Supplementary Online Content


eAppendix. Supplemental Material

This supplementary material has been provided by the authors to give readers additional information about their work.
eAppendix. Supplemental Material

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I. EXAMPLE OF 3 CATEGORY NET TRANSITION PROBABILITY

We leveraged Markov-type transition models and cross-sectional data to estimate 1-year net transition probabilities between BP categories. As an example of net transition probabilities, consider a hypothetical cohort of 80 participants aged 35 years; of these 80 participants, 50 participants have ideal BP (62.5%), 20 participants have prehypertension (25.0%) and 10 participants have hypertension (12.5%).

By age 36, 8 participants with ideal BP have transitioned to prehypertension while 3 participants with prehypertension have transitioned to ideal BP, representing a net transition from ideal to prehypertension of 5 (i.e. 8-3). The one year net transition probability from ideal BP to prehypertension can then be calculated as the net transition divided by the prevalence of prehypertension at age 35 (5/50=0.1 or 10%). Similarly, by age 36, 4 participants with prehypertension have transitioned to hypertension while 2 participants with hypertension transitioned to prehypertension, representing a net transition of 2 (i.e. 4-2) and a net transition probability of 10% (i.e. 2/20). At age 36, 45 participants would have ideal BP (56.3%), 23 participants would have prehypertension (28.8%), and 12 participants would have hypertension (15.0%), reflecting the net transition between categories. Net transition probabilities at age 36 would then use these new prevalences, reflecting both movement into and out of a blood pressure category as the denominator for calculating net transition probabilities to age 37. For simplicity, we assumed no two-step transitions occurred within a single year, however two-step transitions could easily be accommodated by the statistical framework.

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II. ESTIMATION OF NET TRANSITION PROBABILITIES

Markov type models, originally developed to solve transportation problems in operations research, allow for estimation of yearly net transition probabilities between blood pressure categories using cross-sectional data. Transportation problems generally describe the optimal movement of supplies to meet demands by using an objective function to select the best values for resources or decision variables that minimizes shipping costs. The computational methods used to solve transportation problems have been extended to other substantive areas beyond the physical distribution of goods. To calculate our net transition probabilities, supplies were interpreted as smoothed prevalence proportions $\pi_i(a - 1)$, where $a$ signified age and $i$ denoted the blood pressure category at age $a - 1$. Here, demands described the prevalence proportions one year later $\pi_j(a)$, with $j$ indexing the blood pressure category at age $a$; the shipping costs or cost constants for moving from one blood pressure category to another were pre-specified ($c_{ij}$, see below). We calculated the decision variables or in this context, the net transitions $\tau_{ij}(a)$. The objective function $J$ kept track of the total transportation costs of transitioning between blood pressure categories at age $a - 1$ to blood pressure categories at age $a$. The objective function $J$ was then minimized: $\min J = \sum_{i=1}^{3} \sum_{j=1}^{3} c_{ij} \tau_{ij}(a)$, subject to the conditions $\sum_{j=1}^{3} \tau_{ij}(a) = \pi_i(a - 1), \sum_{i=1}^{3} \tau_{ij}(a) = \pi_j(a)$ and $\tau_{ij}(a) \geq 0$. These constraints ensured that the total flow from blood pressure category $i$ represented the smoothed prevalence proportion in that blood pressure category and that the total flow into blood pressure category $j$ equalled the demand of that category. Estimating our net transitions also required the overall supply to always equal the overall demand, and that no transitions were negative. Following the calculation of our net transitions, net transition probabilities $p_{ij}(a)$ were estimated as $p_{ij}(a) = \tau_{ij}(a)/\pi_j(a - 1)$. © 2017 American Medical Association. All rights reserved.
III. CALIBRATION OF NET TRANSITION PROBABILITIES

Overview. Although estimation of net transition probabilities from cross-sectional data necessitates the pre-specification of a cost constant to describe the cost of transitioning from one blood pressure category to another, \(c_{ij}\), previous studies have not calibrated cost constraints using longitudinal data.

Approach. For initial assessment, we arbitrarily assigned zero costs to remaining within the same blood pressure category one year later, a cost of one unit for moving one up or down one blood pressure category (e.g. ideal to prehypertension), and a cost of three units for moving up or down two blood pressure categories (e.g. ideal to hypertension).\(^{20}\) Cost constants were then calculated using longitudinal data from the Coronary Artery Risk Development in Young Adults (CARDIA) study to compare calculated constants with the previously described method. The CARDIA study is a population-based cohort study investigating the development and determinants of cardiovascular disease from young adulthood into later life.\(^{40}\) CARDIA investigators recruited \(n=5,115\) African American (51.5\%) and Caucasians (48.5\%) males and females aged 18-30 at study baseline (1985-1986) from four US centers. Blood pressure was measured at eight visits over 25 years. Although the CARDIA study did not include Mexican Americans or participants younger than 18, the population provides a wide variety of ages in African Americans and Caucasians over 25 years to inform on the likelihood of moving between blood pressure categories.

To calculate the cost constants, we estimated the age-specific cumulative probabilities for ideal (0), prehypertension (1), and hypertension (2) as \(\theta_0\), \(\theta_1\) and \(\theta_2 = 1\), respectively, using a cumulative logistic mixed effects model.

\[
\theta_{ij}(age,b) = \frac{\exp(a_0 + \beta_1 \times age + \beta_2 \times age^2 + \gamma_1 \times I(race = white) + \gamma_2 \times I(sex = female) + \gamma_3 \times I(race = white, sex = female) + b)}{1 + \exp(a_0 + \beta_1 \times age + \beta_2 \times age^2 + \gamma_1 \times I(race = white) + \gamma_2 \times I(sex = female) + \gamma_3 \times I(race = white, sex = female) + b)}
\]

\[
\theta_{i1}(age,b) = \frac{\exp(a_0 + \beta_1 \times age + \beta_2 \times age^2 + \gamma_1 \times I(race = white) + \gamma_2 \times I(sex = female) + \gamma_3 \times I(race = white, sex = female) + b)}{1 + \exp(a_0 + \beta_1 \times age + \beta_2 \times age^2 + \gamma_1 \times I(race = white) + \gamma_2 \times I(sex = female) + \gamma_3 \times I(race = white, sex = female) + b)}
\]

Here, \(a_0, \alpha_1, \beta_1, \beta_2, \gamma_1, \gamma_2\) and \(\gamma_3\) are fixed effects and \(b\) are random effects assumed to follow a normal distribution with mean zero. The probabilities of ideal, prehypertension and hypertension given \(b\) were respectively:

\[
\pi_0 = \theta_0, \pi_1 = \theta_1 - \theta_0, \pi_2 = 1 - \theta_1.
\]

The prevalence for blood pressure category \(j\) at age \((a-1)\) was

\[
\int_{-\infty}^{\infty} \pi_j(a-1,b) \times \frac{1}{\sqrt{2\pi} \sigma} \exp\left(-\frac{b^2}{2\sigma^2}\right) db
\]

and the net transition from group \(j\) to group \(i\) for \(j \neq i\) was

\[
\max\left(\int_{-\infty}^{\infty} \pi_i(a,b) \times \pi_j(a-1,b) \times \frac{1}{\sqrt{2\pi} \sigma} \exp\left(-\frac{b^2}{2\sigma^2}\right) db\right)
\]

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For \( i = j \), the net transition from group \( i \rightarrow i \) at age \( a \) was defined as

\[
\text{prevalence of group } i \text{ at age } (a-1) \times \sum_{k \neq i} \text{ net transition from group } i \rightarrow k.
\]

The net transition probability at age \( a \) from blood pressure category \( i \) to blood pressure category \( j \) was then defined as:

\[
\text{net transition from } i \rightarrow j \text{ at age } a = \frac{\text{prevalence of group } i \text{ at age } a}{\text{prevalence of group } i \text{ at age } a}.
\]

The four race and sex group specific net transition probabilities were then obtained and averaged over the four groups.

We then used a numerical integration approach to calculate the integrals described in the above formulas. These steps yielded net transition probabilities from the cross sectional model using the optimization algorithm approach for a given set of cost parameters as well as net transition probabilities from the longitudinal model obtained by fitting the cumulative logistic mixed effects model. Calibration errors were calculated as:

\[
\sum_{Age} \sum_{BP \text{ group}} \text{net transition probability obtained from the cross sectional model - net transition probability obtained from the longitudinal model}.
\]

To calculate net transition probabilities from the cross sectional model only the baseline value was used. Cost parameters were searched from \([0, 20]\) using an increment of one while restricting the cost of remaining in the same blood pressure to less than that of transitioning to a different blood pressure category and the cost of transitioning from ideal to hypertension or from hypertension to ideal blood pressure to larger than the sum of the other two cost parameters. The optimal cost parameters were then chosen as the parameters for which the calibration error was minimized.

**Results and conclusions.** Using longitudinal CARDIA data, our calculated optimized cost constraints of 4, 8, and 17 produced net transitions and standard errors that differed on average less than 0.01% from net transitions estimated using the initial cost constraints (0, 1, and 3), suggesting the definition used for our cost constraints had little impact on the estimation of net transitions or associated standard errors.


IV. VALIDATION OF NET TRANSITION PROBABILITIES

Overview. Calculation of net transition probabilities from age specific cross-sectional prevalence estimates of blood pressure categories is contingent on the assumption that blood pressure transitions remain stable over time. To assess this assumption in our data, we compared the blood pressure prevalence proportions observed from the 2009-2010 and 2011-2012 NHANES data with the expected 2009-2010 and 2011-2012 blood pressure prevalence proportions estimated from 2007-2008 NHANES data net transition probabilities. Overlap between observed and expected prevalence proportions in 2009-2010 and 2011-2012 would suggest that blood pressure category transitions remained approximately stable across the four years under study.

Approach. To calculate our expected prevalence proportion for 2009-2010 and 2011-2012, we first used Markov-type net transition models to calculate age-specific net transition probabilities for transitioning between ideal, prehypertension and hypertension using the 2007-2008 NHANES data. Second, we defined an age population of $n_{a0}$ participants with ideal blood pressure, $n_{a1}$ participants with prehypertension, and $n_{a2}$ participants with hypertension blood pressure in 2007-2008; we used the same approach to estimate the prevalence proportions of ideal, prehypertension and hypertension in 2011-2012 from 2007-2008 data. At age $a$, the two year (2007-2008 to 2009-2010) net transition probability from blood pressure category $i$ to blood pressure category $j$ was $p_{aij}$. The two year net transition probability was obtained by multiplying the one year net transition probability matrix with itself for each age. We then:

I. Estimated $x_j = (x_{j0}, x_{j1}, x_{j2})$, the expected number of participants in moving from blood pressure category $j$ to each blood pressure category (including $j$) by 2009-2010 as $n_{ai} \times (p_{a,j0}, p_{a,j1}, p_{a,j2})$ for $j \in \{0,1,2\}$.

II. The proportion of participants in each blood pressure category in 2009-2010 (indexed by $k$) is given as $y_{ak} = \sum_{i=0}^{2} x_{ik}$.

III. Lastly, we used locally weighted scatterplot smoothing (LOESS) to smooth the prevalence proportions across age.

Results. The following plots compare expected and observed prevalence proportions in the population in 2009-2010, and 2011-2012. The curve of the smoothed expected and observed prevalence proportions in the plots very closely resemble each other suggesting that the cross-sectional method of predicting prevalence proportions performs well. Though modest discrepancies between observed and expected estimates of ideal and prehypertension in the lower ranges of age in the 2009-2010 NHANES data are observed (eFigure 1, panels A and B), generally our expected blood pressure prevalence estimates coincide with observed results, suggesting that blood pressure category transitions remained approximately stable across time.
V. EXTRAPOLATION OF NET TRANSITION PROBABILITIES TO THE US POPULATION

To better represent our net transition probabilities on a population level, net transition probabilities were extrapolated to the US population to estimate the net number of non-institutionalized AAs, CAs, and MAs transitioning between BP levels at each age. The net number of people was calculated by multiplying the appropriate net transition probabilities by the prevalence of ideal (prehypertension) BP and the age-, ethnic- and sex-specific 2010 noninstitutionalized population size. When net transition probabilities were extrapolated to the 2010 U.S. population of noninstitutionalized AAs, CAs, and MAs ages 8 to 80, substantial differences by race-ethnicity and sex were observed in the ages at which the largest net increases in the population with intermediateprehypertension and poor hypertensionBP were estimated (Figure 4). Differences between estimated net transition probabilities and net population extrapolations reflect both the magnitude of estimated net transition probabilities and the size of the population eligible to transition into the adjacent BP category. Ideal to intermediateprehypertension BP net transition probabilities among males peaked at approximately age 40. When extrapolated to the 2010 the U.S. noninstitutionalized population, the largest age-specific increases in the net number of males transitioning from ideal to intermediateprehypertension BP occurred approximately two decades earlier at age 20, with estimated 1-year net increases of 6,187 in AA males, 22,340 in CA males, and 4,830 in MA males. Consistent with net transition probability estimates, net increases in the population with intermediateprehypertension BP occurred much earlier in males compared to females, with net increases in intermediateprehypertension BP among CAs observed to peak at age 20 in males and approximately 30 years later at age 50 in females.
VI. SUPPLEMENTAL FIGURES

eFigure 1. Simulation results examining the stability of blood pressure category transitions by age in n=17,747 African American and Caucasian NHANES participants, 2007-2012. The stability of blood pressure category transitions across time is assessed by the ability of net transition probabilities estimated in the 2007-2008 NHANES population cross-section to predict the prevalence of ideal, prehypertension and hypertension in the 2009-2010 (panels A, B, and C) and 2011-2012 (panels D, E, and F) NHANES population cross-sector.

a. Observed and expected prevalence of ideal blood pressure in 2009-2010. Expected ideal blood pressure prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2009-2010 NHANES data.

b. Observed and expected prevalence of prehypertension in 2009-2010. Expected prehypertension prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2009-2010 NHANES data.

c. Observed and expected prevalence of hypertension in 2009-2010. Expected hypertension prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2009-2010 NHANES data.

d. Observed and expected prevalence of ideal blood pressure in 2011-2012. Expected ideal blood pressure prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2011-2012 NHANES data.

e. Observed and expected prevalence of prehypertension in 2011-2012. Expected prehypertension prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2011-2012 NHANES data.

f. Observed and expected prevalence of hypertension in 2011-2012. Expected hypertension prevalence estimates were estimated using the net transition method applied to 2007-2008 NHANES data. Observed estimates are calculated directly from the 2011-2012 NHANES data.
Figure 2. One-year age-specific population extrapolations of the net number of non-institutionalized African American, Caucasian, and Mexican American males and females transitioning to prehypertension and hypertension.

VII. SUPPLEMENTAL TABLE

eTable 1. American Heart Association Definition of Ideal Cardiovascular Health for Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Adults ≥20 years of age</th>
<th>Children 8-19 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal</td>
<td>SBP &lt;120/ DBP&lt;80 mm Hg untreated</td>
<td>&lt;90th percentile</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>SBP 120-139, DBP 80-89 mm Hg or treated to goal</td>
<td>90th-95th percentile, SBP ≥120 or DBP ≥80 mm Hg</td>
</tr>
<tr>
<td>Hypertension</td>
<td>SBP ≥140 or DBP ≥90 mm Hg</td>
<td>&gt;95th percentile</td>
</tr>
</tbody>
</table>

*SBP, systolic blood pressure; DBP, diastolic blood pressure
VIII. SUPPLEMENTAL REFERENCES

