Treating Early-Stage CKD With New Medication Therapies

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Kidney Medicine

Treating Early-Stage CKD With New Medication Therapies: Results of a CKD Patient Survey Informing the 2020 NKF-FDA Scientific Workshop on Clinical Trial Considerations for Developing Treatments for Early Stages of Common, Chronic Kidney Diseases

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Rationale & Objective: With a growing number of medications and therapies available to treat chronic kidney disease (CKD), risk-versus-benefit discussions are increasingly critical. Balancing risks and benefits requires assessing patients' understanding of these, as well as incorporating patient preferences and tolerance for side effects into shared decision making.

Study Design: A 26-question online survey was sent to people in the National Kidney Foundation patient email list and posted on associated social media pages to assess the respondents' willingness and comfort with taking preventative medications during earlier-stage CKD to inform a December 2020 scientific workshop co-sponsored by the National Kidney Foundation and the US Food and Drug Administration on clinical trial considerations in developing treatments for individuals with early stages of CKD.

Setting & Population: Online survey of CKD patients, including broad demographic data and responses to risk-benefit scenarios, with surveys emailed to 20,249 people not identified as currently receiving kidney replacement therapy.

Analytical Approach: Survey results are presented as descriptive data.

Results: Of 1,029 respondents, 45 self-identified as at risk for CKD, 566 had CKD, 267 had received kidney transplants, 51 were receiving dialysis, and 100 replied other or did not answer. Respondents reported being willing to assume some risk with the goal of preventing the progression of CKD, with a greater willingness to assume risk and treatment burdens the closer they came to late-stage disease. Clinician recommendations regarding kidney therapies and clinician willingness to work with patients to address any side effects were important in respondents' willingness to initiate and persevere with a new medication.

Limitations: Approximately 10% response rate with limited data on respondents.

Conclusions: Risk-versus-benefit discussions appear key to patients and their care partners making well-informed decisions about taking a new medication that may or may not help the progression of their kidney disease. Future tools and strategies are needed to facilitate informed discussions of treatment in early-stage kidney disease.

Complete author and article information provided before references.

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Chronic kidney disease (CKD) is a major public health problem affecting an estimated 37 million American adults.[1] Most people with CKD are unaware of their disease, even those with more advanced disease.[2] Kidney failure requiring kidney replacement therapy is a relatively uncommon outcome, with a lifetime risk of approximately 3%-4%, although this is higher, approaching 8%-9%, among those of African ancestry.[3-5] Moreover, one-third of US residents develop advanced CKD (defined as a glomerular filtration rate [GFR] <45 mL/min, consistent with CKD stage 3b), with a significant impact on overall health, including increased risk of cardiovascular disease, cognitive impairment, anemia, and mineral and bone disorders.[4,6] All of this contribute to high utilization of health care resources; high costs to governments, insurers, and individuals; and lost productivity with worse quality and duration of life.

Related Article, 100441

In the past 2 decades, there have been significant advances in basic and clinical science related to CKD progression, including validation of surrogates for hard clinical endpoints that can be used in clinical trials of new CKD treatments, even early in the disease course.[7,8] Recent approval of medicines to prevent the progression in later stages of CKD, as well as the use of surrogate endpoints in rare diseases with newer, disease-specific interventions, have established an environment that is primed for development and evaluation of treatments for common causes of CKD early in the disease course.[9-11]

Medications targeting kidney disease will only benefit a subset of individuals with or at risk of early-stage CKD, raising the question of who should receive the medications and when they should be received in the course of the disease. While risk prediction tools may improve the selection of those patients most likely to benefit from interventions that decrease the risk of CKD progression, there is still much to learn about why some patients progress and others do not and, in the absence of precise risk estimates,

PLAIN-LANGUAGE SUMMARY

The goal of the survey was to gain insight into patients' preferences and considerations for determining how much risk (side effects) versus potential future benefits (slowing progression of chronic kidney disease [CKD]) they would be willing to accept when taking a new medication. The results of the survey informed a scientific workshop on clinical trial considerations in developing treatments for early stages of CKD co-sponsored by the National Kidney Foundation and the US Food and Drug Administration in December 2020. The results showed that there was a willingness to assume risk in seeking treatment to slow the progression of kidney disease, which highlighted the need for more frequent and earlier education about the risk of CKD progression and the potential benefits of early-stage treatment.

patients may not be able to quantify their risk to weigh benefits of early treatment. In light of these factors, compounded with patients' unique comorbid conditions, circumstances, and value preferences, it is not surprising that risk-versus-benefit conversations among clinicians, patients, and care partners are challenging.[12-15] Given this, there is a clear imperative to assess peoples' willingness and comfort with taking preventative medications in earlier-stage CKD. As no therapy is without side effects, it is particularly important to capture concerns regarding side effects that may have an impact on willingness to take a medication.

In December 2020, the National Kidney Foundation (NKF) and the US Food and Drug Administration (FDA) co-sponsored a scientific workshop to explore patients', providers', and payers' perceptions of the value of treating early CKD. To inform this workshop, NKF surveyed their patient network on patient perspectives regarding their risk of kidney disease progression, as well as considerations important to patients in deciding whether or not to take new medications that could reduce their risk of progression.

METHODS

This observational survey aimed to assess the baseline knowledge of CKD, level of understanding of respondents' current CKD status, and perceptions of the future risk of progression either to late-stage CKD or kidney failure. Additionally, survey questions were aimed at identifying individuals' values and considerations in decision making about taking a medication that may or may not benefit them. This anonymized survey with minimal demographic data was designed to inform the conference proceedings and was not intended to develop generalizable knowledge; therefore, informed consent was not obtained.

Survey Development

The 26-question survey was developed with input from the conference planning committee, which included the researcher, clinician, patient, and regulatory members (Items S1 and S2). The planning committee first identified key topics that they thought would be critical to inform conference participants, including knowledge of CKD and the individual respondent's current health, perception of their future kidney health risk and progression, and the value placed on minimizing side effects from medications to prevent progression. We used existing validated surveys to assess respondents' knowledge about kidney disease and related signs or symptoms that a person might experience if they have advanced CKD or kidney failure.[16] We reviewed a survey distributed to the heart-failure patient community before a similar conference.[17] Drafts of the survey were then shared with patient reviewers from the NKF's Kidney Advocacy Committee, and edits were made based on their feedback and insights.

To assess perspectives around the risks and benefits of taking a new medication, we developed scenarios that asked respondents to consider whether they would take a new medication that would reduce their risk of developing kidney failure over the next 20, 10, and 5 years, framed with the assumption that they had a 20% risk of developing kidney failure over those time periods. The time frame was selected based on a review of the literature, which describes progression rates in CKD populations that range from 2 to 5 mL/min per year.[18,19] For example, for a patient starting at a GFR of 70 mL/min per 1.73 m^2, the patient would be at CKD stage 5 after 20 years. Responses to risk questions were ranked on a 5-point scale ranging from not likely to very likely. To assess perspectives on the tolerance of specific medications, we asked respondents to consider specific benefits and side effects, including how these side effects would impact their willingness to take the medication and how important certain factors are in deciding to take a new medication. We developed the list based both on common side effects for medications used in general (constipation) and for CKD (dizziness, increased urination), including known sodium/glucose cotransporter 2 side effects (increased urination, urinary tract infections).[20] Many medications require monitoring and more frequent appointments and blood tests. Responses to these questions had 3 possible response choices: not important, important, or very important.

Dissemination

The survey was sent by the NKF in November 2020 via email to their database of 20,249 people not known to be currently receiving dialysis or living with a transplant. Links to the survey were also posted to the NKF's Facebook page, which had 255,130 followers at the time of dissemination, and to 10 other kidney- and diabetes-related Facebook groups. Dissemination was purposefully broad to gain insight into how people think about risk at

various CKD stages. There was no incentive offered for completion.

RESULTS

Of 1,029 respondents, 49% were between 55 and 75 years old, 50% were women, 65% were White, and 52% had either a college or advanced degree; 55% identified as having nondialysis CKD, while 26% identified as a kidney transplant recipient. There was modest missingness on demographic questions. A total of 86% of respondents with CKD had been referred to a kidney specialist or nephrologist. There was a fairly even distribution among CKD stages 3a, 3b, and 4, while 8.7% of respondents indicated that they had CKD stages 1 or 2 (Table 1). A third of respondents were not sure whether they had protein in their urine (33%).

CKD Knowledge

Tables S1 and S2 show the results of respondents on knowledge questions. Respondents answered most knowledge questions correctly, with the lowest correct response rate of 74% elicited from the question, "What is the range that is usually considered to be normal for GFR?" (Table S1). Respondents also correctly identified the signs and symptoms of CKD (Table S2).

Risk-Benefit Assessments

The survey posed 3 major scenarios for respondents. Scenario 1 stated, "Your doctor says that there is a new medication which can reduce your chance of developing kidney failure. Please tell us your likelihood of taking this medication under the following circumstances." Respondents were overall willing to take a medication that reduces their risk of kidney disease progression, and this willingness increased as the imminent threat of kidney failure increased (from 33% to 47% from 20 to 5 years, respectively; Fig 1). The percent of respondents who were not likely to take the medication was fairly stable, regardless of the imminence of kidney failure (12.1%, 9.7%, and 11.9% with 20, 10, and 5 years to kidney failure, respectively), with similar responses for men and women.

Scenario 2 stated, "If your doctor told you that you have a 20% chance of developing kidney failure over 5 years, how likely would you be to take a drug that has the following side effects or concerns?" Most factors listed were not a barrier to taking a medication for many patient respondents (Fig 2). Regular blood tests and more frequent doctor visits would not affect most respondents' willingness to take a medication, with 75.8% and 73.1%, respectively, remaining likely or very likely to take medication. Other side effects, such as increased urination (61.5% likely or very likely), a chance of urinary tract infections (52.8% likely or very likely), occasional dizziness (45.1% likely or very likely), and mild to moderate constipation (43.4% likely or very likely), affected slightly larger percentages of people's decision to take a medication.

Scenario 3 stated, "Imagine that you have started the medication. You notice that the side effects of the new drug are worse than you thought they would be. You talk to your doctor, and your doctor goes over the clinical evidence with you. You are convinced that the data show that the drug would significantly slow or prevent the progression of your kidney disease and that this will lead to a better quality of life down the road. How likely would you be to take this drug?" Respondents were overwhelmingly willing to continue taking the medication even if side effects occurred (93.8%), although the majority (58.7%) were only willing to continue if their doctor worked with them to try to reduce the side effects (Fig 3).

Considerations for Taking a New Medication

The most important factors for patients considering taking a new medication were the severity of the known side effects (60.6% very important), cost and whether the drug was covered by insurance (57.9% very important), and what their doctor recommends (55.4% very important; Table 2). The least concerning to patients was how often they needed to take medication (47.2% not important).

DISCUSSION

In a fairly well-informed population with access to nephrology care, as demonstrated by CKD knowledge questions and referrals to nephrologists, respondents were by and large willing to assume some side effects, particularly as the time frame of the potential benefit of medications to delay kidney failure shortened. Critically, clinician recommendations regarding kidney therapies and clinician willingness to work with patients to address any side effects were important in patients' willingness to initiate and to persevere with a new medication. Risk-versus-benefit discussions appear key to patients and their families making well-informed decisions about taking a new medication that may or may not help the progression of their kidney disease.

When considering treatments for end of life or treatments for chronic conditions, patients typically are willing to accept some level of risk for degrees of potential benefit.[21,22] For example, in 1 study of obesity management, most individuals considering bariatric surgery were willing to accept a 10% risk of death if it meant they would sustain greater than 20% weight loss; however, the majority were unwilling to accept the risk if sustained weight loss were projected to be 20% or less. Of note, a lower baseline quality of life was associated with a greater willingness to accept risk. Similarly, patients with hepatitis C virus infection were willing to accept an increased risk of side effects for a sufficient improvement in the likelihood of a treatment response. While benefits in these disease states are easily quantifiable in a relatively short time,

Table 1. Characteristics by Respondent Self-Identified CKD Status

	At Risk for CKD (n=45)	Have CKD (n=566)	Kidney Transplant (n=267)	Dialysis (n=51)	Other[a] or Blank (n=100)	Total (n=1,029)
Kidney disease causes						
Diabetic kidney disease	0.8% (8)	9.0% (93)	2.7% (28)	1.1% (11)	0.0%	13.6% (140)
Polycystic kidney disease	0.2% (2)	6.3% (65)	5.3% (55)	1.1% (11)	0.0%	12.9% (133)
Glomerulonephritis	0.2% (2)	6.7% (69)	9.3% (96)	1.3% (13)	0.0%	17.5% (180)
Other	1.9% (20)	25.1% (258)	8.5% (87)	1.6% (16)	1.7% (18)	38.8% (399)
Blank	1.5% (15)	10.9% (112)	1.6% (16)	0.6% (6)	8.0% (82)	22.4% (231)
Total	4.6% (47)	58.0% (597)	27.4% (282)	5.5% (57)	9.7% (100)	105.2%
eGFR, mL/min/1.73m^2						
90+	0.9% (9)	0.7% (7)	NA	NA	1.1% (11)	2.6% (27)
60-89	1.2% (12)	4.3% (44)	NA	NA	0.7% (6)	6.1% (63)
45-59	0.7% (7)	14.1% (145)	NA	NA	0.2% (2)	15.0% (154)
30-44	0.6% (6)	13.6% (140)	NA	NA	0.3% (2)	14.5% (149)
15-29	0.0%	13.9% (143)	NA	NA	0.5% (2)	14.4% (148)
<15, nondialysis	0.1% (1)	3.5% (36)	NA	NA	0.1% (1)	3.7% (38)
Unsure	0.9% (9)	3.6% (37)	NA	NA	0.6% (6)	5.1% (52)
Missing	0.1% (1)	1.4% (14)	25.5% (262)	4.9% (50)	6.9% (71)	38.7% (398)
Total	4.4% (45)	55.0% (566)	25.5% (267)	4.9% (51)	10.3% (100)	100.0%
Urine ACR						
<30 mg/g	1.1% (11)	12.7% (131)	NA	NA	1.0% (8)	14.8% (152)
30-300 mg/g	0.1% (1)	8.3% (85)	NA	NA	0.4% (2)	8.8% (90)
>300 mg/g	0.2% (2)	3.1% (32)	NA	NA	0.0%	3.3% (34)
Unsure	2.8% (29)	28.2% (290)	NA	NA	2.0% (17)	33.0% (339)
Blank	0.2% (2)	2.7% (28)	25.5% (262)	4.8% (49)	7.1% (73)	40.2% (414)
Total	4.4% (45)	55.0% (567)	25.5% (269)	4.8% (54)	10.5% (104)	100.1%
Risk factors						
Diabetes	1.3% (13)	12.2% (126)	NA	NA	0.5% (3)	14.0% (144)
Heart condition	0.7% (7)	9.4% (97)	NA	NA	0.3% (1)	10.4% (107)
Overweight or obese	1.5% (15)	19.0% (195)	NA	NA	0.8% (7)	21.2% (218)
High blood pressure	2.7% (28)	37.3% (384)	NA	NA	1.4% (14)	41.4% (426)
Sickle cell disease	0.1% (1)	0.2% (2)	NA	NA	0.0%	0.3% (3)
Kidney cancer	0.4% (4)	1.7% (18)	NA	NA	0.4% (4)	2.5% (26)
HIV or AIDS	0.0%	0.0%	NA	NA	0.0%	0.0%
Other	0.6% (6)	8.6% (88)	NA	NA	1.1% (11)	10.2% (105)
Blank	0.2% (2)	5.9% (61)	25.5% (262)	4.8% (49)	7.2% (74)	43.5% (448)
Total	7.4% (76)	94.4% (971)	26.3% (271)	5.1% (52)	10.4% (107)	143.5%
Age, y						
18-44	0.3% (3)	3.7% (38)	2.0% (21)	0.5% (5)	0.4% (4)	6.9% (71)
45-54	0.3% (3)	4.6% (47)	5.2% (53)	0.5% (5)	0.1% (1)	10.6% (109)
55-64	1.1% (11)	9.4% (97)	7.7% (79)	1.1% (11)	0.6% (6)	19.8% (204)
65-75	1.2% (12)	19.7% (203)	6.4% (66)	1.3% (13)	0.6% (6)	29.2% (300)
76-85	0.5% (5)	7.9% (81)	0.6% (6)	0.7% (7)	0.5% (5)	10.1% (104)
85+	0.1% (1)	1.6% (16)	0.0%	0.0%	0.1% (1)	1.7% (18)
Unanswered	1.0% (10)	8.2% (80)	4.1% (42)	1.0% (10)	7.5% (77)	21.3% (223)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%
Gender						
Male	1.1% (11)	14.9% (153)	10.1% (104)	1.7% (17)	0.9% (9)	28.6% (294)
Female	2.3% (24)	31.6% (325)	11.8% (121)	2.3% (24)	1.5% (15)	49.5% (509)
Unanswered	1.0% (10)	8.6% (88)	4.1% (42)	1.0% (10)	7.4% (76)	22.0% (226)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%
Race						
White	2.2% (23)	40.8% (420)	16.9% (174)	3.3% (34)	2.0% (21)	65.3% (672)
Black or African American	0.6% (6)	2.9% (30)	3.3% (34)	0.5% (5)	0.1% (1)	7.4% (76)

(Continued)

Table 1 (Cont'd). Characteristics by Respondent Self-Identified CKD Status

	At Risk for CKD (n=45)	Have CKD (n=566)	Kidney Transplant (n=267)	Dialysis (n=51)	Other[a] or Blank (n=100)	Total (n=1,029)
Asian American	0.1% (1)	1.3% (13)	0.2% (2)	0.1% (1)	0.0%	1.7% (17)
American Indian or Alaska Native	0.1% (1)	0.3% (3)	0.9% (9)	0.0%	0.0%	1.3% (13)
Native Hawaiian or Pacific Islander	0.0%	0.0%	0.1% (1)	0.0%	0.0%	0.1% (1)
Other	0.4% (4)	1.7% (18)	1.1% (11)	0.2% (2)	0.2% (2)	3.6% (37)
Unanswered	1.1% (11)	9.1% (93)	4.4% (45)	1.0% (10)	7.4% (76)	22.9% (16)
Total	4.5% (46)	56.1% (577)	26.8% (276)	5.1% (52)	9.7% (100)	102.1%
Ethnicity						
Hispanic or Latino	0.3% (3)	2.1% (22)	1.4% (14)	0.3% (3)	0.2% (2)	4.3% (44)
Non-Hispanic or Latino	2.9% (39)	43.5% (448)	20.1% (207)	3.7% (38)	2.0% (21)	72.3% (744)
Unanswered	1.2% (12)	9.4% (96)	4.5% (46)	1.0% (10)	7.5% (77)	23.5% (241)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%
Marital status						
Single or never married	0.5% (5)	4.7% (48)	2.9% (30)	0.8% (8)	0.3% (3)	9.1% (94)
Married or living together	1.9% (20)	28.7% (295)	15.5% (159)	2.2% (23)	1.2% (12)	49.5% (509)
Divorced or separated	0.5% (5)	8.7% (89)	2.1% (22)	0.5% (5)	0.6% (6)	12.4% (127)
Widowed	0.3% (3)	4.0% (41)	1.2% (12)	0.4% (4)	0.2% (2)	6.0% (62)
Unanswered	1.2% (12)	9.1% (93)	4.3% (44)	1.1% (11)	7.5% (77)	23.1% (237)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%
Education						
Non-high-school graduate	0.1% (1)	0.5% (5)	0.1% (1)	0.2% (2)	0.0%	0.9% (9)
High-school graduate or GED	0.4% (4)	5.3% (55)	2.2% (23)	0.7% (7)	0.2% (2)	8.8% (91)
Some college or Associate Degree	1.3% (13)	15.4% (158)	7.1% (73)	1.7% (17)	0.7% (7)	26.0% (268)
College graduate	0.7% (7)	12.0% (123)	6.8% (70)	0.9% (9)	0.9% (9)	21.2% (218)
Advanced degree	0.8% (8)	12.9% (133)	5.5% (57)	0.5% (5)	0.5% (5)	20.2% (208)
Unanswered	1.2% (12)	9.0% (92)	4.2% (43)	1.1% (11)	7.5% (77)	22.9% (235)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%
Employment						
Full-time employed	0.9% (9)	9.0% (93)	7.2% (74)	0.8% (8)	0.8% (8)	18.7% (192)
Part-time employed	0.4% (4)	2.4% (25)	2.2% (23)	0.1% (1)	0.1% (1)	5.2% (54)
Student, homemaker, or volunteer	0.1% (1)	3.8% (39)	2.0% (20)	0.0%	0.0%	5.8% (60)
Retired or disabled	2.1% (21)	31.4% (323)	10.7% (110)	3.1% (31)	1.4% (14)	48.5% (499)
Unemployed	0.1% (1)	1.3% (13)	1.2% (12)	0.1% (1)	0.0%	2.6% (27)
Unanswered	1.0% (10)	9.8% (100)	4.5% (26)	1.0% (10)	7.6% (78)	23.7% (244)
Total	4.5% (46)	57.6% (593)	27.7% (285)	5.0% (51)	9.8% (101)	104.6%
Family history of CKD						
Yes	1.3% (13)	16.0% (165)	9.7% (100)	2.2% (23)	0.6% (6)	29.8% (307)
No	2.4% (25)	34.5% (355)	15.3% (157)	2.3% (24)	1.9% (20)	56.5% (581)
Unknown	0.6% (6)	3.8% (39)	0.9% (9)	0.4% (4)	0.2% (2)	5.8% (60)
Unanswered	0.1% (1)	0.7% (7)	0.1% (1)	0.0%	7.0% (72)	7.9% (81)
Total	4.4% (45)	55.0% (566)	25.9% (267)	5.0% (51)	9.7% (100)	100.0%

Note: Varying sizes of the "total" rows indicate different response sizes for questions, and a total >100% indicates multiple responses were allowed. "Unanswered" includes items left blank and those in which "prefer not to answer" was indicated. The eGFR, ACR, and comorbid conditions were not queried among respondents with a kidney transplant or receiving dialysis.

Abbreviations: ACR, albumin-creatinine ratio; AIDS, acquired immunodeficiency syndrome; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NA, not applicable.

[a]"Other" includes family members, kidney cancer, and kidney cyst patients.

kidney disease poses unique challenges in risk-versus-benefit discussions, with not only relatively low percentages of people with CKD progressing to kidney failure but also a high burden of associated comorbid conditions that may affect a patient's lifestyle, overall health, and mortality.[23-25] While this survey was developed in preparation for the workshop, a clear consensus emerged from the workshop that there is value in preventing the

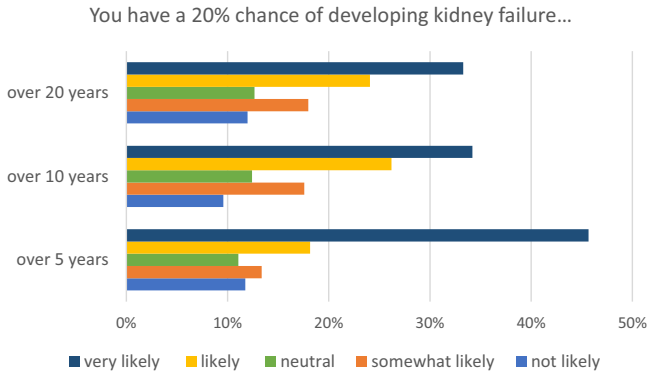

Figure 1. Responses to scenario 1, regarding the likelihood of taking a new medication to prevent kidney failure. Scenario 1 stated, "Your doctor says that there is a new medication which can reduce your chance of developing kidney failure. Please tell us your likelihood of taking this medication under the following circumstances."

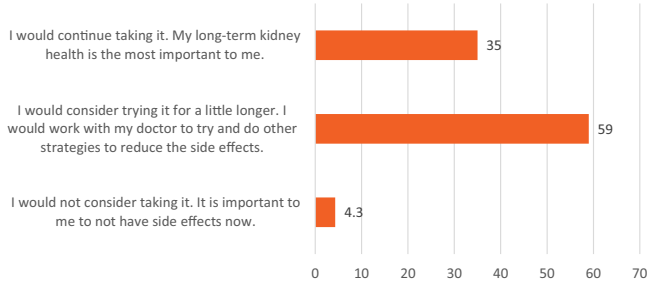

Figure 3. Responses to scenario 3, regarding willingness to continue use if side effects occurred. Scenario 3 stated, "Imagine that you have started the medication. You notice that the side effects of the new drug are worse than you thought they would be. You talk to your doctor, and your doctor goes over the clinical evidence with you. You are convinced that the data show that the drug would significantly slow or prevent the progression of your kidney disease and that this will lead to a better quality of life down the road. How likely would you be to take this drug?"

development or treating the progression of early CKD in people who are at high risk for progression (workshop report in preparation). It is important to gain further insight into the level of risk or side effects patients with early-stage CKD are willing to assume to decrease their chance of progressing to late-stage CKD or kidney failure.

One theme from respondents was that the opinions of their physicians and working with their physicians to address side effects were important for initiating and continuing potentially risk-lowering treatments. Despite the potential reticence of clinicians to have complex risk-progression discussions with patients, the reality is that clinicians' professional insights and opinions carry significant impacts on patients' willingness to consider new medications or treatments.[15,26] This is true even among the well-educated population who responded to the survey reported here. Ideally, these conversations begin early and continue over time, in an iterative process combining education and preference discussions. These efforts are key to engaging patients as partners and can have a significant impact on patient activation and overall health.[27]

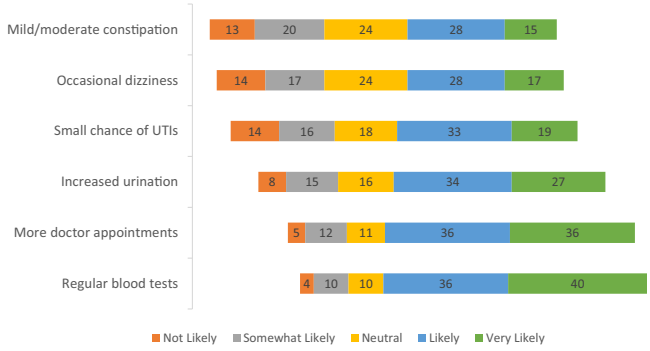

Figure 2. Responses to scenario 2, regarding symptoms that would impact medication willingness. Scenario 2 stated, "If your doctor told you that you have a 20% chance of developing kidney failure over 5 years, how likely would you be to take a drug that has the following side effects or concerns?" More frequent appointments and blood tests refer to approximately every 3 months. Abbreviation: UTI, urinary tract infection.

Newer and emerging treatments to prevent kidney disease progression offer new opportunities and challenges for researchers, regulators, and clinicians. Our results showed that people with CKD are willing to accept some risk and some burden of side effects. This can inform the recommendations that emerge from the workshop about treatments of early CKD. While our survey used a 20% risk over a 5- to 20-year time span to frame this scenario, some patients may internalize a risk differently depending on how the risk is presented; for example, a patient may view a 20% risk as minimal while also viewing a 1 in 5 risk as significant, despite their mathematical equivalence. Further qualitative research is needed to fully understand patients' perspectives and preferences in how this critical information is presented and interpreted and to identify universal best practices for translating statistical risks into narrative frameworks.

CKD is often an asymptomatic disease until late in the disease course. This presents challenges regarding how to assess patients' perceptions and priorities in earlier stages of CKD. The NKF is deeply engaged in this challenge with public health campaigns ("Are You the 33%") and a recently launched CKD Patient Registry (the NKF Patient Network).[28] For the purpose of informing the conference participants, we purposefully elected to send the survey to the broad NKF audience to gain insight into how people think about risk at various CKD stages. Further, people with early-stage CKD may not appreciate the "burden" of CKD yet. Thus, while individuals with late-stage CKD, including those receiving dialysis or living with a kidney transplant, have an inherent bias, they offer valuable

Table 2. Responses to the Question "How Important Are Each of the Following to You When Deciding to Select a New Drug?"

	Not Important	Important	Very Important
The drug is a pill that can be taken by mouth	28.2% (230)	36.7% (303)	35.1% (287)
How often you take the drug	47.2% (376)	38.9% (314)	13.9% (114)
Number of side effects known for the drug	6.5% (52)	51.5% (423)	42% (342)
Severity of side effects known for drug	3.3% (26)	36.1% (288)	60.6% (489)
Cost and/or if covered by insurance	9.8% (79)	32.3% (267)	57.9% (474)
What your physician recommends	3.2% (25)	41.4% (330)	55.4% (443)

insight into questions posed by the survey. Indeed, patients with more advanced CKD often noted a shift in their own personal journey when they became more active and involved in their care. This journey informed the workshop participants and guided recommendations about the importance of educating patients with early CKD before engaging with them in the discussion about treatment options.

Although this study included broad ranges of ages, stages of CKD, and likely causes of kidney disease, there were a number of limitations. First, although the survey was emailed to more than 20,000 individuals identifying with CKD in the NKF database, only approximately 5% of this number completed a survey. Respondents may also have seen the survey on alternative media. Importantly, the population who receive NKF communications or follow NKF on social media likely differ from the broader CKD population, resulting in a largely White, well-educated population of respondents who have been referred to a nephrologist. This has implications for generalizability, as CKD disproportionately affects individuals with a lower socioeconomic status and less health literacy. Second, many respondents had already progressed to advanced kidney disease and, while they may be able to reflect meaningfully on their experience in hindsight, those with newly recognized, earlier-stage disease may have a differing, more nuanced perspective. Additionally, those with genetic diseases like polycystic kidney disease may be more inclined to accept risks even with a higher GFR, as they have seen family members live and die from kidney disease. Third, the 5-, 10- and 20-year time horizons and 20% likelihood posed in scenarios for developing kidney failure are somewhat arbitrary; however, they are consistent with potential patterns of kidney disease progression in people with CKD. Critically, there remains a need to collect additional data in individuals with earlier stages of disease to inform our understanding of the potential acceptability of tradeoffs between treatment benefits and risks in patients with early stages of disease.

While insights gleaned from this work may have some universal applications, additional research into the priorities of a larger population of individuals with earlier-stage kidney disease, as well as those from diverse cultural and socioeconomic backgrounds and those with less education, access to nephrology care, and trust in health care providers, is warranted. Insofar as the respondents are more likely to have access to ongoing health care than are populations not reached by the survey, they may also perceive that delaying disease progression is less critical, as later monitoring and care might address future "problems." Additionally, as lifestyle, behavior, and treatment adherence are increasingly seen as meaningful variables in risk management, further research to explore patient activation and willingness to take a risk-reducing medication may enrich future discussions.

In sum, among a population of well-informed individuals with CKD, there was a willingness to assume risk in seeking treatment to slow the progression of kidney disease, reinforcing the broader population's need for more frequent and earlier education about kidney disease risk progression. For this population, who are likely to have positive engagement with the health care system, physicians' recommendations regarding therapies and input in managing potential side effects are meaningful, and developing best practices for engaging patients, transcending biases and cultural differences, and presenting a risk to patients will aid in increased clinician comfort with these difficult, yet necessary, conversations.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Item S1: Workshop Planning Committee.

Item S2: CKD patient survey.

Table S1: Survey respondent answers to CKD knowledge questions.

Table S2: Knowledge table of signs and symptoms of advanced CKD.

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