

# Factors Influencing the Decline in Stroke Mortality

A Statement from the  
American Heart Association/American Stroke  
Association



Stroke

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**Factors Influencing the Decline in Stroke Mortality: A Statement From the American Heart Association/American Stroke Association**

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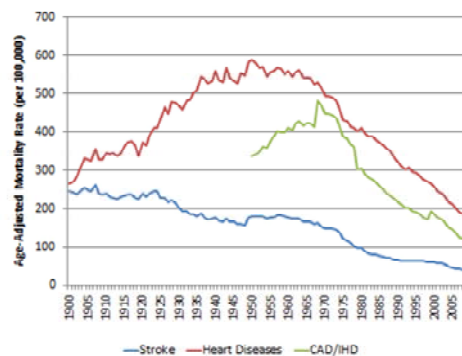
## Introduction

- The remarkable decline in stroke mortality has been acknowledged as one of the 10 great public health achievements for the United States (US) in the 20th century.
- Stroke has now fallen from the third to the fourth leading cause of death in the US.
- While both stroke and ischemic heart disease mortalities have declined substantially, the patterns of their decline stand in stark contrast.

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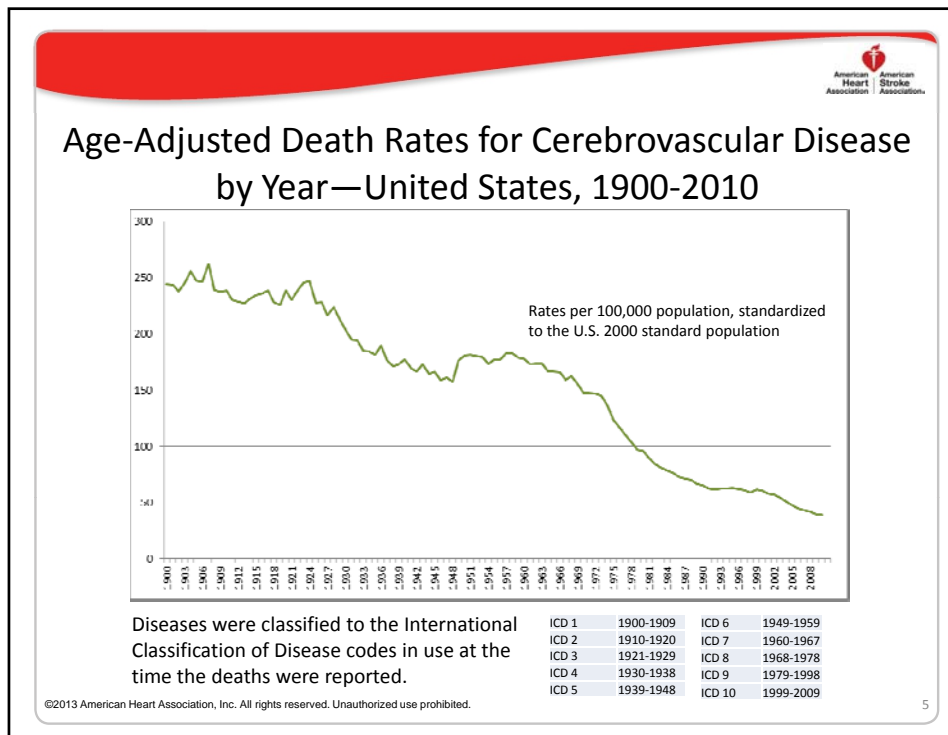
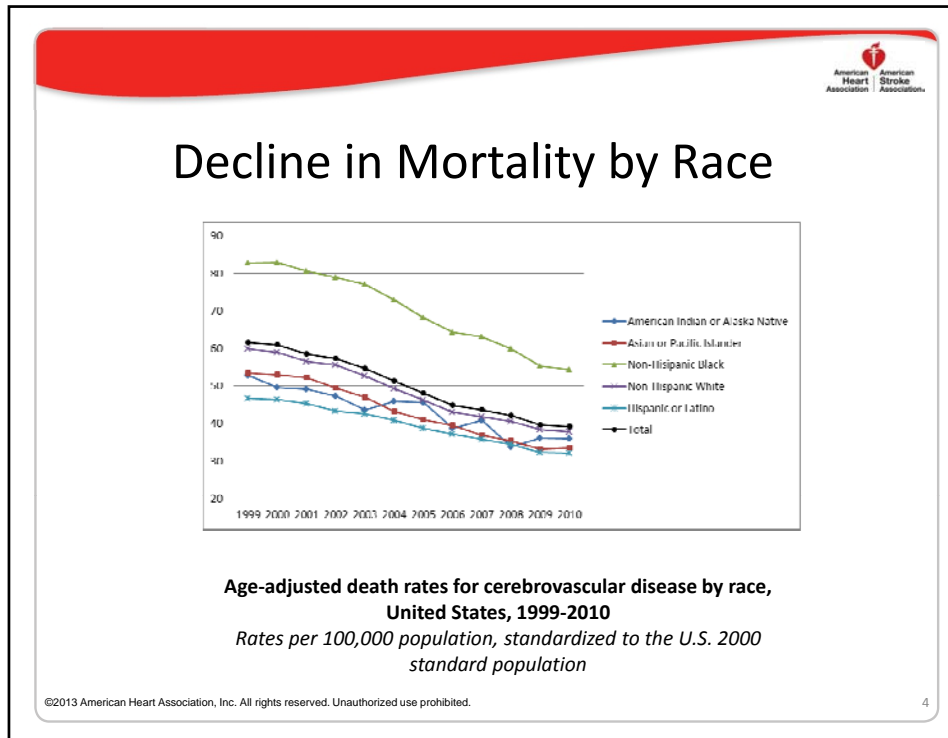
## Decline in Death Rates



Per 100,000 population, standardized to the U.S. 2000 standard population  
 Diseases were classified to the International Classification of Disease codes in  
 use at the time the deaths were reported

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### III. Recurrent and Incident Strokes

- Assessment of stroke mortality includes
  - Case fatality, in-hospital mortality, 30-day mortality, 1-year mortality, and various definitions across studies
    - 30-day mortality rate near double for recurrent stroke
    - Early mortality often related to index stroke
    - Later mortality often related to cardiovascular disease
      - Recommendation that ischemic stroke be included in cardiac risk assessment models as survivors are more likely to die from a cardiovascular event

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### Trends in Recurrence

- Recurrent stroke has declined substantially over the last 5 decades
  - Almost 50% reduction in recurrent stroke rates in the 1990s and 2000s as compared to the 1960s
- Clinical trials over 5 decades have demonstrated benefit of secondary stroke prevention therapies
  - Improved blood pressure control, increased use of antiplatelet and anticoagulant medications, statins, and decreased smoking rates

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## Trends in Stroke Incidence

- Worldwide stroke incidence studies from the 1970s through 2008 show incidence and case fatality rates in high-income countries declined 42% but increased in low to middle income countries
  - Greater Cincinnati Northern Kentucky Stroke Study (GCNKSS)
    - Incidence declined in 2005 compared to 1993-1994 and 1999 among whites but not blacks, with no change in hemorrhage or case fatality rates.

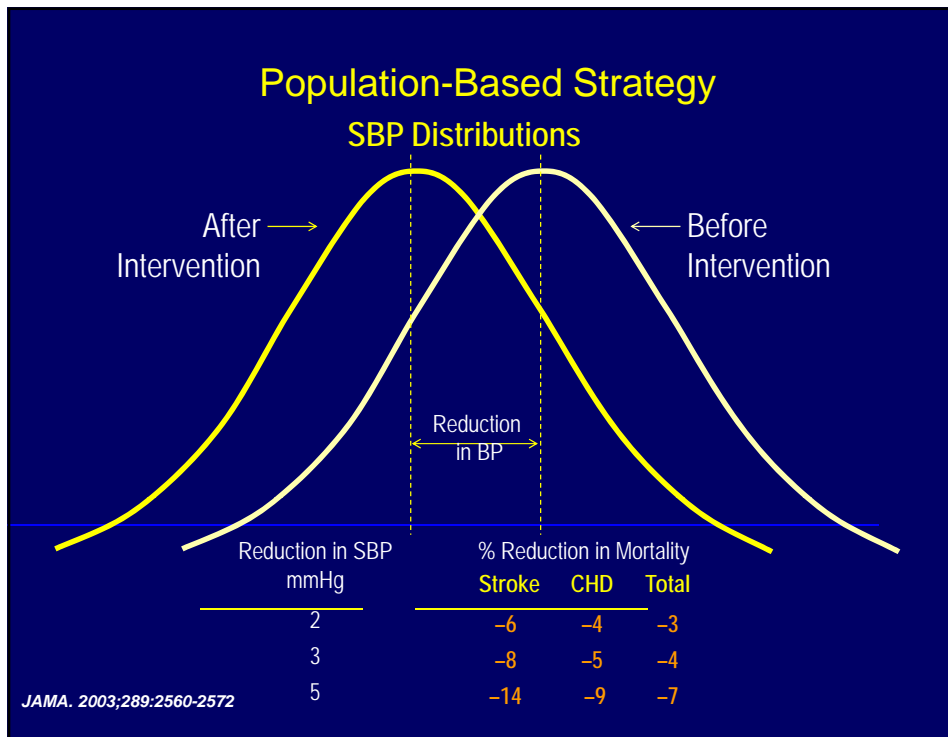
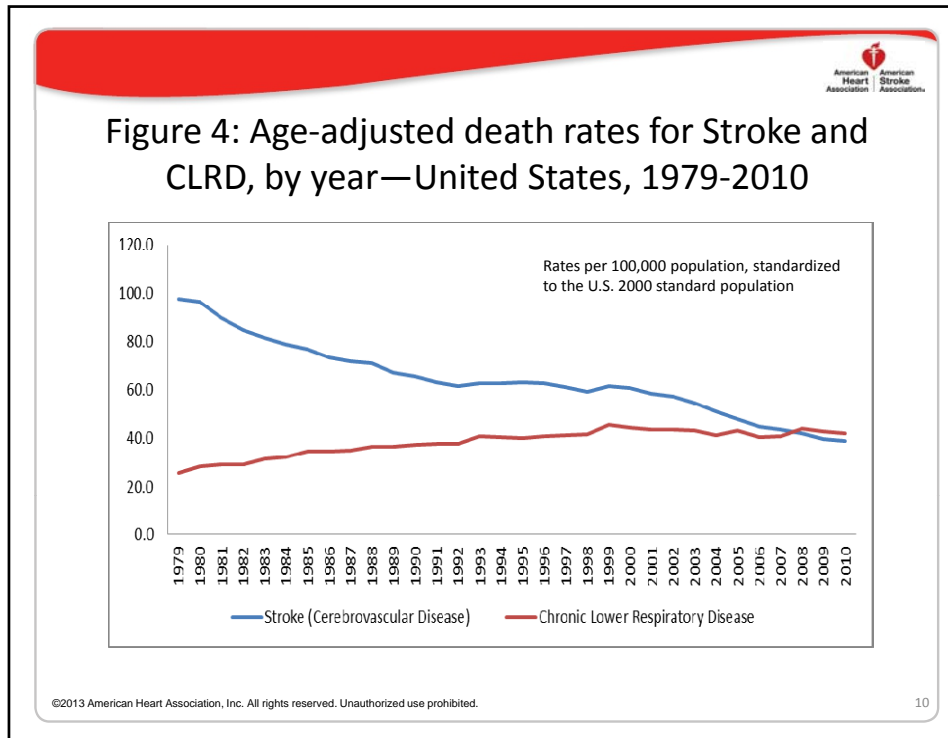
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## IV. Changes in Pulmonary and Lung Disease on the Assessment of Stroke Mortality Trends and Ranking

- Chronic Lower Respiratory Disease (CLRD)
  - Mortality rates slowly increased 1979-1999 then declined from 2000-2008
- Stroke Mortality Rates
  - Declined steadily over the past 100 years
    - 1/2% per year until the 1970s when rate of decline accelerated to 5% per year
- These mortality trends for CLRD and Stroke resulted in a change in the ranking

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## V. Hypertension as a Factor in the Decline in Stroke Mortality

- Society of Actuaries first recognized the association of blood pressure levels and risk of stroke in the 1920s.
- Evidence for the benefits of lower blood pressure and reduced stroke risks is ***strong, continuous, graded, consistent, independent, predictive, and etiologically significant*** for those with and without coronary heart disease

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## Hypertension, *Continued*

- High blood pressure recognition and reduction campaigns are associated with the US age-adjusted stroke mortality rate reduction from 88 in 1950 to 23/100,000 in 2010
  - Blood pressure reduction strategies
    - Clinical interventions
    - Public health efforts focused on lifestyle modification
      - Obesity, high alcohol intake, sodium intake, healthier diets, physical activity, and smoking cessation

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## Prevalence of HTN

- Global estimates of 1 billion individuals and 7.1 million deaths attributable to HTN
- National Health and Nutrition Examination Survey (NHANES) estimates 68 million Americans have HTN
  - 70% treated
  - 46% controlled to below 140/90 mmHg
  - Median SBP declined 16 mmHg between 1959 and 2010

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## Prevalence of HTN (Continued)

### Mean Systolic Blood Pressure (SBP) by Time Period NHANES I-IV

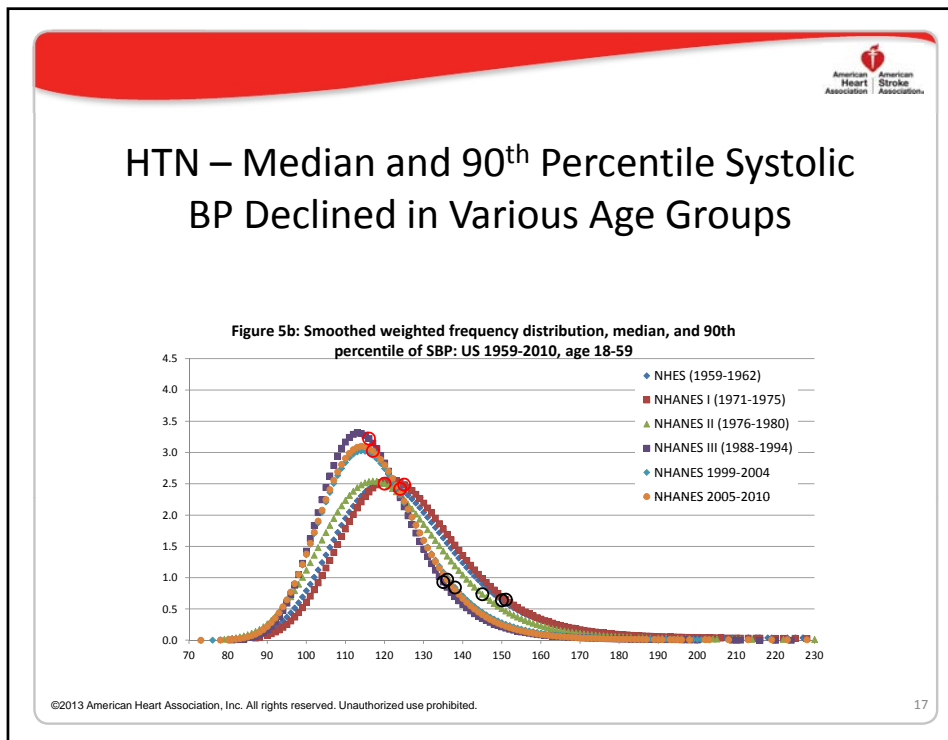
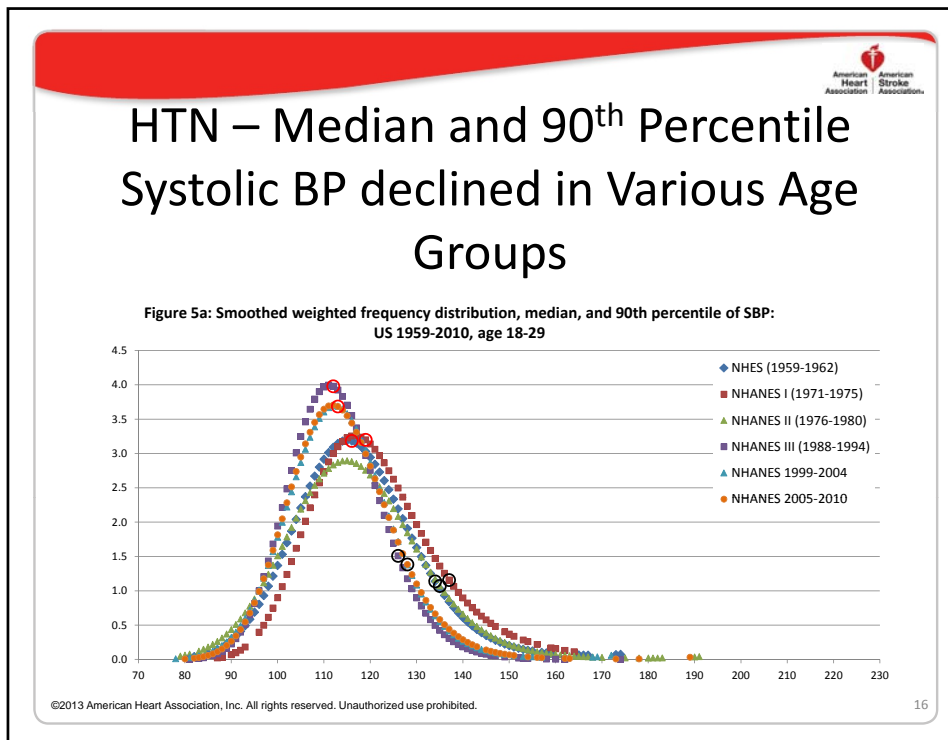
TABLE 1	
YEAR	SBP (Hg)
1960-62	131 mm
1971-74	129 mm
1976-81	126 mm
1988-91	119 mm
1988-94	121 mm
1999-04	123 mm
2001-08	122 mm

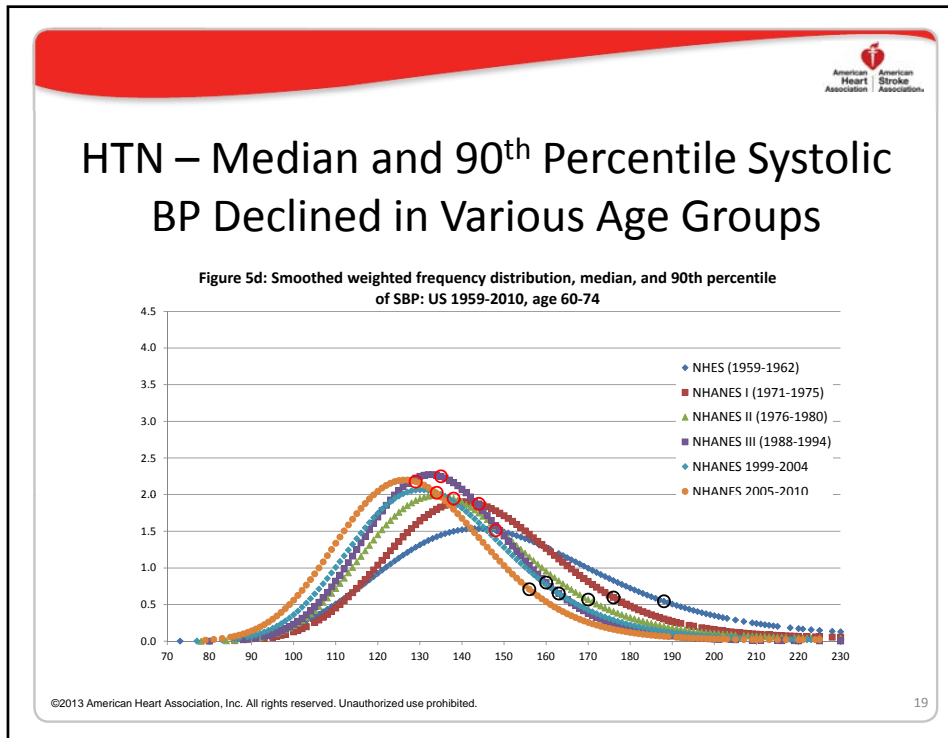
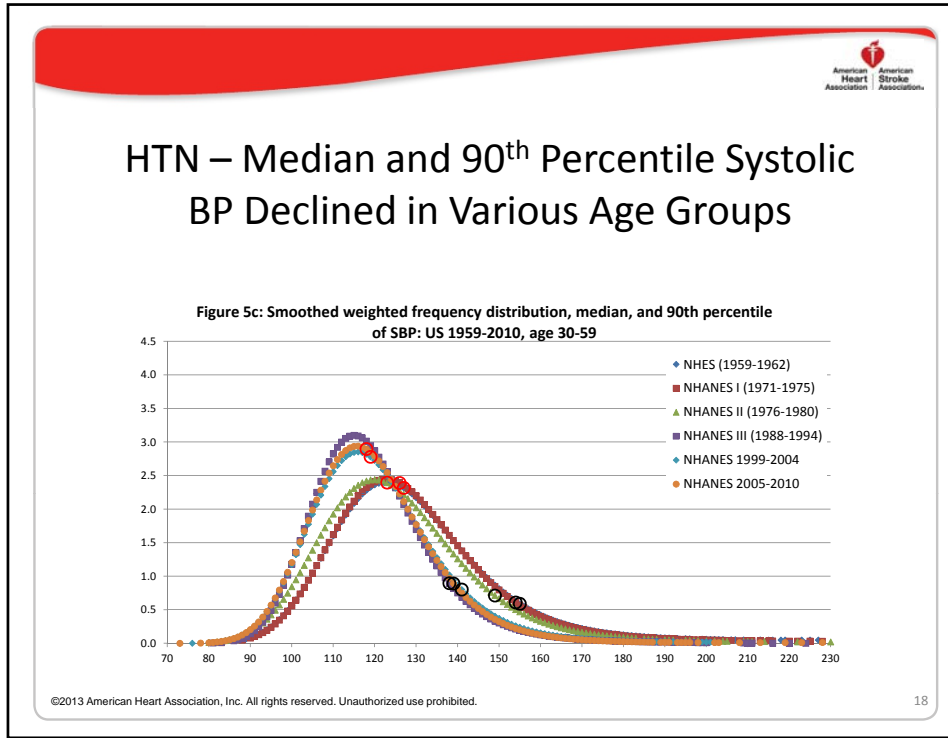
Mean SBP for the US adult population declined from 131 mmHg in 1960 to 122 mmHg in 2008.


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## Summary - HTN

- Declining shift in BP distribution consistent for different age groups
- Population-wide changes in reduced blood pressures associated with large accelerated reductions in stroke mortality
- Shift in mean arterial blood pressure is more pronounced in older Americans than younger Americans

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## HTN – Risk of Stroke begins at BP below 140/90 mmHg

- Meta-analysis of 61 prospective studies observed 1M adults between the ages of 40-69 years with starting BP of 115/75 mmHg
- Each incremental 20 mmHg (SBP) and 10 mmHg (DBP) was associated with a 2x increase in stroke death rates
- This effect is seen in all decades of life.

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## HTN – Clinical Trials: Benefit of HTN Treatment to Reduce Stroke Risks

- In clinical trials, antihypertensive therapy has been associated with reductions
  - Stroke incidence averaging 35-40%
  - Myocardial infarction 20-25%
  - Heart failure more than 50%

Clinical trials have demonstrated that control of isolated systolic hypertension reduces total and stroke mortality

Reducing SBP even if BP control levels are not achieved improves risks and outcomes.

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## HTN – Clinical Trials

- ALLHAT and CONVINCe trials show DBP control rates exceeded 90% but SBP control rates were considerably less (60-70%).
- Hypertension Detection and Follow-up Program (HDFP) showed that reductions of 4.7 mmHg reduced stroke mortality by 17.6%.
- Meta-analysis (32 trials)
  - confirmed HTN treatment reduces stroke risks
  - showed substantial stroke risk reduction with tight BP control and lowered BP levels
  - determined a 41% reduction in stroke risks with systolic BP reductions of 10 mmHg

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## HTN – Clinical Trials: Reduction of Recurrent Strokes

- Secondary Prevention
  - Dutch TIA Trial Study and others have shown significantly lower rates of recurrent stroke with lower blood pressures
  - Secondary Prevention of Small Subcortical Strokes (SPS3) Trial showed targeting a systolic blood pressure < 130 mmHg is likely to reduce recurrent stroke by about 20% and significantly reduced intracerebral hemorrhage by 2/3

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## HTN – Structured Programs to Lower Stroke Risks

- Structured programs are used to implement public health programs that focus on decreasing blood pressure and therefore stroke risks
- Programs are aimed at working with manufacturers, restaurants, and food procurement policymakers to decrease stroke risk factors via
  - Reduction of salt in prepared and processed food
  - Encouragement of fresh produce consumption
  - Increasing community participation in physical activity
  - Detecting and tracking HBP at community places

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## HTN – Structured Programs: Identification of Stroke Belt

- 1970s – NHLBI provided funding and technical assistance to develop state hypertension education and control programs
- Programs developed patient tracking systems to determine what became of those screened
- Results demonstrated a sharp increase in HTN control rates and a marked decline in stroke mortality
- Became evident that the Southeast US experienced greater HTN prevalence and more severe HTN
- 2 landmark studies were published identifying 11 contiguous states in the Southeast had higher stroke mortalities than the rest of nation named the Stroke Belt

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## HTN – Structured Programs: Identification of Stroke Belt

- NHLBI and partners developed structured education efforts in the Southeast.
- To increase the intensity of education activities
  - Blood pressure screening programs were conducted using models from activities in barbershops
  - Mass media campaigns increased to
    - encourage people to know their numbers
    - visit their doctor
    - reduce salt consumption
    - increase physical activity

This compendium of structured community and professional activities was associated with a reduction in stroke mortality in the Southeast.

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## HTN – Research Gaps and Considerations

- How to lower the number of hypertension-related ICH cases in older age-groups currently using antithrombotics
- An increase in prevalence of amyloid angiopathy among aging population could lead to an increase in the number of ICH cases
- Studying cerebral microbleeds (CMB) and HTN as it relates to increased stroke risks has the potential to be an important biomarker
- These studies also facilitate disparities as significant racial differences in CMB prevalence in ICH.

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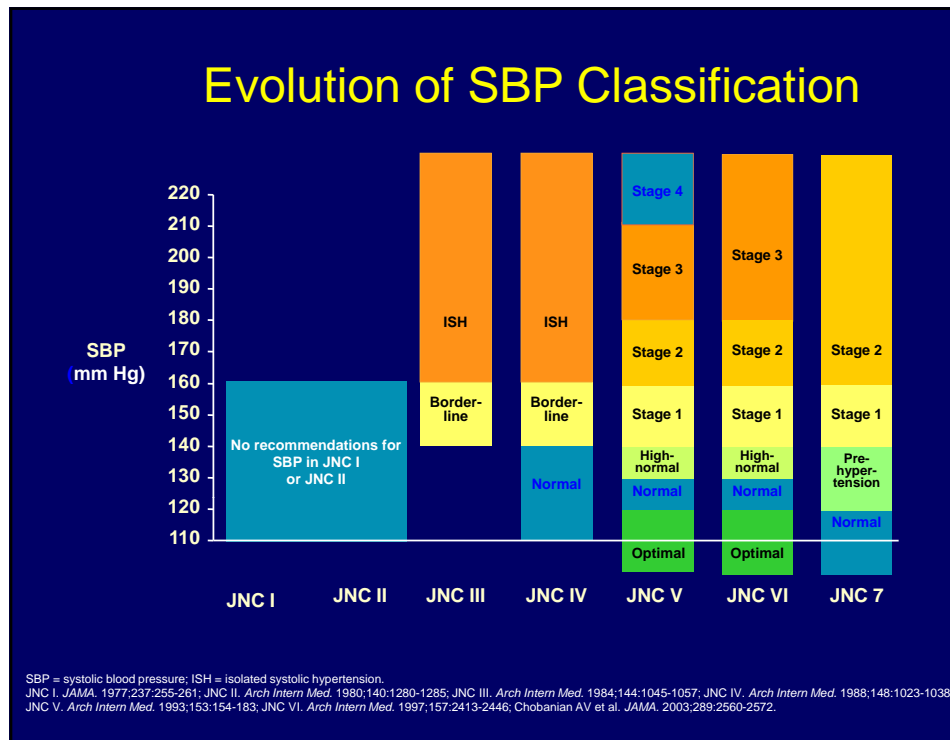
## HTN – Summary

### “Higher BP = Greater Stroke Risk”

- Observational epidemiological study findings are consistent with clinical trial findings that BP reduction results in lower stroke mortality rates
- Major determinant for decrease in stroke prevalence and mortality → decrease in BP with drug therapy

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## HTN – Treatment Guidelines

- JNC’s BP treatment guidelines have included recommendations focused on lowering HTN-related conditions including stroke.
- With each set of JNC guidelines, the BP level for treatment and goals has typically been lowered, possibly impacting the population BP levels as SBPs have been lower (Table 1).

YEAR	SBP (Hg)
1960-62	131 mm
1971-74	129 mm
1976-81	126 mm
1988-91	119 mm
1988-94	121 mm
1999-04	123 mm
2001-08	122 mm

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## 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

### Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C.ushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

#### **Recommendation 1**

In the general population aged  $\geq 60$  years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP)  $\geq 150$  mm Hg or diastolic blood pressure (DBP)  $\geq 90$  mm Hg and treat to a goal SBP  $< 150$  mm Hg and goal DBP  $< 90$  mm Hg. (Strong Recommendation – Grade A)

#### **Corollary Recommendation**

In the general population aged  $\geq 60$  years, if pharmacologic treatment for high BP results in lower achieved SBP (eg,  $< 140$  mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)


While all panel members agreed that the evidence supporting recommendation 1 is very strong, the panel was unable to reach unanimity on the recommendation of a goal SBP of lower than 150 mm Hg. Some members recommended continuing the JNC 7 SBP goal of lower than 140 mm Hg for individuals older than 60 years based on expert opinion.<sup>12</sup> These members concluded that the evidence was insufficient to raise the SBP target from lower than 140 to lower than 150 mm Hg in high-risk groups, such as black persons, those with CVD including stroke, and those with multiple risk factors. The

**Annals of Internal Medicine**

**SPECIAL ARTICLE**

### **Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View**


Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, PhD; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP



## Diabetes Treatment and Effect on Stroke Prevalence

- Diabetes mellitus is a risk factor for stroke and stroke mortality
- Diabetes prevalence has been increasing in US and the world
- Sparse data are available regarding trends in population prevalence of diabetes treatment or treatment intensity
- Temporal effect of changes in diabetes treatment on risk of stroke death cannot be determined


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## Atrial Fibrillation Treatment Effect on Stroke Mortality Decline

- Data on trends in age-adjusted prevalence of AF are limited by ascertainment bias
  - Framingham study showed increasing trend in prevalence of AF among men aged 65-84 years
    - 2% in 1968-70 to 5.3% in 1987-1989 (p=0.08)
- Anticoagulation with warfarin for AF reduces fatal and non-fatal stroke by approximately 50%
- Between 2003 and 2009, Get with the Guidelines showed anticoagulation for AF increased from 28% to 69%


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## Recent Trends in Dyslipidemia Prevalence in the United States

- Dyslipidemia remains highly prevalent in the United States
- NHANES population
  - Total Cholesterol  $\geq 240$  mg/dL decreased
    - 20.5% in 1988-94 to 14.2% in 2005-10
  - Mean low-density lipoprotein cholesterol (LDL-C)
    - 134 mg/dL in 1976-80 to 119 mg/dL in 1999-2006
- Estimated 33.5 million adults >20 years have total cholesterol levels  $\geq 240$  mg/dL


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## Effects of Antiplatelet Drugs on Decline in Stroke Mortality

- Use of aspirin following acute ischemic stroke is well established without opportunity for improvement
- In outpatient setting, large number of individuals with known cardiovascular disease are not taking aspirin
  - Opportunity exists to further reduce incidence of mortality rate from stroke

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## Contribution of Neurological and Technical Advances in Stroke Treatment

- Technological advances, medical treatment options, and systems of delivering care have affected stroke mortality rates
- 1920s and 1930s: cerebral angiography
- 1940s and 1950s: measurement and assessment of cerebral flow metabolism
  - Principles used currently for identifying mismatch between blood flow and tissue injury to identify patients for reperfusion therapies

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## Contribution of Neurological and Technical Advances in Stroke Treatment, *Continued*

- 1950s: Carotid Endarterectomy and Prosthetic Heart Valves for Rheumatic Heart Disease
  - Reduced incidence of stroke from carotid stenosis
  - Reduced risk for embolic stroke
- 1960s: Doppler Ultrasonography
  - Enhanced technology permitted the use of transcranial sonography
    - Proven useful in sickle cell disease

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## Neurological and Technical Advances in Stroke Treatment, *Continued*

- 1970s: Computed Tomography (CT)
  - Main diagnostic tool available for evaluation of brain injury; essential component of all acute treatment protocols
  - There is insufficient evidence identifying a relationship between MRI imaging and stroke mortality
- 1990s: tissue plasminogen activator (rtPA) approved by FDA and endovascular therapy become available

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## rtPA Use on Decline in Stroke Mortality

- Use of rtPA is unlikely to have contributed to decline in stroke mortality rates
  - Randomized controlled trials failed to show that IV rtPA prevents post-stroke death, although it does prevent post-stroke disability
  - Small proportion of ischemic stroke patients treated with rtPA
    - Increased from 1.1% in 2004-2005 to 3.4% in 2009

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## Contribution of Stroke Systems of Care on Decline in Stroke Mortality

- Primary or Comprehensive Stroke Centers and Stroke Systems of Care
  - Primary stroke centers (PSC) may have lower rates of mortality at discharge compared to non-stroke centers, although outcomes were better even prior to certification
    - Certification did not produce reduced mortality rates
  - 11 major criteria for establishing PSCs are not associated with changes in stroke mortality


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## Stroke Systems of Care on Decline in Stroke Mortality Continued

- Telemedicine
  - Geographic barriers exist in treatment of acute stroke patients
    - High-quality video teleconferencing is reasonable for performing a general neurological exam and a non-acute NIHSS assessment
    - FDA-approved teleradiology systems are recommended for timely review of CT scans
    - If stroke specialist is not immediately available, high-quality video teleconferencing can facilitate appropriate use of IV rtPA

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## Contribution of Smoking on Decline in Stroke Mortality

- Cigarette smoking is an independent risk factor for stroke and abstinence from smoking after stroke is associated with better outcomes
- Any decline in prevalence of smoking would contribute to the decline in stroke mortality

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## Contribution of Obstructive Sleep Apnea (OSA) on Decline in Stroke Mortality

- OSA is increasing in the US (due to the rising obesity epidemic) and is an independent risk factor for ischemic stroke and combined endpoint of stroke and death
  - OSA is associated with post-stroke mortality.
  - OSA treatment with continuous positive air pressure (CPAP) reduces cardiovascular events
  - OSA is underdiagnosed and there is poor compliance with the use of CPAP

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## Air Pollution and Environmental Factors on Decline in Stroke Mortality

- The Clean Air Act and implementation of clean air standards have resulted in significant reduction in particulate matter (PM) over time
- Inconclusive epidemiologic evidence of a causal effect of PM on stroke mortality
  - Pollution levels increased from 1900-1970 while stroke mortality was declining.
  - Short-term PM exposure was associated with an increased stroke risk and mortality.
  - Long-term PM exposure studies (in the US) have not been consistent in association with risk of stroke, mortality, or both.

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## Contribution of Exercise on Decline in Stroke Mortality

- Few studies have examined the role of physical activity and stroke mortality
- Significant inverse associations between cardiorespiratory fitness and age-adjusted data, nonfatal, and total stroke rates found in both women and men

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## Obesity and Body Mass Patterns on Decline in Stroke Mortality

- Obesity prevalence rates are rising in the US
  - 36% of US adults are obese
  - 33% of US adults are overweight
- Body mass index (BMI) association with stroke mortality
  - Each 5 kg/m<sup>2</sup> increase in BMI from 25-50 kg/m<sup>2</sup> yielded 40% higher stroke mortality, any stroke subtype
    - Mostly accounted for effects of BMI on blood pressure


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## Impact of Research and Program Funding on Decline in Stroke Mortality, *Continued*

- Significant contribution to the reduction in stroke mortality accomplished
  - Research findings on stroke risk and prevention
  - Funding of studies
  - Intervention programs
- Control rates for hypertension have improved six-fold during the last four decades
  - Driven by an increase in public awareness and treatment

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## Impact of Other Factors on Decline in Stroke Mortality

- Sickle Cell Disease
  - Increased risk of stroke among young African Americans
  - Reduced stroke risk over past 2 decades
    - Use of transcranial Doppler
    - Transfusion therapy
- Salt Intake
  - Reduced sodium intake associated with reduced stroke rates as well as improved blood pressure control

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## Conclusions and Discussion

- Stroke has moved from 3<sup>rd</sup> to 4<sup>th</sup> leading cause of death in the United States
- Decline seen in both genders as well as all races and age groups
- No marked increase in death rates from respiratory disease

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## Conclusions and Discussion, *Continued*

- Combination of different parameters and programs contributes to the significant decline
  - Improved control of blood pressure has resulted in a significant and accelerated decline in stroke deaths
  - Treatment and control of diabetes and hyperlipidemia contribute to decline
  - Systems of care, rtPA use, smoking cessation, air pollution, exercise, atrial fibrillation, and other factors may play a small role in the decline in stroke deaths

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## Conclusions and Discussion, Continued

- The decline in stroke mortality is one of the major public health successes of the past 50 years.
- With implementation of evidence-based primary, secondary, and tertiary stroke prevention strategies, these trends should continue.

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