Bayesian Estimation of Population-Level Trends in Measures of Health Status

Mariel M. Finucane, Christopher J. Paciorek, Goodarz Danaei and Majid Ezzati

Abstract. Improving health worldwide will require rigorous quantification of population-level trends in health status. However, global-level surveys are not available, forcing researchers to rely on fragmentary country-specific data of varying quality. We present a Bayesian model that systematically combines disparate data to make country-, region- and global-level estimates of time trends in important health indicators.

The model allows for time and age nonlinearity, and it borrows strength in time, age, covariates, and within and across regional country clusters to make estimates where data are sparse. The Bayesian approach allows us to account for uncertainty from the various aspects of missingness as well as sampling and parameter uncertainty. MCMC sampling allows for inference in a high-dimensional, constrained parameter space, while providing posterior draws that allow straightforward inference on the wide variety of functionals of interest.

Here we use blood pressure as an example health metric. High blood pressure is the leading risk factor for cardiovascular disease, the leading cause of death worldwide. The results highlight a risk transition, with decreasing blood pressure in high-income regions and increasing levels in many lower-income regions.

Key words and phrases: Bayesian inference, hierarchical models, combining data sources.

1. INTRODUCTION

Variations and trends in health outcomes and risk factors across the globe have received greatly increased attention in recent years, in part driven by the UN's Millennium Development Goals, the increase in in-

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ternational funding for global health and the demand for objective evidence about the effectiveness of interventions. There has been a concomitant focus on data sources and quantitative methods for population-level measures of health status. However, global-level surveys are not available, forcing researchers to rely on fragmentary country-specific data of varying quality.

The Global Burden of Diseases, Injuries and Risk Factors Study (GBD, www.globalburden.org), which aims to quantify the relative contributions of different diseases and injuries, and their risk factors, to morbidity and mortality worldwide, offers a demonstration of these challenges. For example, despite cardiovascular diseases being the leading causes of death worldwide (Lozano et al., 2013), our understanding of their trends is almost entirely based on specific cohorts and communities, primarily in high-income countries. As part of the GBD Study, we set out to estimate trends in cardiometabolic risk factors over the past 30 years for all nations.

In this paper we present a Bayesian model developed to address these issues by combining disparate data sources to complete the largest-ever analysis of metabolic risk factors and the first global analysis of trends. Our model has been used to analyze global trends in systolic blood pressure (Danaei et al., 2011b), serum total cholesterol (Farzadfar et al., 2011), body mass index (Finucane et al., 2011) and fasting plasma glucose (Danaei et al., 2011a).

Here, we focus on the blood pressure analysis as an illustrative example of model development and the advantages of using the Bayesian paradigm. Kearney et al. (2004, 2005) and Lawes et al. (2004) were influential in demonstrating the importance of this risk factor, which is responsible for more than 9 million annual deaths, more than any other risk factor (Lim et al., 2013). These analyses, however, were based on only a small subset of available data. Further, they did not assess trends over time systematically, did not distinguish nationally-representative surveys from subnational and community-based studies, and did not take into account the missingness of data from entire countries or age groups when quantifying uncertainty.

In addition to addressing these deficiencies, our approach differs in important ways from other recent modeling of global health. Rajaratnam et al. (2010) and Hogan et al. (2010), for example, modeled global adult and maternal mortality, respectively. These studies used investigator-chosen smoothing parameters and implemented a two-stage estimation procedure, which prevents uncertainty from propagating through the modeling process. We, on the other hand, estimate all parameters as part of a single model, allowing all sources of uncertainty to be reflected in our inference. Furthermore, whereas they decided a priori how much weight to give high- vs. low-quality studies, our model estimates these weights empirically based on the noisiness observed in the different types of data sources.

2. THE DATA

For 199 countries and territories, from 1980 to 2008, we estimate trends in mean systolic blood pressure (SBP) for adults 25 years of age and older. We accessed numerous unpublished studies and reviewed published studies to collate comprehensive data on SBP. We grouped the 199 analysis countries into 21 subregions using the classifications of the GBD Study. We grouped the subregions into seven merged regions. Details are given in Danaei et al. (2011b).

The primary challenge of this analysis is the fragmented nature and varying quality of the data, available only from some countries, in some years and for some age groups. For roughly one-third of all countries, no data exist at all. Furthermore, many studies cover only rural or only urban populations. Although a portion of the data comes from national surveys with sample weights, most data come from epidemiologic studies not intended to be nationally representative. In addition, many data sources suffer from small sample sizes.

3. WHY BAYES?

Given these patterns of data sparsity and missingness, a hierarchical model is needed to provide inference for all country–year–age triplets and to account for missingness when aggregating to the regional and global levels. The hierarchy provides prior distributions that enable us to borrow strength over time, countries and age, while enforcing plausible parameter constraints.

In principle, a non-Bayesian hierarchical mixed model is an alternative, fit by maximum marginal likelihood after integrating over all the random effects, but the predictive uncertainty would not have included the substantial uncertainty from hyperparameter estimation. Furthermore, with 23 hyperparameters, this would have been a challenging optimization in practice, especially given the parameter constraints. In addition, it would have been difficult to interpret the hierarchical model in a non-Bayesian fashion, with mean blood pressure for a country as a random effect, given that the fixed countries of the world are not drawn from some large population of possible countries.

MCMC sampling has the added advantage of providing Bayesian imputations of risk factor levels at any level of aggregation (over age groups, times, countries, etc.) as a product that the many stakeholders in this work can use to do their own analyses that easily incorporate uncertainty; our analysis includes functionals such as the linear component of blood pressure time trends and the population-weighted, age-standardized global mean blood pressure level (see Section 6).

4. THE MODEL

Our basic strategy is to fit a Bayesian hierarchical model that clusters countries within geographical subregions and regions of the globe, thereby borrowing strength from countries with data. Our approach treats

countries as exchangeable in the absence of other information, after accounting for covariates. To the basic model we add smooth time trends and age effects as well as country- and study-level covariates. We specify a heteroscedastic, multi-component error structure to account for the fact that not all studies are nationally representative. Models for women and men are fit separately.

Throughout, bold characters denote vectors and matrices. For each age group h from study i, the model inputs a sample average and a sample standard deviation of SBP values ($y_{h,i}$ and $s_{h,i}$) as well as a sample size ($n_{h,i}$). We let t_i denote the year in which study i was conducted and we use square brackets to denote group membership such that $j[i]$ is the country j in which study i was conducted. The likelihood is

$$y_{h,i} | a_{j[i]}, b_{j[i]}, u_{j[i],t_i}, \boldsymbol{\beta}, \gamma_i, e_i, \tau_i^2$$

$$(4.1) \quad \sim \mathcal{N}\Big(a_{j[i]} + b_{j[i]} t_i + u_{j[i],t_i}$$

$$+ \mathbf{X}_i' \boldsymbol{\beta} + \gamma_i(z_h) + e_i, \frac{s_{h,i}^2}{n_{h,i}} + \tau_i^2 \Big).$$

a_j and b_j denote the country-specific intercept and linear time slope for the jth country ($j = 1, \ldots, J = 199$). These intercepts and slopes are modeled hierarchically, as discussed in Section 4.1. $\mathbf{u}_j$, a vector of length $T = 29$, models smooth nonlinear change over discretized time ($t = 1980, \ldots, 2008$) in country j (Section 4.2). The matrix $\mathbf{X}$ contains study- and country-level covariates (Section 4.3). The z_h's are age-group values and the $\gamma_i(\cdot)$'s are their smoothly-varying study-specific effects; we describe the flexible age model in Section 4.4. Finally we add a random effect, e_i, to capture study-level heterogeneity, allowing us to combine data from disparate sources, as described in Section 4.5.

The likelihood variance has two terms. $s_{h,i}^2 / n_{h,i}$ represents the known sampling uncertainty of mean SBP for a given age group within a study. We model additional residual variability across age groups within a study as τ_i^2 (Section 4.5).

4.1 Linear Components of the Time Trends

We model the intercepts and slopes in a hierarchical fashion, with each country-specific intercept, a_j, and slope, b_j, composed of country- (c), subregion- (s), region- (r) and global-level (g) components. Letting k index subregions and l index regions, we have

$$a_j = a_j^c + a_{k[j]}^s + a_{l[j]}^r + a^g,$$
$$b_j = b_j^c + b_{k[j]}^s + b_{l[j]}^r + b^g.$$

The constituent random intercepts (a^c, a^s and a^r) and slopes (b^c, b^s and b^r) each have a normal prior with mean zero and variance equal to κ_a^c, κ_a^s, κ_a^r, κ_b^c, κ_b^s or κ_b^r, respectively. The variance parameters determine the degree of intercept (κ_a) and slope (κ_b) shrinkage performed at the country- (κ^c), subregion- (κ^s) and region-levels (κ^r). For the variance parameters, we use a flat prior on the standard deviation scale (Gelman, 2006). We use flat priors for a^g and b^g as well. All flat priors were truncated at 0 and 1000.

4.2 Nonlinear Change in Time

We also model smooth nonlinear change over time in country j hierarchically: $\mathbf{u}_j = \mathbf{u}_j^c + \mathbf{u}_{k[j]}^s + \mathbf{u}_{l[j]}^r + \mathbf{u}^g$, with each component of the nonlinear trend modeled using a discrete second-order Gaussian autoregressive prior (Rue and Held, 2005). In particular, we model each of the vectors $\mathbf{u}_j^c$ ($j = 1, \ldots, J$), $\mathbf{u}_k^s$ ($k = 1, \ldots, K$), $\mathbf{u}_l^r$ ($l = 1, \ldots, L$) and $\mathbf{u}^g$ using a normal prior with mean zero and precision $\lambda_c \mathbf{P}$, $\lambda_s \mathbf{P}$, $\lambda_r \mathbf{P}$ and $\lambda_g \mathbf{P}$, respectively. The fixed matrix $\mathbf{P}$ penalizes second differences.

In this portion of the model, we enforce two constraints to achieve identifiability. We give the precision parameters a flat prior on the standard deviation scale (Gelman, 2006), truncating $\log \lambda \leq 15$, as larger values correspond to essentially no extra-linear temporal variability. We also enforce orthogonality between the linear and nonlinear components of the time trends by constraining the mean and slope of each $\mathbf{u}^c$, $\mathbf{u}^s$, $\mathbf{u}^r$ and $\mathbf{u}^g$ to be zero.

4.3 Covariate Effects

We include six time-varying, country-level covariates: national income, national urbanization and four measures of national food availability (namely, the first four terms from a principal components analysis summarizing the availability of many food types, e.g., meats, pulses, spices). We include interactions of income and urbanization with time because the associations may have changed over time (e.g., as treatment for high blood pressure became available). We smoothed the country-level covariates using a triangularly-weighted moving average with weights decreasing from the year of data collection to the ninth year prior.

At the study level, we include two covariates to account for potential bias from data sources that are not representative of national populations. We account for potentially time-varying effects of sources that are not nationally representative. In addition, we account for differences between study- and country-level urbanization using an interaction term.

4.4 Age Model

Mean SBP generally varies as a nonlinear function of age (Singh et al., 2012). We model the age effect using cubic splines with fixed knots at 45 and 60 years:

$$\gamma_i(z_h) = \gamma_{1i}z_h + \gamma_{2i}z_h^2 + \gamma_{3i}z_h^3$$
$$+ \gamma_{4i}(z_h - 45)_+^3 + \gamma_{5i}(z_h - 60)_+^3.$$

We centered the age variable (z_h) at 50 years of age to reduce dependence among model parameters. The γ's are modeled as $\gamma_{si} = \psi_s + \phi_s\mu_i + c_{sj[i]}$ for $s = 1, \ldots, 5$, where $\mu_i = a_{j[i]} + b_{j[i]}t + \mathbf{X}_i'\boldsymbol{\beta} + u_{j[i],t_i} + e_i$ is the blood pressure level for the 50-year-old age group. We model the spline coefficients for study i as a linear effect of the level for this baseline group because blood pressure tends to increase more sharply as a function of age in countries with higher SBP levels (Singh et al., 2012). To this, we add a country-specific random effect to account for additional country-specific variation in the age effect, with $c_{sj}|\sigma_s^2 \sim \mathcal{N}(0, \sigma_s^2)$ and flat priors for the σ_s's (Gelman, 2006).

The age model above is continuous in age. However, the blood pressure means are reported for discrete age groups (e.g., mean SBP for 35–44-year-olds). As a simplification, we used the midpoint of each age range (e.g., 40 years) as the age value for each data point.

4.5 Study-Specific Random Effects and Residual Age-by-Study Variability

We account for study-level effects (above and beyond sampling variability) that are consistent across age groups by including a study-specific random effect, e_i. We model these random effects as being normally distributed with a variance that depends on how representative the study is of the country's population:

$$\text{Var}(e_i) = \begin{cases} v_w, & \text{if study } i \text{ is nationally} \\ & \text{representative with sample weights,} \\ v_u, & \text{if study } i \text{ is nationally} \\ & \text{representative without sample} \\ & \text{weights,} \\ v_s, & \text{if study } i \text{ is "sub-national" (i.e.,} \\ & \text{covers multiple provinces/states),} \\ v_c, & \text{if study } i \text{ is from} \\ & \text{an individual community.} \end{cases}$$

Exploratory analysis and subject-matter knowledge suggest that even weighted national studies may have more variability than can be accounted for by sampling variability because of issues with study design and quality; this is accounted for through the v_w variance term. We then assume that studies that are increasingly less representative have increasing random effects variances, imposing the set of constraints $v_w < v_u < v_s < v_c$. The assumption that we should smooth over (rather than fitting) aberrant data points is substantiated by the larger-than-expected variability among studies from country-years in which we have multiple nationally representative studies with sample weights.

We also include a variance term for within-study errors (above and beyond sampling variability) that differ between age groups. As with the study-specific random effects, we use variance parameters that differ depending on the representativeness of the study, where τ_w^2, τ_u^2, τ_s^2 and τ_c^2 are defined in an analogous fashion to v_w, v_w, v_s and v_s and with an analogous ordering constraint.

5. COMPUTATION

We fit the model via Markov chain Monte Carlo (MCMC), using a combination of conjugate sampling steps and Metropolis–Hastings updates, with details provided in Danaei et al. (2011b). We note that in hierarchical models there can be strong dependence between parameters across levels of the model, in particular, dependence of random effects and their associated variance components. To address this, we jointly sampled random effects with their hyperparameters (Rue and Held, 2005, Section 4.1.2), which greatly improved convergence and mixing. Finally, we note that while it is possible to analytically integrate out those parameters in the mean of the normal likelihood whose priors were also normal, we avoided doing so because it would result in off-diagonal structure in the covariance of the likelihood, requiring large matrix manipulations in order to calculate the marginal likelihood.

6. MODEL CHECKING AND INFERENCE

We used posterior predictive checks to ensure that we had not omitted important interactions and used cross-validation to ensure that we had not overfit our data. In addition, we assessed the sensitivity of our inference to the inclusion of country-level covariates. All model checks were reassuring and full results are given in Danaei et al. (2011b). In particular, in the cross-validation our model predicted the known-but-masked data very well: the 95% prediction intervals covered 94% of excluded study mean values for both men and women, consistent with the expected 95%.

We draw from the posterior predictive distribution for the mean SBP in each country, age and year with covariates corresponding to a weighted national study that represents both urban and rural populations. We then estimate year- and age-group-specific mean SBP at the subregion level using a population-weighted average of the mean SBP values for the countries within the subregion, with analogous estimates for the regions and globe. We also estimate mean SBP marginalizing over age by calculating age-standardized values, with weights for each age group from the World Health Organization standard population. Epidemiologists are interested in the linear component of the SBP time trends to assess whether health status has generally been improving. To linearize, at each iteration we fit a simple linear regression of the country's mean SBP values against year, collecting the resulting slopes across MCMC iterations.

7. RESULTS

We additively decomposed the variability in the country–year predictions for 50-year-olds to understand the variation attributable to mean and time trends at each of the levels of the hierarchy. For each country and MCMC iteration, we decomposed the predicted time series into mean, linear trend and nonlinear trend (residual). We then decomposed each of these terms into country-specific variation, subregional variation, regional variation and global variation, treating country–time points as the units—that is, the subregional, regional and global terms were averages of the countries within each subregion, region and globe. This weighting gives greater emphasis to subregions with more countries than would treating subregions as units

within regions and regions as units within the globe. As can be seen in Table 1, country and region variation predominate, and cross-country variation is more important than temporal variation.

For females, we note that v_c (the variance of random effects specific to community studies) is large (33.0, 27.9–38.8), suggesting that studies of individual communities do not reflect the country's mean SBP level accurately. Although v_w (the analogous variance for nationally representative studies with sample weights) is smaller (10.8, 6.5–16.0), its magnitude is nonnegligible. Consistent with this, if we include study-specific variation for weighted national studies in the variance decomposition above, this accounts for 22.8% (13.6–34.4%) of the variation for females. This indicates that even weighted national studies, the highest quality studies in this analysis, may have imperfect study design and quality, reflected in the anomalous 2004 study in the U.S. (Figure 1). Similar conclusions hold for males.

Figure 1 shows example model fits for 50-year-old females from three countries with differing data density and study representativeness.

Comparing across subregions in 2008, female SBP was highest in some east and west African countries, with means of 135 mmHg or greater. Male SBP was highest in Baltic and east and west African countries, where mean SBP reached 138 mmHg or more. Men and women in western Europe had the highest SBP among high-income regions.

Figure 2 shows age-standardized regional and global trends, highlighting a global transition in which cardiovascular disease risk factor levels have increased in lower-income regions to become comparable to—and

TABLE 1
Decomposition of variability in predictions (%), with 95% credible intervals subscripted

|	Country	Subregion	Region	Globe	Total
			Female		
Mean	$_{26.5}38.6_{51.8}$	$_{3.4}7.6_{14.2}$	$_{16.9}26.9_{38.5}$		$_{60.3}73.1_{84.4}$
Lin. trend	$_{2.0}6.8_{15.0}$	$_{0.7}2.7_{6.9}$	$_{3.6}8.5_{15.2}$	$_{0.0}2.6_{10.1}$	$_{11.5}20.6_{31.5}$
Nonlin. trend	$_{0.8}4.0_{9.3}$	$_{0.1}1.0_{2.8}$	$_{0.1}1.0_{3.2}$	$_{0.0}0.3_{1.4}$	$_{1.5}6.3_{13.8}$
Total	$_{37.4}49.4_{61.0}$	$_{6.2}11.3_{19.8}$	$_{25.2}36.4_{48.5}$	$_{0.1}2.9_{10.7}$	
			Male		
Mean	$_{26.4}40.1_{54.1}$	$_{5.7}10.3_{17.1}$	$_{15.2}26.0_{37.3}$		$_{63.0}76.5_{87.3}$
Lin. trend	$_{0.9}3.5_{8.7}$	$_{0.3}2.3_{6.9}$	$_{1.1}4.0_{8.2}$	$_{0.0}1.5_{7.2}$	$_{5.1}11.3_{19.9}$
Nonlin. trend	$_{1.9}6.6_{13.7}$	$_{0.4}1.8_{4.4}$	$_{0.4}2.0_{4.9}$	$_{0.1}2.0_{6.4}$	$_{4.3}12.3_{23.2}$
Total	$_{37.3}50.2_{63.5}$	$_{8.4}14.4_{22.9}$	$_{20.7}32.0_{43.9}$	$_{0.3}3.5_{11.0}$	
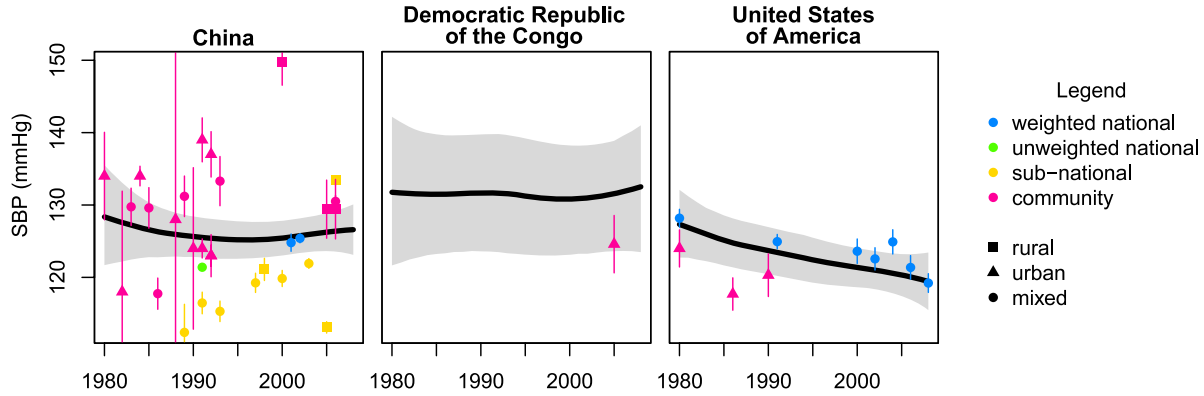
FIG. 1. *Raw data with model fits for 50-year-old females. The solid line represents the posterior mean, the shaded area the pointwise 95% credible interval. The vertical error bars show the 95% intervals due to sampling variability* ($\pm 2s/\sqrt{n}$).

in places even surpass—those in high-income regions, in which levels have decreased. A costly epidemic of high blood pressure in low-income countries may be the most salient feature of the global cardiovascular risk transition in the coming decades.

8. DISCUSSION

The results of our analyses using this modeling strategy were published in a series of four risk-factor-specific papers in 2011 in *The Lancet* that received

press coverage at the national and global level (including the *Washington Post*, *International Herald Tribune*, *Guardian*, *Times of India* and *BBC*). The results were used in the WHO Global Status Report on noncommunicable diseases (NCDs; WHO, 2011) and The World Health Statistics, and were presented at the First Global Ministerial Conference on Healthy Lifestyles and NCD Control. They were used to select ambitious but achievable targets for cardiovascular disease risk factors for the UN high-level meeting
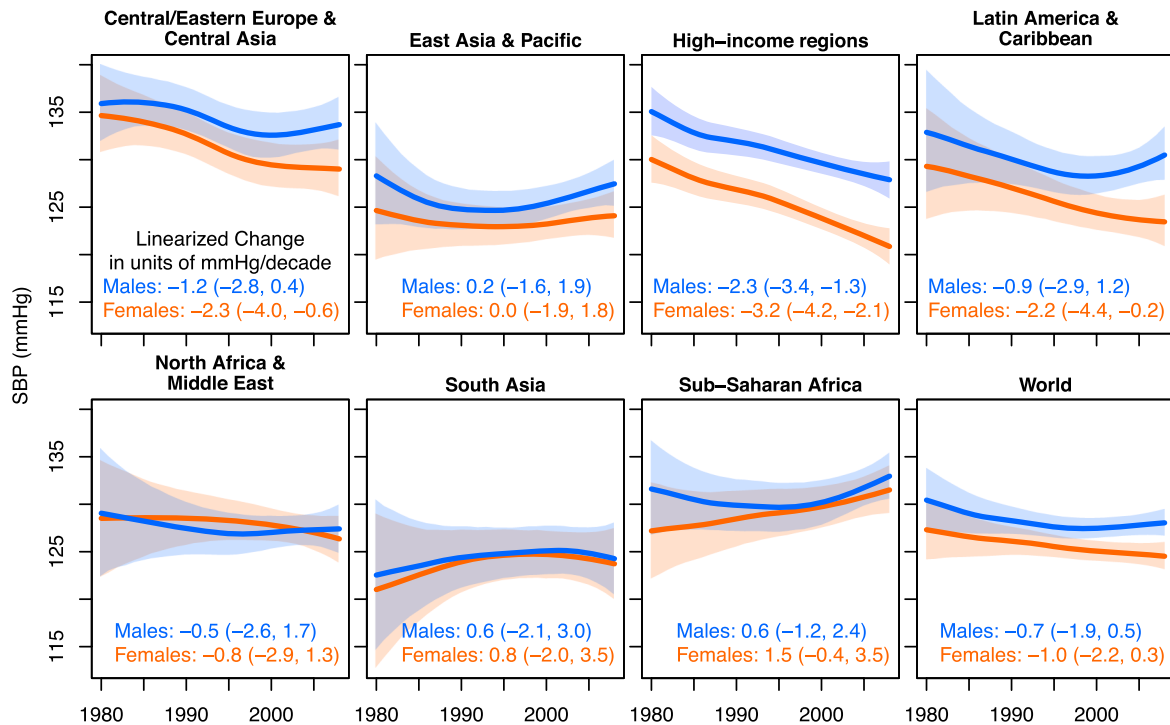

FIG. 2. *Male (blue) and female (orange) trends (estimated separately) by region. The solid line represents the posterior mean and the shaded area the pointwise 95% credible interval. Numerical values are the estimated linearized time trends.*

on NCDs, a task that requires a thorough understanding of past trends. In addition, our results were used by the US National Academy of Sciences Panel on *International Health Differences in High Income Countries* (Woolf and Aron, 2013) to understand the role of risk factors for cardiovascular disease in cross-population health differentials. Our results were also used to calculate the global burden of disease attributable to CVD risk factors (Lim et al., 2013), a calculation which requires comparable estimates by age, sex, year and country. Researchers working on non-CVD conditions have also used our results on CVD risk factors, for example, to examine the role of obesity on cancers and of maternal obesity on stillbirths in different countries (Flenady et al., 2011). Finally, our close collaboration with leading global health researchers is helping to place Bayesian methods that rigorously synthesize fragmentary data at the heart of the conversation about methods for measures of health status.

While our confidence in the model is bolstered by the cross-validation results that indicate that our inference reflects the important sources of variability, there are a number of potential model improvements. These include further consideration of additional covariates, nonlinear covariate effects and covariate interactions, including covariate effects that vary by region. In addition, we would like to have considered more flexible models for the effects of nonnationally representative studies and studies representing only rural or urban populations. While data sparsity led us to assume that a number of model parameters were constant across region, it would be worthwhile to investigate allowing the country-level variance components, including the autoregressive smoothing parameters, to vary by region. Finally, our model assessment indicated room for improvement in the fitted age effect in some countries; in particular, age effects may vary with time beyond our modeled interaction with the overall time-varying level of mean SBP.

Beyond such model selection issues, we close by noting two important open issues. First, cross-validation can only assess our quantification of predictive uncertainty in relation to the observed data; the presence of additional variability (beyond sampling variability) related to shortcomings in study quality in the weighted nationally representative studies makes it difficult to assess our quantification of uncertainty in the true country-level trends. Second, we assume that the presence/absence of data is noninformative; if the studies or countries represented in the data set are not missing at random, our results would be biased, with

trend estimates affected by data collection patterns. For example, if countries with more airports tend to attract both researchers and fast food franchises, then we could be at risk for overestimating SBP levels.

In summary, efforts to improve global health will depend on reliable estimates of health status, and many of these estimates will be based on fragmentary data from disparate sources. The Bayesian paradigm provides a framework for rigorously combining these data sources to obtain coherent country-, region- and global-level inference.

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