

## Letters

### TO THE EDITOR

## Origins and Previous Applications of Causal-Benefit Models



We commend the authors for their comprehensive overview of current challenges in optimizing the selection of individuals for timely prevention of atherosclerotic cardiovascular disease.<sup>1</sup> This review clearly explains how preventive treatment decisions can be optimized by combining predicted 10-year or lifetime risk with causal estimates from trials. While introduced as a “new paradigm,” we believe it is pertinent to note the historical antecedents of this causal-benefit model. Indeed, the methodological concept was first postulated by Glasziou and Irwig as early as 1995.<sup>2</sup> Subsequent studies have corroborated the utility of this concept in cardiovascular trial settings<sup>3</sup> and elucidated its translation into a lifetime perspective.<sup>4</sup> Particularly noteworthy are the lifetime benefit models, offering invaluable insights into selecting young and middle-aged adults who stand to gain from early preventive interventions. These models, leveraging age as the time scale and accounting for competing risks, render lifetime benefit contingent upon risk, causal benefit, and age of treatment initiation, in alignment with the conceptualization by Kohli-Lynch et al. Presently, such models are readily accessible for clinical use through online risk calculators like the European Society of Cardiology (ESC) CVD Risk Calculation App and <https://U-Prevent.com>. Encouragingly, the 2021 ESC guidelines on cardiovascular disease prevention in clinical practice have already embraced the incorporation of causal-benefit models, recommending their utilization in shared decision-making regarding step 2 intensified preventive treatment options.<sup>5</sup> Notably, these guidelines have even incorporated causal-benefit tables delineating the individual lifetime effects of interventions such as blood pressure reduction, low-density lipoprotein-cholesterol lowering, and smoking cessation. Furthermore, the ESC guidelines recommended application of causal-benefit models extends beyond merely prescribing statins for primary prevention.

It also involves identifying high-risk patients with diabetes or established cardiovascular disease who would benefit most from intensive preventive medications like proprotein convertase subtilisin/kexin type 9 inhibitors, intensive blood pressure management, sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide-1-receptor agonists, eicosapentaenoic acid, or low-dose colchicine. We concur with the authors on the persisting challenges in implementing these models in clinical care, particularly in integrating algorithm-based calculations into the workflow of health care professionals and facilitating education, both for health care professionals and patients, and on the interpretation of predicted benefits.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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