A Risk Score for Risk Factors
Rationale and Roadmap for Preventing Hypertension

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I find it increasingly helpful to distinguish two kinds of aetiological questions. The first seeks the causes of cases, and the second seeks the causes of incidence. “Why do some individuals have hypertension?” is a quite different question from “Why do some populations have much hypertension, whereas in others it is rare?” The questions require different kinds of study, and they have different answers.

—Geoffrey Rose

High blood pressure (BP) is a common problem and a major cause of morbidity and mortality. It is estimated that there are $\approx 972$ million people with hypertension worldwide, and a much larger number of people have nonoptimal BP (defined as a systolic pressure $\geq 115$ mm Hg). From a global perspective, “suboptimal” BP accounts annually for $\approx 7.6$ million premature deaths and a loss of $92$ million disability-adjusted life-years (1 disability-adjusted life-year is equivalent to 1 lost year of healthy life).

Suboptimal BP is also common in the United States, with an estimated $73.6$ million people having hypertension (33% of the population $\geq 20$ years of age) and another $53.6$ million individuals with prehypertension (25% of the population $\geq 20$ years of age). More than 70% of patients with a first stroke, heart attack, or heart failure have had antecedent hypertension, and the condition accounts for 1 in 5 deaths in the United States, rivaling the impact of smoking on mortality. It is also an expensive condition, with an estimated cost of over $73$ billion in terms of healthcare expenses in 2009. Given the burden posed by suboptimal BP in general and by hypertension in particular, preventing the condition is a major public health priority.

Causes of Diseases in Cases Versus Determinants of Disease Incidence in the Population

The last 6 decades have led to major advances in our understanding of the epidemiology of high BP. It is increasingly acknowledged that hypertension is best regarded as “a level of BP above which treatment does more good than harm,” an epidemiological concept illustrated by the progressive lowering of BP thresholds defining hypertension in successive guidelines over time. Observational studies have highlighted the conjoint and synergistic influences of socioeconomic factors, race, behavioral characteristics, and metabolic risk factors in determining the propensity of individuals and populations for developing high BP. Randomized, controlled trials have established that both nonpharmacological (lifestyle and dietary) and pharmacological interventions can delay the progression to hypertension in high-risk nonhypertensive individuals. Although we understand the epidemiology of hypertension and suboptimal BP and recognize the societal toll, efforts have thus far focused more (and with good reason) on improving the detection, awareness, and the control of BP in those with established hypertension.

In this context, it is perhaps relevant to revisit a landmark commentary by Geoffrey Rose, in which he distinguished the “causes of disease in cases” from the “determinants of disease incidence in the population.” The 2 concepts represent complementary approaches that define prevention strategies at the level of the individual (for identifying susceptible individuals) and at the level of the population, respectively. Rose himself prioritized elucidating the determinants of hypertension incidence in populations from a public health standpoint because, “if causes of incidence can be removed, susceptibility ceases to matter.” However, he acknowledged that the population-wide approach was challenged by the “prevention paradox,” ie, “a preventive measure that brings much benefit to the population offers little to each participating individual.” In other words, BP lowering at the level of the population is achievable if everyone chooses to exercise more, maintains an ideal body weight, and eats well, ie, consumes a diet low in salt and rich in fruits, fiber, and vegetable proteins. Yet, few among the $\approx 53$ million million with prehypertension may feel motivated to do so because of the prevention paradox.

Perhaps if we had the means of identifying a higher-risk subgroup among the millions with prehypertension, we could focus our resources more efficiently to motivate and intervene in the “more susceptible” among this larger group. The development of a risk score for predicting hypertension may be seen as 1 step in alleviating the prevention paradox by identifying people who are more likely to gain at an individual level and targeting them for nonpharmacological measures (and presumably pharmacological ones), in concert with public health measures to lower the societal burden of suboptimal BP.

Role of Hypertension Risk Scores

At least 3 different groups of investigators have developed risk scores for predicting hypertension. In this issue of

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Hypertension. Kivimäki et al.\textsuperscript{12} provide us with an elegant roadmap of how to develop and validate a risk score for predicting the very development of risk factors, in this case, hypertension. Using the longitudinal design of the large Whitehall II Study cohort to their advantage and dividing their sample into derivation and validation sets, the investigators formulated a risk score for hypertension and compared its performance with that of the Framingham hypertension risk score. The authors used a range of appropriate metrics to compare the validity and transportability of the Framingham score with the Whitehall sample, including the discrimination and calibration statistics, the net reclassification index, and assessment of predictive use in distinct subgroups. The investigators demonstrated the excellent performance of the Framingham hypertension score in their sample and noted that the Whitehall score did not necessarily perform better than the Framingham one, although it was developed from within a subset of the Whitehall cohort.

These studies\textsuperscript{12,13} and another recent report\textsuperscript{12,14} (of a hypertension risk score) from the Women’s Health Study serve to illustrate some key points. First, and not surprisingly, baseline BP emerged as a key predictor of hypertension risk, a phenomenon referred to as the ‘horse racing effect’ in epidemiology. However, a risk score that additionally incorporates age, sex, and body mass index identifies the propensity for developing hypertension on short-term follow-up (4 to 8 years) better than simply using the baseline BP or the prehypertension category.\textsuperscript{12–14} Second, the risk scores seem to perform reasonably well across different subgroups defined on the basis of age, sex, body mass index, smoking status, or parental history, confirming the robustness of the scores.\textsuperscript{12} Third, the Women’s Health Study investigations indicated that adding biochemical variables to the scoring system did not enhance predictive utility over a parsimonious score with few easily measured clinical variables.\textsuperscript{14} Fourth, these scores were developed in predominantly white people living in developed countries, who likely hailed from a middle-class (or higher) socioeconomic position.\textsuperscript{12–14} Additional studies are warranted to assess their transportability to other races, social classes, and other countries (with appropriate recalibration to the local rates of hypertension). Fifth, it should be remembered that scores predicting risk over a short time frame (4 to 8 years) tend to underestimate risks in younger people who may experience a greater risk over longer periods of follow-up. Sixth, 2 of these risk scores\textsuperscript{12,13} excluded individuals with diabetes mellitus from their samples, acknowledging the emphasis on lower BP goals in people with diabetes mellitus.\textsuperscript{7}

What might be the potential use of these risk scores? At the level of the individual, these risk scores can be used for risk assessment and for risk communication. In a world of finite resources, the absolute risk of developing events has been used as a yardstick for focusing interventions on those with greatest risk to maximize the cost-effectiveness of interventions. The aforementioned studies\textsuperscript{12–14} demonstrate that we gain information when we factor in other simple clinical variables (components of the risk score) in addition to an individual’s current BP for predicting the future probability of developing hypertension. So, we can more precisely, and perhaps more efficiently, target high-risk individuals for preventive measures. Also, in the context of lifestyle and dietary interventions, one can hopefully avoid the prevention paradox by focusing efforts on people who stand to gain the most from these interventions. Because these risk scores are developed for short-term prediction of hypertension risk, the gains to individuals are likely to also accrue in the short run, which may motivate them further to adopt the interventions.

The hypertension risk scores can also be used for designing clinical trials of hypertension prevention by enrolling higher-risk individuals. At a population level, health policy planners may also find the risk scores useful for projecting the future burden of hypertension in communities and for allocating...
resources based on mean levels of the various components of the hypertension risk score in the communities. Temporal trends in hypertension risk scores among the nonhypertensive segment of the community may help us gauge the relative success of societal measures in preventing hypertension (eg, effectiveness of interventions to promote physical activity or smoking cessation).

Preventing Risk Factors in the First Place: Notions of Primordial Prevention of High BP and Promotion of Optimal BP Levels

It is estimated that the global burden of hypertension will increase to \( \approx 1.56 \) billion afflicted individuals by 2025.\(^2\) Framingham data indicate that the lifetime risk of developing hypertension is a staggering 90%. In the United States, the Healthy People 2010 Program aimed to reduce the proportion of individuals with high BP from 25% to 16%, and interim assessments suggest that we have moved away from that target, in part because of the burgeoning burden of obesity. These projections underscore both the opportunity and the “urgency of now” for preventing hypertension.

As noted above, the past few decades have helped us develop a good understanding of how high BP develops over the life course, with presumably antenatal and early childhood influences that are followed by BP changes during adolescence and young adulthood and BP tracking going through midlife and beyond (Figure). Notwithstanding the potential key role of genetic influences, we understand that high BP is, to a large extent, a lifestyle-related and life-course disease that is strongly determined by environmental influences. We remain physiologically “hunter-gatherers in the fast lane”\(^15\) who have acculturated to a sedentary lifestyle in a motorized economy, in which physical inactivity and consumption of energy-dense, salt-replete, processed foods are rampant. Accelerated vascular aging and conduit artery stiffness translate into steeper increases in BP with age (yellow and red dotted lines in the Figure). Primitive tribes do exist on this very planet (such as the Yanomami Indians), who demonstrate a flat BP trajectory with aging (green line in the Figure). If such a desirable BP trajectory were achieved, it would greatly mitigate the cardiovascular consequences of suboptimal BP.

In 1978, Toma Strasser\(^16\) coined the term “primordial prevention” to describe the promotion of social conditions under which risk factors do not develop. A more recent National Heart, Lung, and Blood task force\(^17\) preferred the term “prevention of risk factors in the first place.” Overall, it is clear that preventing hypertension and reducing the global burden of suboptimal BP require a multifaceted intersectoral approach involving and promoting active partnerships among individuals, academia, healthcare providers, communities, civic bodies, and industry. Although we can use the hypertension risk score to understand the causes of diseases in individuals to identify susceptible people, we must not lose sight of our efforts to understand and target the causes of the disease in the population that must proceed in parallel.

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