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Commentary

Advances in predicting cardiovascular risk: Applying the PREVENT equations

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Given the increasing prevalence of patients with metabolic risk factors and chronic kidney disease, which disproportionately affect systemically disenfranchised communities, new constructs for risk stratification of cardiometabolic disease are needed. Moreover, the shift in relative contributions of risk factors such as decreased smoking, increase in lipid-lowering treatment, and availability of novel therapies to reduce cardiometabolic risk have often biased previous equations for atherosclerotic cardiovascular disease (ASCVD) risk assessment, such as the Pooled Cohort Equations (PCEs), to overestimate the 10-year risk of ASCVD in the general population [1,2].

In response, the American Heart Association (AHA) defined a novel construct known as cardiovascular-kidney-metabolic (CKM) syndrome, with progressively greater risk for adverse outcomes indicated by higher CKM stages [3]. A quantitative approach to absolute risk estimation of cardiovascular disease (CVD) includes the Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) equations, which highlight the need for global CVD risk assessment [3-5]. The PREVENT equations were created by the American Heart Association's Cardiovascular-Kidney-Metabolic Scientific Advisory Group, arising from a need for a more comprehensive risk assessment tool for cardiovascular disease that incorporated both traditional factors and factors related to cardiovascular, kidney, and metabolic health. In order to validate these tools for generalizability, they were subsequently applied to a large cohort of US adults aged 30 to 79 without known cardiovascular disease that included 25 different datasets and over 3 million individuals.

The PREVENT equations assess CVD risk as a composite outcome of ASCVD and heart failure (HF) specifically by incorporating CKM factors such as body mass index (BMI) and estimated glomerular filtration rate (eGFR) with traditional risk factors. As such, the PREVENT equations build upon prior multivariable risk prediction models that have predominately focused on atherosclerotic outcomes (myocardial infarction and stroke) [4,5]. Importantly, while the PREVENT equations begin at 30 years, primordial prevention begins at birth and comprises Stage 0 of CKM health (i.e., no CKM risk factors), highlighting the importance of early intervention in reducing CVD risk along an individual's lifespan.

The burden of CVD continues to increase within the United States, with a disproportionate burden borne by individuals identifying as non-Hispanic Black, American Indian, Alaskan native, and South Asian Americans [6,7]. Historically disenfranchised communities in particular

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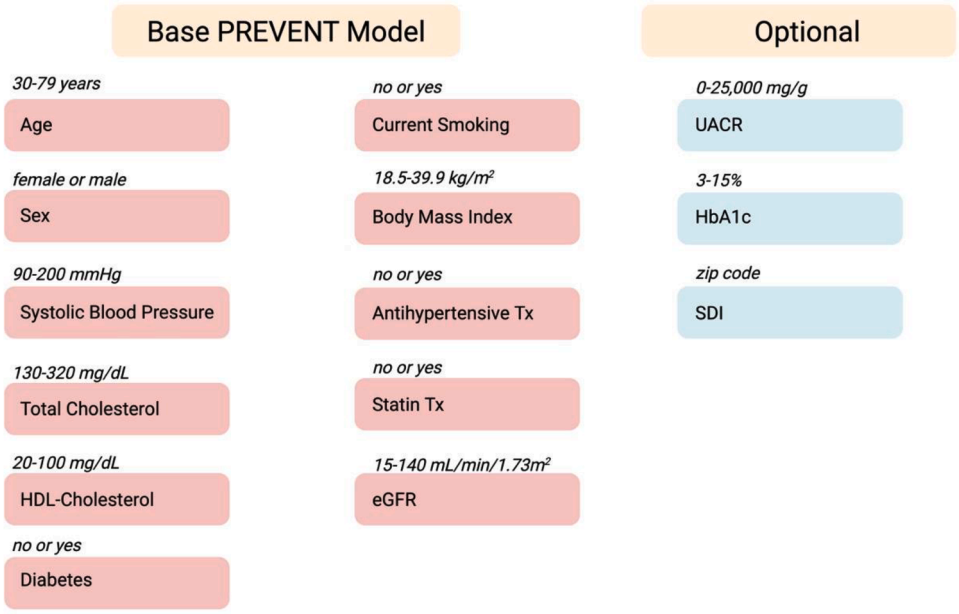

Fig. 1. Schematic of variables included within the PREVENT equations.

face higher risks of CVD due to disparities in medical risk factors as well as social determinants of health. Furthermore, clinicians have frequently endorsed that current risk stratification tools used to counsel patients fail to incorporate socioeconomic factors when assessing long-term risk of developing CVD. Given that CVD risk is increasingly being shown to be linked to factors such as access to healthcare, it is imperative that emerging risk assessment tools account for factors such as structural racism and barriers to health access [8-10].

Among the many advantages of the PREVENT equations are that non-race-based variables are used in estimating CVD risk, thereby reducing the bias of race as an individual predictor of CVD. Therefore, by implementing the PREVENT equations, the AHA has taken a vital step towards promoting overall health equity and improving health outcomes of historically marginalized populations through more accurate cardiovascular risk estimates and effective counseling towards primary prevention for both HF and ASCVD. The PREVENT equations serve as a starting point, and ongoing refinement for the incorporation of social determinants of health within risk assessment can help identify the factors that are most important in outcome prediction and the clinician-patient encounter [9-11]. Factors included in the PREVENT model, including the optional variables, are highlighted in Fig. 1.

Clinical subtypes of CVD that portend higher morbidity and mortality also warrant more tailored risk stratification. For example, determining risk of developing HF is an essential aspect of assessing overall risk as an individual's CKM stage progresses. While PREVENT focuses largely on incident risk, it incorporates multivariable risk prediction for subtypes of CVD such as HF, which could enable more accurate prognostication for individuals at risk of disease progression [12, 13]. Importantly, the PREVENT equations also allow for assessment of lifelong risk starting at age 30, thereby enabling more timely counseling of younger adults who require more nuanced conversations prior to initiation of therapies. This is especially important where earlier counseling and intervention is warranted, such as for those with a strong family history of clinically significant CVD who have yet to become symptomatic or present with imaging evidence of subclinical disease; incident CVD risk is affected by cumulative exposures to factors such as elevated LDL and blood pressure, which highlights the critical importance of early intervention [14].

Other novel risk equations that predict lifetime CVD risk have been tested practically, such as the PREDICT equations assessed in New Zealand and Australia, which incorporate ethnicity and socioeconomic status. Using specifically defined selection criteria, the equations were shown to detect lifelong CVD risk better than the preexisting Framingham risk equations [15]. The PREVENT equations build upon these risk estimates by adding a standardized framework towards assessing multivariable risk that incorporates important CVD subtypes while also emphasizing the impacts of health behaviors on risk of long-term CKM progression [4,5]. The inclusion of social determinants of health (SDOH) as an optional factor in the PREVENT equation is another advancement. However, calculating CVD risk with or without SDOH (zip code) could result in significantly different PREVENT scores. The authors of the PREVENT paper have indicated that the best estimation of risk is when zip code is added. However, we feel clinicians should use whichever version places the patient at a higher risk, to ensure any risk factors are addressed as early and effectively as possible to mitigate long-term CVD risk.

Lastly, the new PREVENT equations – as population risk estimates – should be personalized alongside individual contextual factors such as access to healthy foods, ability to participate in physical activity, and personal health literacy. The importance of an overall healthy lifestyle should be emphasized, including healthy eating and incorporating Life's Essential 8 which include sleeping well, maintaining a healthy diet, increasing physical activity, quitting tobacco, maintaining a healthy weight, controlling cholesterol, managing blood sugar and controlling blood pressure [16]. Incorporating shared decision-making involves combining these factors and comprehensive risk assessment tools with an individual's lived experiences, leading to more personalized, holistic discussions regarding follow-up, appropriate monitoring, and response to therapeutic interventions. This approach should help foster more informative conversations between patients and providers within the shared decision-making framework as clinicians assist patients to take control of their modifiable risk factors and prevent CKM progression.

The PREVENT equations hold significant promise for improving clinical practice by offering a more comprehensive assessment of cardiovascular disease (CVD) risk. We anticipate this can lead to earlier intervention and improved patient outcomes. Future applications might include integrating the equations into electronic health records, thereby allowing for real-time risk calculation and prompting for preventive measures. Furthermore, research opportunities lie in exploring the PREVENT equations' effectiveness in diverse populations and refining

them to incorporate additional risk factors like social determinants of health. Additionally, researchers could investigate the equations' ability to predict specific types of CVD (atherosclerotic cardiovascular disease vs. heart failure) or in helping to guide treatment decisions. However, despite these advantages, some challenges and limitations remain. The equations were validated in a specific population, and their generalizability requires further study in more diverse populations. Additionally, further research will be essential in order to determine the cost-effectiveness of implementing the PREVENT equations in clinical settings.

In summary, risk assessment of CVD remains an essential aspect of primary prevention for cardiologists, internists, and other primary care clinicians. The new PREVENT equations provide a more comprehensive, holistic, and patient-centered approach to assessing individual risk of CVD progression, especially within the CKM framework. As the global burden of CVD continues to rise, shifting trends in risk factor prevalence, availability of therapeutic modalities, and refinement of social and biological predictors continue to influence how clinicians approach discussions with patients regarding their overall risk of cardiovascular disease. Accordingly, the PREVENT equations afford health practitioners an opportunity to counsel patients more effectively as we aim to improve individual health and achieve societal health equity.

CRediT authorship contribution statement

Deen L. Garba: Conceptualization, Writing – review & editing. **Alexander C. Razavi:** Writing – review & editing. **Roger S. Blumenthal:** Conceptualization, Writing – review & editing. **Neil J. Stone:** Writing – review & editing. **Tamar Polonsky:** Writing – review & editing, Writing – original draft. **Sadiya S. Khan:** Conceptualization, Writing – review & editing. **Lili A. Barouch:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

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