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The Potential for Pragmatic Trials to Reduce Racial and Ethnic Disparities in Kidney Disease

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The well-documented and unacceptable racial and ethnic disparities in the prevalence and outcomes of kidney disease are receiving increased attention within and beyond the nephrology community, with numerous calls for intentional, active approaches to ensure that care is equitable and that disparities are eliminated.[1,2] In 2003, the Institute of Medicine (now the National Academy of Medicine) concluded that elimination of racial disparities in health outcomes requires a multilevel approach directed at health systems, patients, care providers, and payors.[3] While some strategies should be adopted because they are clearly the right thing to do, others require rigorous evaluation before broad uptake to understand the benefits, unanticipated harms, relative value, and challenges to implementation. Pragmatic or "real-world" clinical trials have received substantial interest during the past decade because they yield results that are highly generalizable to the nontrial setting, evaluate interventions that can be readily transferred to clinical practice, and save money by leveraging clinical care systems rather than relying on separate research infrastructure.[4] Pragmatic trials are most often used for comparative effectiveness research to identify advantages and disadvantages of treatment approaches already in widespread clinical use, or to evaluate strategies for implementing or increasing uptake of interventions known to have efficacy. This article makes the case that pragmatic clinical trials can advance equity in both research and clinical care, and that they are well suited for evaluating interventions that aim to reduce racial and ethnic disparities in kidney disease outcomes.

PRAGMATIC TRIALS CAN MAKE RESEARCH MORE EQUITABLE

According to a 2020 report by the US Food and Drug Administration on newly approved drugs, only 8% of research participants were Black and 11% were Hispanic—a clear underrepresentation relative to their proportions of 13.4% and 18.1%, respectively, within the overall US population.[5] While this may in part reflect the global nature of many of these trials, numerous studies have demonstrated that Black and Hispanic individuals are under-represented in research performed in the United States, including in clinical trials evaluating interventions for kidney disease, which disproportionately affects members of these racial and ethnic groups.[6] By making research more accessible, pragmatic trials should make research more equitable. In contrast to typical conventional clinical trials that enroll highly selected participants who meet a long list of eligibility criteria, pragmatic trials aim to be nonrestrictive and thus, by intention, have trial cohorts that reflect the population of patients with the condition of interest. By incorporating trials into clinical care delivery, pragmatic trials in effect bring the trial to the patient and make research available to people who might otherwise have difficulty with the time commitment, transportation requirements, or other barriers to research participation that have been well documented among members of racial and ethnic minority groups. However, the greater accessibility achieved by incorporating research into care delivery reduces research inequity only to the extent that the barriers to clinical care are minimized and the health setting serves a diverse population. The effect of barriers to clinical care on research equity can potentially be overcome through community-based pragmatic trials, a notable example being a cluster-randomized trial of a highly successful pharmacist-led intervention to improve blood pressure

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control that was implemented in neighborhood barbershops to make research more accessible to Black men.[7]

Another source of inequitable access to research participation are biases among members of research teams about which patients are appropriate for trial participation.[8] Approaches used in pragmatic trials to identify potential research participants can be designed to minimize such biases. Algorithm-based screening of the electronic health record is frequently used as an initial strategy to identify patients likely to meet trial eligibility criteria. For pragmatic trials that enroll patients by default and either do not require informed consent or use opt-out approaches for consenting, biases by researchers should not interfere with inclusivity if only the electronic health record–based algorithms are used for participant identification. For trials that have, after the initial automated screening, a second step that involves decisions by research team members about who to approach for research participation, eliminating factors that contribute to biases, such as race, age, and home address, from the information provided in the electronic health record–generated lists, can increase inclusivity and advance research equity. Importantly, electronic health record–based approaches to identifying trial participants will not overcome biases that are ultimately incorporated into the health record, such as the underdiagnosing of conditions among members of racial or ethnic minorities.

PRAGMATIC TRIALS CAN REDUCE BIASES IN CLINICAL CARE

In addition to biases held by researchers about the suitability of patients for participation in clinical trials, biases by clinicians about suitability of patients for established medical interventions contribute to disparities in outcomes. Pragmatic trials are often used to evaluate approaches to increase uptake of interventions with known efficacy. An example of such a trial is the ongoing ICD-PIECES trial, evaluating the effect on clinical outcomes of practice facilitators embedded in primary care clinics to improve blood pressure and blood glucose control and increase the use of angiotensin converting enzyme or angiotensin receptor blockers among patients with the triad of CKD, hypertension, and diabetes.[9] While ICD-PIECES was not designed primarily to address racial and ethnic disparities, the strategy of implementing the trial intervention broadly using a standardized approach should counteract differential implementation of best practices that often occurs in routine clinical practice. Differential implementation of clinical care on the basis of racial, ethnic, or socioeconomic biases is especially frequent with new interventions because of preconceived ideas about barriers related to cost and/or challenges in monitoring for adverse effects. Pragmatic trials can be designed specifically to reduce the effect of these biases and resulting inequities. For example, one could envision a randomized trial evaluating the effect on initiating sodium glucose co-transporter 2 inhibitor therapy, of a physician-targeted intervention consisting of electronic health record–generated notification about patients with CKD who meet medical criteria for the medication plus materials to support safe prescribing and monitoring (Nwamaka Eneanya, MD, MPH, personal communication). The notifications, while perhaps not sufficient to eliminate disparities in prescribing without other supportive measures, should, at a minimum, help eliminate biases that clinicians might not be aware they hold about suitability for a beneficial medical intervention.

PRAGMATIC TRIALS CAN TARGET CHALLENGES RESULTING FROM STRUCTURAL RACISM

While pragmatic trials cannot by themselves dismantle structural racism, which is the root of racial disparities in health outcomes, they can rigorously evaluate interventions that target its downstream effects and provide evidence to support policies that directly increase health equity. Relevant types of interventions that have been or can be evaluated through pragmatic trials include care navigators, peer coaches, self-management support, health screening programs, culturally customized educational materials, decision aids, financial incentives, nutritional support, and community-based educational activities.[10] An important benefit of embedding the evaluation of these interventions into clinical care delivery or the community, a defining characteristic of pragmatic trials, is that patients hear about research directly from their providers or community members—an approach that helps overcome the distrust of researchers that is experienced by many people, but especially by those from racial or ethnic minority groups.[11]

SUMMARY

While clearly only one component of what is needed to address health inequities, pragmatic trials have the potential to reduce disparities by making participation in research more accessible and by evaluating, using rigorous methods for evidence generation, interventions targeting downstream effects of structural racism. The nephrology community is encouraged to embrace this approach, to include experts in health equity research and implementation science as members of research teams, and to engage patients directly in the planning and conduct of research. By adopting multiple strategies for addressing inequities, we can continue to work toward the goal of attaining optimal health outcomes for all people with kidney disease.

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AUTHOR CONTRIBUTIONS

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