Predicting the Benefit of Statins in Patients With Diabetes Mellitus

A Case of Perfect Being the Enemy of Good?

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The main goal of personalized medicine is to tailor medical decisions to the individual patient based on his or her predicted response or risk of disease. Although traditionally, the concept of personalized medicine has referred to genetic personalization, this also applies to traditional clinical and demographic factors, which may affect the balance of risks and benefits a patient is expected to derive from a treatment. Clinical trial results report mean effects across the study population, and subgroup analyses are inherently limited. As such, we often conclude that the benefits of treatment apply consistently to the entirety of the study population, and the practice guidelines and performance measures generally reflect these conclusions. However, multivariable models can sometimes effectively quantify the heterogeneity of treatment benefit. In this way, patients can be identified who are at most (and least) likely to benefit from a treatment; such information could provide critically important guidance to clinicians and patients for many day-to-day management decisions. While this is a noble goal, the number of risk models that are created far exceed those used in clinical practice. There are multiple reasons for this, including the use of variables that are difficult to collect in routine clinic practice, modeling outcomes that are not clinically relevant or actionable, lack of external validation or concerns about model performance, and simple technology limitations and the ability to integrate these models into clinical care. Importantly, for a model to be useful, it should (1) be accurate at estimating risk, (2) be able to separate patients into distinct risk categories, (3) be able to be used with available data at the time of decision making, and (4) exert a substantial impact on a treatment decision. 

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having to take a statin is a superior approach to simply treating all patients with diabetes mellitus.

Multiple studies have shown a disconnect between the practice guidelines and clinical practice. Is the answer to improving this conundrum more personalization—or is it simplification of the guidelines? The authors argue that patients will be more likely to buy in to treatment with estimation of risk; however, there is no clear proof of this concept; of which, we are aware. The disconnect between guidelines and practice likely lies in a combination of physicians either not being aware of or not believing that the guideline recommendations apply to their patients. It is unclear whether personalization would help physicians think that the guideline applies or if it would add confusion by creating a subset of patients for which the guideline does not apply. In addition, for this approach to be effective, the model must save a patient from a treatment that carries a substantial risk. For example, using risk modeling to estimate benefit from carotid endarterectomy in asymptomatic carotid stenosis could save a patient from undergoing a costly surgery with real potential hazards, or predicting risk and benefit with prolonged dual antiplatelet therapy after myocardial infarction could save a patient from taking a medication with a substantial risk of bleeding. However, in the case of statins for primary prevention, the treatment is a medication that is generic and with low risk of serious adverse side effects. Furthermore, risks change over time. In particular, a patient may not need a statin but then will meet threshold for treatment in 5 years (because of the effect of age on absolute risk of cardiovascular events).

Although we are strongly supportive of personalized care based on a patient’s individual risk, models to guide this must move the needle and impact care substantially enough to be clinically useful. When the harm in treating a small proportion of additional patients is minimal, it is hard to justify adding further complexity to the current treatment paradigm. As we move into a medical landscape in which such models can be run with minimal to no effort by the treating clinician, perhaps this can provide additional value, or if an individual patient questions the benefit of a statin, the information from such a model could be useful. Sometimes, however, standardization has a role, allowing for simple, uniform rules that provide benefit to the vast majority of patients and allow for easy tracking and feedback of performance so as to improve the quality of care, and ultimately patient outcomes. Such standardization and tracking of care has proven useful in improving outcomes in cardiovascular disease during the past several decades, despite evidence of heterogeneity of benefit even for those treatments that are included in performance metrics. Estimating the heterogeneity of treatment benefit and using this information to guide treatment decisions can have great effect in improving care. However, until technology improves to make prediction models integrated into routine medical care with minimal to no additional input from the treating clinicians, the models we use must provide substantial value beyond the established benefit of standardization and trackable metrics.

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References


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