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


Introduction
High blood pressure is the leading risk factor for cardiovascular disease mortality, causing more than 7 million deaths every year worldwide.1–3 Multicountry studies4–7 have shown large differences in mean population blood pressure, associated with variations in adiposity and dietary salt. Studies in a few countries and communities with repeated data show that change in population blood pressure can range from remaining almost unchanged to 10 mm Hg per decade.4–8

Reliable information about trends in blood pressure is needed to understand its dietary, lifestyle, and pharmacological determinants within populations; set intervention priorities; and evaluate national programmes. Despite decades of research on health consequences of high blood pressure and benefits of interventions, our knowledge of trends, with few exceptions,9–12,16–18 is based on cohort and community studies, mainly from high-income countries.14,15 Previous analyses reviewed published studies to estimate mean blood pressure or hypertension prevalence worldwide.15,16 These studies advanced our knowledge of worldwide levels, but were based on only a few dozen studies, did not assess time trends, did not explicitly address missing data for entire countries or for older ages, combined data from nationally representative surveys with subnational and community studies without distinguishing them, and did not account for all sources of uncertainty including missing and older country data. Many health examination surveys have measured blood pressure, providing an opportunity to

Methods
We estimated trends and their uncertainties in mean SBP for adults 25 years and older in 199 countries and territories. We obtained data from published and unpublished health examination surveys and epidemiological studies (786 country-years and 5.4 million participants). For each sex, we used a Bayesian hierarchical model to estimate mean SBP by age, country, and year, accounting for whether a study was nationally representative.

Findings
In 2008, age-standardised mean SBP worldwide was 128·1 mm Hg (95% uncertainty interval 126·7–129·4) in men and 124·4 mm Hg (123·0–125·9) in women. Globally, between 1980 and 2008, SBP decreased by 0·8 mm Hg per decade (–0·4 to 2·2, posterior probability of being a true decline=0·90) in men and 0·0 mm Hg per decade (–0·3 to 2·3, posterior probability=0·93) in women. Female SBP decreased by 3·5 mm Hg or more per decade in western Europe and Australasia (posterior probabilities ≥0·999). Male SBP fell most in high-income North America, by 2·8 mm Hg per decade (1·3–4·5, posterior probability=0·999), followed by Australasia and western Europe where it decreased by more than 2·0 mm Hg per decade (posterior probabilities ≥0·98). SBP rose in Oceania, east Africa, and south and southeast Asia for both sexes, and in west Africa for women, with the increases ranging 0·8–1·6 mm Hg per decade in men (posterior probabilities 0·72–0·91) and 1·0–2·7 mm Hg per decade for women (posterior probabilities 0·75–0·98). Female SBP was highest in some east and west African countries, with means of 135 mm Hg or greater. Male SBP was highest in Baltic and east and west African countries, where mean SBP reached 138 mm Hg or more. Men and women in western Europe had the highest SBP in high-income regions.

Interpretation
On average, global population SBP decreased slightly since 1980, but trends varied significantly across regions and countries. SBP is currently highest in low-income and middle-income countries. Effective population-based and personal interventions should be targeted towards low-income and middle-income countries.

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systematically and comprehensively assess regional and national trends.

We reviewed and accessed unpublished and published studies to collate comprehensive data for blood pressure. We developed and applied statistical methods to systematically address measurement comparability, missing data, non-linear trends, age patterns, and national versus subnational and community representativeness. With these data and methods, we estimated blood pressure trends and their uncertainties by country.

Methods
Study design
We estimated 1980–2008 trends in mean systolic blood pressure (SBP) and their uncertainties, by sex, for 199 countries and territories in 21 subregions of the Global Burden of Diseases, Injuries, and Risk Factors study, which are grouped into seven merged regions (webappendix p 21). We estimated trends in SBP, rather than diastolic blood pressure (DBP), because prospective studies strongly suggest that SBP is a better predictor of cardiovascular disease risk, especially in older adults (≥55 years), in whom most deaths from cardiovascular disease occur. We used mean SBP rather than hypertension prevalence, because shifting the blood pressure distribution (measured by population mean) reduces risk of cardiovascular disease irrespective of how blood pressure is lowered.1,27

Our analysis included three steps: (1) identification of data sources, and accessing and extracting data; (2) conversion of extracted data to a comparable metric (namely, mean SBP); and (3) application of a statistical model to estimate SBP trends by country and sex. We analysed the uncertainty in estimates, taking into account sampling error and uncertainty from statistical modelling in steps 2 and 3.

Data identification, access, and extraction
We obtained data from health examination surveys and epidemiological studies with anonymised data available to Collaborating Group members, multicentre studies, review of published articles, and unpublished data identified through the WHO Global InfoBase (figure 1 and webappendix pp 2–3). We identified duplicate sources by comparing studies from the same population-year (eg, when data from a multicentre study site were also reported separately, or when a national survey available to Collaborating Group members was also reported in a publication); and we used the source with most detail.

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**Figure 1: Flow diagram for data identification and access**

324 health surveys and epidemiological studies analysed by Collaborating Group members representing 380 country-years

3 multicentre epidemiological studies representing 169 country-years

14 763 articles identified in Medline and Embase

10 682 articles excluded based on title and abstract review

4081 articles remaining after exclusion based on title and abstract review

2113 articles excluded based on full text review and 285 articles excluded because we could not retrieve the full text or because we could not translate the article

1683 articles remaining after exclusion based on full text review

1 543 articles excluded because data were not accessible by age and sex, because they were based on the same study as another article, or because the same data were available from Collaborating Group members

3 articles received through personal communication

Data extracted from 143 published studies representing 198 country-years

39 additional country-years of data retrieved from WHO Global InfoBase

Data extracted for 786 country-years with 5.4 million participants
Collaborating Group members analysed anonymised data from health examination surveys and epidemiological studies. Mean SBP was calculated by sex and age group, incorporating appropriate sample weights when applicable. When more than one SBP measurement was taken, we excluded the first because it tends to be higher than subsequent measurements.

We identified data sources by searching Medline and Embase for relevant articles; webappendix pp 2–3 and figure 1 provide detailed information about the search strategy, exclusion criteria, and the number of articles identified and retained. In brief, studies were included if they were from a representative sample, including from a national, subnational, or community population, and if the data were based on measured (vs self-reported) blood pressure. If a published article met the inclusion criteria but did not report data by age and sex, we invited the corresponding author to join the Collaborating Group by contributing stratified data. There were no restrictions on the language of publication. All articles for which we could identify a translator were screened for inclusion in the data sources.

We identified additional data sources through personal communications with researchers, including inquiries about additional data from authors of published studies. We also searched the WHO Global InfoBase for additional data sources. These additional searches led to data from multicentre studies (eg, the MONICA Project and INTERSALT and INTERMAP studies), published government reports, published sources not identified in our review, and unpublished data. These data were used only if information about study population and measurement methods were available. We applied the same exclusion criteria to these data sources as to published articles.

Data stratified by age and sex were extracted into standard data extraction files. Extracted data included age-stratified and sex-stratified SBP mean and SD, prevalence of hypertension, or both; sample sizes, standard errors, or confidence intervals; survey population and sampling strategy; and selected other study characteristics (webappendix pp 22–47). Importantly, for each data source, we recorded whether the data were national (separated into weighted and unweighted), subnational (covered multiple communities, provinces, or states), or from individual communities (denoted as coverage hereafter); and whether the study population was rural, urban, or both (webappendix pp 22–47). This information was used to account for potential bias and additional uncertainty in data sources that were not representative of their national populations.

Conversion to a comparable blood pressure metric

Many published studies reported hypertension prevalence but not mean SBP. In such cases, we developed linear regressions to estimate mean SBP, which is our primary outcome, from hypertension prevalence for these data sources. A separate linear regression was developed for each hypertension definition extracted from published studies. The dependent variable in these so-called cross-walking regressions was mean SBP; independent variables were hypertension prevalence, age, sex, year of survey, and whether the country was high income. Webappendix pp 48–50 provides the details of these regression models and their coefficients.

Statistical analysis

Despite our extensive data access, many country-years were without data or without nationally representative data, because yearly risk factor data are available for very few countries. Further, some studies covered only some age or sex groups, or only rural or urban populations. We developed a statistical model to estimate mean SBP over time, by age group, sex, and country. We did all analyses by sex, because SBP levels or trends can differ in men and women.11 We used a Bayesian hierarchical model to make estimates for each age-country-year unit; the estimates were informed by data from that unit itself, if available, and by data from other units. Specific model features, and their motivations, are described briefly below. Webappendix pp 4–19 provides complete details about the statistical model and about model validation and testing.

We used a hierarchical model in which SBP levels and trends in countries were, in turn, nested in subregional, regional, and global levels and trends. The hierarchical model borrows information across countries, subregions, and regions, appropriately compromising between (overly) uncertain within-unit estimates and (overly) simplified aggregate cross-unit estimates. It borrows information to a greater degree when data are non-existent or non-informative (ie, have large uncertainty), and to a lesser degree in data-rich countries, subregions, and regions.

Trends over time were modelled as a linear trend plus a smooth non-linear trend, at all levels. Both components were modelled hierarchically. Time-varying country-level covariates informed estimates. The covariates, described in webappendix p 20, were national income (Ln per-head gross domestic product converted to international dollars in 1990), urbanisation (proportion of population that lived in urban areas), and national availability of multiple food types. The associations of SBP with the first two covariates were allowed to change over time—eg, because income association might change as antihypertensive drugs become more accessible. To reduce the effect of fluctuations of covariates between years and to reflect potentially cumulative associations, we used a weighted average of the past 10 years, with progressively smaller weights in the more distant past.

Subnational and community studies might systematically differ from nationally representative ones, because they might be undertaken in areas with high or low blood pressure; they might also have larger variation
Figure 2: Trends in age-standardised mean SBP by subregion between 1980 and 2008 for men (A) and women (B)

Webappendix pp 72–74 shows trends by region and webappendix pp 82–116 trends by country. The solid line represents the posterior mean and the shaded area the 95% uncertainty interval. SBP=systolic blood pressure.
than national studies. Our model included time-varying offsets for subnational and community data, and additional variance components for subnational and community data and for national data without sample weights. These variance components were estimated empirically, and allowed national data with sample weights to have a stronger effect on estimates than other sources. Blood pressure might differ systematically between rural and urban populations, with the difference depending on the country’s extent of urbanisation. Therefore, our model accounted for the differences between study-level and country-level urbanisation.

Mean SBP might be non-linearly associated with age and the age association might flatten or even decrease in older ages. The age association of SBP might vary across countries, and SBP generally rises steeply when mean SBP is high. Therefore, we used a cubic spline age model, with parameters estimated as a function of SBP at a baseline age.

Mean SBP was estimated from the model for 5–10-year age groups, by country and year, for adults 25 years and older. Subregional and regional estimates for every year were calculated as population-weighted averages of the constituent country estimates by age group and sex. For presentation, age-specific estimates for each country or region and year were age-standardised to the WHO reference population.

We quantified the following sources of uncertainty (webappendix pp 4–19): sampling uncertainty of original data sources; uncertainty associated with fluctuations between years in national data, because of unmeasured study design and quality factors (eg, national data from USA in webappendix pp 117–449) or because some had not used sample weights; additional uncertainty associated with data sources that were not national, because of subgroup variation within each country; uncertainty associated with statistical methods for estimating mean SBP from hypertension prevalence; and uncertainty due to use of a model to estimate mean SBP by age group, country, and year when data were missing.

We fitted the Bayesian model with the Markov chain Monte Carlo (MCMC) algorithm and obtained samples from the posterior distribution of model parameters, reflecting the sources of uncertainty, which were in turn used to obtain the posterior distribution of mean SBP for each age, country, and year (webappendix pp 4–19). The uncertainty intervals represent the 2.5–97.5 percentiles of the posterior distribution of estimated mean SBP. Change was estimated as linear trend over the 28 years of analysis and is reported as change per decade. We also report the posterior probability that an estimated increase or decrease corresponds to a truly increasing or decreasing trend. The posterior probability is not a p value; the posterior probability would be 0.50 in a country or region in which an increase is statistically indistinguishable from a decrease, and larger posterior probability indicates more certainty.

Role of the funding source
The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The Writing and Global Analysis Group had access to all data sources and has responsibility for the contents of the report and the decision to submit for publication.

Results
Our analysis included 786 country-years with 5.4 million participants (figure 1). 406 country-years were from 28 high-income countries and 380 from 107 low-income and middle-income countries. High-income subregions of east Asia, North America, and western Europe had the most data per country (webappendix pp 67–69). National surveys provided 20% of all data, subnational studies 15%, and community studies the remainder (webappendix pp 70–71). Japan had the most national data with 28 years, followed by the USA with 7 years. Conversely, we could not identify any population-based data for 64 countries. Andean and central Latin America, central Asia, and sub-Saharan Africa had the largest proportion of countries without data. The data were spread almost equally among the three decades of analysis, but more than 60% of national surveys were from the 2000s (webappendix pp 70–71).

In 2008, women in Australasia had the lowest worldwide age-standardised mean SBP (117.6 mm Hg, 95% uncertainty interval 117.2–122.7), followed by high-income North America (118.4 mm Hg, 115.1–121.8) and Asia-Pacific (120.5 mm Hg, 117.5–123.3). Men had higher mean SBP than did women in every subregion apart from west Africa, by up to 9 mm Hg (figure 2). SBP for men was lowest in North America (123.3 mm Hg, 120.0–126.6). Western European women and men had the highest mean SBP of high-income regions. Western European women (123.1 mm Hg, 120.6–125.7) had mean SBP more similar to women in central Latin America and south Asia than to those in other high-income countries (figure 2); male SBP in western Europe (131.3 mm Hg, 128.8–133.8) was similar to that in central Asia (figure 2). The highest SBP values in men and women in 2008 were in central and eastern Europe and sub-Saharan Africa, with mean SBP ranging 129.2–132.7 mm Hg for women and 132.6–134.8 mm Hg for men.

Globally, between 1980 and 2008, age-standardised mean SBP decreased from 130.5 mm Hg (127.3–134.0) to 128.1 mm Hg (126.7–129.4) in men, by 0.8 mm Hg per decade (–0.4 to 2.2, posterior probability of being a true decline=0.90); female SBP decreased from 127.2 mm Hg (124.1–130.6) to 124.4 mm Hg (123.0–125.9), by 1.0 mm Hg per decade (–0.3 to 2.3, posterior probability=0.93). Although western European women had higher SBP than did women in other high-income subregions in 1980, they had the second largest fall since 1980, after Australasia (figure 2). As a result,
Figure 3: Change in country age-standardised mean SBP between 1980 and 2008 in relation to its uncertainty for men (A) and women (B).

The shaded areas roughly represent the following ranges of posterior probability (PP) of an estimated increase or decrease being a true increase or decrease:

- **PP > 0.975 (A)**; 0.95 < PP < 0.975 (B); 0.75 < PP < 0.95 (C); and PP < 0.75 (D).
female SBP in western Europe moved from fourth highest in 1980, to eighth lowest in 2008; Australasia moved from 12th lowest to lowest worldwide SBP. Female SBP also fell by 2·9 mm Hg or more per decade in tropical Latin America (posterior probability = 0·98) and high-income Asia-Pacific (posterior probability = 0·999).

The decrease in North America was less than 60% of that of Australasia (figure 2). The largest decrease in SBP in men was in high-income North America (figure 2), moving from tenth lowest SBP in 1980, to lowest in 2008. Male SBP decreased in Australasia and western Europe by more than 2·0 mm Hg per decade (posterior probabilities > 0·98). SBP rose in east Africa, Oceania, and south and southeast Asia for both sexes, and in west Africa for women (figure 2). The increase in these subregions ranged 0·8–1·6 mm Hg per decade in men, and posterior probabilities were 0·72–0·91; the rise in women ranged 1·0–2·7 mm Hg per decade, and posterior probabilities were 0·75–0·98.

The cross-country correlation between male and female SBP was 0·76 in 2008. SBP for women in 2008 was lowest in South Korea (116·9 mm Hg, 111·6–121·8), followed by Australia, Cambodia, Taiwan, Canada, and USA, where women had mean SBP of 117·4–118·5 mm Hg; it was highest in some east and west African countries with mean values greater than 135 mm Hg (figure appendix, and webappendix pp 75–81). The lowest mean SBP in men was in Papua New Guinea (122·6 mm Hg, 117·1–128·1), followed by Cambodia, USA, Canada, and Turkey, where mean SBP ranged 123·2–123·6 mm Hg; the highest values were in Baltic and east and west African countries, where SBP reached 138 mm Hg or greater. By comparison, this level was recorded in western European countries such as Finland in the 1980s, before their SBP fell substantially (figure appendix). Whereas estimates in low-income and middle-income countries had higher uncertainty, many countries with low or high estimated SBP had recent health examination surveys, including national surveys in Cambodia, Mozambique, São Tomé and Príncipe, Papua New Guinea, Turkey, and Niger (webappendix pp 22–47 and 67–69). High-income countries with highest mean SBP were Portugal and Finland (both sexes), and Ireland and Norway (men only). Finland had high SBP in 2008 despite a substantial decrease of 2·9 mm Hg per decade (1·2–4·9) for men, and 4·3 mm Hg per decade (2·1–6·7) for women, because of very high values in 1980.

Between 1980 and 2008, male SBP decreased in 136 countries with varying degrees of uncertainty, with the largest falls of 3·0 mm Hg or more per decade (figure 3). The decreases in 21 high-income nations and in the United Arab Emirates had posterior probabilities of 0·975 or higher. Female SBP decreased in 122 countries, some by 4·0 mm Hg or more per decade. 32, mostly high-income, countries had posterior probabilities of 0·975 or higher. Male SBP might have increased in 63 countries and female SBP in 77 countries, with posterior probabilities of 0·75 or higher in 25 countries for men and in 46 for women. When applying a posterior probability cutoff of 0·975, arguably an overly strict bar for harmful trends, SBP increased only for women in two countries. Male SBP rose by 2·0 mm Hg or more per decade in three countries in east Africa and southeast Asia (posterior probabilities 0·88–0·93). Female SBP rose by 2·5 mm Hg or more per decade in nine countries in Oceania, east Africa, and southeast Asia (posterior probabilities ≥ 0·89).

Discussion

We systematically analysed health examination surveys and epidemiological studies, and estimated worldwide trends in SBP, the leading cardiovascular risk factor. We noted that, after standardising for population age structure, mean SBP decreased by about 1 mm Hg per decade for men and women between 1980 and 2008. The estimated trends changed the age-standardised prevalence of uncontrolled hypertension (SBP ≥140 mm Hg or DBP ≥ 90 mm Hg) from 33% (95% CI 28–39) in 1980 to 29% (27–31) in 2008 in men, and from 29% (25–34) to 25% (23–27) in women. However, the number of people with uncontrolled hypertension increased from 605 million (537–680 million) in 1980, to 978 million (921–1040 million) in 2008, because of population growth and ageing.

Men and women in Australasia, North America, and western Europe had large SBP decreases. Conversely, SBP rose in Oceania, east Africa, and south and southeast Asia for both sexes, and in west Africa for women. In view of the established health benefits of low blood pressure, these trends might have partly contributed to the recorded trends in adult mortality worldwide, and its variations by region and sex. Future research should quantify the mortality effects of estimated SBP trends, as done in previous country-specific or cross-country analyses.

The strengths and innovations of this study include analysis of long-term trends; the large amount of data accessed and used; inclusion of data for either mean SBP or hypertension prevalence, and systematic conversion of all metrics to mean SBP; the Bayesian hierarchical model to estimate mean SBP; incorporation of non-linear age associations and time trends; incorporation of study coverage as offset and variance components in the statistical model; and systematic quantitative analysis and reporting of uncertainty. Coverage-specific offsets and variances allowed our estimates to use all available data and to follow data from nationally representative studies more closely than other sources. Further, the coverage-specific variance components are larger for less representative data sources, resulting in larger uncertainty when we did not have nationally representative data, propagating through the Bayesian model into our uncertainty intervals, thereby representing the true availability of information.

Our model did well in external predictive validity tests. Specifically, in each of five separate model runs with 10%
of studies excluded, the model was used to predict the excluded values. The 95% uncertainty intervals of model predictions included 94% of (excluded) study means for both men and women. Our model also had good predictive validity by region (covering 89–98% of excluded study means) and age group (91–98%), and at different income and urbanisation levels (89–98%). When we excluded all data for some countries (ie, created the appearance of no data when data were available), the uncertainty intervals of model predictions included more than 95% of the known but excluded study means. Finally, we examined how our results changed in a model that excluded country-level covariates. The median absolute differences with and without covariates were only 0·30 mm Hg (women) and 0·35 mm Hg (men) for subregion SBP, and 0·68 mm Hg and 0·78 mm Hg for country SBP across all 29 analysis years; the results between the covariate and no-covariate models were also highly correlated (r=0·90–0·98). When the two models yielded estimates with larger differences, the uncertainty intervals of estimates were wider and still overlapped, indicating that when covariates affected our results more, the estimates had larger uncertainty, reflecting the absence of direct information. Webappendix pp 4–19 provides the detailed designs and results of these tests and additional tests about model performance.

The main limitation of our study is that despite extensive data seeking, many country-years still did not have data. In particular, although we used several data sources from low-income and middle-income countries in the 2000s, these countries had fewer data in the preceding two decades. In our analysis, this data disparity is reflected in larger uncertainty in low-income and middle-income countries and in the 1980s. Our findings of data availability and sparseness should initiate a discussion on SBP surveillance needs, including frequency and comparability of measurements. In high-income and some middle-income countries with universal insurance and mandatory or near-complete periodic check-ups, linked records could provide estimates of population blood pressure that are either unbiased or affected by biases that might be quantifiable in small validation studies. However, in most low-income and middle-income countries, health examination surveys will probably remain the only source in the near future. The global health community should assess whether and how high-quality and standardised surveys related to chronic disease risk factors can be started and supported, similar to those for fertility and maternal and child health in the 1980s. Further, although we incorporated information about study coverage into our model, other quality indicators related to blood pressure measurement, such as standardisation for resting time, position of the arm, and exclusion of the first measurement, could lead to variability between studies. We did not estimate trends in DBP, which although secondary to SBP within populations, is an important determinant of cardiovascular disease risk, especially at ages younger than 55 years. Finally, because our analysis unit was age-country-year, we could use only covariates for which we had data for every country-year. As a result we could not incorporate important predictors of blood pressure with sparse data, especially salt intake and antihypertensive use, in the model.

Our findings are consistent with national or multisite studies of blood pressure trends, including modest to large decreases in Japan, central and western Europe, Russia, South Korea, and USA; a near steady pattern in Seychelles; and a possible rise in India. Our results differed from published studies in China, where investigators of the MONICA Project recorded an increase in one community; however, our analysis with many additional national and subnational sources found almost no change in SBP. A study in (West) Germany found a slight rise in female SBP in mid-1980s, followed by flattening later in the decade. We used these same data and additional sources, and estimated a decrease. Similarly, SBP trends seem to have been flat in the Danish MONICA population, but with additional sources our model estimated a decrease.

Although the observed trends of this leading risk factor are highly relevant for national and regional cardiovascular mortality patterns, we can only postulate about their drivers in most regions. Within populations, the main determinants of blood pressure might be consumption of salt and fruits and vegetables, adiposity, and antihypertensive use. Few data exist for trends in salt intake, with the exception of a few high-income countries; one study quantitatively related SBP decline in Japan to salt reduction. Mean body-mass index (BMI) increased in most regions, indicating that SBP trends might have been more favourable had BMI stayed at the levels recorded in 1980. Although data are scarce for trends in screening and antihypertensive use, the VA Cooperative Studies and subsequent trials have increased attention to hypertension detection and management, with worldwide dissemination of clinical guidelines and increase in treatment. Some previous studies have quantitatively or qualitatively attributed blood pressure decrease to wider antihypertensive use, but concerns remain about screening, and physician and patient compliance. Access to screening and antihypertensive drugs is likely to vary across countries, and is particularly low in low-income countries.

Epidemiological studies have shown the health benefits of lowering of blood pressure and the efficacy of specific lifestyle or pharmacological interventions. However, little has been achieved in understanding of worldwide trends, their drivers, and their mortality effects. National trends in SBP estimated in this study are an important component of such an understanding. Subsequent analyses should estimate the effect of these trends on cardiovascular mortality, and examine their behavioural, environmental, nutritional, and health systems drivers to
provide lessons for programmes and policies that accelerate the falling trends, and curb and reverse the rise in developing regions.

Contributors
GD and ME developed the study concept. GMS and JKL reviewed published studies and managed databases. JKL, MJC, GMS, and members of Country Data Group analysed health survey and epidemiological study data. NPM and CJP developed the Bayesian statistical model with input from GD and MMF. JKL, GMS, and GMS analysed databases and prepared results. ME wrote the first draft of the report. Other members of the Writing and Global Analysis Group contributed to study design, analysis, and writing of the report. ME, GD, and CJP oversaw the research. ME is the study guarantor for this report.

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