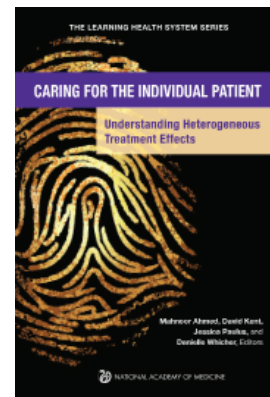


Caring for the Individual Patient

Understanding Heterogeneous Treatment Effects

A Special Publication of the National Academy of Medicine



Clinical trials are for the average; how can we best treat the individual?

Evidence-based medicine arose from a clear need and represents a major advance in the science of clinical decision-making. Despite broad acceptance of evidence-based medicine, however, a fundamental issue remains unresolved: evidence is derived from groups of people, yet medical decisions are made by and for individuals. Despite persistent assertions from clinicians that determining the best therapy for each patient is a more complicated endeavor than just picking the best treatment on average, traditional approaches have been overly reliant on the average effects estimated from the outcomes of clinical trials.

This Special Publication is based on a workshop, held by the NAM, that considered patient and stakeholder perspectives on the importance of understanding heterogeneous treatment effects (HTE) and best practices for implementing clinical programs that take HTE into account. For evidence to be more applicable to individual patients, we need to combine methods for strong causal inference (first and foremost, randomization) with methods for prediction that permit inferences about which particular patients are likely to benefit and which are not. Better population-based outcomes will only be realized when we understand more completely how to treat patients as the unique individuals that they are.

Key directions for the field

- Develop guidance on approaches for assessing the effectiveness or the validity of predictive and prognostic models for predicting treatment effects
- Understand the comparative performance of supervised machine learning methods that can be applied to understand HTE
- Facilitate collaboration and leadership across various sectors of the research ecosystem to create and prioritize opportunities for large trial re-analyses or collaborative individual patient analyses to examine HTE most likely to impact population health
- Describe approaches to implementing risk models in clinical care and provide guidance on which approaches are most effective at informing decisions both at the point of care and at the level of the health care system
- Consider approaches for integrating data related to the social determinants of health in risk-prediction models
- Determine the role for observational data and when it is appropriate to combine randomized controlled trials and observational data
- Reform the predominant fee-for-service payment system in the United States to one that rewards value and population health improvements
- Promote dissemination of innovative trial designs, including those sampling larger and broader populations to enrich patient heterogeneity
- Establish or extend research reporting guidelines to promote the conduct of predictive HTE analyses

Research considerations in moving toward individual patient treatment

By understanding the reasons for treatment effect heterogeneity and developing ways to predict how patients who typically vary from one another in many different and important attributes will respond to a treatment, medical researchers and physicians should be able to personalize medicine to a far greater degree than is possible today. Such an ability would open the door to treatments that are more effective with fewer side effects and would also allow patients to make more informed decisions about the types of medical treatments they choose to receive. But, to reach this potential will require advances on the research side, the clinical side, and deep collaboration with patients and families. Not only will patient cooperation be critical in the design and performance of clinical trials that aim to understand HTE, the patients themselves will also inevitably be partners with clinicians in making treatment decisions about their care whenever HTE is present.

“The premise of traditional research is to put a treatment at the center of consideration and decide, Is this treatment helpful for an average patient? Trouble is, there aren’t very many average patients out there, and I, like most people, am not an average patient. So traditional research could not answer the question, the basic question that everyone wants to know, including patients and their caregivers, and that is, What is the treatment that is most likely to help me or my patient with their specific issues?”

-Seth Morgan, American Academy of Neurology

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