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Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015

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IMPORTANCE Elevated systolic blood (SBP) pressure is a leading global health risk. Quantifying the levels of SBP is important to guide prevention policies and interventions.

OBJECTIVE To estimate the association between SBP of at least 110 to 115 mm Hg and SBP of 140 mm Hg or higher and the burden of different causes of death and disability by age and sex for 195 countries and territories, 1990-2015.

DESIGN A comparative risk assessment of health loss related to SBP. Estimated distribution of SBP was based on 844 studies from 154 countries (published 1980-2015) of 8.69 million participants. Spatiotemporal Gaussian process regression was used to generate estimates of mean SBP and adjusted variance for each age, sex, country, and year. Diseases with sufficient evidence for a causal relationship with high SBP (eg, ischemic heart disease, ischemic stroke, and hemorrhagic stroke) were included in the primary analysis.

MAIN OUTCOMES AND MEASURES Mean SBP level, cause-specific deaths, and health burden related to SBP (\geq 110-115 mm Hg and also \geq 140 mm Hg) by age, sex, country, and year.

RESULTS Between 1990-2015, the rate of SBP of at least 110 to 115 mm Hg increased from 73 119 (95% uncertainty interval [UI], 67 949-78 241) to 81 373 (95% UI, 76 814-85 770) per 100 000, and SBP of 140 mm Hg or higher increased from 17 307 (95% UI, 17 117-17 492) to 20 526 (95% UI, 20 283-20 746) per 100 000. The estimated annual death rate per 100 000 associated with SBP of at least 110 to 115 mm Hg increased from 135.6 (95% UI, 122.4-148.1) to 145.2 (95% UI 130.3-159.9) and the rate for SBP of 140 mm Hg or higher increased from 97.9 (95% UI, 87.5-108.1) to 106.3 (95% UI, 94.6-118.1). Loss of disability-adjusted life-years (DALYs) associated with SBP of at least 110 to 115 mm Hg increased from 148 million (95% UI, 134-162 million) to 211 million (95% UI, 193-231 million), and for SBP of 140 mm Hg or higher, the loss increased from 95.9 million (95% UI, 87.0-104.9 million) to 143.0 million (95% UI, 130.2-157.0 million). The largest numbers of SBP-related deaths were caused by ischemic heart disease (4.9 million [95% UI, 4.0-5.7 million]; 54.5%), hemorrhagic stroke (2.0 million [95% UI, 16-2.3 million]; 58.3%), and ischemic stroke (1.5 million [95% UI, 1.2-1.8 million]; 50.0%). In 2015, China, India, Russia, Indonesia, and the United States accounted for more than half of the global DALYs related to SBP of at least 110 to 115 mm Hg.

CONCLUSIONS AND RELEVANCE In international surveys, although there is uncertainty in some estimates, the rate of elevated SBP (\geq 110-115 and \geq 140 mm Hg) increased substantially between 1990 and 2015, and DALYs and deaths associated with elevated SBP also increased. Projections based on this sample suggest that in 2015, an estimated 3.5 billion adults had SBP of at least 110 to 115 mm Hg and 874 million adults had SBP of 140 mm Hg or higher. *JAMA*. 2017;317(2):165-182. doi:10.1001/jama.2016.19043 Corrected on January 19, 2017.

Editorial page 142

Supplemental content

 CME Quiz at jamanetworkcme.com and CME Questions page 206

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Corresponding Author: Christopher J. L. Murray, DPhil, Institute for Health Metrics and Evaluation, 2301 Fifth Ave, Ste 600, Seattle, WA 98121 (cjlm@uw.edu). Systolic blood pressure (SBP) of at least 110 mm Hg has been related to multiple cardiovascular and renal outcomes, including ischemic heart disease, cerebrovascular disease, and chronic kidney disease.¹⁻³ The global obesity epidemic may further increase SBP in some populations.⁴⁻⁶ The burden of SBP of at least 110 mm Hg remains high despite the availability of preventive interventions and low-cost, effective antihypertensive medications.^{4,7}

Several studies have assessed SBP measurements from population-based examination surveys.^{4,5} The global burden related to high SBP has been reported in detail for 1997, 2001, 2005, and 2010.^{5,6,8,9} Results from the Global Burden of Disease, Injuries, and Risk Factor study 2015 (GBD 2015) related risk factors to 41% of all disabilityadjusted life-years (DALYs) in 2015.¹⁰ In GBD 2015, SBP was associated with the highest burden among risk factors-more than either smoking or obesity.¹⁰ In the current study, we used the results of the GBD 2015 comparative risk assessment to explore patterns of SBP above 110 to 115 mm Hg and related deaths and DALYs for 195 countries and territories from 1990 to 2015.10 This analysis reports separately the disease burden for participants aged 25 years and older related to SBP levels of at least 110 to 115 mm Hg and SBP levels of 140 mm Hg or higher.^{11,12}

This analysis supersedes all previous global burden of disease study results for SBP because all data from 1990 to present have been re-analyzed using consistent methods.

Methods

This analysis was part of the GBD 2015 comparative risk assessment to assess health loss (DALYs) related to specific risk factors.⁹ In contrast to pooling studies or primary studies that analyze individual record data to estimate the magnitude of related burden and the number of people at different levels of SBP, the GBD study is a descriptive meta-analysis of available study results. Thus, the data are projections for a population rather than direct estimates for a sample population and should be assessed considering the availability of primary data for a given country and year, uncertainty of the pooled estimates, and the overall modeling strategy and assumptions.

Prior to the 1990s, diastolic blood pressure was considered to be a better predictor of health outcomes than SBP. Later, epidemiological studies showed a greater association and better predictive validity with outcomes for SBP, especially for patients who were older (in whom incidence of related disease is higher).^{13,14} Atherosclerosis is known to increase SBP and strengthen the association with heart, central nervous system, and renal vascular diseases.¹⁵⁻¹⁷ Due to the strong correlation between SBP and diastolic blood pressure burden, measures of SBP alone are now used in studies of the global and national burdens of risk factors. Only SBP was included in this analysis. For this study, estimates were first produced at age-, sex-, country-, year-, and cause-specific strata before being aggregated.

Key Points

Question What is the worldwide association between elevated blood pressure and the burden of disease?

Findings In studies from 154 countries that included 8.69 million participants, it is estimated that between 1990 and 2015 the rate of systolic blood pressure (SBP) of at least 110 to 115 mm Hg increased from 73 119 to 81 373 per 100 000 persons, and SBP of 140 mm Hg or higher increased from 17 307 to 20 526 per 100 000 persons. The estimated rate of annual deaths associated with SBP of of at least 110 to 115 mm Hg increased from 135.6 to 145.2 per 100 000 persons, and for SBP of 140 mm Hg or higher increased from 97.9 to 106.3 per 100 000 persons.

Meaning Over the past 25 years, the number of individuals with worldwide SBP levels of at least 110 to 115 mm Hg and of 140 mm Hg or higher and the estimated associated deaths have increased substantially.

The analysis was divided into 5 components in the following sequence: (1) the distribution (mean and variance) of SBP in each age, sex, and country group was estimated; (2) the relative risks (RRs) of 10 cardiovascular and renal outcomes, including chronic kidney disease, associated with SBP of at least 110 to 115 mm Hg based on pooled prospective cohort studies were estimated; (3) a level of minimum risk for SBP was determined; (4) the cause-specific population-attributable fraction (PAF) related to SBP that was elevated above this minimum level of risk was calculated; and (5) deaths and DALYs related to SBP of at least 110 to 115 mm Hg were computed by multiplying each outcome by the PAF for each country, age, sex, and year group.

Estimating SBP Distributions

Data for this study were obtained from an update to the systematic review of health examination surveys reporting SBP originally conducted as part of the GBD 2010 study.^{9,18} Using PubMed, studies published between July 15, 2009, and December 31, 2015, were added to the original review. Studies were included if they were population-based and measured SBP using a sphygmomanometer (either manual or electronic; see eAppendix in the Supplement for details on the evaluation of study quality and identifying and removing outliers). All measurements of blood pressure were categorized by sex, and data points were divided by age groups based on the global age distribution of mean SBP using the available detailed ageand sex-specific data. Mean SBP was estimated in each age-, sex-, country-, and year-specific stratum using spatiotemporal Gaussian process regression (method has been widely applied in global health estimation, including for tobacco prevalence estimation and obesity).^{19,20} Detailed methods for this estimation procedure are described in the eAppendix (Supplement) and country data sources are provided in searchable form online through the Global Health Data Exchange.²¹

Accounting for Blood Pressure Variation

The standard deviation of SBP was estimated for every age, sex, country, and year by estimating the relationship between the mean of SBP and the standard deviation in available studies; the proportion of variance of SBP due to measurement error was also estimated (eAppendix in the Supplement).²²⁻²⁷ SBP varies over time with circadian rhythm, changes in diet, physical activity, and treatment, which add substantial random noise to the long-term exposure average.²⁸ Random measurement error of SBP also causes an attenuation of the association between the SBP level and incidence of disease outcomes called regression dilution bias.²⁹ A correction for usual SBP is commonly used in cohort studies to estimate the association between the level of SBP and the outcome risk. Using these corrected RRs in burden of disease estimates requires the same adjustment be applied to the distributions of SBP from surveys that are based on 2 to 3 measurements taken during a single encounter. Multiple measurements in a cohort of participants over time can provide an estimate of the random variation that needs to be taken out of the single (time) measurement to correct for this underestimation of effect size.

Relative Risks for Outcomes Related to SBP

The GBD comparative risk assessment framework pairs each risk with known disease-specific outcomes. To be paired, sufficient evidence for a causal relationship between risk and disease outcome is needed. The strength of evidence for association between risk-outcome pairs, including elevated SBP, was evaluated as part of the GBD 2015 study (see eAppendix in the Supplement for detailed methods of the risk-outcome evaluation).¹⁰ On the basis of analysis from pooled cohort studies,³⁰ the following diseases were identified as having sufficient evidence to support a relationship with high SBP (≥110-115 mm Hg): ischemic heart disease, ischemic stroke, hemorrhagic stroke, hypertensive heart disease, cardiomyopathy, atrial fibrillation, aortic aneurysm, rheumatic heart disease, peripheral vascular disease, endocarditis, chronic kidney disease, and other cardiovascular diseases (CVDs [cardiovascular outcomes other than those previously listed]). Although the cause of rheumatic heart disease and endocarditis is infection, high SBP has been associated with an increasing risk of death, accelerating adverse heart effects caused by infection or autoimmune response. The aggregated outcome was assumed to include death and morbidity.

Cohort studies and a meta-analysis of 147 clinical trials of blood pressure-lowering drugs found improved outcomes due to blood pressure lowering were similar across the range of 120 to 180 mm Hg SBP levels at pretreatment.^{31,32} The RRs that were based on blood pressure lowering in these metaanalyses were similar to the results from the Prospective Studies Collaboration.³³ For the present study, age-specific RRs for cardiovascular outcomes based on pooled cohort studies were used including the Prospective Studies Collaboration and the Asia Pacific Cohort Studies Collaboration (eFigure 1 and eTable 1 in the Supplement).^{18,34} For this study, a meta-analysis of cohort studies was completed to estimate the relationship between SBP and chronic kidney disease. Citation information for the data sources used for RRs are provided by the Global Health Data Exchange in a searchable web tool.²¹

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Minimum Risk Level

The GBD comparative risk assessment framework is based on the observation that risk caused by a given exposure begins at a certain level and then ascends as exposure increases above that level. This counterfactual level is referred to as the theoretical minimum-risk exposure level which, when compared with an observed level of SBP, allows for estimation of the PAF. The theoretical minimum-risk exposure level of SBP was estimated to range from 110 to 115 mm Hg based on pooled prospective cohort studies that show risk of mortality increases for SBP above that level.^{30,35} Recent randomized clinical trial results, including the Systolic Blood Pressure Intervention Trial (SPRINT) and the Heart Outcomes Prevention Evaluation (HOPE-3), show that lifestyle modification early in life is likely to be a major component for lowering SBP to near this level given the variable range of benefit observed in these studies when blood pressure was lowered with antihypertensive medications alone.³⁶⁻³⁸ The selection of a theoretical minimum-risk exposure level of an SBP level of 110 to 115 mm Hg-the level that captures the maximum attributable burden-is consistent with the GBD study approach of estimating all attributable health loss that could be prevented even if current interventions did not exist that could achieve such a change in exposure level (eg, a tobaccosmoking prevalence of 0%). Some studies, such as the Framingham cohort, have found an increase in SBP with increasing age and it has been suggested that the theoretical minimum-risk exposure level should also follow this age pattern.³⁹ Other studies that found no change in SBP with age⁴⁰⁻⁴² support maintaining a single theoretical minimum-risk exposure level across age groups. Based on the current evidence,⁴³ we determined that a difference in theoretical minimum-risk exposure level by age group was not sufficiently supported and decided to retain a single level across age groups. Further investigations in the form of cohorts or pooled cohort studies are needed to determine if varying the theoretical minimum-risk exposure level for SBP with age group is justified. To include the uncertainty in the theoretical minimum-risk exposure level, 1000 random draws from the uniform distribution of the interval between 110 and 115 mm Hg were taken; unertainty in the theoretical minimum-risk exposure level was propagated by sampling between the 110- and 115-mm Hg interval each time the population-attributable burden was calculated.

Population-Attributable Fractions

The equation in this section describes the formula used for computing a PAF for a continuous risk factor; the PAF for SBP in an age-sex-country-year for a cause (*o*) is defined as follows:

$$PAF_{oasct} = \frac{\int_{x=l}^{u} RR_{oas}(x)P_{asct}(x)dx - RR_{oas}(\text{theoretical})}{\int_{x=l}^{u} RR_{oas}(x)P_{asct}(x)dx}.$$

 $RR_{oas}(x)$ is the relative risk as a function of exposure level (*x*) for SBP, cause (*o*), age group (*a*) and sex (*s*). $P_{asct}(x)$ is the distribution of exposure of SBP in age group (*a*), sex (*s*), country (*c*), and year (*t*). The lowest level of exposure (*l*) and the highest level of exposure possible (*u*) (300 mm Hg) are also

described in this equation. The log-normal function, rather than normal, ⁴⁴ β , or γ distributions, gave the best fit of the distribution of SBP in multiple health examination surveys such as the US National Health and Nutrition Examination Survey (NHANES), China Longitudinal Healthy Longevity Survey, and Indonesia Family Life Survey.

Burden Related to SBP

Deaths and DALYs related to SBP of at least 110 to 115 mm Hg were computed by multiplying an age-, sex-, country-, year-, and cause-specific PAF by the estimated deaths or DALYs for the same strata. Total (all-causes) burden related to SBP of at least 110 to 115 mm Hg was calculated by the following:

All-cause-associated burden_{asct} =
$$\sum_{o=1}^{W} \text{DALY}_{oasct} \text{PAF}_{oasct}$$
.

Hypertensive heart disease and hypertensive chronic kidney disease were treated as conditions that would not have occurred without elevated systolic blood pressure, and all disease burden for these causes was attributed to this risk factor. The PAFs and related deaths and DALYs for each 1-mm Hg increment of SBP were evaluated to provide the distribution of health burden across the range of possible SBP levels.

Uncertainty Intervals

We computed 95% uncertainty intervals (UIs) for all estimates of deaths and DALYs related to SBP of at least 110 to 115 mm Hg. A Monte Carlo simulation approach was used to propagate uncertainty from all sources in the final burden estimations. These intervals incorporated sampling uncertainty in the examination surveys, parameter estimation in the spatiotemporal Gaussian process regression model for blood pressure mean, the RRs for each outcome from the analysis of pooled cohort studies, the theoretical minimum-risk exposure level, and the deaths and DALYs estimated for each age, sex, country, year, and cause. The 1000 draws of the posterior distribution of mean SBP and outcomes by country, age, and sex were calculated independently so the variance of estimation for the aggregate groups (eg, all-age, both sexes, or global burden) were more likely to be underestimated because of possible covariance between different risk levels and outcome, countries, or sexes. Despite efforts to incorporate all sources of uncertainty, uncertainties from some intermediate predictive steps were not propagated due to existing data and methodological constraints. Therefore, the UIs presented may be optimistic estimates. Analyses and computations were completed using Stata version 13.1, R version 3.1.2, and Python version 2.7.11.

Results

Global

In total, 844 studies from 154 countries (N=8.69 million individual participants) published from 1980 to 2015 were included in GBD 2015.¹⁰ Between 1990 and 2015, the rate of SBP of at least 110 to 115 mm Hg increased from 73 119 (95% UI, 67 949-78 241) to 81 373 (95% UI, 76 814-85 770) per 100 000; the rate of SBP of 140 mm Hg or higher increased from 17 307 (95% UI, 17 117-17 492) to 20 526 (95% UI, 20 283-20 746) per 100 000. The associated estimated annual deaths for SBP of at least 110 to 115 mm Hg and of 140 mm Hg or higher increased from 135.6 deaths (95% UI, 122.4-148.1) to 145.2 deaths (95% UI 130.3-159.9) per 100 000 and from 97.9 deaths (95% UI, 87.5-108.1) to 106.3 deaths (95% UI, 94.6-118.1) per 100 000.

Table 1 shows the projected number of individuals, deaths, and DALYs related to SBP of at least 110 to 115 mm Hg and SBP of 140 mm Hg or higher for 6 time points between 1990 and 2015. The projected number of individuals with SBP of at least 110 to 115 mm Hg increased from 1.87 billion (95% UI, 1.74-2.0 billion) in 1990 to 3.47 billion (95% UI, 3.27-3.65 billion) in 2015, and the associated annual number of projected deaths increased from 7.2 million (95% UI, 6.5-7.9 million) in 1990 to 10.7 million (95% UI, 9.6-11.8 million) in 2015, a 1.6% increase per year (Table 1). Projected DALYs related to SBP of at least 110 to 115 mm Hg increased from 148 million (95% UI, 134-162 million) in 1990 to 211 million (95% UI 193-231 million) in 2015. The projected number of individuals with SBP of 140 mm Hg or higher increased from 442 million (95% UI, 437-447 million) in 1990 to 874 million (95% UI, 864-884 million) in 2015, and the associated annual number of projected deaths in 2015 (7.8 million [95% UI, 7.0-8.7 million]) or 14.0% of total deaths (95% UI, 12.5%-15.5%) and 143 million DALYs (95% UI, 130.2-157.0 million) were related to SBP of 140 mm Hg or higher.

Similar to DALYs, age-standardized death rates associated with SBP of at least 110 to 115 mm Hg declined from 225 (95% UI, 200-247) per 100 000 to 170 (95% UI, 151-188) per 100 000 (eTable 4 in the Supplement), which suggests population growth and aging may have been the main driver of the observed increase in total projected DALYs related to SBP of at least 110 to 115 mm Hg since 1990 (Table 1). Age-standardized rate per capita (an adjusted measure for population size and age structure) of deaths and DALYs related to SBP of at least 110 to 115 mm Hg decreased despite increased average SBP. The downward change in the age-standardized rate of deaths was 0.92% (95% UI, 0.80%-1.03%) per year for men and 1.37% (95% UI, 1.26%-1.50%) per year for women (eTable 6 in the Supplement). Age-standardized DALYs per capita decreased from 4.1 (95% UI, 3.7-4.5) per 100 persons in 1990 to 3.2 (95% UI, 2.9-3.4) per 100 persons in 2015 (see data reported as per 100 000 individuals in eTable 4 in the Supplement).

Figure 1 shows 2 views of global trends for individuals with SBP of 140 mm Hg or higher. Panel A shows that the rate of high SBP of 140 mm Hg or higher increased from 17 307 (95% UI, 17 116.9-17 492) per 100 000 in 1990 to 20 525 (95% UI, 20 283-20 746) per 100 000 in 2015. Although the rate initially decreased between 1990 and 1995, the initial trend was followed by an increase to 2015. Panel B shows that after controlling for changes in population aging, the age-standardized rate increased after 2000 (eFigure 2 and eFigure 3 in the Supplement).

Figure 2 shows the distribution of DALYs in the world by level of SBP and by cause. At the global level, 29% of DALYs related to SBP of at least 110 to 115 mm Hg occurred in

Table 1. Projected Number of Individuals Globally With Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher, Deaths, and Disability-Adjusted Life-Years, 1990-2015^a

	Projected No. (95% Uncertainty Interv	al)	
	1990	1995	2000
SBP ≥110-115 mm Hg			
Individuals, thousands	1 868 253 (1 736 165-1 999 123)	2 119 822 (1 967 808-2 270 838)	2 427 524 (2 259 371-2 591 634)
Deaths, thousands	7191 (6493-7852)	7946 (7187-8702)	8514 (7684-9329)
DALYs, thousands	147 625 (134 192-161 520)	163 476 (148 256-178 742)	175 618 (159 592-191 887)
SBP ≥140 mm Hg			
Individuals, thousands	442 214 (437 354-446 928)	478 941 (473 708-484 088)	535 993 (530 228-541 646)
Deaths, thousands	5191 (4641-5731)	5670 (5054-6266)	6014 (5382-6658)
DALYs, thousands	95 900 (86 962-104 856)	105 249 (95 326-115 157)	112 630 (102 225-123 351)
	2005	2010	2015
SBP ≥110-115 mm Hg			
Individuals, thousands	2 752 925 (2 577 041-2 924 177)	3 104 244 (2 922 179-3 281 536)	3 466 261 (3 272 051-3 653 550)
Deaths, thousands	9212 (8326-1010)	9826 (8835-10790)	10 704 (9601-11 787)
DALYs, thousands	189 579 (172 703-206 696)	198 389 (180 979-216 006)	211 816 (192 712-231 114)
SBP ≥140 mm Hg			
Individuals, thousands	619 320 (613 021-626 064)	743 995 (736 480-752 041)	874 332 (864 013-883 705)
Deaths, thousands	6531 (5842-7225)	7103 (6338-7840)	7834 (6973-8706)
DALYs, thousands	123 241 (111 943-134 737)	132 018 (120 214-144 095)	143 037 (130 198-156 961)

Abbreviation: DALYs, disability-adjusted life years; SBP, systolic blood pressure.

^a All data are for individuals aged 25 years and older and both sexes combined.

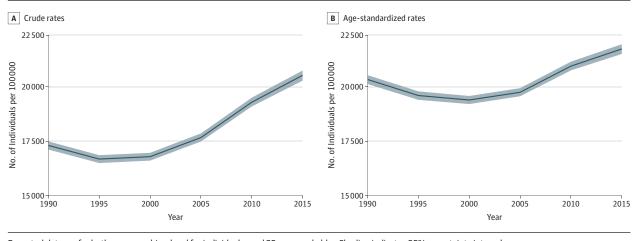


Figure 1. Projected Global Rates of Systolic Blood Pressure of 140 mm Hg or Higher

Reported data are for both sexes combined and for individuals aged 25 years and older. Shading indicates 95% uncertainty intervals.

individuals who had SBP between 115 and 140 mm Hg. Another 26% of DALYs occurred in individuals with SBP between 140 and 150 mm Hg, and the remaining 45% of DALYs occurred in individuals with SBP 150 mm Hg or higher. At all levels of SBP, ischemic heart disease was the most important contributor to SBP-related deaths followed by hemorrhagic stroke and then ischemic stroke.

Projected global deaths and DALYs associated with SBP of at least 110 to 115 mm Hg and SBP of 140 mm Hg or higher by specific outcome and the PAFs for those outcomes in 2015 are shown in **Table 2**. Forty-one percent (95% UI, 35.9%-45.4%) of deaths related to SBP of 140 mm Hg or higher were related to CVDs (and the rest through chronic kidney disease), among which 40.1% (95% UI, 32.2%-48.1%) were related to ischemic heart disease, 40.4% (95% UI, 34.5%-46.4%) to cerebrovascular diseases (38.1% [95% UI, 29.9%-46.7%] to ischemic stroke and 42.5% [95% UI, 34.2%-50.8%] to hemorrhagic stroke) (death PAFs for SBP ≥140 mm Hg; Table 2). SBP of at least 110 to 115 mm Hg was associated with all hypertensive heart disease deaths, 68.7% (95% UI, 63.7%-73.5%) of chronic kidney disease deaths, 54.4% (95% UI, 46.8%-62.4%) of cerebrovascular disease deaths (50.0% [95% UI, 39.4.0%-60.8%] of ischemic stroke and 58.3% [95% UI, 48.0%-68.5%] of hemorrhagic stroke deaths), and 54.5% (95% UI, 44.4%-64.2%) of ischemic heart disease deaths (Table 2). Overall, SBP of 140 mm Hg or higher was associated with 73.2% (95% UI,

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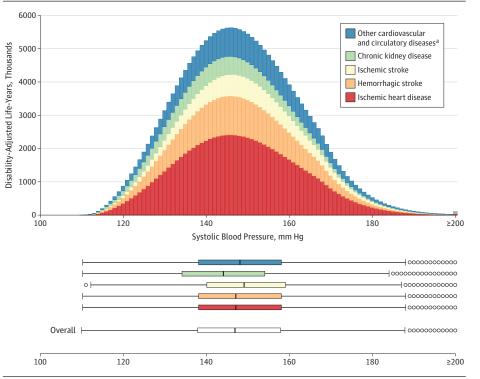


Figure 2. Projected Global Disability-Adjusted Life-Years by Systolic Blood Pressure Level and Cause, 2015

Reported data are for both sexes combined and for individuals aged 25 years and older. The boxes show the median and extend from the 25th to the 75th percentiles. The upper whiskers extend from the third quartile to the highest value within 1.5 × the IQR of the third quartile; the lower whiskers extend from the first quartile to the lowest value within 1.5 × the IQR of the first quartile. Data outside the the whisker range are plotted as open circles.

^a Category includes rheumatic heart disease, hypertensive heart disease, cardiomyopathy and myocarditis, atrial fibrillation and flutter, aortic aneurysm, peripheral vascular disease, endocarditis, and other cardiovascular and circulatory diseases.

Table 2. Projected Number of Global Deaths and Disability-Adjusted Life-Years Related to Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher and Population-Attributable Fractions^a

	Systolic Blood P	ressure						
	≥110 to 115 mm	n Hg			≥140 mm Hg			
	Deaths, No. (95% UI), Thousands	Death PAFs, % (95% UI)	DALYs, No. (95% UI), Thousands	DALY PAFs, % (95% UI)	Deaths, No. (95% UI), Thousands	Death PAFs, % (95% UI)	DALYs, No. (95% UI), Thousands	DALY PAFs, % (95% UI)
All-cause deaths and DALYs	10 704 (9601-11 787)	19.18 (17.21-21.11)	211 816 (192 712-231 114)	8.61 (7.66-9.55)	7834 (6973-8706)	14.04 (12.51-15.55)	143 037 (130 198-156 961)	5.81 (5.14-6.48)
lschemic heart disease	4862 (3955-5740)	54.53 (44.39-64.23)	90 298 (77 837-102 138)	55.05 (47.29-62.29)	3573 (2867-4277)	40.08 (32.28-48.14)	61 736 (52 823-70 417)	37.64 (32.13-43.10)
Ischemic stroke	1489 (1167-1821)	49.98 (39.43-60.76)	24 198 (19 500-28 264)	53.52 (43.61-61.89)	1134 (879-1399)	38.07 (29.89-46.65)	17 653 (14 135-20 671)	39.05 (31.63-45.15)
Hemorrhagic stroke	1953 (1588-2313)	58.32 (47.94-68.53)	43 412 (36 092-49 999)	59.13 (49.03-67.41)	1423 (1152-1705)	42.51 (34.22-50.82)	29 708 (24 529-34 286)	40.46 (33.61-46.77)
Other cardiovascular diseases ^b	1552 (1457-1653)	57.95 (54.97-61.02)	33 209 (30 711-36 020)	51.19 (48.21-54.37)	1151 (1054-1285)	42.98 (39.54-47.68)	22 472 (20 464-24 911)	34.65 (32.00-38.24)
Chronic kidney disease	848 (759-925)	68.69 (63.72-73.49)	20 699 (18 196-22 879)	58.71 (54.00-63.16)	553 (494-608)	44.78 (40.98-48.29)	11 468 (10 005-12 803)	32.53 (29.33-35.52)
Abbreviations: DA	LYs, disability-adju	isted life years; PA	Fs, population-attribut	able ^b Categ	ory includes rhe	umatic heart dise	ase, hypertensive hea	

Abbreviations: DALYs, disability-adjusted life years; PAFs, population-attributable fractions; UI, uncertainty interval.

cardiomyopathy and myocarditis, atrial fibrillation and flutter, aortic aneurysm, peripheral vascular disease, endocarditis, and other cardiovascular and circulatory diseases.

^a All data are for year 2015, individuals aged 25 years and older, and both sexes combined.

71.5%-75.0%) of all SBP-related deaths of at least 110 to 115 mm Hg, or 14.0% (95% UI, 12.5%-15.5%) of global deaths (Table 2).

Table 3 shows projected deaths and DALYs associated with SBP 110 to 115 mm Hg and higher and SBP of 140 mm Hg and higher by age and sex. With increasing cardiovascular DALYs as reported by age, SBP-related deaths and DALYs increase substantially (Table 3). Deaths and DALYS increased by age beginning with 2.5 million DALYs related to SBP of at least 110 to 115 mm Hg for men aged 25 to 29 years, 1.1 million DALYs for women in that age group, and increasing to 11.0 million DALYs for men aged 80 years and older, and 15.6 million DALYs for women in that age group. The total burden is greater in men than women except after age 75, when more burden is observed in women because of longer life expectancy. Among those aged 60 years and older, more than 66% of burden is in

	SBP, Men				SBP, Women			
	≥110-115 mm	Hg	≥140 mm Hg		≥110-115 mm	Hg	≥140 mm Hg	
Age Group, y	Deaths, No. (95% UI), Thousands	DALYs, No. (95% UI), Thousands						
25-29	38	2468	11	718	15	1049	3	181
	(30-47)	(1967-2992)	(8-15)	(505-950)	(12-19)	(823-1317)	(2-4)	(126-249)
30-34	68	3960	37	2148	25	1556	9	558
	(57-79)	(3326-4565)	(30-45)	(1722-2607)	(21-30)	(1290-1873)	(7-12)	(430-711)
35-39	94	4982	52	2725	36	1994	15	799
	(82-108)	(4326-5660)	(44-61)	(2323-3208)	(30-42)	(1679-2334)	(12-18)	(649-988)
40-44	143	6776	76	3595	59	2929	26	1300
	(123-164)	(5847-7780)	(64-89)	(3034-4222)	(50-68)	(2462-3377)	(22-32)	(1072-1570)
45-49	235	9954	136	5764	107	4721	57	2481
	(205-266)	(8712-11 220)	(118-157)	(4988-6646)	(93-121)	(4076-5314)	(48-66)	(2117-2892)
50-54	352	13 179	219	8200	172	6654	102	3911
	(313-391)	(11 752-14 638)	(193-246)	(7252-9238)	(153-192)	(5906-7392)	(90-114)	(3452-4409)
55-59	465	15 148	309	10 075	246	8297	162	5427
	(420-510)	(13 706-16 573)	(278-341)	(9065-11 121)	(222-269)	(7510-9100)	(146-179)	(4882-6015)
60-64	643	17 890	451	12 535	381	10 898	270	7698
	(584-700)	(16 237-19 456)	(408-494)	(11 298-13 720)	(349-414)	(9946-11 880)	(244-294)	(6958-8392)
65-69	629	14 567	455	10 532	449	10 581	338	7962
	(552-697)	(12 778-16 115)	(397-506)	(9190-11 755)	(400-495)	(9406-11 671)	(300-375)	(7036-8836)
70-74	727	13 548	544	10 110	603	11 404	474	8950
	(627-813)	(11 684-15 125)	(470-613)	(8705-11 342)	(527-669)	(9955-12 664)	(413-529)	(7761-9995)
75-79	751	10 796	571	8196	715	10 370	568	8228
	(667-834)	(9608-11 962)	(507-640)	(7231-9174)	(637-793)	(9257-11 450)	(506-634)	(7308-9199)
≥80	1449	10 958	1100	8316	2278	15 549	1848	12 629
	(1168-1717)	(8874-12 942)	(886-1313)	(6697-9901)	(1833-2699)	(12 548-18 291)	(1489-2187)	(10 204-14 914)
All ages ^a	5608	125 124	3963	82 915	5096	86 692	3872	60 122
	(5073-6156)	(113 463-136 730)	(3564-4372)	(75 255-90 813)	(4503-5671)	(78 653-94 918)	(3406-4337)	(54 210-66 029)

Table 3. Projected Number of Deaths and Disability-Adjusted Life-Years Related to Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher by Age and by Sex in 2015

Abbreviation: DALYs, disability-adjusted life-years.

^a Indicates individuals aged 25 years and older.

those with SBP of 140 mm Hg or higher, whereas among those aged 25 to 29 years, 30% of CVD burden is in those with SBP of 140 mm Hg or higher.

Regional and Country Results

Figure 3 shows age-standardized DALY rates associated with SBP of at least 110 to 115 mm Hg for 21 GBD regions and by cause. Regions were ordered by life expectancy. Age-standardized DALY rates varied substantially-from 1025.66 (95% UI, 916.51-1136.97) in the Asia-Pacific high-income region to 7022.18 (95% UI, 5259.73-9652.2) in Oceania. The variation in 2015 for SBP of at least 110 to 115 mm Hg was greater across countries ranging from 923 DALYs (95% UI, 794-1046) per 100 000 in Switzerland to 13 639 (95% UI, 10 696-17 151) per 100 000 in Afghanistan (eTable 4 in the Supplement). Age-standardized DALYs associated with SBP of at least 110 to 115 mm Hg were highest in Oceania, Eastern Europe, Central Asia, and Central sub-Saharan Africa. Relative to life expectancy, the burden of SBP was comparatively high in East Asia and Central Europe (eTable 4 in the Supplement). The relative contributions of different outcomes to the global age-standardized DALY rate associated with SBP of at least 110 to 115 mm Hg varied by region. In sub-Saharan Africa, cerebrovascular diseases predominated, while in Oceania, Central Asia, and Eastern Europe, ischemic heart disease predominated.

Table 4 and Table 5 provide deaths and DALYs associated with SBP 110 to 115 mm Hg and of 140 mm Hg or higher for all

ages and both sexes combined, by region, and for the 25 most populous countries in the world from 1990 to 2015. The last column in Table 4 and Table 5 lists the number of individuals measured for each country for all included data sources. Estimates for all countries can be found in eTables 2, 3, and 4 in the **Supplement**. The highest age-standardized death rate was estimated for Afghanistan with 637 deaths (95% UI, 511-579) per 100 000, Vanuatu with 420 (95% UI, 309-584) per 100 000, and Iraq with 415 (95% UI, 336-506) per 100 000. The lowest age-standardized rates of SBP-related deaths were in Andorra with 61 (95% UI, 51-71) per 100 000, France with 62 (95% UI, 54-72) per 100 000, and Canada with 64 (95% UI, 53-75) per 100 000. The age-standardized mortality rate for women was 145 (95% UI, 129-162) per 100 000 vs 197 (95% UI, 176-217) per 100 000 for men (eTable 6 in the **Supplement**).

Of the global burden of 212 million DALYs related to SBP of at least 110 to 115 mm Hg, 60% occurred in 10 countries, with the majority of DALYs in China with 45.1 million and in India with 38.7 million (**Figure 4**). Age-standardized DALYs from SBP decreased globally, but the trend varied between countries. Although age-standardized DALYs per capita associated with SBP of at least 110 to 115 mm Hg decreased between 1990 and 2015 in South Korea by 77.2% (95% UI, 75.6%-78.8%) and in the the United Kingdom by 65.6% (95% UI, 64.1%-67.1%), a significant increase of 18.9% (95% UI, 1.6%-41.4%) was observed in Bangladesh. Countries in sub-Saharan Africa (except Southern sub-Saharan Africa),

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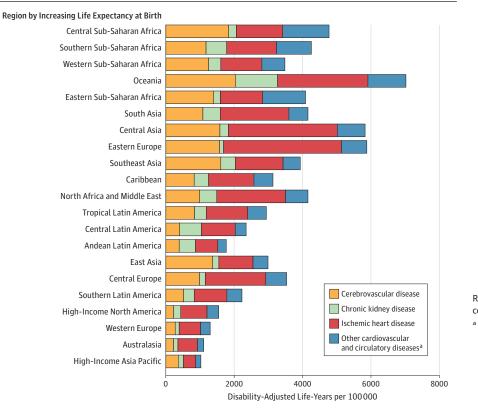


Figure 3. Projected Age-Standardized Disability-Adjusted Life-Years by Systolic Blood Pressure of at Least 110 to 115 mm Hg, by Region and Cause, 2015

South Asia, Central Asia, Southeast Asia, and Central Latin America generally increased in age-standardized DALYs per capita associated with SBPs of at least 110 to 115 mm Hg. In China, the total burden of SBP has increased since 1990, and SBP levels increased after 1995 but were offset by decreases in mortality until 2005, at which point the overall agestandardized burden started increasing.

Discussion

In this study, we used an expanded set of blood pressure prevalence surveys to assess, for the first time to our knowledge, the full distribution of the population by level of SBP and the burden of mortality and DALYs associated with each level of SBP for 195 countries and territories. This study showed that SBP of at least 110 to 115 mm Hg was associated with more than 10 million deaths (95% UI, 9.6-11.8 million) and more than 212 million DALYs (95% UI, 193-231 million) in 2015, a 1.4-fold increase since 1990. Compared with all other specific risks quantified in the GBD, SBP of at least 110 to 115 mm Hg was the leading global contributor to preventable death in 2015.¹⁰ These estimates are concerning given that in 2015, an estimated 3.5 billion individuals had an SBP level of at least 110 to 115 mm Hg.

This analysis, the first to be performed at a comprehensive global scale, found considerable variation among the 195 countries and territories and 21 regions studied. Five counReported data include both sexes combined.

^a Includes rheumatic heart disease, hypertensive heart disease, cardiomyopathy and myocarditis, atrial fibrillation and flutter, aortic aneurysm, peripheral vascular disease, endocarditis, and other cardiovascular and circulatory diseases.

tries accounted for more than half of global DALYs associated with SBP of at least 110 to 115 mm Hg: China, India, Russia, Indonesia, and the United States. Both the projected number and prevalence rate of SBP of at least 110 to 115 mm Hg are likely to continue to increase globally. These findings support increased efforts to control the burden of SBP of at least 110 to 115 mm Hg to reduce disease burden.

In this study, ischemic heart disease and stroke accounted for the majority of health loss (DALYs, which include deaths and nonfatal burden) related to SBP of at least 110 to 115 mm Hg. Although the majority of the burden associated with SBP occurred in persons with hypertension (SBP ≥140 mm Hg), nearly 30% occurred in individuals with an SBP between 115 and 140 mm Hg. A broad range of other conditions contributed to health loss associated with SBP of at least 110 to 115 mm Hg, with chronic kidney disease notable for contributing almost as many DALYs globally in 2015 as hypertensive heart disease.

There have been claims that the burden of SBP of at least 110 to 115 mm Hg is an increasing problem globally.^{4,5,8,45} The finding that the total projected number of individuals with SBP of 140 mm Hg or higher is increasing globally supports those claims. Although the drivers of trends in hypertension were not quantified in this study, other research has documented that dietary salt intake, fruit and vegetable consumption, overweight and obesity, and physical activity have also changed substantially over the same time period.¹⁰ Among these factors at the global scale, the prevalence of obesity and

	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
Region ^b	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	- No. of Individuals Measured
Global	7191.1 (6493.5 to 7852.1)	10703.8 (9601.3 to 11787.5)	48.8 (45.3 to 52.8)	5190.8 (4640.9 to 5731.0)	7834.4 (6972.5 to 8705.7)	50.9 (47.3 to 55.0)	8 694 616
Sociodemographic index							
High	2637.2 (2319.5 to 2916.8)	2573.0 (2222.8 to 2896.1)	-2.4 (-5.4 to 0.3)	2197.4 (1924.4 to 2453.0)	1955.6 (1680.2 to 2218.6)	-11.0 (-14.5 to -7.3)	2 442 846
High-middle	1815.9 (1634.4 to 1996.3)	2844.5 (2528.5 to 3128.3)	56.6 (50.8 to 63.0)	1288.2 (1155.2 to 1427.7)	2175.5 (1928.7 to 2413.9)	68.9 (62.3 to 75.3)	811 015
Middle	1648.5 (1483.7 to 1819.3)	3066.8 (2759.2 to 3367.2)	86.0 (75.3 to 96.5)	1043.9 (932.3 to 1161.4)	2253.4 (2016.5 to 2489.2)	115.9 (102.6 to 128.9)	5 028 555
Low-middle	867.0 (774.2 to 962.3)	1796.0 (1616.4 to 1994.8)	107.1 (93.2 to 123.7)	511.7 (452.9 to 572.8)	1150.5 (1031.5 to 1287.0)	124.8 (108.6 to 143.0)	303 749
Low	217.5 (192.8 to 244.5)	414.2 (358.9 to 478.6)	90.5 (67.0 to 118.8)	146.2 (128.9 to 164.3)	292.9 (253.8 to 338.5)	100.4 (76.8 to 130.4)	108 448
High-income Asia Pacific	243.3 (219.4 to 266.8)	272.7 (237.9 to 309.6)	12.1 (6.5 to 17.3)	201.5 (180.9 to 221.9)	196.9 (170.7 to 223.7)	-2.3 (-7.3 to 2.8)	316 591
Japan	189.1 (169.8 to 207.1)	227.3 (198.2 to 256.9)	20.2 (14.8 to 25.6)	164.4 (147.5 to 180.9)	172.0 (148.7 to 195.3)	4.6 (-0.7 to 10.2)	183 118
Australasia	38.3 (33.6 to 43.0)	34.5 (28.9 to 40.3)	-9.8 (-15.5 to -3.5)	31.7 (27.5 to 35.7)	23.5 (19.4 to 27.9)	-25.6 (-31.4 to -19.4)	79 614
Western Europe	1018.8 (900.2 to 1124.9)	806.4 (695.4 to 921.9)	-20.8 (-24.1 to -17.4)	881.1 (772.0 to 979.4)	609.1 (518.1 to 703.4)	-30.9 (-34.8 to -26.1)	1 753 322
France	98.2 (85.3 to 110.4)	90.1 (74.7 to 106.2)	-8.2 (-18.3 to 1.0)	79.5 (68.6 to 89.7)	62.1 (48.7 to 76.0)	-21.9 (-34.5 to -8.0)	211 177
Germany	279.1 (241.3 to 310.4)	219.1 (187.8 to 249.0)	-21.5 (-26.5 to -16.4)	248.5 (212.8 to 281.5)	178.2 (148.0 to 207.8)	-28.3 (-35.2 to -20.0)	244 689
Italy	149.2 (133.7 to 163.9)	142.0 (120.6 to 163.7)	-4.9 (-12.3 to 2.8)	135.4 (114.3 to 150.3)	102.5 (85.6 to 122.4)	-24.3 (-33.9 to -11.3)	146 864
United Kingdom	186.7 (166.6 to 204.9)	93.9 (80.2 to 108.1)	-49.7 (-52.7 to -46.7)	170.3 (150.0 to 188.6)	65.8 (55.8 to 76.7)	-61.3 (-64.2 to -57.2)	315 420
High-income North America	538.1 (461.5 to 609.1)	495.5 (418.8 to 569.6)	-7.9 (-10.6 to -4.9)	416.9 (353.6 to 476.5)	314.4 (260.7 to 369.1)	-24.6 (-27.5 to -21.5)	79 190
United States	496.2 (425.7 to 562.1)	456.2 (386.8 to 523.6)	-8.1 (-10.8 to -5.3)	384.2 (325.9 to 439.0)	290.2 (240.9 to 340.3)	-24.5 (-27.4 to -21.4)	53 304
Southern Latin America	85.4 (76.7 to 94.5)	104.8 (92.8 to 116.0)	22.7 (16.6 to 29.2)	66.8 (58.5 to 74.5)	85.0 (73.6 to 95.4)	27.3 (17.7 to 37.5)	5972
Andean Latin America	21.2 (18.4 to 23.9)	42.4 (36.9 to 47.9)	100.3 (84.4 to 117.8)	10.7 (9.1 to 12.3)	28.5 (24.3 to 32.6)	166.5 (143.3 to 194.0)	48 013
Central Europe	454.2 (404.3 to 496.5)	418.1 (365.8 to 463.5)	-7.9 (-10.9 to -5.2)	402.6 (355.3 to 442.1)	370.3 (322.9 to 412.0)	-8.0 (-11.7 to -2.3)	129 565

Table 4. Projected Number of Deaths Related to Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher for All Causes Combined for All Regions and the 25 Most Populous Countries

	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
Region ^b	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	
East Asia	1272.0 (1122.2 to 1424.9)	2405.5 (2156.0 to 2660.9)	89.1 (74.2 to 105.5)	729.9 (632.6 to 829.1)	1838.8 (1646.8 to 2042.7)	151.9 (130.2 to 177.5)	2 488 341
China	1232.6 (1082.3 to 1383.4)	2334.5 (2090.3 to 2581.9)	89.4 (74.2 to 106.5)	703.9 (607.8 to 801.5)	1791.8 (1605.9 to 1984.9)	154.6 (131.8 to 181.1)	2 464 184
Central Latin America	107.9 (97.6 to 118.4)	235.7 (210.1 to 261.2)	118.5 (110.2 to 125.9)	72.9 (65.5 to 80.7)	163.8 (144.4 to 182.8)	124.7 (115.7 to 133.3)	227 218
Mexico	45.0 (40.4 to 49.6)	116.5 (102.6 to 129.8)	158.6 (147.7 to 168.1)	27.6 (24.6 to 30.8)	74.9 (65.4 to 84.1)	171.2 (159.4 to 182.3)	202 139
Tropical Latin America	153.5 (138.6 to 168.2)	272.8 (243.8 to 302.0)	77.8 (68.6 to 88.2)	101.5 (90.7 to 112.2)	208.6 (186.1 to 231.2)	105.6 (94.0 to 119.0)	20 225
Brazil	150.5 (135.9 to 164.9)	265.4 (237.1 to 293.4)	76.3 (67.2 to 87.1)	99.4 (88.8 to 110.0)	203.0 (181.4 to 225.0)	104.2 (92.5 to 118.0)	18919
Caribbean	47.7 (42.1 to 53.3)	74.3 (65.5 to 82.7)	55.8 (46.9 to 65.6)	30.5 (26.7 to 34.3)	51.7 (45.0 to 57.9)	69.5 (58.6 to 81.6)	106 176
North Africa and Middle East	381.4 (343.7 to 418.1)	650.0 (582.9 to 717.2)	70.4 (60.6 to 80.9)	266.6 (239.3 to 294.6)	445.9 (398.5 to 495.2)	67.2 (57.4 to 78.2)	344 363
Egypt	83.0 (74.7 to 91.2)	141.8 (127.6 to 155.4)	70.7 (60.7 to 80.7)	51.4 (45.1 to 58.3)	99.9 (88.7 to 110.9)	94.5 (77.5 to 113.6)	9417
Iran	49.2 (41.8 to 56.8)	88.1 (71.1 to 106.2)	78.9 (43.2 to 118.4)	31.5 (26.6 to 36.4)	44.0 (35.0 to 54.1)	39.7 (11.1 to 72.2)	142 296
Turkey	75.2 (65.8 to 85.0)	72.9 (63.9 to 81.7)	-3.0 (-11.9 to 7.0)	56.4 (48.9 to 64.4)	54.4 (46.9 to 61.7)	-3.5 (-13.6 to 8.6)	62 723
Southeast Asia	459.0 (407.0 to 509.9)	884.1 (779.1 to 991.4)	92.6 (74.3 to 113.8)	329.9 (290.8 to 368.1)	663.3 (575.7 to 749.2)	101.0 (80.1 to 125.7)	242 679
Indonesia	197.3 (173.9 to 219.5)	394.4 (322.6 to 469.7)	99.9 (64.5 to 136.3)	158.8 (138.9 to 178.5)	324.1 (264.5 to 384.5)	104.1 (67.3 to 144.3)	61841
Myanmar	49.6 (31.3 to 71.2)	67.4 (42.8 to 94.6)	36.0 (-15.5 to 127.6)	36.3 (22.9 to 52.9)	50.0 (31.9 to 70.0)	37.9 (-13.0 to 132.0)	19 334
Philippines	40.8 (36.8 to 45.1)	108.7 (95.8 to 122.7)	166.3 (144.2 to 190.2)	25.0 (22.2 to 28.2)	62.5 (53.7 to 71.7)	149.7 (125.5 to 176.8)	19778
Thailand	43.7 (38.0 to 50.2)	84.8 (70.3 to 101.0)	94.1 (65.4 to 123.9)	23.3 (19.6 to 27.5)	52.1 (43.0 to 62.3)	123.7 (84.9 to 164.7)	26 876
Vietnam	74.5 (62.0 to 89.1)	139.9 (110.4 to 169.2)	87.8 (42.7 to 135.8)	51.0 (41.7 to 61.4)	110.3 (86.3 to 133.4)	116.2 (60.9 to 170.4)	41 206
Central Asia	136.1 (119.9 to 151.2)	184.7 (162.4 to 204.3)	35.7 (31.7 to 39.8)	102.9 (89.7 to 115.1)	141.8 (123.8 to 157.9)	37.7 (33.5 to 42.3)	37 598
Eastern Europe	863.5 (760.4 to 956.2)	1070.6 (920.8 to 1194.8)	24.0 (18.3 to 29.0)	733.1 (643.9 to 818.9)	911.6 (786.0 to 1026.8)	24.3 (16.6 to 31.5)	144 710
Russia	544.4 (483.1 to 602.7)	682.5 (589.5 to 758.8)	25.4 (18.1 to 31.6)	452.3 (396 5 to 505 0)	568.0 (487 8 to 640 2)	25.6 (16.0 to 34.6)	89 858

174 JAMA January 10, 2017 Volume 317, Number 2

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	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
Region ^b	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	Deaths 1990, No. (95% UI), Thousands	Deaths 2015, No. (95% UI), Thousands	% Change, (95% UI)	
South Asia	1003.6 (895.9 to 1119.2)	2097.0 (1879.6 to 2319.9)	108.9 (97.7 to 121.2)	565.3 (501.7 to 637.2)	1304.4 (1158.8 to 1462.8)	130.8 (117.8 to 145.2)	2 376 370
Bangladesh	56.1 (48.1 to 64.8)	165.0 (136.9 to 194.4)	194.1 (148.8 to 252.7)	27.6 (23.1 to 32.4)	88.9 (73.1 to 106.7)	222.8 (168.0 to 294.9)	93 910
India	812.4 (723.6 to 906.8)	1638.1 (1464.4 to 1811.0)	101.6 (90.3 to 114.3)	449.2 (397.9 to 504.6)	1012.3 (900.2 to 1130.4)	125.4 (111.7 to 139.0)	2 253 394
Pakistan	120.8 (101.5 to 142.4)	264.2 (223.6 to 315.0)	118.7 (79.6 to 168.3)	79.3 (66.4 to 94.3)	180.5 (150.2 to 216.2)	127.8 (86.5 to 180.4)	9239
Western Sub-Saharan Africa	112.3 (94.3 to 135.1)	202.4 (168.0 to 248.7)	80.3 (43.6 to 129.5)	71.6 (60.7 to 85.9)	146.5 (121.7 to 181.2)	104.5 (63.5 to 156.7)	138 922
Nigeria	43.6 (29.7 to 64.1)	62.5 (43.4 to 99.9)	43.4 (-14.1 to 153.4)	24.1 (16.2 to 35.7)	47.1 (32.7 to 75.5)	95.3 (16.7 to 245.4)	46 876
Oceania	7.1 (5.6 to 9.0)	16.7 (12.6 to 22.8)	134.4 (75.4 to 219.2)	3.7 (3.0 to 4.6)	9.5 (7.4 to 12.6)	156.2 (97.3 to 238.1)	31 439
Eastern Sub-Saharan Africa	147.5 (128.2 to 168.8)	254.5 (210.4 to 309.1)	72.5 (43.2 to 109.2)	97.4 (84.4 to 111.9)	185.5 (153.8 to 225.7)	90.3 (58.1 to 128.9)	85 436
Ethiopia	46.7 (38.4 to 55.7)	66.0 (40.9 to 100.1)	41.3 (-13.5 to 119.6)	25.6 (20.7 to 31.4)	42.9 (26.9 to 65.0)	67.2 (5.6 to 158.8)	22 093
Southern Sub-Saharan Africa	56.2 (50.2 to 62.5)	93.7 (82.9 to 105.9)	66.6 (49.4 to 87.7)	44.1 (39.4 to 49.1)	74.6 (65.8 to 84.1)	69.2 (51.9 to 90.3)	32 297
South Africa	46.8 (41.8 to 51.8)	75.1 (66.5 to 84.8)	60.3 (44.1 to 78.0)	36.9 (32.9 to 41.0)	60.1 (53.2 to 68.1)	62.9 (46.7 to 80.9)	13 580
Central Sub-Saharan Africa	44.1 (31.6 to 59.2)	87.4 (58.1 to 124.8)	98.1 (29.6 to 203.1)	29.9 (21.6 to 40.2)	60.7 (40.3 to 87.1)	102.7 (30.7 to 211.1)	6575
Democratic Republic of the Congo	23.3 (15.2 to 33.9)	52.7 (32.5 to 77.2)	126.2 (35.0 to 279.7)	15.1 (9.7 to 22.0)	35.2 (21.6 to 51.8)	132.9 (36.7 to 294.1)	4646

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Table 5. Projected Number of Disability-Adjusted Life-Years Related to Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher for All Causes Combined for All Regions

	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
	DALYs, No. (95% UI), Thousands	sands	% Change	DALYs, No. (95% UI), Thousands	sands	0, Change	alcubinibul to oN
Region ^b	1990	2015	(95% UI)	1990	2015	% UIAII96, (95% UI)	No. of Individuals Measured
Global	147 625.5 (134 192.1 to 161 520.3)	211 816.4 (192 712.1 to 231 114.4)	43.5 (39.8 to 47.4)	95 899.8 (86 961.6 to 104 855.7)	143 037.0 (130 197.6 to 156 960.8)	49.2 (45.5 to 53.3)	8 694 616
Sociodemographic index							
High	44 868.2 (40 877.6 to 48 613.5)	39 221.2 (35 078.7 to 42 911.1)	-12.6 (-14.8 to -10.6)	35 298.7 (31 823.5 to 38 397.1)	27959.7 (24936.0 to 30846.3)	-20.8 (-23.2 to -18.4)	2 442 846
High-middle	37 056.4 (33 593.8 to 40 590.2)	53 865.0 (48 948.8 to 58 642.2)	45.4 (40.0 to 51.3)	23807.0 (21601.7 to 26147.5)	38515.7 (34951.6 to 42211.7)	61.8 (56.1 to 68.5)	811 015
Middle	37 915.1 (33 941.3 to 41 809.6)	65 305.7 (59 390.3 to 71 660.6)	72.2 (62.3 to 82.5)	21545.5 (19286.1 to 23992.0)	44559.6 (40 258.9 to 48977.8)	106.8 (94.3 to 119.3)	5 028 555
Low -middle	21 974.1 (19 686.0 to 24 464.3)	42 648.4 (38 47 3.4 to 47 093.3)	94.1 (80.9 to 109.9)	11672.6 (10355.2 to 13082.1)	24947.4 (22346.5 to 27864.2)	113.7 (97.8 to 131.7)	303 749
Low	5708.1 (5037.2 to 6453.2)	10592.9 (9172.3 to 12237.3)	85.6 (62.4 to 113.1)	3511.9 (3079.4 to 3984.8)	6936.9 (5985.3 to 8047.1)	97.5 (72.9 to 126.9)	108 448
High-income Asia Pacific	4350.0 (3989.2 to 4702.5)	3635.4 (3231.3 to 4034.6)	-16.4 (-20.0 to -13.1)	3361.2 (3076.7 to 3653.6)	2481.8 (2200.7 to 2768.0)	-26.2 (-29.5 to -23.2)	316 591
Japan	3190.1 (2928.0 to 3443.2)	2915.1 (2587.4 to 3227.7)	-8.6 (-12.2 to -5.2)	2647.4 (2427.3 to 2858.4)	2115.9 (1878.0 to 2361.9)	-20.1 (-23.4 to -16.9)	183 118
Australasia	617.7 (556.5 to 674.4)	446.3 (390.5 to 499.1)	-27.8 (-31.1 to -24.4)	483.1 (433.8 to 533.1)	287.8 (248.5 to 327.3)	-40.4 (-44.0 to -36.8)	79 614
Western Europe	15 607.6 (14 216.5 to 16 893.3)	10080.4 (8968.3 to 11143.4)	-35.4 (-37.7 to -33.3)	12990.8 (11751.1 to 14121.3)	7214.7 (6363.1 to 8078.6)	-44.5 (-46.8 to -41.6)	1 753 322
France	1457.2 (1311.3 to 1596.4)	1152.7 (1015.0 to 1310.1)	-20.9 (-26.1 to -15.7)	1128.7 (1006.6 to 1241.7)	781.5 (673.0 to 900.7)	-30.8 (-37.5 to -23.9)	211 177
Germany	4229.0 (3834.5 to 4577.3)	2632.4 (2325.3 to 2913.4)	-37.8 (-41.0 to -34.7)	3650.5 (3242.2 to 3986.6)	1958.1 (1691.5 to 2212.5)	-46.4 (-50.5 to -41.2)	244 689
Italy	2206.3 (2028.5 to 2370.1)	1584.3 (1410.1 to 1763.8)	-28.2 (-32.3 to -23.9)	1925.8 (1720.9 to 2089.6)	1104.8 (963.5 to 1247.3)	-42.6 (-47.8 to -36.0)	146 864
United Kingdom	3002.1 (2735.4 to 3226.8)	1329.8 (1171.3 to 1475.4)	-55.7 (-57.8 to -53.6)	2653.1 (2411.6 to 2869.9)	889.2 (780.4 to 997.0)	-66.5 (-68.5 to -63.9)	315 420
High-income North America	8829.9 (7869.0 to 9752.1)	7781.3 (6886.2 to 8702.9)	-11.9 (-14.4 to -9.3)	6145.2 (5434.5 to 6856.6)	4218.8 (3650.6 to 4785.5)	-31.3 (-34.1 to -28.7)	79 190
United States	8133.8 (7248.1 to 8987.7)	7217.4 (6393.3 to 8066.4)	-11.3 (-13.9 to -8.6)	5643.5 (4987.8 to 6299.2)	3902.2 (3380.3 to 4427.3)	-30.9 (-33.7 to -28.3)	53 304
Southern Latin America	1527.6 (1384.8 to 1667.4)	1587.2 (1441.9 to 1723.7)	3.9 (-0.3 to 8.8)	1066.8 (956.4 to 1176.3)	1171.2 (1050.3 to 1284.6)	9.8 (3.4 to 16.6)	5972
Andean Latin America	480.7 (421.3 to 538.7)	779.6 (685.1 to 872.7)	62.2 (49.5 to 76.4)	194.9 (168.2 to 224.8)	446.0 (386.3 to 504.1)	128.8 (109.5 to 152.3)	48 013

176

Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015

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	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
	DALYs, No. (95% UI), Thousands	ands	opured) %	DALYs, No. (95% UI), Thousands	ands	epuch) %	of Individuals
Region ^b	1990	2015	(95% UI)	1990	2015	(95% UI)	Measured
Central Europe	8270.9 (7620.7 to 8866.2)	6440.2 (5869.5 to 6943.8)	-22.1 (-24.3 to -20.1)	7025.8 (6382.4 to 7593.5)	5525.2 (5012.6 to 5987.9)	-21.4 (-23.9 to -18.4)	129 565
East Asia	27 070.2 (23 829.9 to 30 324.4)	46 474.4 (41 949.7 to 51 163.3)	71.7 (58.7 to 87.2)	13636.8 (11793.3 to 15535.6)	33 618.4 (30 372.6 to 37 096.8)	146.5 (126.9 to 171.0)	2 488 341
China	26 178.5 (22 992.4 to 29 387.4)	45 062.6 (40 761.9 to 49 610.2)	72.1 (58.8 to 88.1)	13104.0 (11273.3 to 14933.9)	32 751.3 (29 564.7 to 36 158.7)	149.9 (129.1 to 176.0)	2 464 184
Central Latin America	2335.8 (2129.8 to 2544.4)	4445.1 (4011.5 to 4876.4)	90.3 (83.2 to 96.9)	1403.9 (1267.5 to 1541.4)	2764.5 (2480.0 to 3045.1)	96.9 (89.4 to 104.3)	227 218
Mexico	953.8 (865.3 to 1045.3)	2173.1 (1939.9 to 2409.4)	127.8 (118.1 to 136.8)	524.5 (471.8 to 579.5)	1246.7 (1105.0 to 1387.5)	137.7 (127.0 to 147.7)	202 139
Tropical Latin America	3690.6 (3319.3 to 4062.7)	5625.4 (5061.8 to 6164.7)	52.4 (44.9 to 62.3)	2204.1 (1972.1 to 2442.4)	3977.8 (3580.7 to 4373.5)	80.5 (71.0 to 92.1)	20 225
Brazil	3625.4 (3259.9 to 3988.5)	5476.6 (4927.9 to 6007.0)	51.1 (43.2 to 60.9)	2162.2 (1934.0 to 2395.7)	3874.7 (3483.7 to 4261.7)	79.2 (69.4 to 90.9)	18919
Caribbean	981.8 (878.2 to 1088.3)	1368.2 (1229.5 to 1515.9)	39.4 (30.3 to 49.6)	576.6 (513.0 to 643.9)	883.8 (785.1 to 987.1)	53.3 (43.4 to 65.1)	106 176
North Africa and Middle East	9163.2 (8304.4 to 10094.5)	15215.0 (13688.5 to 16846.8)	66.0 (55.3 to 77.5)	5838.7 (5260.7 to 6474.6)	9725.0 (8706.9 to 10 792.8)	66.6 (55.5 to 78.5)	344 363
Egypt	2012.2 (1827.0 to 2211.2)	3394.5 (3105.7 to 3680.3)	68.7 (58.8 to 81.2)	1133.8 (1004.0 to 1273.1)	2315.3 (2097.2 to 2547.8)	104.2 (87.9 to 123.4)	9417
Iran	1188.9 (994.3 to 1386.8)	1933.0 (1549.0 to 2364.6)	62.6 (29.7 to 103.0)	699.2 (583.7 to 817.0)	926.1 (729.5 to 1147.9)	32.5 (4.9 to 67.2)	142 296
Turkey	1605.6 (1407.9 to 1813.0)	1446.1 (1294.8 to 1598.3)	-9.9 (-18.9 to -0.5)	1096.8 (954.3 to 1251.9)	996.9 (878.5 to 1107.5)	-9.1 (-18.8 to 1.1)	62 723
Southeast Asia	11 016.6 (9758.4 to 12 268.7)	20111.3 (17656.0 to 22817.8)	82.6 (63.9 to 103.9)	7141.6 (6322.1 to 8000.9)	13 890.4 (12 074.8 to 15 824.0)	94.5 (73.6 to 118.3)	242 679
Indonesia	4942.1 (4350.4 to 5517.3)	9686.0 (7777.4 to 11648.5)	96.0 (60.3 to 136.2)	3584.9 (3130.3 to 4030.1)	7307.6 (5933.3 to 8765.6)	103.8 (68.3 to 145.3)	61 841
Myanmar	1180.7 (743.8 to 1744.3)	1578.6 (994.3 to 2301.3)	33.7 (-18.4 to 129.8)	786.5 (489.9 to 1173.3)	1087.2 (690.5 to 1593.4)	38.2 (-15.3 to 137.0)	19 334
Philippines	1095.4 (978.6 to 1213.7)	2729.3 (2385.7 to 3092.7)	149.2 (127.8 to 173.3)	614.4 (542.3 to 691.3)	1450.5 (1245.7 to 1660.6)	136.1 (113.4 to 161.0)	19 778
Thailand	1072.8 (937.9 to 1218.8)	1704.3 (1396.6 to 2022.0)	58.9 (33.2 to 86.8)	491.1 (416.5 to 577.4)	936.2 (768.6 to 1114.9)	90.6 (59.0 to 127.4)	26 876
Vietnam	1438.8 (1213.4 to 1721.0)	2393.0 (1860.4 to 2984.5)	66.3 (21.5 to 113.9)	888.9 (737.2 to 1060.8)	1738.7 (1350.0 to 2152.5)	95.6 (43.6 to 153.0)	41 206
Central Asia	2741.7 (2490.5 to 2985.6)	3760.1 (3417.6 to 4096.7)	37.1 (32.8 to 41.9)	1945.8 (1753.8 to 2128.9)	2730.0 (2461.9 to 2992.9)	40.3 (35.8 to 45.2)	37 598

(continued)

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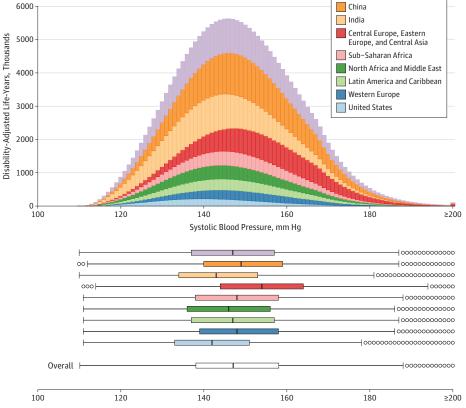
Table 5. Projected Number of Disability-Adjusted Life-Years Related to Systolic Blood Pressure of at Least 110 to 115 mm Hg and of 140 mm Hg or Higher for All Causes Combined for All Regions

	SBP ≥110-115 mm Hg			SBP ≥140 mm Hg			
	DALYs, No. (95% UI), Thousands	ands		DALYs, No. (95% UI), Thousands	ands		elevitivities for the
Region ^b	1990	2015	% cnange, (95% UI)	1990	2015	% cnange, (95% UI)	No. ot individuals Measured
Eastern Europe	15 967.5 (14 552.1 to 17 219.0)	18513.2 (16665.4 to 20106.1)	15.9 (12.2 to 19.9)	13084.1 (11891.4 to 14202.9)	15106.9 (13489.9 to 16560.1)	15.5 (10.4 to 20.9)	144 710
Russia	10 333.3 (9412.6 to 11 187.3)	12 209.7 (10 945.0 to 13 319.2)	18.2 (12.9 to 23.5)	8267.8 (7500.1 to 8990.3)	9672.7 (8585.8 to 10 629.9)	17.0 (10.5 to 23.9)	89 858
South Asia	25 649.9 (22 887.3 to 28 705.5)	49198.4 (44123.9 to 54512.3)	91.8 (81.2 to 103.3)	13126.2 (11643.9 to 14754.8)	27 991.3 (24 903.3 to 31 258.3)	113.2 (101.0 to 126.2)	2 376 370
Bangladesh	1581.4 (1363.3 to 1813.3)	3892.3 (3232.2 to 4595.6)	146.1 (109.0 to 193.9)	686.0 (573.3 to 805.4)	1874.5 (1539.6 to 2244.1)	173.2 (127.0 to 231.6)	93 910
India	20 890.0 (18 631.5 to 23 346.0)	38 670.4 (34 701.0 to 42 654.8)	85.1 (75.0 to 97.1)	10524.9 (9309.6 to 11 858.8)	22 019.2 (19 658.0 to 24 566.5)	109.2 (96.5 to 122.8)	2 253 394
Pakistan	2803.1 (2344.2 to 3325.6)	5956.0 (4977.9 to 7168.3)	112.5 (72.7 to 166.3)	1686.8 (1408.5 to 2000.4)	3610.1 (3009.1 to 4377.9)	114.0 (73.0 to 167.2)	9239
Western Sub-Saharan Africa	3094.1 (2628.2 to 3710.7)	5593.7 (4663.1 to 6846.4)	80.8 (46.4 to 125.5)	1765.6 (1497.2 to 2109.5)	3660.8 (3032.7 to 4493.9)	107.3 (67.6 to 157.8)	138 922
Nigeria	1215.1 (845.2 to 1764.5)	1793.8 (1294.0 to 2731.6)	47.6 (-7.5 to 149.8)	596.2 (404.4 to 874.5)	1205.5 (860.1 to 1831.6)	102.2 (25.5 to 244.5)	46 876
Oceania	202.9 (157.0 to 262.5)	466.6 (338.8 to 665.0)	129.9 (66.7 to 224.2)	91.2 (72.3 to 114.2)	239.4 (176.7 to 330.9)	162.4 (97.0 to 255.1)	31 439
Eastern Sub-Saharan Africa	3748.8 (3247.9 to 4324.5)	6165.7 (5076.1 to 7584.4)	64.5 (34.7 to 100.2)	2248.6 (1942.1 to 2613.9)	4180.3 (3439.4 to 5123.1)	85.9 (53.4 to 125.3)	85 436
Ethiopia	1151.8 (928.8 to 1393.7)	1483.1 (916.3 to 2297.3)	28.8 (-22.7 to 105.0)	550.0 (433.2 to 680.4)	868.4 (539.3 to 1355.6)	57.9 (-2.5 to 151.1)	22 093
Southern Sub-Saharan Africa	1157.9 (1035.1 to 1290.3)	1953.8 (1713.3 to 2223.6)	68.7 (49.8 to 93.3)	836.4 (746.3 to 936.1)	1455.4 (1275.7 to 1658.7)	74.0 (55.0 to 98.2)	32 297
South Africa	938.5 (842.8 to 1036.7)	1518.6 (1342.9 to 1713.5)	61.8 (44.6 to 81.5)	682.2 (613.7 to 756.2)	1145.2 (1010.0 to 1288.4)	67.9 (50.0 to 87.6)	13 580
Central Sub-Saharan Africa	1120.0 (801.8 to 1527.5)	2175.2 (1436.6 to 3159.8)	94.2 (23.0 to 203.3)	732.5 (522.6 to 998.9)	1467.8 (958.4 to 2146.9)	100.4 (25.5 to 216.4)	6575
Democratic Republic of the Congo	590.2 (379.1 to 844.7)	1295.9 (794.5 to 1925.2)	119.6 (30.0 to 269.2)	373.6 (237.0 to 538.8)	850.8 (519.1 to 1252.9)	127.7 (33.7 to 282.3)	4646

178 JAMA January 10, 2017 Volume 317, Number 2



Figure 4. Projected Global Disability-Adjusted Life-Years by Systolic Blood Pressure Level



Reported data include both sexes combined and individuals aged 25 years and older. Data are reported for the 3 most populous countries (United States, China, and India) to highlight burden at the highest population levels and utility of country-specific results. Data for other countries and regions are presented on a regional scale using super regions from the Global Burden of Diseases, Injuries, and Risk Factors study 2015 (the regions that contain the United States, China, and India were excluded to prevent double representation of the following results: high income, South Asia, Southeast Asia, East Asia, and Oceania) and have presented the remainder of countries from those super regions as an additional group. The boxes show the median and extend from the 25th to the 75th percentiles. The upper whiskers extend from the third quartile to the highest value within 1.5 × the IOR of the third quartile; the lower whiskers extend from the first quartile to the lowest value within 1.5 × the IQR of the first quartile. Data outside the whisker range are plotted as open circles.

^a Category includes 45 countries.

overweight in particular increased substantially over the period 1990 to 2015.20

With population growth and aging and the fact that SBP levels increase with age, the number of persons with hypertension and related adverse health outcomes are expected to increase in the world. Despite the increase in global SBP levels in terms of numbers (per individual with SBP \geq 140 mm Hg), rates, and age-standardized rates of SBP of 140 mm Hg or higher, deaths and DALYs associated with SBP of at least 110 to 115 mm Hg and SBP of 140 mm Hg or higher have decreased. The difference in trends between exposure to SBP of at least 110 to 115 mm Hg and the rates of related outcomes is likely related to background trends downward in global agespecific cardiovascular death rates. Previous studies have attributed those declines in CVD death rates to changes in risk factors such as tobacco as well as improved access to treatment.⁴⁶⁻⁴⁸ Although declines in elevated blood pressure may have contributed to CVD declines in some high-income countries such as Japan, globally, the downward trend in hypertension is not a driver of CVD rate reductions.⁴⁹ Yet SBP of at least 110 to 115 mm Hg remains one of the larger risks for decreased human health, greater than tobacco or high body mass index, for which SBP probably mediates a portion of the risk.⁹ Prevention and control of high blood pressure through a combination of behavioral, lifestyle, and drug treatment strategies as a health system priority could mitigate the growing burden associated with high SBP.

The results of the current study are informed by, but do not help to resolve, the significant debate about appropriate clinical use and targets for blood pressure-lowering medications. Meta-analyses performed by Law et al and Ettehad et al showed cardiovascular mortality benefits for a target SBP as low as 120 mm Hg.^{31,32} SPRINT showed significant mortality benefits among individuals in the United States with elevated cardiovascular risk, 90% of whom were already receiving prior treatment with blood pressure-lowering medication, when they received intensive blood pressure reduction therapy and achieved an average SBP below 120 mm Hg.³⁸ The HOPE-3 trial did not observe this same benefit when less intensive blood pressure reduction was achieved. However, unlike the SPRINT trial, the population enrolled in HOPE-3 had an initial mean SBP of 138 mm Hg (and only 22% were receiving prior treatment with blood pressure-lowering medications), more tobacco smokers, and more women. In a prespecified analysis, HOPE-3 found benefit only among those whose SBP remained above 143 mm Hg.

These results support the model assumption that elevated SBP is a modifiable risk factor for mortality even though the precise subpopulation and SBP target for blood pressurelowering medications remains less clear. The purpose of this study was to estimate the full extent of health burden lost related to elevated SBP and not to determine the optimum SBP level for the current population. This estimation is an essential step in understanding the contribution of SBP as a risk factor for global health loss. Quantification of the modifiable health loss due to SBP, given scale-up of the technologies currently available for SBP lowering, would require an alternate estimation strategy than used for this study. However in 2015, 7.8 million deaths and 143 million DALYs were estimated to be related to SBP of 140 mm Hg or higher, suggesting that large health gains from expanded treatment with blood pressurelowering medications are possible. It is likely that more evidence will be needed to define the role of pharmacotherapy in reducing the burden associated with SBP of at least 110 mm Hg and less than an SBP of 140 mm Hg.

This study has important limitations. First, the burden of high diastolic blood pressure, including cases of isolated high diastolic blood pressure, was not included. Second, burden was only associated with SBP for individuals aged 25 years and older, except for hypertensive heart disease, which included all ages. Third, estimates of population mean SBP were based on 814 studies in 154 countries. For 41 countries with no examination survey data, estimates of blood pressure levels were based on spatiotemporal Gaussian process regression statistical models; there is a need for population-based health surveys in these countries as well as broader implementation of surveys that track access to treatment. Fourth, measured standard deviations of blood pressure were converted to narrower ranges of usual blood pressure using a single correction factor based on cohort studies in 5 countries.¹⁰ The conversion from measurements taken at a given point in time to usual blood pressure were based on an intertemporal

ARTICLE INFORMATION

Correction: This article was corrected on January 19, 2017, for incorrect values in the Abstract and for missing units of measure in Table 1.

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variation in SBP for each individual. This intertemporal variation may well vary across countries. Moreover, uncertainty in this correction was not captured in this study. Fifth, the relative risk of each 10-mm increment of SBP was assumed to be the same from 115 mm Hg to SBP above 200 mm Hg. The metaanalyses by Lv et al and by Law et al of all blood pressurelowering trials support this assumption; showing that there was no statistically different RR as a function of starting level of SBP.^{31,50} Sixth, the RRs for each outcome were assumed to be generalizable across populations. Higher RRs have been reported for 6 countries in the East Asia, high-income Asia Pacific, and Australasia regions including China (and Hong Kong), Japan, New Zealand, Singapore, South Korea, and Taiwan.^{35,51,52} Other studies found RRs varied by race.^{7,53,54} Large cohort pooling studies are required to establish statistically significant location- and time-specific RRs. While acknowledging these limitations, this study was based on the largest available set of data and applied the same methods to previous years to provide a consistent analysis of time trends from 1990 to 2015.

Conclusions

In international surveys, although there is uncertainty in some estimates, the prevalence of elevated SBP (≥110-115 and ≥140 mm Hg) increased substantially between 1990 and 2015, with a corresponding increase in DALYs and deaths associated with elevated SBP. Projections based on this sample suggest that in 2015, an estimated 3.5 billion adults had SBP of at least 110 to 115 mm Hg and 874 million adults had SBP of 140 mm Hg or higher.

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REFERENCES

1. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease: part 2, short-term reductions in blood pressure. *Lancet*. 1990;335(8693):827-838.

2. Wright JT Jr, Bakris G, Greene T, et al; African American Study of Kidney Disease and Hypertension Study Group. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. *JAMA*. 2002;288(19):2421-2431.

3. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. *Nature*. 2006;444(7121):875-880.

4. Kearney PM, Whelton M, Reynolds K, Whelton PK, He J. Worldwide prevalence of hypertension. *J Hypertens*. 2004;22(1):11-19.

5. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension. *Lancet*. 2005;365(9455):217-223.

6. Murray CJL, Lopez AD. Global mortality, disability, and the contribution of risk factors. *Lancet*. 1997;349(9063):1436-1442.

7. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA*. 2003; 290(2):199-206.

8. Lawes CMM, Vander Hoorn S, Rodgers A; International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. *Lancet*. 2008;371(9623):1513-1518.

9. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010. *Lancet*. 2012;380 (9859):2224-2260.

10. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388(10053): 1659-1724.

11. Chobanian AV, Bakris GL, Black HR, et al; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206-1252.

12. James PA, Oparil S, Carter BL, et al. 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). *JAMA*. 2014;311(5):507-520.

13. García-Donaire JA, Ruilope LM. Systolic pressure, diastolic pressure, or pulse pressure as a cardiovascular risk factor in renal disease. *Curr Hypertens Rep*. 2010;12(4):307-312.

14. Piper MA, Evans CV, Burda BU, et al. Screening for High Blood Pressure in Adults: A Systematic Evidence Review for the US Preventive Services Task Force. Rockville (MD). US: Agency for

jama.com

Healthcare Research and Quality; 2014. http://www .ncbi.nlm.nih.gov/books/NBK269495/. Accessed December 17, 2015.

15. Zheng X, Jin C, Liu Y, et al. Arterial stiffness as a predictor of clinical hypertension. *J Clin Hypertens* (*Greenwich*). 2015;17(8):582-591.

16. Kaess BM, Rong J, Larson MG, et al. Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA*. 2012;308(9):875-881.

17. Townsend RR, Wilkinson IB, Schiffrin EL, et al; American Heart Association Council on Hypertension. Recommendations for improving and standardizing vascular research on arterial stiffness: a scientific statement from the American Heart Association. *Hypertension*. 2015;66(3): 698-722.

18. Danaei G, Finucane MM, Lin JK, et al; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Pressure). National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5-4 million participants. *Lancet*. 2011;377(9765):568-577.

19. Ng M, Freeman MK, Fleming TD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *JAMA*. 2014;311(2):183-192.

20. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014;384(9945):766-781.

21. Institute for Health Metrics and Evaluation. Global Health Data Exchange. http://ghdx .healthdata.org/. Accessed November 21, 2016.

22. China Center for Economic Research. *China Health and Retirement Longitudinal Study (CHARLS)*. Beijing, China: Peking University; 2008.

23. California Center for Population Research, University of California Los Angeles, Center, for Research and Teaching in Economics, National Institute of Public Health, Universidad Iberoamericana. Mexican Family Life Survey. http://www.ennvih-mxfls.org/english/index.html. Accessed October 14, 2016.

24. Adair LS, Popkin BM, Akin JS, et al. Cohort profile: the Cebu longitudinal health and nutrition survey. *Int J Epidemiol*. 2011;40(3):619-625.

25. Macro International, RAND Corporation, University of California Los Angeles, University of Indonesia. Indonesian Family Life Survey, 1993. http://www.rand.org/labor/FLS/IFLS.html. Accessed October 14, 2016.

26. Yi Z, Vaupel JW, Zhenyu X, Yuzhi L, Chunyuan Z. Chinese Longitudinal Healthy Longevity Survey (CLHLS), 1998-2005: Version 2. 2009. http://www.icpsr.umich.edu/NACDA/studies/24901/version/2 Accessed September 30, 2015.

27. National Center for Health Statistics, Centers for Disease Control and Prevention, Westat, Inc. *United States National Health and Nutrition Examination Survey*. Hyattsville, MD: National Center for Health Statistics, Centers for Disease Control and Prevention; 1980.

28. Giles TD. Circadian rhythm of blood pressure and the relation to cardiovascular events. *J Hypertens Suppl*. 2006;24(2):S11-S16.

29. Hutcheon JA, Chiolero A, Hanley JA. Random measurement error and regression dilution bias. *BMJ*. 2010;340:c2289.

30. Singh GM, Danaei G, Farzadfar F, et al; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group; Asia-Pacific Cohort Studies Collaboration (APCSC); Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe (DECODE); Emerging Risk Factor Collaboration (ERFC); Prospective Studies Collaboration (PSC). The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One*. 2013;8(7):e65174.

31. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009;338:b1665.

32. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016;387(10022):957-967. doi:10.1016/S0140-6736(15)01225-8

33. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360(9349):1903-1913.

34. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet*. 2016;387(10017):435-443.

35. Lawes CM, Rodgers A, Bennett DA, et al; Asia Pacific Cohort Studies Collaboration. Blood pressure and cardiovascular disease in the Asia Pacific region. *J Hypertens*. 2003;21(4):707-716.

36. Lonn EM, Bosch J, López-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med*. 2016;374(21):2009-2020.

37. Wright JT Jr, Williamson JD, Whelton PK, et al; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103-2116.

38. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: a randomized clinical trial. JAMA. 2016; 315(24):2673-2682.

39. Franklin SS, Gustin W IV, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure: the Framingham Heart Study. *Circulation*. 1997;96(1):308-315.

40. Gurven M, Blackwell AD, Rodríguez DE, Stieglitz J, Kaplan H. Does blood pressure inevitably rise with age?: longitudinal evidence among forager-horticulturalists. *Hypertension*. 2012;60(1): 25-33.

41. Bjerregaard P, Jørgensen ME, Lumholt P, Mosgaard L, Borch-Johnsen K; Greenland Population Study. Higher blood pressure among Inuit migrants in Denmark than among the Inuit in Greenland. *J Epidemiol Community Health*. 2002; 56(4):279-284. **42**. Timio M, Verdecchia P, Venanzi S, et al Age and blood pressure changes: a 20-year follow-up study in nuns in a secluded order. *Hypertension*. 1988;12 (4):457-461.

43. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014;383(9932):1899-1911.

44. Lu Y, Hajifathalian K, Ezzati M, Woodward M, Rimm EB, Danaei G; Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects). Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1-8 million participants. *Lancet*. 2014;383(9921): 970-983.

45. Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. *J Atheroscler Thromb*. 2005;12(6):295-300.

46. Taylor R, Dobson A, Mirzaei M. Contribution of changes in risk factors to the decline of coronary heart disease mortality in Australia over three decades. *Eur J Cardiovasc Prev Rehabil*. 2006;13(5): 760-768.

47. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. *Circulation*. 2004;109(9):1101-1107.

48. Luepker RV. Decline in incident coronary heart disease: why are the rates falling? *Circulation*. 2008;117(5):592-593.

49. Hata J, Ninomiya T, Hirakawa Y, et al. Secular trends in cardiovascular disease and its risk factors in Japanese: half-century data from the Hisayama Study (1961-2009). *Circulation*. 2013;128(11):1198-1205.

50. Lv J, Ehteshami P, Sarnak MJ, et al Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. *CMAJ*. 2013;185(11): 949-957.

51. Kelly TN, Gu D, Chen J, et al. Hypertension subtype and risk of cardiovascular disease in Chinese adults. *Circulation*. 2008;118(15):1558-1566.

52. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol, and stroke in eastern Asia. *Lancet*. 1998;352(9143):1801-1807.

53. Howard G, Lackland DT, Kleindorfer DO, et al. Racial differences in the impact of elevated systolic blood pressure on stroke risk. *JAMA Intern Med*. 2013;173(1):46-51.

54. Mountford WK, Hunt KJ, Lackland DT. Assessment of racial variation in risk of coronary heart disease and stroke mortality for elevated levels of systolic blood pressure. *Ann Epidemiol*. 2007;17(9):729. doi:10.1016/j.annepidem .2007.07.023

55. Forouzanfar MH, Alexander L, Anderson HR, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet.* 2015;386(10010):2287-2323.