COMMENTARY

A Novel Approach for Estimating Cost-Effectiveness of Pharmacological Treatment in Drug Naïve Adults with Hypertension

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In this edition of the journal, an article by Vasudeva *et al.*[1] report on the cost-effectiveness of extending pharmacological treatment to untreated non-Hispanic Black and White adult men and women aged 35–74 years with hypertension according to the recommended treatment thresholds espoused in the recently published JNC 8 report.[2] The general approach they took to arrive at these estimates was to execute computer simulations to produce their cardiovascular disease (CVD) policy model based on multiple inputs from epidemiological studies, randomized clinical trials, and hospital discharge surveys. Population projections for the 2014–2024 time frame were obtained from the census bureau. Hypertension treatment was recommended as follows: (i) Blood pressure (BP) <140/90 mm Hg for those with diabetes and/or chronic kidney disease (CKD), (ii) diastolic BP <90 mm Hg if <60 years of age, or (iii) BP <150/90 mm Hg if 60 years or older without either diabetes or CKD. The reduction in BP was estimated taking into account the baseline BP level and the number of standard medication doses needed to reach the guideline BP goal according to a trial-based formula.[3]

An initial simulation was undertaken to estimate the number of CVD events, CVD deaths and heart failure deaths, costs and quality-adjusted life years (QALY); this simulation was repeated in non-Hispanic Black and White adults with stratification by age, sex, and the presence/absence of CVD, CKD, or diabetes after treatment to their respective JNC 8 BP target. Incremental cost-effectiveness ratios (ICERs) were computed as the change in costs divided by the incremental change in QALYs. The range of ICERs was characterized as: (i) <$50,000 per QALY gained (cost effective), (ii) $50,000 to $149,999 (intermediate value), and (iii) $150,000 and higher (low value). Systolic BP was classified as stage 1 hypertension (140–159 mm Hg) and stage 2 was 160 mm Hg or higher; diastolic BP was classified as stage 1 (90–99 mm Hg) and stage 2 was 100 mm Hg or higher.

Over the time frame 2014–2024, 1.7 million non-Hispanic Blacks and 5.4 million non-Hispanic Whites in the 35- to 74-year age range were eligible for treatment of their hypertension for primary prevention of CVD. Cost-effectiveness of pharmacological antihypertensive treatment was demonstrated in non-Hispanic Black men and women in the 35- to 44- and 45- to 74-year age categories for hypertension stages 1 and 2 irrespective of diabetes or CKD status. Similar results were observed in non-Hispanic Whites except for 35- to 44-year-old men without diabetes or CKD (intermediate value) and women aged 35–44 years with stage 1 hypertension with or without diabetes where pharmacological treatment was of intermediate or low value.

The authors are to be commended for undertaking and completing this daunting analysis requiring the interrogation and integration of multiple, diverse datasets. Meticulous effort was required to ensure that the assumptions made were reasonable and the estimates produced by the CVD policy model were as free from bias and error as possible. In addition, risk estimates were adjusted for quantifiable racial differences in CVD risk when possible. The results of this CVD Policy simulation are somewhat consistent with our prior recommendations for earlier initiation of pharmacological treatment and lower a lower BP target (<135/85 mm Hg) in African Americans with hypertension.[4]

The treatment assumptions in this simulation were, however, conservative and therefore can be legitimately questioned. The BP thresholds used for initiation of pharmacological treatment were considerably higher than the level of pretreatment BP for which a pre-SPRINT meta-analysis showed CVD risk reduction.[5] The recently published SPRINT study[6] included high-risk men and women aged 50–80 years with BP 130–180 mm Hg at baseline; this trial, stopped early because of a clear benefit of intensive pharmacological treatment (<120 mm Hg systolic) on the composite CVD endpoint, confirmed the CVD risk reduction at pretreatment BP levels lower than conventional BP thresholds

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(<140/90 mm Hg) and also highlighted that the more aggressive BP targets than those promulgated in JNC 8[2] did indeed lower CVD risk. Though definitive post-SPRINT pharmacological BP initiation thresholds and treatment targets have not been put forth, they almost assuredly will be more aggressive than those promulgated in the JNC 8 report.[2] Also, most hypertensive patients will receive many decades of antihypertensive drug therapy meaning that observations made in randomized trials and meta-analyses or even decade-long simulations emanate from a much shorter time frame than actual patients will be treated for.

Analyses such as these will not likely substitute for well-done adequately powered randomized controlled trials (or meta-analyses) designed to determine the benefits of pharmacological BP treatment on the prevention of pressure-related CVD events. Rather, similar simulations will most plausibly provide complementary data to well-done randomized controlled trials and careful meta-analyses of these trials. The data reported herein showed more consistent cost-effectiveness from pharmacological treatment across risk strata in non-Hispanic Blacks than in non-Hispanic Whites. Accordingly, does this mean that pharmacological treatment in younger (35- to 44-year old) White men without diabetes and same aged White women, irrespective of diabetes status, should be eschewed? The answer, I believe is no—at least a qualified no.

The observed difference in cost-effectiveness plausibly reflects racial differences in pretreatment absolute CVD risk. And though we previously made the argument for a lower BP threshold for the initiation of pharmacological treatment in African Americans, there is perhaps a better, more individualized strategy for ensuring optimal treatment for those at high CVD risk. That is, to base the decision to initiate pharmacological BP treatment on absolute CVD risk.[7] In the emerging era of personalized medicine, it seems outdated to use broad race–ethnicity categories that mask widely varying risk profiles to produce identical treatment recommendations for all "individuals" self-identifying as being a member of a given race–ethnicity group.

Simulations can easily provide data regarding cost-effectiveness over extended periods of time—more reflective of a lifetime of treatment—as opposed to simply providing them at one, more proximal, time point. There is also the opportunity to utilize risk estimates for CVD based on long term (many decades) of BP differences in Mendelian randomized BP cohorts.[8] This type of analysis, arguably, serves as a proxy for an extended duration of pharmacological BP control. Furthermore, the risk reduction coefficients for a given magnitude of BP difference in Mendelian BP cohorts are several-fold larger than those derived from short-term randomized trials. Further, the ability to model varied assumptions (e.g., different BP initiation thresholds, on-treatment BP targets) can also be done and should prove to be highly informative. Importantly, the effects of pharmacological treatment can be modelled according to the level of pretreatment absolute CVD risk.

Carefully done simulations such as the one reported in this edition of the journal by Vasudeva *et al.*[1] merit consideration as substantive, informative, and complimentary data to traditional sources (trials, meta-analyses) when evaluating hypertension treatment strategies for the lowering of CVD risk. Such simulations leverage the vast knowledge within the existing hypertension database and facilitate the exploration of varied diagnostic and therapeutic approaches, many of which may never be investigated in future randomized controlled trials.

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