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In the last three years, JEF has received speaking honoraria from multiple universities and investigator-initiated research funding unrelated to this project from the Renal Research Institute, a subsidiary of Fresenius Medical Care, North America. She serves on a medical advisory board for Fresenius Medical Care, North America and a scientific advisory board and Data and Safety Monitoring Committee for NIDDK. J. Flythe also reports Consultancy: Fresenius Medical Care Medical Advisory Board; and Advisory or Leadership Role: KHI Patient Preferences Project Chairperson (2019-), Kidney 360 Associate Editor (2019-), PCORI Peer Review Associate Editor (2022-). DW is an employee of RTI, which received funding for the conduct of this study. RCH is Co-Chairperson of the Kidney Health Initiative. He receives research funding from Bayer. R. Harris also reports Ownership Interest: Apple; and Patents or Royalties: eNOS db/db mouse. D. Forfang reports Employer: ASN Kidney Health Initiative (KHI); Consultancy: University of North Carolina Kidney Center, CareDX, Ardelyx Inc Scientific Advisory Board, ASN and Responsum, ASN, HSAG; Honoraria: Health Service Advisory Group; Advisory or Leadership Role: HSAG ESRD Network #17 Board Member; National Forum of ESRD Networks Board Member, National Forum of ESRD Networks, Kidney Patient Advisory Council Chair, Kidney Health Initiative Patient Advisory Committee, National Kidney Foundation, SONG Group, European Association for Dialysis, Arbor Research and Unity Health Toronto OPPUS, UCSF Kidney Project Patient Advisor; and Other Interests or Relationships: Volunteer for The Forum of ESRD Networks as Kidney Patient Advisory Council Chair and Board Member; Volunteer for ESRD Network #17 as Patient Advisory Committee Chair and Network Board Member; Volunteer for the NKF as a member of their Public Policy Committee; Volunteer for the NKF as a Regional Leader of their Kidney Advocacy Committee, KHI PFPC Member. All remaining authors have nothing to disclose.

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Abstract:

Significance Statement

**Risk Tolerance in the Setting of Wearable Dialysis Devices: A Patient Preference Study
Using the Threshold Technique**

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Individuals receiving maintenance dialysis often have worse quality of life than people treated with kidney transplant.¹ Many patients feel constrained by dialysis, particularly in-center hemodialysis, and patients desire more freedom to pursue their life interests.²⁻⁴ Wearable dialysis devices offer more flexible therapy and are in varying development stages.⁵ However, just like current, on-market dialysis devices, wearable devices have risks, including the risks of bleeding and infection. It is unknown how patients may trade off the potential benefits and risks of wearable devices with those of other dialysis types.

In a quantitative patient preference study, we elicited benefit-risk preferences from individuals receiving dialysis for a wearable dialysis device (compared to in-center hemodialysis) and explored whether preferences differ by respondent characteristics. We administered a cross-sectional, on-line survey⁶ that used the threshold technique⁷ to assess the maximum increase in the risk of serious bleeding and serious infection over baseline risk that patients would accept in exchange for the potential benefits of a wearable dialysis device. Eligibility criteria included age ≥ 22 years, English- or Spanish-speaking, and receipt of dialysis for ≥ 3 months. We estimated the average maximum acceptable risk (MAR) above baseline for serious bleeding and separately, serious infection, by estimating a regression model including only a constant term, for the entire sample and across subgroups (**Supplement:** detailed methods).

Of the 599 survey respondents (**Supplemental Figure S1; Supplemental Table S2**), 253 (42%) received in-center hemodialysis, 206 (34%) received home hemodialysis, 137 (23%) received peritoneal dialysis, and 3 (0.5%) did not specify modality. Overall, 51% respondents were female, 23% were Black Non-Hispanic, 25% were Hispanic, and 33% had a bachelor's degree or higher level of education.

In the first question about serious bleeding (annual bleeding risk: $< 1\%$ for in-center hemodialysis and 8% for wearable device), 247 (41.7%) respondents selected the wearable device. Respondents currently receiving peritoneal dialysis were more likely to select the

wearable device (n=81, 59.1%) than respondents receiving home hemodialysis (n=67, 32.5%) or in-center hemodialysis (n=99, 39.6%). The sample response distribution was bimodal, with about equal proportions of respondents willing to accept an increased risk of serious bleeding of <1% (22.5%) and >22% (25.6%) with the wearable device (**Supplemental Figure S2**). The maximum increase in the risk of serious bleeding that the mean respondent was willing to accept exceeded the additional risk of serious bleeding posed by a hypothetical wearable device (8.0%): the mean MAR above baseline for serious bleeding was 11.1% (95% confidence intervals (CI), 10.0 – 12.1). The mean MAR above baseline for serious bleeding was higher for respondents receiving peritoneal dialysis than for respondents using other modalities (**Figure 1A**). In subgroup analyses (**Supplemental Table S3**), the mean MAR above baseline for serious bleeding increased with patient age and was higher among female (vs. male), White non-Hispanic (vs. Black non-Hispanic), and non-Hispanic (vs. Hispanic) respondents.

In the first question about serious infection (annual infection risk: 6% for in-center hemodialysis and 31% for wearable device), 197 (33.2%) respondents selected the wearable device. Respondents currently receiving peritoneal dialysis were more likely to select the wearable device (n=74, 54.0%) than respondents receiving home hemodialysis (n=58, 28.2%) or in-center hemodialysis (n=65, 25.9%). The sample response distribution was concentrated in the lower range of presented risk levels for serious infection (**Supplemental Figure S2**). The maximum increase in the risk of serious infection that the mean respondent was willing to accept did not exceed the additional risk of serious infection posed by a hypothetical wearable device (31%): the mean MAR above baseline for serious infection was 15.0% (13.1 – 17.0). The mean MAR above baseline for serious infection was higher for respondents receiving peritoneal dialysis than for respondents using other modalities (**Figure 1B**). In subgroup analyses (**Supplemental Table S3**), the mean MAR above baseline for serious infection was higher among non-Hispanic (vs. Hispanic) respondents.

In covariate-adjusted models, the respondent characteristics of receiving peritoneal dialysis (vs. in-center hemodialysis) and lower (vs. higher) health literacy influenced the serious bleeding and serious infection mean MARs (**Supplemental Table S4**).

In conclusion, we examined the risk tolerance for serious bleeding and serious infection of individuals receiving dialysis in the setting of a wearable device compared to in-center hemodialysis. Results suggest that there may be preference heterogeneity for wearable devices in the dialysis population. While these findings must be contextualized within study limitations such as potential bias from insufficient respondent understanding of the presented devices and risks as well as inclusion of more hemodialysis than peritoneal patients and a disproportionate number of home hemodialysis patients, they highlight the importance of powering clinical trials of such devices to assess safety and efficacy in certain subpopulations. Post-authorization, they emphasize the need for shared decision-making accounting for variable risk tolerance. Moreover, we showed that, in partnership with diverse stakeholders, collecting preference information from individuals receiving dialysis using a web-based survey is feasible and has potential to yield data relevant to the regulatory environment.

AUTHOR CONTRIBUTIONS

Research idea and study design: all authors; data acquisition: Dallas Wood; statistical analysis: Dallas Wood; data interpretation: all authors; supervision or mentorship: Jennifer Flythe and Michelle Tarver. All authors drafted the manuscript or revised it critically for important intellectual content. All authors approved the final version of the manuscript and agreed to be accountable for the work.

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DISCLOSURES

In the last three years, JEF has received speaking honoraria from multiple universities and investigator-initiated research funding unrelated to this project from the Renal Research Institute, a subsidiary of Fresenius Medical Care, North America. She serves on a medical advisory board for Fresenius Medical Care, North America and a scientific advisory board and Data and Safety Monitoring Committee for NIDDK. J. Flythe also reports Consultancy: Fresenius Medical Care Medical Advisory Board; and Advisory or Leadership Role: KHI Patient Preferences Project Chairperson (2019-), Kidney 360 Associate Editor (2019-), PCORI Peer Review Associate Editor (2022-). DW is an employee of RTI, which received funding for the conduct of this study. RCH is Co-Chairperson of the Kidney Health Initiative. He receives research funding from Bayer. R. Harris also reports Ownership Interest: Apple; and Patents or Royalties: eNOS db/db mouse. D. Forfang reports Employer: ASN Kidney Health Initiative (KHI); Consultancy: University of North Carolina Kidney Center, CareDX, Ardelyx Inc Scientific Advisory Board, ASN and Responsum, ASN, HSAG; Honoraria: Health Service Advisory Group; Advisory or Leadership Role: HSAG ESRD Network #17 Board Member; National Forum of ESRD Networks Board Member, National Forum of ESRD Networks, Kidney Patient Advisory Council Chair, Kidney Health Initiative Patient Advisory Committee, National Kidney Foundation,

SONG Group, European Association for Dialysis, Arbor Research and Unity Health Toronto
OPPUS, UCSF Kidney Project Patient Advisor; and Other Interests or Relationships: Volunteer
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necessarily reflect the official policies of any KHI member organization, the US Department of
Veterans Affairs, or the US Department of Health and Human Services, nor does any mention of
trade names, commercial practices, or organizations imply endorsement by the US
Government.

DATA SHARING STATEMENT

Because of a contractual data use agreement, the authors cannot make the data collected in this study publicly available. Provision of de-identified data to outside investigators upon request under formal data use agreements with the American Society of Nephrology and appropriate external Institutional Review Board oversight may be possible.

JASN-2022-001016R1 Supplemental File -- <http://links.lww.com/JSN/E39>

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SUPPLEMENTAL MATERIAL

Supplemental Table S1. Additional authors: steering committee and survey workgroup members.

Supplemental Methods

Supplemental Figure S1. Flow diagram for survey response dataset construction.

Supplemental Table S2. Respondent characteristics and responses for all survey background questions.

Supplemental Figure S2. Distribution of risk intervals for serious bleeding and serious infection.

Supplemental Table S3. Mean maximum increase in the risks of serious bleeding and infection respondents were willing to accept in exchange for a wearable dialysis device by patient subgroup.

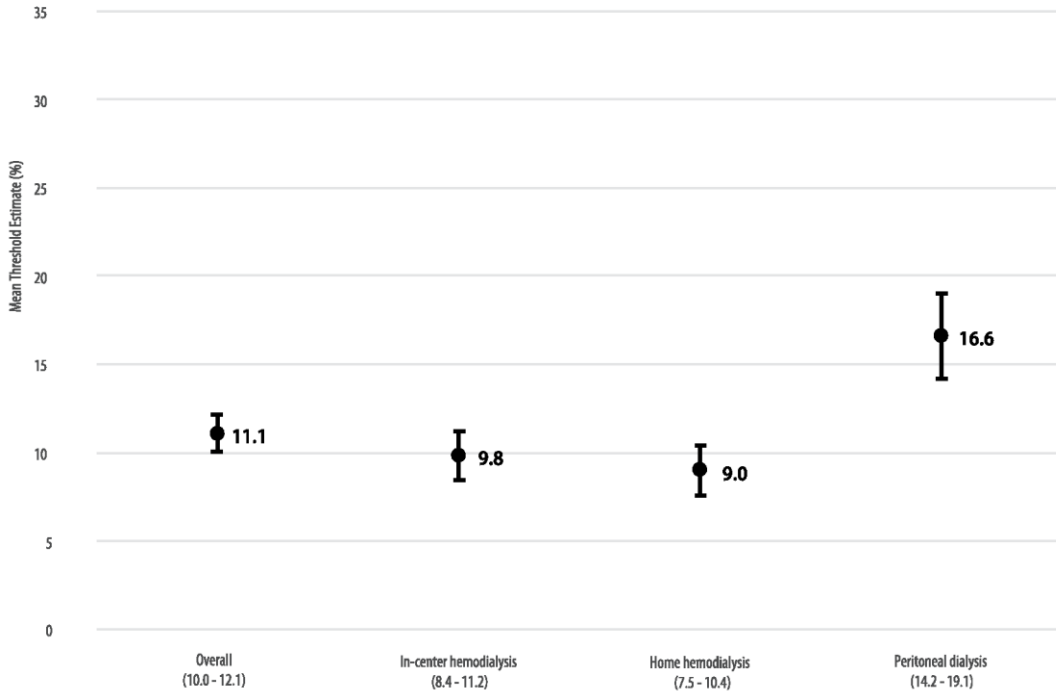
Supplemental Table S4. Interval regression results for risk trade-offs when controlling for covariates.

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Figure 1. Mean threshold estimates overall and by current dialysis modality type for serious bleeding (Panel A) and serious infection (Panel B).^a

^a Point estimates show mean threshold rates or MAR above baseline that were estimated using interval regressions. These threshold rates measure the maximum increase in the risk of serious bleeding (and serious infection) the mean respondent was willing to accept in exchange for the described benefits of a wearable dialysis device (over in-center hemodialysis). Upper and lower bars indicate 95% confidence intervals.

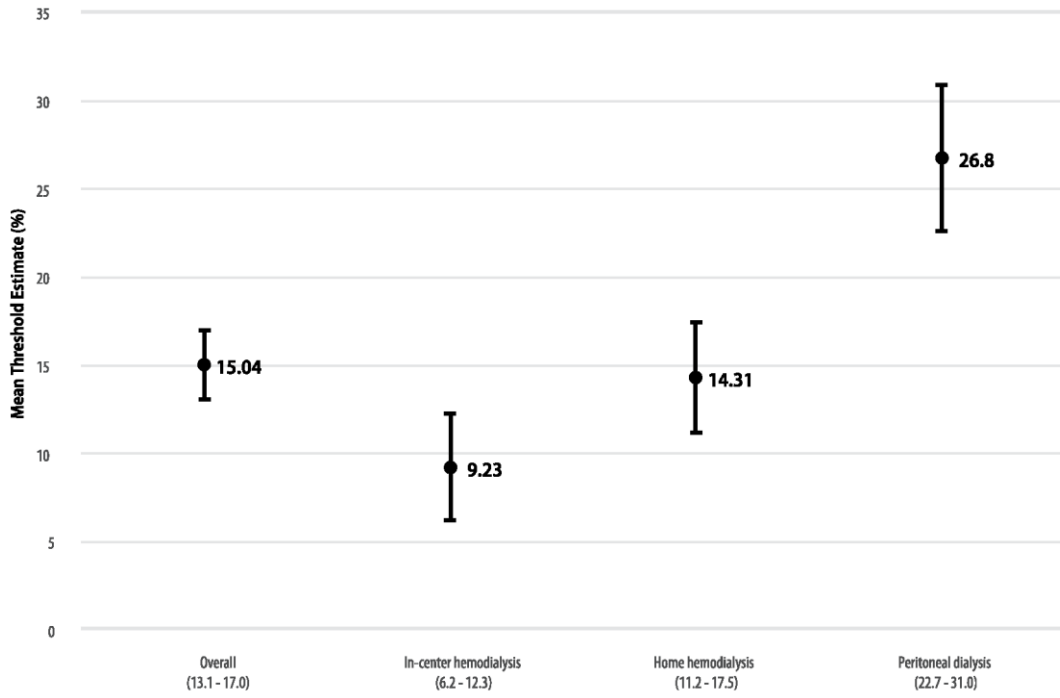
Panel A



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Panel B



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