

# Stroke and Hypertension: Recent Trends of High Blood Pressure and the Decline in Stroke Mortality

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## ABSTRACT

High blood pressure has long been recognized as associated with increased risk of stroke. Basically, the higher the systolic blood pressure, the greater the risk of stroke. The high blood pressure risks are evident in both genders, all ages and all population. Since the 1970s, evidence has been generated determining that lowering the blood pressure reduces the risks of stroke. At the population level, the blood pressure distributions in the United States have shifted to the left, i.e. current population blood pressure levels are lower than previous decades. These lower blood pressures are associated with lower stroke risks. The lower blood pressures are attributed to structured programs implemented specifically to lower blood pressure in the population, clinical guidelines detailed to pharmacologically lower pressures, hypertension prevention efforts and programs, and additional resources devoted to lower blood pressure. These intervention and prevention have been effective in lowering blood pressures and stroke risk reduction. While additional improvements remain to be accomplished globally, the models of lower blood pressures and hypertension should be considered one of the major public health success stories in the past 50 years and a major objective for population risk reduction throughout the world.

**Keywords:** Blood pressure, Disease risks, Hypertension, Population, Stroke.

**How to cite this article:** Lackland DT. Stroke and Hypertension: Recent Trends of High Blood Pressure and the Decline in Stroke Mortality. *Hypertens J* 2015;1(1):22-27.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

The diagnosis, treatment, management and prevention of high blood pressure (BP) represent one of the major global public health issues of the past century. Every country and population is affected by elevated BP with adverse outcomes, such as stroke and end-stage renal disease

with the associated economic burden. However, the successful efforts for hypertension control and prevention have manifested into a public health success story with global implications.<sup>1</sup> The World Hypertension League is positioned to address the global issues through member societies and regional offices.

## HYPERTENSION RISKS

Hypertension risks were first recognized with the association of BP levels and stroke risks in the 1920s.<sup>2</sup> Early clinical studies identified clear benefits of lowering BP on reducing stroke deaths.<sup>3</sup> Several studies were stopped earlier as the benefits of the treatment of high BP were evident.<sup>4,5</sup> Similarly, other studies reported a consistent pattern of benefit of hypertension treatment.<sup>6,7</sup> The evidence for the benefits of lower blood is strong, continuous, graded, consistent, independent, predictive, and etiologically significant for those with or without comorbid conditions including coronary heart disease.<sup>8,9</sup> These results were so significant such to be used in development and implement the national programs, such as National High BP Education Program (NHBPEP) in the USA that promoted hypertension screenings and patient treatment.<sup>10</sup>

Lowering high BP is proposed as a major factor for the reduction in stroke death rates during the last half of the 20th century and early 21st century.<sup>11</sup> Specifically, hypertension-related outcomes, such as stroke mortality was reduced from 88/100,000 in 1950 to 23/100,000 in 2010, with consistent reductions in mortality for all age, race and sex groups in the US as well as other countries is consistent with high BP recognition and reduction campaigns initiated during the same period.<sup>12</sup> These BP reduction strategies included clinical interventions for hypertension and public health efforts focused on lifestyle for the shifting of BP distributions.<sup>1</sup> The decline in hypertension-related outcomes significantly accelerated after the introduction of tolerable antihypertensive drug therapy in the 1960s.<sup>13</sup>

Epidemiological studies have shown elevated BP is the most important determinant of the risk of stroke with a linear relationship beginning at relatively low levels of systolic and diastolic BP.<sup>14</sup> Risk factors for high BP, including increased body mass, obesity, increased waist

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circumference, higher alcohol intake, and greater sodium intake are also associated with increased risks for high BP related outcomes.<sup>15</sup> It is estimated that the overwhelming majority of strokes each year could be prevented through awareness and optimal management of hypertension.<sup>16</sup>

## PREVALENCE OF HIGH BLOOD PRESSURE AND BLOOD PRESSURE DISTRIBUTION

Recent estimates from population surveillance identify over 68 million individuals with high BP warranting some form of monitoring or treatment in the US alone.<sup>17-19</sup> Global hypertension prevalence estimates of 1 billion individuals, with an estimated 7.1 million deaths per year attributable to hypertension.<sup>20</sup> As the population ages, the number of individuals with elevated BP increases.<sup>1,21,22</sup> The substantial and increasing prevalence of elevated BP combined with the evidence-based benefit of hypertension treatment have led to the prioritization of prevention and control programs among governmental, professional and voluntary agencies with considerable success achieved.<sup>1</sup> The percentage of patients with hypertension receiving treatment has increased to where more than 90% of the population knows the relationship between high BP and stroke, nearly 70% of the adult hypertensive population are treated, and nearly half of those treated for high BP are controlled to below 140/90 mm Hg.<sup>23,24</sup>

The mean systolic BP (SBP) for the US adult population declined from 131 mm Hg in 1960 to 122 mm Hg in 2008.<sup>1,25,26</sup> Between 1959 and 2010, median and 90th percentile systolic BP declined by approximately 16 mm Hg.<sup>1</sup> This declining shift in BP distributions was consistent for different age groups, including 18 to 29 years, 18 to 39 years, 30 to 59 years, and 60 to 74 years.<sup>1</sup> These population wide changes in reduced BP seen within the last five decades have been associated with the large accelerated reductions in stroke mortality.<sup>1</sup> The shift to the left in mean arterial BP is more pronounced in older Americans who have a greater prevalence, who are more likely to visit physicians and who are on BP treatment, than in younger people, even though they may be less likely to achieve goal BP. Goff et al described a gradual downward shift of the entire distribution of BP levels in the general population going back to the early 1900s.<sup>27</sup> The recognition of elevated BP as a risk factor appears to have affected BP levels and subsequent stroke mortality risks. While the decline in stroke mortality and lowering BP may have appeared to be evident before this recognition and treatment of hypertension, the effects of lowered BP is most evident after the population-based campaigns.<sup>1</sup> Hypertension treatment and control rates have consistently increased since the early 1970s.<sup>1</sup> This improvement is seen in all subsets of the population. Further demonstrating the impact of treatment, SBP is

lower for treated hypertensive than untreated groups. All populations have shown significant improvements during the time period. Likewise a reduction in mean SBP has been observed for all age, race, and gender groups.<sup>1</sup> The 90th percentile SBP levels have been lowered over the past decades suggesting significant impact of hypertension treatment and control. Similarly, the 10th percentiles have also been lower through the past years.<sup>1</sup> The reduction in these lower BP levels is most likely the result of lifestyle and nonpharmacologic interventions and public health activities.

Pharmacological treatment of BP focuses on individuals with hypertension defined as a value of 140/90 mm Hg or greater, the risk of stroke begins at BP below 140/90 mm Hg levels.<sup>28</sup> A meta-analysis of 61 studies found each incremental rise of 20 mm Hg SBP and 10 mm Hg DBP was associated with a two-fold increase in death rates from stroke.<sup>1</sup> In addition, age-related rise in SBP is primarily responsible for an increase in both incidence and prevalence of hypertension with a lifetime risk of hypertension to be approximately 90% for men and women, who were nonhypertensive at 55 or 65 years and survived to age 80 to 85.<sup>29,30</sup> These risks demonstrate the impact of BP on outcomes.<sup>31</sup> The increase of BP to hypertensive categories with increasing age is evident by patterns and trends indicating that the 4-year rates of progression to hypertension are 50% for those 65 years and older with BP in the 130 to 139/85 to 89 mm Hg range and 26% for those with BP between 120 and 129/80 to 84 mm Hg range.<sup>32</sup>

Greatest benefits of BP reduction are evident in the severe category of elevated BP levels.<sup>33,34</sup> These extreme BP levels are more prevalent among the high stroke risk populations, especially African Americans, but the values have been reduced with treatment with corresponding risk reduction.<sup>35,36</sup> However, hypertension emergencies, crises and malignant hypertension represent a small percent of the population with high BP. Up to 2% of patients with hypertension develop a hypertensive crisis at some point in their lifetime.<sup>37,38</sup>

## OBSERVATIONAL STUDIES

Cohort studies have demonstrated increased attributable risks associated with elevated BP levels.<sup>1,39,40</sup> High BP was identified as responsible for the largest number of cardiovascular and stroke deaths in the US.<sup>1,36</sup> The INTERSTROKE study concluded the contribution of various risk factors to the burden of stroke worldwide to be 34.6% for hypertension (CI 30.4–39.1).<sup>41</sup> In addition, it was estimated that among treated hypertensives, approximately 45% of all strokes might be attributed to uncontrolled BP.<sup>42</sup> Such risk estimates are consistent for all components of the population with significant

population-attributable risk for elevated BP and stroke mortality.<sup>1</sup> The relationship between BP and risk of cardiovascular disease (CVD) events is demonstrated over time, continuous, consistent, and independent of other risk factors. The linear relationship holds true for all demographics indicating the higher BP the greater the risk of stroke mortality.

## CLINICAL TRIALS

The benefit of hypertension treatment to reduce stroke risks is evident with the effective number needed-to-treat (NNT) estimates. Treatment of high BP has been associated with reductions in stroke incidence by 35 to 40%; myocardial infarction, 20 to 25%; and heart failure, more than 50%.<sup>43</sup> It is estimated that among patients with stage one hypertension (SBP 140–159 mm Hg and/or DBP 90–99 mm Hg) and additional cardiovascular risk factors, achieving a sustained 12 mm Hg reduction in SBP over 10 years will prevent one cardiovascular event for every 11 patients treated. In the presence of CVD or target organ damage, only nine patients would require such BP reductions to prevent death.<sup>44</sup> Clinical trials have demonstrated that control of systolic hypertension reduces stroke risks.<sup>45–48</sup> Results from the hypertension detection and follow-up program (HDFP) showed that reductions of 4.7 mm Hg reduced stroke mortality by 17.6%.<sup>49</sup>

Several studies focused on secondary prevention. The Dutch TIA trial study and other major trials have shown significant lower rates of recurrent stroke with lower BP.<sup>50</sup> The secondary prevention of small subcortical strokes (SPS3) trial showed targeting a systolic BP less than 130 mm Hg is likely to reduce recurrent stroke by about 20% ( $p = 0.08$ ) and significantly reduced intracerebral hemorrhage by two-third.<sup>51</sup> The ongoing systolic blood pressure intervention trial (SPRINT) is a 2-arm, multicenter, randomized clinical trial designed to test whether a treatment program aimed at reducing SBP to a lower goal than currently recommended will reduce cardiovascular disease and stroke risk as well as cognitive function.<sup>52</sup>

## HYPERTENSION TREATMENT GUIDELINES

From the 1970s, high BP guidelines have been developed to guide clinical practice with high impact on elevated BP control and management of high BP.<sup>8,14,53–61</sup> The treatment guidelines have included recommendations focused on the reduction of hypertension-related conditions including stroke. The guidelines have evolved as evidence about the benefits of treating to lower BP levels becomes available as well as study results, which differentiate the effectiveness of the different classes of treatment. A

major contribution of the clinical guidelines remains the definition of hypertension and BP treatment goals. With each set of guidelines, the BP level for treatment and goals have typically been lowered. These recommendations may have impact population BP levels as systolic BP have been lower with the evolving guidelines. These guidelines recommendations for clinical management are also used for public health hypertension control efforts. The implementation of the guidelines to address the population at risks is designed to impact the disease risk.<sup>62</sup>

## STRUCTURED PROGRAMS

The impact of elevated BP on the population has led to the establishment of prevention and management strategies for hypertension as major public health objectives with the premise that if the elevation of BP with age can be prevented or reduced, outcomes, such as stroke will be affected.<sup>1</sup> This concept has led to the implementation of public health strategies and programs to reduce BP in the population as an effort to lower risks. The traditional global risk factors include excess body weight; excess dietary sodium intake; suboptimal physical activity; inadequate intake of fruits, vegetables, and potassium; and excess alcohol intake.<sup>63</sup> These programs are aimed at working with the food industry and restaurants as well as establishing policies to reduce salt in the prepared and processed food, encouraging the consumption of more fresh fruits and vegetables, increasing community participation in physical activity, detecting and tracking high BP at churches, worksites and community events and public education campaigns.<sup>64,65</sup>

This population-based approach complements the clinical hypertension treatment and management. Primary prevention strategies are implemented to reduce the BP levels in the population. The desired outcome is the shift to the left of BP distributions in the general population delays in onset of hypertension and BP-associated morbidity and mortality.<sup>1</sup> Risk estimates from the two decades ago predicted a 5 mm Hg reduction of SBP in the adult population would result in a 14% overall reduction in mortality due to stroke.<sup>66</sup> The reduction in SBP is consistent with the decline in stroke mortality, and corresponds to the predicted lower stroke mortality rates.<sup>1</sup>

In summary, multiple evidence sources identify the impact of BP reduction on stroke mortality decline in many population demonstrating the impact of high BP control and prevention. Epidemiological and observational studies over the past five decades consistently identify a significant association of BP level and stroke mortality for all genders, races and cultures, as well as all age groups. Clinical trials have confirmed the consistent findings of reduced BP and lower stroke mortality rates. The trends in stroke risks with BP



level identified from the observational epidemiologic studies are consistent with the evidence for the levels of BP reduction from clinical trials. The evidence is strong such that clinical guidelines and intervention programs focus on BP management and lower BP levels for primary and secondary stroke prevention. These comprehensive components of population risk reduction are ideal models for the clinical medicine and population health partnership. The accelerated decline in stroke mortality beginning in the 1970s is consistent with the aggressive hypertension treatment and control strategies implemented in that time period. In addition, with an aging and heavier population, the pool of at-risk individuals has increased substantially during this time period. The decrease in BP with drug therapy as assessed in clinical settings and widespread public health interventions in the general population appears to be the major determinant for reduction in the risk of hypertension-related outcomes. These success stories provide a tremendous opportunity for partnerships and the world hypertension league specifically addressing the global burden of elevated BP.

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