Restating Well-Known Determinants for Blood Pressure: Do Classification Trees Help?

Yuri V. Sebastião,[1,*] Chighaf Bakour,[2,*] and Skai W. Schwartz[2,*]

Over the 4 decades since the CARDIA longitudinal cohort study began, several reports have characterized risk factors, incidence, and cardiovascular disease outcomes associated with prehypertension and hypertension in that study population.[1–3] The recent report by Reges *et al.* on risk factors and risk factor interactions for blood pressure (BP) in the CARDIA cohort is the latest in this line of studies.[4] There are 2 aspects that differentiate the general approach by Reges *et al.* from the previous CARDIA study reports on this subject.

First, the outcome studied by Reges *et al.* was defined as the probability of maintaining normal BP throughout middle age rather than the risk of developing above-normal BP (i.e., prehypertension and hypertension). The reasons for focusing on the positive complement of the risk of developing higher BP are not discussed in the report but this approach is in part reminiscent of a "positive epidemiology" focus, which some authors have argued can help advance epidemiology and public health research.[5] The general argument in favor of positive epidemiology is that we would have a more complete understanding of the factors that shape population health by supplementing the study of disease distribution and traditional risk factors with a broader examination of positive health assets and outcomes.[5] However, the main findings from the report by Reges *et al.* are limited to a handful of known risk factors for hypertension.

Second, Reges *et al.* used a classification tree algorithm, one of many segmentation techniques that have been in use since the 1960s.[6] The Chi-square Automatic Interaction Detection technique (CHAID) used by Reges *et al.* provides an interpretable visual summary of population subgroups formed by combinations of multiple (in this case, up to 3) risk factors.[6] Having such a visual representation of how different risk factors combine to influence the likelihood of maintaining normal BP may provide advantages for translating study findings into prevention efforts. However, as Reges *et al.* acknowledge, the results from CHAID classification trees are not robust to (i.e., they vary with) changes in the sample being studied.[4] Furthermore, unlike regression modeling, classification trees do not estimate the adjusted effect of a given variable while controlling for multiple covariates; they only show the additional discriminative value provided by a given variable conditional to the risk factor combinations that form a subgroup in the tree diagram.[6]

As its name suggests, the CHAID algorithm selects predictors based on statistical significance, and in the study by Reges *et al.* baseline BP was the most significant predictor, followed by race. The finding that participants with low BP measured at age 18–30 were more likely to remain normotensive throughout midlife is consistent with earlier reports from the CARDIA cohort and elsewhere.[7,8] What is surprising at first, is the systolic cut point of ≤92 mm Hg, which defined the subgroup with highest likelihood of remaining normotensive. This cut point suggests that at least some young adults in the subgroup met the definition for hypotension at systolic blood pressure <90 mm Hg. Yet we are reminded that what we consider to be "normal" BP still conveys considerable risk: A report from the Framingham cohort indicated that young people with systolic blood pressure of 120–129 or diastolic blood pressure of 80–84 mm Hg were about 3 times as likely to develop hypertension as were those with systolic blood pressure <120 and diastolic blood pressure <80 over the next 10 years.[9] Reges *et al.* did not predefine the systolic cut point of ≤92; instead, the cut point was selected empirically by the classification tree algorithm. We are unaware of any previous studies that have examined a cut point for "ideal" systolic blood pressure as low as ≤92. Could it be that that with optimal lifestyle choices, a systolic blood of 92 is not only obtainable in a young person but also healthy? Reges *et al.* suggest that this is a question worth examining in future research.

The CARDIA project stands out from its peer cohort studies because of its overwhelming concentration on cardiovascular risk factor disparities between Black (51.5% of the study population) and White urban Americans. As such, the finding that Whites were likely to remain normotensive

Correspondence: Skai W. Schwartz (skaisw@aol.com or sschwar2@usf.edu).

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[1]Division of Global Women's Health, School of Medicine, University of North Carolina, Chapel Hill, North Carolina, USA; [2]College of Public Health, University of South Florida, Tampa, Florida, USA.

***These authors contributed equally to this work.**

than Blacks is consistent with several previous CARDIA reports, published as early as 1989.[1,10–13] However, the study by Reges *et al.* highlighted only a few factors that modified the racial association with staying normotensive (low body mass index, nonsmoking, and no family history), thus providing little insight into race as a marker for higher risk of hypertension. In their analysis, Reges *et al.* included dietary sodium consumption, cardiorespiratory fitness (duration of a treadmill test), and exercise total intensity score, all of which were not selected among the most statistically significant predictors by the classification tree algorithm. While we acknowledge that not all potentially important factors were known or measured at baseline, the limited inclusion of candidate variables related to lifestyle is surprising as we note some early CARDIA analyses that concluded that lifestyle and/or dietary factors taken together explain a nontrivial portion of the association between race and hypertension.[1,11] With regard to diet, both consumption of potassium and isoflavone have been shown to be lower in Blacks than Whites, and both higher consumption of potassium and isoflavone were protective against hypertension within some subgroups defined by race and/or sex in the CARDIA cohort.[11,14] Additionally, the only measure of socioeconomic status included in the study by Reges *et al.* was education, which does not fully account for the influence of income, socioeconomic mobility, and neighborhood characteristics, all which have been found to contribute to the risk of hypertension, particularly among African Americans.[15,16]

As has been discussed by many, and briefly mentioned by Reges *et al.* in their report, race "may be a marker for psychosocial factors resulting from societal disparities/racism…."[4] This warrants a deeper discussion of race as a risk factor. First, when examining racial disparities in health outcomes it is important to recognize that biological race is rarely the variable of concern. The true risk factor is often racial inequalities, structural racism, and a host of socioeconomic factors that come with being Black in the United States. As reported by Krieger and Sidney, internalized responses to racial discrimination, and accepting unfair treatment as part of life were associated with elevated BP among Black men and women in their 20s and 30s, while those who were able to articulate their experience of discrimination or do something about it were at a lower risk of hypertension in the CARDIA cohort.[13] Likewise, Forde *et al.* discussed mechanisms by which discrimination may induce hypertension, including stress response and dysfunctional coping mechanisms leading to poor diet, smoking, and alcohol consumption.[17] They found that, among African Americans in the Jackson Heart Study, both high levels of lifetime discrimination and higher stress from lifetime discrimination increased the risk of hypertension but the latter association was attenuated after adjusting for other risk factors.[17] Similarly, Borrell *et al.* found that discrimination was much more common among African Americans (89.1%) compared with Whites (40.0%) and was associated with health behaviors such as smoking and alcohol use among African Americans in the CARDIA cohort.[18]

Finally, it is a common practice to examine the interaction between race and risk factors for a health outcome in epidemiological studies. In some cases, a risk factors that is significantly associated with the outcome may not contribute to the racial disparity in the outcome, which leads to the appearance of a negative interaction, where the deleterious exposure–outcome relationship appears to be stronger among the more advantaged group. However, the higher burden from both the exposure and the outcome may still be carried by the disadvantaged group.[19] In this case, race and its accompanying socioeconomic factors, discrimination, and the resulting stress are the stronger risk factors for the outcome, and are strongly correlated with other modifiable risk factors, causing these risk factors to contribute very little additional risk of the outcome. This pattern has been observed in several studies examining the interaction between race and other risk factors for health outcomes[19,20] and again points to the contribution of racial inequalities and racism. Therefore, we urge caution in interpreting the interactions reported in the study by Reges *et al.* and when determining the implications of these results for prevention.

In conclusion, based on their approach, the study by Reges *et al.* provides a fresh perspective on the epidemiology of BP in the CARDIA cohort. However, several questions for the prevention of hypertension remain unanswered due to omission from the analysis or lack of discussion about diet, lifestyle, and psychosocial determinants of BP.

DISCLOSURE

The authors declared no conflict of interest.

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