, the target SBP varied by trial but was generally below 150 mm Hg (8). The results showed decreased total and cardiovascular mortality and reduced nonfatal cardiovascular events, particularly stroke, among the treated patients. A more recent Cochrane Database review included 15 trials with 24,055 patients, with the notable addition of the Hypertension in the Very Elderly Trials (HYVET), and came to a similar conclusion. They estimated a modest reduction in total mortality (relative risk 0.90, 95 percent CI 0.84–0.97) and reduction in cardiovascular mortality and morbidity (relative risk 0.72, 95 percent CI 0.68–0.77) with treatment of hypertension (9). However, it should be noted that achieved SBP was not less than 140 mm Hg in any of these trials and was often greater than 150 mm Hg. Nevertheless, the SHEP and HYVET trials, which did attain mean SBPs between 140 and 150 mm Hg, also reported favorable outcomes. The Cochrane review included a subgroup analysis of treatment in very elderly patients (80 years or older), which showed no significant benefit in terms of all-cause mortality, including cardiovascular, coronary heart disease, or cerebrovascular disease mortality.

Although clinical trial results provide solid evidence that controlling SBP below 150 to 160 mm Hg improves mortality in the elderly, the optimal target blood pressure is still unclear. Two relatively recent randomized trials have studied strict blood pressure control (SBP less than 140 mm Hg) versus moderate control (SBP 140 to 160 mm Hg) among older individuals and have shown no difference in outcomes, including cardiovascular and cerebrovascular events (10, 11). In addition, a secondary analysis of the International Verapamil-Trandolapril study (INVEST), which compared the efficacy of a calcium antagonist versus a noncalcium antagonist hypertension treatment strategy (12), examined the relationship between blood pressure and adverse outcomes in elderly patients with coronary artery disease (13). The target blood pressure for both arms of the trial was less than 140/90 mm Hg (and less than 130/85 mm Hg in patients with diabetes or renal impairment). In a secondary analysis, outcomes were examined according to achieved blood pressure after the participants were divided into four age categories ranging from less than 60 years to 80 years or older. At baseline, the older participants had higher SBP and the highest prevalence of myocardial infarction (MI), stroke, heart failure, chronic kidney disease, and other comorbid conditions and risk factors for cardiovascular events and death. During the trial, the very old had the highest incidence of adverse outcomes, including death, nonfatal MI, nonfatal stroke, all stroke, and the primary outcome, which combined death, nonfatal MI, and nonfatal stroke. The hazard ratios for the association of SBP during the trial with the combined outcome were “J-shaped” or “U-shaped” for all age groups, but the “optimal” SBP (i.e., the SBP at which the hazard ratio was at its nadir) was higher among older individuals. Whereas risk was lowest at SBPs of 110 to 120 mm Hg among patients under age 70, the lowest risk was at SBPs of 140 to 145 mm Hg for patients 70 and older.

In consideration of these data, members of the Eighth Joint National Committee (JNC 8) recommended more lenient blood pressure goals for individuals aged 60 years and older than in the previous guidelines, setting a target below 150/90 mm Hg (14). Although this target is in agreement with European guidelines (15), there is an interesting difference in that the European guidelines recommend beginning treatment when SBP is above 160 mm Hg to match the population included in the trials showing benefit. Of note, not all members of the JNC 8 panel agreed with raising the target blood pressure to below 150/90 mm Hg in the over-60 age group. The dissenting panel members recently presented a minority view (16) in which they argued that increasing the target will likely lead to a reduction in the intensity of antihypertensive treatment in this group, reversing the decades-long trend of better blood pressure control. They also point out that because older individuals are at higher risk of cardiovascular events than are younger persons, this recommendation for less aggressive treatment applies to the group at the highest absolute risk of adverse events who stand to benefit the most.

The impact of frailty and comorbidity

These disagreements among experts reflect a lack of definitive RCT evidence to determine the optimum SBP for maximal cardiovascular event-free survival among older individuals. It must also be recognized that the elderly population is heterogeneous and includes individuals who are completely independent and robust in addition to those who are frail or even disabled. Therefore, setting blood pressure targets according to age alone may not be prudent. Some who support higher
blood pressure targets in the elderly have emphasized that clinical trial participants represent a relatively healthy subgroup. In particular, the HYVET study excluded patients with most major comorbid conditions and individuals requiring nursing care (17). In clinical practice, decisions regarding blood pressure targets are particularly difficult in poor-functioning older adults who do not meet the inclusion criteria of the RCTs, and it is not clear whether the risks and benefits in this population differ.

Several studies have raised concerns that aggressive blood pressure treatment may increase the risk of falls in the elderly. A recent study of Medicare beneficiaries over age 70 with hypertension compared the incidence of serious fall injuries among patients receiving no antihypertensive medication, those receiving moderate-intensity, and those receiving high-intensity antihypertensive treatment (18). Antihypertensive medications were associated with a higher risk of serious fall injuries, particularly among patients with a history of previous fall injuries.

Cognitive function is another important determinant of independent living and quality of life among the elderly that might be affected by hypertension or its treatment (either positively or negatively). Although hypertension has been associated with cognitive decline, data on the treatment of hypertension on cognitive function has been confined mainly to low-risk trials. The study of the Syst-Eur trial reported a significantly lower incidence of dementia in the treatment group (19), the SHEP and HYVET trials did not show any significant difference between the treatment arms versus placebo (20, 21). Thus, available RCT evidence does not show clear cognitive benefit or harm with treatment of hypertension in the elderly. It is important to note that the relatively short follow-up of some studies could limit the power to detect differences in cognitive function with treatment.

A recent observational study published in the Archives of Internal Medicine assessed whether the risk of hospitalization for hip fracture among elderly NHANES participants 65 years and older into three groups according to gait speed over a 20-foot walk: faster (greater than or equal to 8 m/sec), slower (less than 8 m/sec), and unable to complete the test (22). Among individuals with faster gait speed, higher SBP was associated with higher mortality. However, there was no association between SBP and mortality among slow walkers. Furthermore, among individuals who were unable to complete the walk test, the risk of death was actually lower among those with elevated blood pressures. Similarly, a population-based study of institutionalized Very Aged People in the Netherlands showed that although there was no significant association between SBP and stroke overall, the risk of stroke was higher among those with lower SBP in individuals with impaired cognitive or physical function (23). It has been suggested that in frail older adults, higher blood pressure may be necessary to maintain perfusion of vital organs. It is also possible that lower blood pressure among frail elders could be related to underlying malnourishment, heart failure, or other comorbidities, which themselves carry a poor prognosis.

Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized Very Aged Population (PART-AGE), a longitudinal study of 1130 frail individuals aged 80 years or older who were living in nursing homes, addressed the association of blood pressure and antihypertensive medications with mortality (24). At baseline, almost 80 percent of the participants were receiving treatment, and 79 percent of them were taking one agent. A total of 53 percent of women had an SBP of less than 140 mm Hg. After 2 years of follow-up, there was an inverse relationship between baseline SBP levels and all-cause mortality, even after adjustment for age, sex, comorbidity, and level of independence. Further analysis revealed an interaction between low SBP and treatment with multiple antihypertensive medications, such that mortality risk was higher among those with lower blood pressure who were receiving multiple antihypertensive medications (24). These data raise the possibility that hypertension is overtreated among frail nursing home residents.

**Treatment recommendations**

The RCT data clearly support starting antihypertensive therapy at SBP above 160 mm Hg and lowering to a target between 140 and 150 mm Hg. Experts disagree on how these data should be extrapolated in clinical practice, with some recommending beginning treatment at a lower SBP (greater than 150 mm Hg) (14) or targeting a lower SBP (less than 140 mm Hg) (25), particularly among relatively healthy individuals aged 60 to 79 years. There has been less emphasis on how to reach these goals. Although some have raised concerns about the safety of sodium restriction and weight loss, an RCT showed benefit of salt restriction among individuals aged 60 to 80 years (26). Weight loss among older participants also resulted in better blood pressure control and fewer cardiovascular events. The American Heart Association and the European Society of Hypertension have emphasized the importance of total blood pressure reduction over the choice of antihypertensive medication based on the results of several studies and meta-analyses comparing different classes of antihypertensives.

Cognitive function with treatment. Guity Farahmand, MD, and Carol Lee, MD, are affiliated with the Division of Nephrology, University of California, San Francisco. Kirsten L. Johansen, MD, is affiliated with the Division of Nephrology, University of California, San Francisco, and San Francisco VA Medical Center.

**References**


