JACC: ADVANCES VOL. 3, NO. 9, 2024

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.[1] 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.[2] Subsequent studies have corroborated the utility of this concept in cardiovascular trial settings[3] and elucidated its translation into a lifetime perspective.[4] 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.[5] 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.

*Jannick A.N. Dorresteijn, MD, PhD, MSc[a]
Steven H.J. Hageman, MD, PhD, MSc[a]
Frank L.J. Visseren, MD, PhD[a]
Deepak L. Bhatt, MD, MPH, MBA[b]

*University Medical Center Utrecht
Department of Vascular Medicine
PO Box 85500
3508 GA
Utrecht, the Netherlands
E-mail: J.A.N.Dorresteijn-2@umcutrecht.nl

From the [a]University Medical Centre Utrecht, Utrecht, the Netherlands; and the [b]Mount Sinai Fuster Heart Hospital, Icahn School of Medicine at Mount Sinai Health System, New York, New York, USA.

Dr Bhatt is on the Advisory Board for Angiowave, Bayer, Boehringer Ingelheim, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, High Enroll, Janssen, Level Ex, McKinsey, Medscape Cardiology, Merck, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, Stasys; is on the Board of Directors for American Heart Association New York City, Angiowave (stock options), Bristol Myers Squibb (stock), DRS.LINQ (stock options), High Enroll (stock); is a consultant for Broadview Ventures, GlaxoSmithKline, Hims, SFJ, Youngene; is on the Data Monitoring Committees for Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (Chair, PEITHO trial), Cleveland Clinic, Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo; for the ABILITY-DM trial, funded by Concept Medical; for ALLAY-HF, funded by Alleviant Medical), Novartis, Population Health Research Institute; Rutgers University (for the NIH-funded MINT Trial); has received honoraria from American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Chair, ACC Accreditation Oversight Committee), Arnold and Porter law firm (work related to Sanofi/Bristol-Myers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2024.101089

committees), CSL Behring (AHA lecture), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, Journal of Invasive Cardiology), *Journal of the American College of Cardiology* (Guest Editor; Associate Editor), K2P (Co-Chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Oakstone CME (Course Director, Comprehensive Review of Interventional Cardiology), Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), WebMD (CME steering committees), Wiley (steering committee); Other: Clinical Cardiology (Deputy Editor); holds a patent on Sotagliflozin (named on a patent for sotagliflozin assigned to Brigham and Women's Hospital who assigned to Lexicon; neither I nor Brigham and Women's Hospital receive any income from this patent); has received research funding from Abbott, Acesion Pharma, Afimmune, Aker Biomarine, Alnylam, Amarin, Amgen, AstraZeneca, Bayer, Beren, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CinCor, Cleerly, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix, Janssen, Javelin, Lexicon, Lilly, Medtronic, Merck, Moderna, MyoKardia, NirvaMed, Novartis, Novo Nordisk, Otsuka, Owkin, Pfizer, PhaseBio, PLx Pharma, Recardio, Regeneron, Reid Hoffman Foundation, Roche, Sanofi, Stasys, Synaptic, The Medicines Company, Youngene, 89Bio; Royalties: Elsevier (Editor, Braunwald's Heart Disease); is a site coinvestigator for Abbott, Biotronik, Boston Scientific, CSI, Endotronix, St. Jude Medical (now Abbott), Philips, SpectraWAVE, Svelte, Vascular Solutions; Trustee: American College of Cardiology; Unfunded Research: FlowCo. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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.

REFERENCES

1. Kohli-Lynch C, Thanassoulis G, Pencina M, et al. The causal-benefit model to prevent cardiovascular events. *JACC Adv*. 2024;3:100825.

2. Glasziou PP, Irwig LM. An evidence based approach to individualising treatment. *BMJ*. 1995;311:1356–1359.

3. Dorresteijn JAN, Visseren FLJ, Ridker PM, et al. Estimating treatment effects for individual patients based on the results of randomised clinical trials. *BMJ*. 2011;343:d5888.

4. Dorresteijn JAN, Kaasenbrood L, Cook NR, et al. How to translate clinical trial results into gain in healthy life expectancy for individual patients. *BMJ*. 2016;352:i1548.

5. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J*. 2021;42:3227–3337.