Using Patient Preference Information to Inform Regulatory Decision Making

An Opportunity to Spur Patient-Centered Innovation in Kidney Replacement Therapy Devices

Jennifer E. Flythe[1,2] *and Melissa West*[3]

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[1]Division of Nephrology and Hypertension, Department of Medicine, University of North Carolina School of Medicine, University of North Carolina Kidney Center, Chapel Hill, North Carolina
[2]Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, North Carolina
[3]Kidney Health Initiative and American Society of Nephrology, Washington, DC

Correspondence:
Dr. Jennifer E. Flythe, University of North Carolina Kidney Center, 7024 Burnett-Womack CB #7155, Chapel Hill, NC 27599. Email: jflythe@med.unc.edu

Medical devices play an essential role in the health care system, often facilitating patients' management of their own health. Such devices—items used for the "diagnosis. . .cure, mitigation, treatment, or prevention of disease that are not absorbed or metabolized by the body" (1)—range in type and function from supportive equipment (*e.g.*, walkers and wheelchairs) to life-sustaining therapies (*e.g.*, cardiac defibrillators and dialysis machines). In the United States, over 500,000 individuals with kidney failure rely on dialysis machines and supportive vascular access and monitoring devices to perform the critical kidney functions of waste and fluid removal. Although dialysis therapy undoubtedly sustains life, its side effects and burdensome nature leave many with constrained livelihoods and diminished quality of life.

Despite the central role of dialysis in the treatment of kidney failure, there has been little innovation in its underlying therapeutic paradigm since its inception in the 1960s. Moreover, opportunities for patient perspectives to inform KRT-related regulatory decision making have been limited. However, in 2016, the Food and Drug Administration (FDA) Center for Device and Radiologic Health (CDRH), the US regulatory body for medical devices, identified partnering with patients as a strategic priority (2). The FDA recognizes patients as experts on their own conditions and acknowledges the potential benefits of incorporating patient perspectives throughout the total product life cycle, from designing medical devices to planning and conducting clinical trials and monitoring safety to providing insights into how specific populations may weigh the benefits and risks of devices (2). The latter, termed patient preference information, "captures the value that patients place on aspects of the medical device in a way that accounts for differing patient perspectives on benefits and risks that come with using that device or treating the condition" (3). Patient tolerance for risk may be influenced by factors such as severity and/or chronicity of disease, and/or availability of alternative therapeutic options. It is essential to obtain this information directly from patients to avoid undue influence from nonpatient standards and/or misperceptions (4). Understanding variations in risk tolerance helps regulators define what constitutes meaningful risks and benefits to different individuals and focuses innovators on aspects of device design and/or function that are most important to patients (5)—two critical elements in bringing patient-centered devices to market.

Although there is growing appreciation for the value of patient-centered innovation, there are limited scientifically valid tools and processes to support patient preference information collection and analysis (6). In 2019, FDA CDRH received funding from the Patient-Centered Outcome Research (PCOR) Trust Fund to enhance its efforts to develop coordinated research networks. Coordinated research networks advance medical device safety and effectiveness by strengthening infrastructure for integrating real-world data, including patient-generated data such as patient preference information, into regulatory decision making (7). Among other projects, the PCOR Trust funding supports the development of a patient preference survey for individuals with kidney failure. The planned patient preference survey will capture perspectives from individuals with kidney failure on potential benefit and risk trade-off considerations related to new innovative technologies. To maximize effect, the development and administration of such patient preference tools benefit from participatory codesign approaches that are supported by partnerships with patients, regulators, and an array of community stakeholders (*e.g.*, device developers, dialysis providers, clinicians, and payors). Such a collaborative approach is intended to yield information that is important to patients and usable to both regulators and innovators. Moreover, strong community partnerships are essential to building capacity for sustained patient preference information collection.

As such, and given their shared commitment to accelerating patient-centered device development, FDA CDRH and the Kidney Health Initiative (KHI) partnered to develop and implement the patient preference survey for individuals with kidney failure. KHI is a public-private partnership that uses diverse stakeholder engagement to catalyze innovation and the development of safe and effective patient-centered therapies for people with kidney disease (8). In 2018,

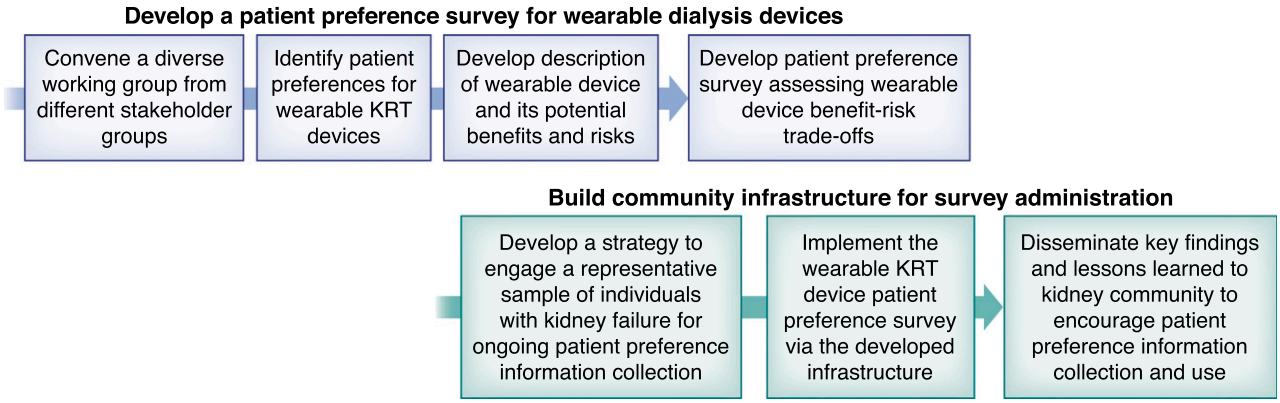

Figure 1. | The KHI-FDA patient preference information initiative will develop a patient preference survey for wearable dialysis devices and build community infrastructure for survey administration.

KHI published the "Technology Roadmap for Innovative Approaches to RRT" with the intent of increasing interest, investment, and innovation in KRT (9). Developed by a diverse group of stakeholders, including patients, care partners, clinicians, innovators, device manufacturers, regulators, payors, and funders, the roadmap provides requisite strategies and research pathways to more effectively and efficiently develop commercially viable, patient-centered alternatives to existing KRT. Facilitating the incorporation of patient perspectives into the development, evaluation, and surveillance of innovative KRTs is a central roadmap objective, and patient priorities, such as being more active, freer to work and travel, and less burdened by dietary and medication regimens, are benchmarks for roadmap success.

In October 2019, FDA CDRH and KHI launched the PCOR Trust–supported initiative "Building Capacity to Incorporate Patient Preferences into the Development of Innovative Alternatives to Kidney Replacement Therapy." This initiative is led by a steering committee composed of patients, clinicians, FDA CDRH representatives, preference methodology experts, and statisticians with expertise in regulatory patient preference information. The group aims to develop a valid patient preference survey for individuals with dialysis-dependent kidney failure, as well as conceptualize sustainable strategies and engagement tools to support future collection of patient preference data from the kidney failure population (Figure 1). Specifically, the team will develop, pretest, and administer an initial patient preference survey using rigorous methodology (*e.g.*, treatment threshold or discrete choice experiments) focused on wearable dialysis devices. As survey results will be used to inform clinical trial design for wearable dialysis devices, survey respondents will be individuals with dialysis-dependent kidney failure who may be eligible to enroll in a clinical trial of a wearable dialysis device (*i.e.*, individuals currently receiving maintenance dialysis therapy). Wearable devices were selected as the focus of the prototype survey because these devices may offer the most near-term, achievable alternative to existing KRT technologies. This foundational work will inform the development of future patient preference instruments directed at other innovative KRT approaches, such as implantable technologies. In addition, the group will develop community partnerships and build the infrastructure necessary to support administration of the developed survey and similar preference surveys, enabling longitudinal patient preference data collection from individuals with kidney failure.

The primary patient preference survey objectives are to (*1*) quantify the level of risk that patients are willing to accept for different types of harms in exchange for the benefits of using a wearable dialysis device and (2) assess differences in how much risk patients are willing to accept on the basis of their current treatment modality and other individual characteristics. Survey output will be used in a Bayesian decision analysis that incorporates patient preferences into the statistical threshold, balancing the overall consequences of approving an ineffective and possibly harmful treatment (false approval) against the consequences of rejecting an effective treatment (false rejection) in a clinical trial (10). In addition, the team will develop a community engagement strategy for collecting patient preference information over time, with a focus on reaching a representative sample of individuals living with kidney failure. Key initiative steps include survey development, pretesting, administration, analysis, and publications on patient preference information best practices and lessons learned.

Nearly every day, people with kidney failure undergo dialysis treatments with medical devices designed with limited patient input. In response, FDA CDRH and KHI have committed to incorporate patient voices into innovative medical product development and evaluation, starting with a patient preference survey focused on wearable dialysis devices, to be followed by other KRT technologies such as the bioartificial implantable kidney. In doing so, FDA CDRH and KHI are paving the way for the enduring collection and integration of diverse patient perspectives into the total product life cycle, thereby catalyzing patient-centered innovation in kidney devices.

Disclosures

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