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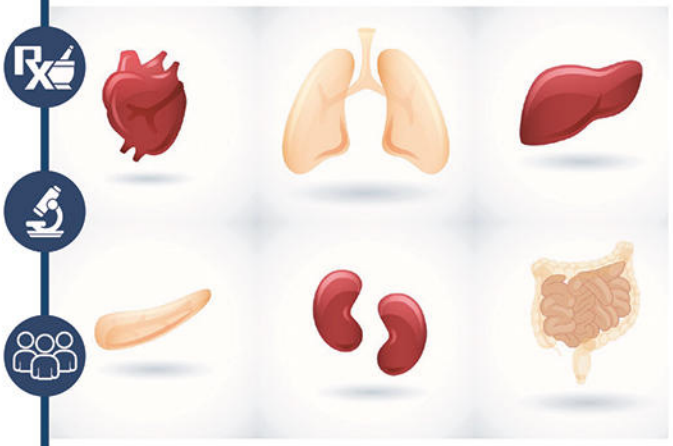

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Received: 26 September 2017 | Revised: 31 August 2018 | Accepted: 8 September 2018

DOI: 10.1111/ctr.13408

ORIGINAL ARTICLE

WILEY Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research

Outcomes for individuals turned down for living kidney donation

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Funding information
Greenwall Foundation; University of Pennsylvania

Abstract

Background: A better understanding of the consequences of being turned down for living kidney donation could help transplant professionals to counsel individuals considering donation.

Methods: In this exploratory study, we used survey instruments and qualitative interviews to characterize nonmedical outcomes among individuals turned down for living kidney donation between July 1, 2010 and December 31, 2013. We assembled a comparator group of kidney donors.

Results: Among 83 turned-down donors with contact information at a single center, 43 (52%) participated in the study (median age 53 years; 53% female; 19% black). Quality of life, depression, financial stress, and provider empathy scores were similar between individuals turned down for donation (n = 43) and donors (n = 128). Participants selected a discrete choice response to a statement about the overall quality of their lives; 32% of turned-down donors versus 7% of donors ($P < 0.01$) assessed that their lives were worse after the center's decision about whether they could donate a kidney. Among turned-down donors who reported that life had worsened, 77% had an intended recipient who was never transplanted, versus 36% among individuals who assessed life as the same or better ($P = 0.02$). In interviews, the majority of turned-down donors reported emotional impact, including empathy, stress, and other challenges, related to having someone in their lives with end-stage kidney disease.

Conclusions: Generic instruments measuring quality of life, depression, financial stress, and provider empathy revealed no significant differences between kidney donors and turned-down donors. However, qualitative interviews revealed preliminary evidence that some turned-down donors experienced emotional consequences. These findings warrant confirmation in larger studies.

KEYWORDS
kidney transplantation, living kidney donor, outcomes, qualitative research

1 | INTRODUCTION

Living organ donation poses a unique ethical scenario in which the donor accepts medical risks without the possibility of medical benefit. As a result, transplant professionals and ethicists have affirmed the need for comprehensive informed consent related to live organ donation.[1,2] Knowledge about risks of living kidney donors has rapidly expanded.[3] However, almost nothing is known about outcomes for individuals who are turned down for living kidney donation. This information deficit may limit the ability of transplant professionals to counsel potential living donors, decide which individuals are appropriate for donation, and prepare these individuals for potential challenges if donation is not permitted.[4]

In clinical practice, it is evident that donors are often highly motivated and feel an obligation to relieve the recipient's suffering. For some, the decision to donate is made rapidly, prior to careful deliberation about risks.[5] Fortunately, donors should expect similar survival and risk of cardiovascular events compared to healthy individuals in the general population.[6-8] Kidney donation is associated with an elevated relative risk of end-stage renal disease, but absolute rates are less than one percent by 15 years.[9,10] Kidney donors enjoy good quality of life. [11-14] The majority of this research has involved generic quality of life instruments, [15-17] although at least one study has used qualitative methods to try to understand the meaning of the donation act for the donor.[18] A prospective study by Rodrigue et al suggests that more than half of kidney donors anticipate nonmedical benefits from donation that may be categorized as personal growth, interpersonal (ie, changes in relationships), and spiritual benefits. While some donors later realize these positive nonmedical outcomes, others express disappointment, particularly when the recipient experienced allograft failure or other complications.[19]

Our group reported about the absence of data on individuals turned down for live kidney donation.[4] Potential explanations for this absence include ambiguity about whether these individuals are the patients of transplant professionals, with associated responsibilities for their outcomes. As a result, transplant centers may have minimal interaction with these individuals after they are turned down. Second, the medical risks of kidney donation may be more easily measured than the nonmedical outcomes for donors and individuals turned down for donation.[4]

Yet, being turned down for kidney donation might cause emotional distress, particularly when the potential donor and recipient have a strong relationship. In some circumstances, such as when the transplant candidate and donor share the same household, a turned-down donor might also perceive that the transplant center's decision had prevented the family from enjoying the financial benefits of transplantation—which may include the ability to work or avoid costs associated with remaining on dialysis.[20] Additionally, a well-informed candidate might sense that his or her autonomy was infringed upon if not accepted as a donor, particularly since there is wide variation in practice and in guidelines about acceptable health and psychosocial criteria for kidney donation.[21,22]

The primary aims of this exploratory study were to describe quality of life, depression, and financial stress among individuals turned down for donation. A secondary aim was to compare outcomes of individuals turned down for kidney donation to kidney donors. We therefore also enrolled a comparator group of living kidney donors, with the recognition that this group would differ from turned-down donors in terms of duration and type of interactions with the transplant center. We measured quality of life for both groups because the effects of living kidney donation on quality of life have been a frequent focus of attention by transplant researchers.[11,15,23] Likewise, for an individual turned down for kidney donation, having a family member who was sick due to kidney disease might also affect quality of life. We assessed for depression, emotional distress, and financial stress, because all are identified by the United Network for Organ Sharing as necessary elements for counseling of potential living kidney donors about the risks of donation,[24] but might also relate to living with or worrying about another person who is suffering from ESRD. We asked participants to assess provider empathy because the process of being evaluated for kidney donation typically involves potentially sensitive topics such as family relationships, health behaviors, risks, and in some cases, communicating a negative decision from the donor selection committee. Provider empathy could be important to the perception that the decision to turn down an individual for kidney donation was reasonable and in that individual's best interests. Finally, we asked participants to describe the effect of either donating or being turned down on their lives, personally and in the context of their relationships with their intended recipient.[4] These data were assessed using qualitative methods, as well as a forced-choice response to a survey item.

2 | MATERIALS AND METHODS

This is a retrospective cohort study of individuals evaluated for living kidney donation. Inclusion criteria included adults (≥18 years) who underwent in-person evaluation for kidney donation at the Hospital of the University of Pennsylvania (HUP) between July 1, 2010 and December 31, 2013. HUP is a large volume US transplant center that performed between 152 and 177 kidney transplants annually during the years 2010 through 2013. Among these transplants, 44-70 (25%-43%) annually were from living kidney donors, a percentage that is similar to overall trends in the United States during this period.[25] Kidney transplant recipients at HUP were 35% black race, 60% male, and 15% were >65 years of age during these years.

Individuals who opted-out of evaluation, potential non-directed donors, and individuals who had expressed documented resentment toward staff (eg, threatening litigation) were excluded. All potential participants were mailed and emailed (when addresses were available) a study information sheet and informed consent document.

Participant demographics, participant relationship to the intended recipient, and the intended recipient's vital status at the time of the interview were abstracted from the electronic medical record. One investigator (PR) categorized reasons recorded by the

donor selection committee for turning down individuals for donation (Appendix S1).

Participants were offered a $20 gift voucher from Amazon.com for completing the study. The University of Pennsylvania Institutional Review Board (protocol #819578) approved the study.

2.1 | Study instruments

Participants completed questionnaires and semi-structured interviews by telephone. The investigators developed an interview guide, which underwent iterative revisions. The guide was piloted among individuals undergoing evaluation as live kidney donors (n = 4; none were in the cohort) and revised. The guide focused on the participant's situation before and after the evaluation for donation. Domains included the participant's relationship with the potential recipient, the care received at the transplant center, and whether the potential recipient's kidney disease affected the participant's finances or lifestyle (Appendix S2).

The guide included some discrete choice questions. Specifically, we asked donors to select a category of agreement (strongly agree, agree, neutral, disagree, or strongly disagree) with the statement "My life is better than it would have been if I had not donated a kidney," and non-donors to respond to the statement "My life is better than it would have been if I had donated a kidney." Responses were categorized as "life is better," "life is the same," or "life is worse" as a result of donation or non-donation. Subsequently, subjects were given the opportunity to respond to an open-ended follow-up probe about how donor evaluation process and the donation/non-donation decision affected their lives (Appendix S2).

2.2 | Questionnaires

All participants completed the Medical Outcomes Study Short Form-12 (SF-12, a quality of life measure), the Patient Health Questionnaire-9 (PHQ-9, an instrument to diagnose, monitor, and measure depression),[26] the Consultation And Relational Empathy measure (CARE, a patient-centered measure of provider empathy),[27] and questions related to financial security (taken from the Health and Retirement Study).[28,29]

2.3 | Data collection

Members of the research team (CC, DL, SL, FB, RP, and AM) conducted telephone interviews and transcribed the interviews. Sustained efforts were made to contact each individual—letter, multiple phone calls (up to 5), and email, when available. Study staff scheduled times when participants had sufficient time to complete questionnaires and interviews. The questionnaires were administered first, followed by the interviews. Questionnaire items were read to participants over the phone. The qualitative interview portion of the research encounter was audio recorded. The median interview duration was 14 minutes (IQR 12, 19 minutes).

2.4 | Data analysis

Interview transcripts were coded using NVivo (version 11.0, QSR International, Melbourne, Australia). With supervision from two experts in qualitative research (SK, CT), four investigators (CC, DL, SL, and RP) developed and iteratively revised a codebook. The coding process started after the team had conducted and transcribed over 100 interviews. The team used a grounded theory approach to analyze the qualitative interviews. Specifically, during the coding process, study staff used the content of participant responses to the interview probes to generate the codebook elements. First, study staff selected 10 representative transcripts from both the turned-down donors and the donors and read the content together. Coders independently reviewed the transcripts to develop a set of major themes apparent in the data; these codes were then revised through a series of team discussions. After major coding was completed, the coders employed a similar process to develop a list of sub-themes.[30,31] For these transcripts, double-coding demonstrated kappa statistics of >0.9 for all domains, indicating a high level of agreement between investigators. The research staff resolved discrepancies between coding decisions through discussion of the rationales for coding decisions and achieving consensus.

Given the primary focus of the research on individuals turned down for kidney donation and the mixed methods analysis, all transcripts from the turned-down donors (n = 41) were coded and categorized according to the relationship with the recipient (parent, child, sibling, spouse/partner, and other). Because of the large number of donors, we did not code and analyze all the donor manuscripts. The initial coding process revealed that relationship to the recipient was a prominent feature of how turned-down donors processed their experiences. Therefore, within each relationship category, we randomly selected donor transcripts to code and analyze. For the three relationship categories of sibling, spouse/partner, and other, we selected and coded the same number of donor transcripts as turned-down donor transcripts. Because the parent and child categories of turned-down donors had a small number of participants (n = 4 in each category), we coded two additional transcripts from parental donors (n = 6 total coded) and three additional transcripts from children donors (n = 7 total coded). All the matched donor manuscripts were double coded.

2.5 | Statistical analysis

We made initial comparisons between individuals turned down for kidney donation (n = 43) and donors (n = 128) using the rank-sum test for continuous variables and using the chi-square test or Fisher's exact test, as appropriate, for categorical variables. We subsequently compared responses to a forced-choice question about overall quality of life after donation or non-donation between turned-down donors (n = 41) and matched donors (n = 46) using Fisher's exact test. We did not use pairwise matching for these analyses. Instead, the turned-down donors and matched donors were analyzed as groups. Among turned-down donors, we examined for associations between

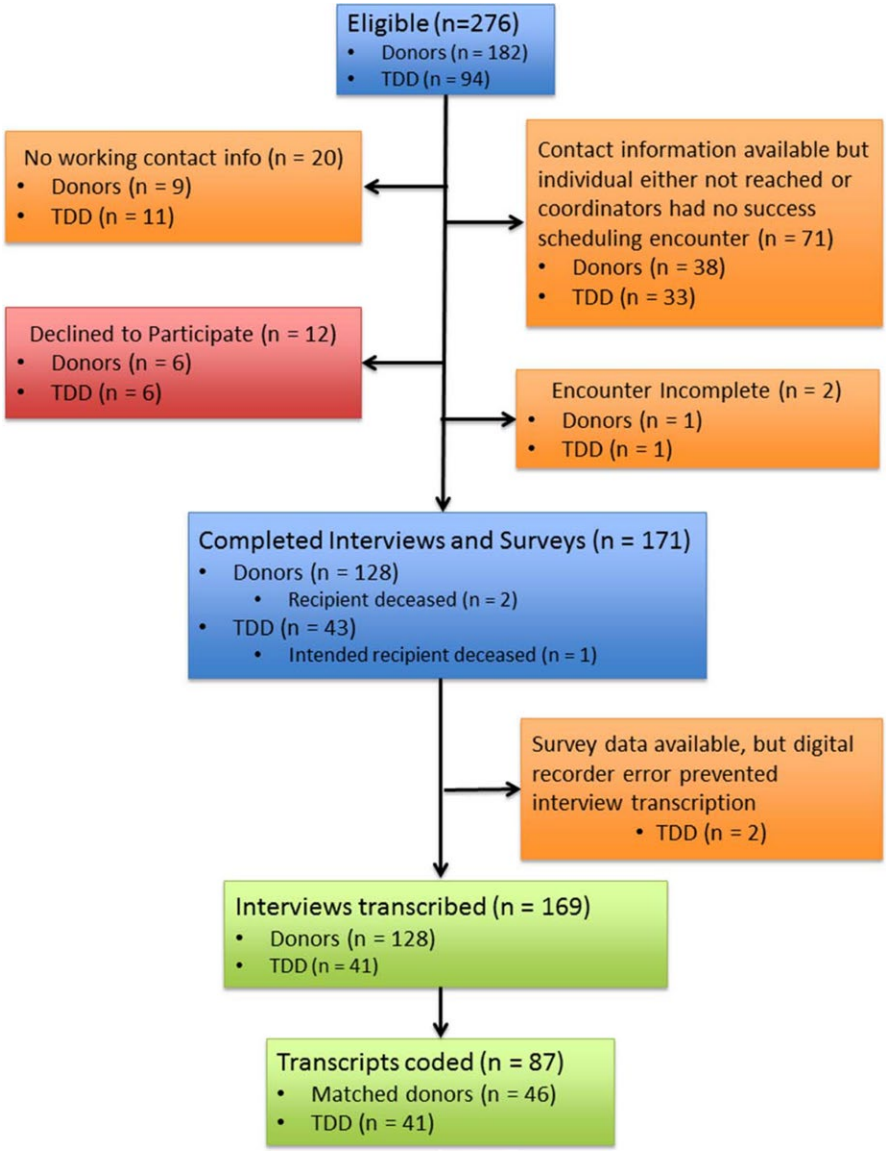

FIGURE 1 Cohort generation flowchart of individuals turned down for kidney donation and donors at a single US center between July 1, 2010 and December 31, 2013. TDD, turned down for kidney donation

the outcome of assessing life as worse because of being turned down as a kidney donor and participant characteristics using the rank-sum test (for age) and Fisher's exact test for binary variables. Given the small sample size, we did not perform multivariable analyses.

3 | RESULTS

Figure 1 shows cohort generation. Among 276 initially eligible participants, a total of 256 had working contact information and 171 completed interviews. Among individuals with contact information, the response rate was lower among turned-down donors (52%) vs donors (73%). The median time between initial center evaluation and the research encounter was 772 days. Table 1 shows characteristics of the 43 individuals turned down for kidney donation, 46 matched donors, and all 128 participating donors. The median age of individuals turned down for kidney donation was 53 years vs 47 years for all kidney donors. Fifty-three percent of individuals turned down for kidney donation were female, versus 66% of kidney donors. Among individuals turned down for kidney donation, 51% of their intended recipients eventually received a kidney transplant.

Turned-down donors generally had good quality of life scores using the SF-12. When comparing groups, quality of life scores ($P = 0.76$ and $P = 0.33$ for the physical and mental components of the SF-12) were nearly identical between kidney donors and individuals turned down for donation.

Responses to the financial stress questions by turned-down donors were not consistent with high levels of financial stress, although some individuals turned down for donation identified specific areas of financial concern in the qualitative interviews (described below). Turned-down donors and donors made similar assessments of financial distress ($P = 0.29$).

The PHQ-9 scale revealed little evidence of depression among most turned-down donors (median = 2). While the difference in depression scores between donors and turned-down donors approached statistical significance ($P = 0.06$), this differences should

TABLE 1 Characteristics of individuals turned down for kidney donation and kidney donors at a single transplant program (July 1, 2010 and December 31, 2013)

Characteristics	Individuals turned down for kidney donation (n = 43)	Selected donors, matched on category of relationship to recipient (n = 46)	Donors (n = 128)	Test statistic[a]	*P*-value[b]
Median age in years (IQR)	53 (35, 58)	45 (41, 50)	47 (41, 54)		0.06
Female (%)	23 (53)	34 (74)	84 (66)	$\chi^2 = 2.02$	0.16
Black race (%)	8 (19)	7 (15)	20 (16)	$\chi^2 = 0.21$	0.65
Relationship to intended recipient (%)					0.25
Parent	4 (9)	6 (13)	18 (14)		
Child	4 (9)	7 (15)	7 (5)		
Sibling	6 (14)	6 (13)	34 (27)		
Spouse/Partner	7 (16)	7 (15)	23 (18)		
Other	22 (51)	20 (43)	46 (35)		
Recipient transplanted (%)	22 (51)	46 (100)	128 (100)		<0.01
Year of donor evaluation initiation					0.03
2010	3 (7)	7 (15)	16 (13)		
2011	4 (9)	44 (30)	34 (27)		
2012	14 (33)	14 (30)	39 (31)		
2013	22 (51)	11 (24)	39 (31)		
Median days between in-center donor evaluation and study encounter	700 (635, 890)	872 (648, 1285)	806 (640, 1225)		0.02
Median SF-12 Physical component score (IQR)[c]	57 (56, 59)	58 (56, 59)	57 (56, 59)		0.76
Median SF-12 Mental component score (IQR)[c]	56 (50, 60)	57 (52, 60)	57 (54, 60)		0.33
Median PHQ-9 Depression scores (IQR)[c]	2 (0, 5)	1 (0,3)	1 (0, 3)		0.06
Median Financial stress (IQR)[c]	0 (0, 1)	1 (0, 3)	0 (0, 2)		0.29
Median CARE (Provider empathy) scale (IQR)[c]	43 (34, 50)	48 (40, 50)	46 (40, 50)		0.10

[a]Test statistic provided for chi-square

[b]Comparison of turned-down individuals to entire cohort of donors (n = 128)

[c]SF-12: Medical Outcomes Study Short Form 12 (higher scores indicate better self-reported quality of life); PHQ-9: Patient Health Questionnaire (higher scores indicate evidence of more severe depression); Financial stress questions taken from the Health and Retirement Study (higher scores indicate more financial stress); CARE: Consultation and Relational Empathy measure (higher scores indicate more provider empathy)

not be considered clinically important because the depression scores in both groups were low. The two groups also made similar assessments of provider empathy ($P = 0.10$).

Figure 2 shows how turned-down donors and matched donors responded on a forced-choice Likert scale to a general statement about changes in their life as a consequence of being accepted or turned down for kidney donation. Thirty-two percent of participants turned down for kidney donation assessed their life as worse ($P < 0.01$ versus donors), after receiving a decision from the transplant center about whether they could donate a kidney.

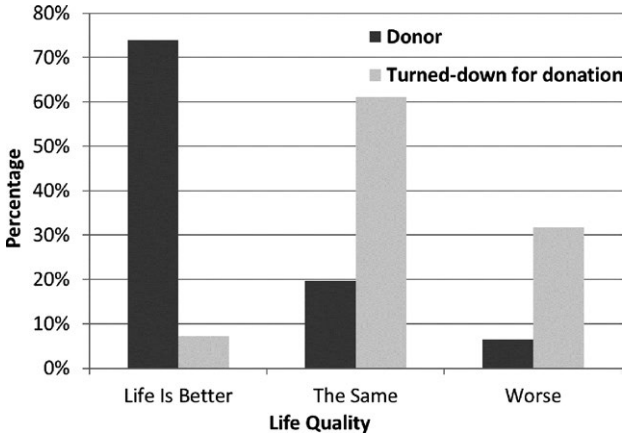

FIGURE 2 Assessments by participants about the effect of being turned down for kidney donation (n = 41) or accepted for kidney donation (matched individuals turned down for donation, n = 46) on their lives*. *$P < 0.01$ for comparison of responses across donors and non-donors using Fisher's exact

We coded transcripts for 41 turned-down donors (two transcripts from the original 43 turned-down donors were lost due to failure of the digital transcription file) and 46 matched donors. Table 2 shows representative quotes from individuals turned down for donation and donors. For individuals turned down, the most common reason for evaluating their lives as worse for having been turned down was because they lost an opportunity to carry out their goal of helping another person. Some also expressed that donation was highly consistent with their sense of purpose and frustration at being unable to carry out that purpose. Notably, many donors endorsed a similar theme. The most common reason why donors (41%) reported that their life was better after donation was gratitude at having had the opportunity to tangibly improve someone else's life. Twenty-six percent of donors also spoke about themes related to personal growth from the experience of organ donation.

We also examined more closely the specific experiences of turned-down donors, without reference to living kidney donors. We found that the turned-down donors' descriptions about the effect of the intended recipients' ESRD on their lives could be categorized as emotional, financial, and lifestyle impact. Table 3 presents representative quotes from these three domains. Twenty-four (59%) reported emotional impact, including compassion and empathy for the intended recipient, stress, and anxiety related to the intended recipient's end-stage kidney disease, and the intense emotional challenge of supporting someone with end-stage kidney disease through their illness and the transplant evaluation process. Six subjects noted reduced ability to travel due to the intended kidney recipient's illness. Four subjects reported financial impact, such as missed workdays. Some kidney donors also reported emotional, financial, and lifestyle impact of their recipient's kidney disease prior to the transplantation (data not shown).

Table 4 shows univariate analyses of the outcome of whether participants assessed their life as worse based on having been turned down as a kidney donor. Seventy-seven percent of turned-down donors who reported that life was worse had an intended recipient who was never transplanted versus 36% who reported that life was the same or better ($P = 0.02$). (We found no significant associations between this outcome and participant age, sex, race, having parental, child, sibling, or spousal relationship with the intended recipient, or reporting specific emotional, financial, or impact related to activity or other limitations.).

Only one individual turned down for donation experienced a worse relationship with the intended recipient. Only one donor reported that donation worsened his relationship with the recipient.

4 | DISCUSSION

This study presents novel data on outcomes for individuals turned down for living kidney donation. Individuals turned down for kidney donation reported good quality of life in a validated questionnaire. Most participants reported only limited evidence of depression or financial distress and assessed their transplant providers as having high levels of empathy. Yet, in discrete choice responses to a statement about their experiences, a third of individuals turned down for kidney donation rated their lives as worse than it would have been if they had been allowed to donate. These individuals commonly reported personal disappointment and highlighted the suffering of their intended recipient. While these findings must be considered exploratory, they warrant further study and suggest that transplant professionals may have opportunities to help turned-down donors cope with disappointment.

The published literature on living kidney donation has focused intensely on physical health consequences attributable to living in a single kidney state.[32] Clinical practice guidelines, and a number of high-quality studies, including the RELIVE multicenter cohort, have also recognized that many kidney donors think about kidney donation as a meaningful act.[23,33-35] A number of detailed, qualitative studies have demonstrated the ways that kidney donors consider donation as an important act of gift-giving that is often tied deeply to complex relationships and duties [36,37]. Kidney donors also commonly anticipate personal "benefits" that may be characterized as emotional or spiritual development.[19,38] If a sense of satisfaction or benefit from kidney donation is anticipated, then it is not surprising that individuals turned down for donation could experience disappointment and psychological distress.[39] The current work adds new empirical information about individuals turned down for kidney donation who described the meaning of this experience and their outcomes afterward.

In our cohort, negative outcomes from being turned down for kidney donation related in some cases to a sense of lost autonomy. A number of these individuals noted the extensive investment of time and resources required both to support the potential recipient through the rigors of dialysis treatment and also to complete the donor evaluation. Other individuals turned down for donation expressed that stepping forward to donate was consistent with their sense of purpose. Such statements align with the concept of

TABLE 2 Themes and representative quotes from interviews with kidney donors and individuals turned down for donation at a single center about their experiences

	Individuals turned down for kidney donation (n = 41)	Selected donors, matched on category of relationship to recipient (n = 46)
Life is better	n = 3	n = 34
	Theme: *Avoiding the adverse physical consequences of donor nephrectomy* n = 2 (5%)	Theme: *Gratitude at witnessing the recipient's health improve* n = 19 (41%)
	274: "Not going through the stress of surgery and not worrying about having one kidney later in life."	25: "Knowing that I was able to help him, giving him I guess a new lease on life." 58: "Seeing him happy and healthy."
	Theme: *Better personal health due to evaluation during donation workup* n = 1 (2%)	Theme: *Personal growth* n = 12 (26%)
	111: "Well I have two kidneys and my blood pressure is being managed pretty well… certainly all the testing that they went through that I experienced through there I'm probably more aware of my own health than I would have otherwise been, and that was at no cost to me, so that was definitely a benefit. Eventually my blood pressure issue that probably would have been realized by my own doctor that I regularly see."	278: "I did something good for somebody else and I feel like I have been a good example to people around me. And I think that my donation has caused others to pay it forward in different ways…" 310: "I feel like I've done something very noble and saved a life. And I can go to my grave knowing that I did something extraordinary for somebody moving forward not knowing how it might affect me."
		Theme: *Better personal health due to evaluation and counseling and focus on health* n = 4 (9%)
		141: "I'm living an even better life. When I first got tested for [the recipient], they told me I was overweight, and they told me I had to lose 10 lbs. to donate my kidney. And … I lost 20 lbs. in that month. And I felt so good that I just kept on doing it, and over 50 lbs. and I've still kept the weight off to this day… Before I had high cholesterol, high blood pressure, and now my blood pressure, and everything is right on perfect, excellent, excellent health."
		Theme: *Less stress in-personal/family life* n = 4 (9%)
		66: "Being concerned about her health, worried about her getting to and from dialysis appointments, and her health deteriorating, I think it's made my family's life easier as a result of it. We're all better off that way."
		Theme: *Improved relationship with recipient* n = 2 (4%)
		153: "He's my husband, we have a great relationship, we love each other. I feel better because I know he feels better. It's improved our whole outlook and relationship because now he's not sick."

(Continues)

TABLE 2 (Continued)

	Individuals turned down for kidney donation (n = 41)	Selected donors, matched on category of relationship to recipient (n = 46)
Life is the same	n = 25	n = 9
	Theme: *Donor evaluation and turndown did not have substantial effects on quality of life, activities or relationships* n = 25 (61%)	Theme: *Kidney donation did not have substantial effects on quality of life, activities or relationships* n = 9 (20%)
	102: "I'm back to doing the same old things as I usually do." 108: "I don't think my life is better or worse…From what they told me it seems like losing a kidney I don't think would have limited [me] really at all from what they were saying. Not being able to… I would have liked to help Mom out, but I wasn't able to, and it's not going to change anything at this point."	282: "As it is right now, I guess I think down the road you know if something adverse happens, you know I just have this one kidney now, and it's a negative thing, you know it still can change. But for right now, no it doesn't."
Life is worse	n = 13	n = 3
	Theme: *Lost opportunity to help a loved one* n = 9 (22%)	Theme: *Health and psychosocial concerns related to donation* n = 2 (4%)
	77: "Because I would have known that I could do something positive for somebody that I care about. That would have made me feel better. A lot better."	253: "Well if I hadn't donated my kidney I know I wouldn't be dealing with the physical issues I am dealing with, I wouldn't be dealing with the struggle with my [family], so I wouldn't have those stresses you know? So in that regard it would be better. It would not have harmed my relationship with [the recipient] if I had not donated a kidney, she would not have thought any less of me."
	Theme: *Unable to fulfill sense of purpose* n = 2 (5%)	
	100: "…you have to look at what your core values are. I'm a nurse practitioner; I want to help people. The person I love most in the world I am a perfect match for. And even if I were to die as a result of giving a kidney, this is so important that I would be living true to my core. My life would be 100% better if I could give him [my husband] a kidney."	
	Theme: *Donation and transplantation would have reduced stress in the family* n = 2 (5%)	
	432: "Well I feel that we would be a healthier household: I would be happier, our whole family would actually be happier because we would know that it would hopefully lift us longer than it did otherwise, and he would be here for our grandchildren. There are just a myriad of reasons and we would just be very, very happy."	

TABLE 3 Reported impact of the intended recipient's ESRD on individuals turned-down for donation

Emotional impact (n = 24)	
Compassion/empathy (n = 10)	014: "[I] just felt compassion for another human being who was younger than me and didn't seem to be able to live or look forward to the happy life that I was already living."
Stress/anxiety (n = 9)	369: "worrying about her passing away and trying to help her out…I did get scared of the surgery, but I was going to go through it no matter what for her. It affected me a lot. I went to bed crying a lot scared for her and scared for myself."
Intense emotional challenge (n = 5)	455: "Well you know I think it's like a gut punch, all of a sudden you see your child isn't going to have the life that you envisioned for them or you would wish for them, so it's heart wrenching, it's gut wrenching and the reality of it is overwhelming."
Impact on activities and lifestyle (n = 14)[a]	
Travel (n = 6)	280: "I am sure there were some times where he talked about maybe going on a trip or vacation, but then there would be an issue of him finding a place to do dialysis while we were on vacation. I mean I think that's the reason he didn't go on vacation for the past 6 y or so."
Activities (n = 4)	419: "It affects me because with dialysis, he gives up portions of his day and he is tired and he just doesn't feel well at times. And that affects me because instead of asking him to do something, I allow him to rest."
Eating (n = 4)	281: "Well we would go out a lot so I would have to monitor what she was eating and what I was eating because I didn't want to order something that would tempt her into having something that wasn't good for her."
Other (n = 5)	108: "She has slowed down a little so I have had to pick up a little extra slack around the house." 417: "it affected my performance at school, and I wasn't able to do things as strongly as I was able to do before." 337: "she [the intended recipient] is still not working and can't work. Nobody will hire her, which affects me and her mother to a point… That's a little bit of a problem, her being at home and not doing anything and us trying to get her to go find a job or look for a job or find somebody that'll help her."
Financial impact (n = 6)	
Manageable (n = 3)	274: "Losing days at work…we live 50 min to an hour away from Philadelphia. We were taking turns, me and my wife, taking him to all of his appointments, and mostly her more than me…She works for a company, so it is easy for her to take off and just lose the hours, whereas I am running a company and when I am not there, it doesn't run. So financially, it was fine, you just work through it and it is something you deal with. "
Substantial (n = 3)	100: "We have a huge dialysis bill. But the center was very gracious and they worked with us and we paid off those bills and now that we came on Medicare I think it will be much easier."

[a]Some participants reported more than one impact on activities and lifestyle.

TABLE 4 Associations between participant characteristics and self-assessment that being turned down for kidney donation made their lives worse (n = 41)

Characteristics	Life worse (n = 13)	Life unchanged or better (n = 28)	*P*-value
Median age (IQR)	54 (46, 56)	53 (36, 58)	0.96
Female (%)	10 (77)	13 (46)	0.10
Black race vs other race (%)	3 (23)	5 (18)	0.69
Parent, spouse, sibling, or child of transplant candidate vs other relationship (%)	9 (69)	11 (39)	0.10
Transplant candidate never received a kidney transplant vs transplanted (%)	10 (77)	10 (36)	0.02
Reported emotional impact related to being turned down for kidney donation vs no impact (%)	8 (62)	16 (57)	1.0
Reported financial impact related to being turned down for kidney donation vs no impact (%)	4 (31)	2 (8)	0.15
Reported impact on activities and lifestyle related to being turned down for kidney donation vs no impact (%)	6 (46)	8 (29)	0.31

relational autonomy, the idea that well-being is embedded in relationships and not simply about control over one's individual existence.[40,41] Other subjects appeared to experience distress from watching the intended transplant recipient endure chronic dialysis and a sense of powerlessness to improve the situation. Consistent with this concept of shared suffering, we found that among turned-down donors, those participants whose intended recipients never received a transplant were much more likely to evaluate their life as worse because of being unable to donate compared with participants whose intended recipient did receive a transplant.

These results do not carry the implication that transplant centers should accept all candidates who are committed to donation. Notably, only a third of turned-down donors assessed that their lives were worse after being refused the opportunity to donate. Transplant professionals should accept potential donors when a reasonable balance of risk and benefit to the donor exists.[42] Nonetheless, transplant professionals should consider the social and psychological outcomes as well as medical outcomes of donor selection for both donors and individuals judged ineligible to donate an organ. They should acknowledge that declining some individuals for kidney donation carries risks—of disappointment, distress, and loss of life purpose.

While turned-down donors reported good quality of life when responding to the SF-12 instrument, the study did identify opportunities to improve the donor evaluation process and consequences for individuals who are turned down. First, physicians and other members of the transplant team should engage with donor candidates about their motivations and expectations for benefit. In some cases, transplant professionals may try to talk to potential donors about the meaning of the act. When individuals are turned down for donation, the donor clinical team should recognize that some patients will conclude that being declined for kidney donation was not in their best interest. Clinicians may anticipate that outcomes may be worse for individuals turned down for donation when the only other plausible path for the intended recipient to get transplanted is a long waiting time for a deceased donor kidney. Second, the donor's clinical team must decide whether they have duties to attend to the needs of unsatisfied individuals who are turned down for kidney donation. If so, then some turned-down donors may be best served by referrals for support and advice that are provided in their local community, for example, by primary care physicians, psychologists, or counselors with whom these individuals have existing relationships. However, in other cases, it may be easier to directly arrange counseling or follow-up of medical problems (commonly identified in the donor workup) in the transplant program hospital. This support for individuals turned down for kidney donation has been endorsed in previous expert commentaries, including the KDIGO Living Kidney Donor Work Group.[43] Additionally, individuals turned down for kidney donation should be informed about the option to seek second opinions at other centers. Third, some individuals turned down for living kidney donation may be encouraged to spread the word in their community about the donor evaluation process, in case another donor might emerge. Motivated individuals might even be offered training on how to effectively attract the interest of other potential donors.[44,45]

The study has several limitations. As a single-center study, the findings may not be broadly generalizable. The response rate among individuals turned down as donors was 52%. Donors had a higher response rate (73%), which is not surprising given that donors had more and longer interactions with the transplant center and may have felt a greater interest in research participation compared with turned-down individuals. This differential response rate may limit the validity of comparisons across groups. However, this study focuses primarily on the group of turned-down donors rather than comparisons between groups. Future studies may attempt to augment response rates with prospective enrollment of individuals considering kidney donation, which may allow study staff to form relationships with participants prior to some individuals being turned down. Yet, this exploratory study provides important initial findings that can provide valuable guidance for investigators designing future studies. There may be response bias. Individuals with the worst outcomes after evaluation for kidney donation might be either underrepresented or overrepresented. Because of the small sample size of turned-down donors, multivariable analysis was not attempted. On the other hand, these are some of the only data reported about turned-down donors. We also acknowledge the limitation that substantial time passed between donor evaluation and interviews, creating the potential that emotions and memories related to the event of being turned down for kidney evaluation changed over time.

We also acknowledge that much of the literature about the ethics and epidemiology of kidney donation focuses on long-term outcomes, such as kidney disease.[9,10,32,46,47] Given follow-up time of only several years, most donors in this cohort would not have yet had time to experience long-term health consequences, which might change their assessment of whether the donation decision was a good one. On the other hand, other studies have revealed that donors rarely regret their decision to donate.[48,49] Finally, the self-assessment about changes in life as a consequence of being accepted or turned down for kidney donation was not a validated measure. Some of these limitations should be addressed by future, prospective studies of outcomes for individuals who pursue living kidney donor evaluation. We also suggest that the association of sex with outcomes among potential donors be a focus of this future research. We draw attention to the non-significant, but interesting finding that among turned-down donors who assessed their life as worse, 77% were female (while among those who assessed their lives as unchanged or better, 46% were female). The experiences of turned-down non-directed donors also warrant study.

In summary, this exploratory study found that individuals declined for kidney donation had good outcomes as assessed by generic instruments that measured quality of life, depression, financial distress, and provider empathy. However, in interviews, some individuals turned down for kidney donation expressed disappointment as a result of the donor selection committee's decision. While declining some candidates for kidney donation is supported by ethical principles, transplant professionals should consider potential

adverse consequences related to turning individuals down for kidney donation.[39,43] Transplant centers may take the opportunity to address patient distress from being declined as a donor. These findings require confirmation in a larger study.

ACKNOWLEDGEMENTS

The authors acknowledge Renee Fox, PhD, for contributions to the study concept and review of the manuscript. The authors also acknowledge the assistance of Donna Collins, MSN, and Maral Palanjian, BSN, in reviewing center records to identify the cohort of patients evaluated for kidney donation. Peter Reese and Carrie Thiessen were supported by the Greenwall Foundation. The University of Pennsylvania also provided research funding for the study. Preliminary data were presented at the 2016 American Transplant Congress, Philadelphia, PA.

CONFLICT OF INTEREST

None.

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REFERENCES

1. Veatch RM, Ross LF. *Transplantation Ethics*. Washington, DC: Georgetown University Press; 2015.
2. Tan JC, Gordon EJ, Dew MA, et al. Living donor kidney transplantation: facilitating education about live kidney donation-recommendations from a consensus conference. *Clin J Am Soc Nephrol*. 2015;10(9):1670-1677.
3. Lam NN, Lentine KL, Levey AS, Kasiske BL, Garg AX. Long-term medical risks to the living kidney donor. *Nat Rev Nephrol*. 2015;11(7):411-419.
4. Allen MB, Abt PL, Reese PP. What are the harms of refusing to allow living kidney donation? An expanded view of risks and benefits. *Am J Transplant*. 2014;14(3):531-537.
5. Valapour M, Kahn JP, Bailey RF, Matas AJ. Assessing elements of informed consent among living donors. *Clinical Transplant*. 2011;25(2):185-190.
6. Garg AX, Meirambayeva A, Huang A, et al. Cardiovascular disease in kidney donors: matched cohort study. *BMJ*. 2012;344:e1203.
7. Reese PP, Bloom RD, Feldman HI, et al. Mortality and cardiovascular disease among older live kidney donors. *Am J Transplant*. 2014;14(8):1853-1861.
8. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. *JAMA*. 2010;303(10):959-966.
9. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. *JAMA*. 2014;311(6):579-586.
10. Mjoen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. *Kidney Int*. 2014;86(1):162-167.
11. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. *Am J Transplant*. 2006;6(12):2965-2977.
12. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. *Am J Kidney Dis*. 2012;60(1):15-26.
13. Clemens K, Boudville N, Dew MA, et al. The long-term quality of life of living kidney donors: a multicenter cohort study. *Am J Transplant*. 2011;11(3):463-469.
14. Johnson EM, Anderson JK, Jacobs C, et al. Long-term follow-up of living kidney donors: quality of life after donation. *Transplantation*. 1999;67(5):717-721.
15. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. *Am J Transplant*. 2013;13(11):2924-2934.
16. Wiedebusch S, Reiermann S, Steinke C, et al. Quality of life, coping, and mental health status after living kidney donation. *Transplant Proc*. 2009;41(5):1483-1488.
17. Lima DX, Petroianu A, Hauter HL. Quality of life and surgical complications of kidney donors in the late post-operative period in Brazil. *Nephrol Dial Transplant*. 2006;21(11):3238-3242.
18. Mazaris EM, Warrens AN, Smith G, Tekkis P, Papalois VE. Live kidney donation: attitudes towards donor approach, motives and factors promoting donation. *Nephrol Dial Transplant*. 2012;27(6):2517-2525.
19. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: association with donor characteristics and recipient outcomes. *Transplantation*. 2014;97(7):762-768.
20. Danuser B, Simcox A, Studer R, Koller M, Wild P. Psychosocial Interest Group STCS, employment 12 months after kidney transplantation: an in-depth bio-psycho-social analysis of the Swiss Transplant Cohort. *PLoS One*. 2017;12(4):e0175161.
21. Reese PP, Feldman HI, McBride MA, Anderson K, Asch DA, Bloom RD. Substantial variation in the acceptance of medically complex live kidney donors across US renal transplant centers. *Am J Transplant*. 2008;8(10):2062-2070.
22. Thiessen C, Gordon EJ, Reese PP, Kulkarni S. Development of a donor-centered approach to risk assessment: rebalancing nonmaleficence and autonomy. *Am J Transplant*. 2015;15(9):2314-2323.
23. Jowsey SG, Jacobs C, Gross CR, et al. Emotional well-being of living kidney donors: findings from the RELIVE Study. *Am J Transplant*. 2014;14(11):2535-2544.
24. Organ Procurement and Transplantation Network Policies. Policy 14: Living donation. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_14. Accessed April 11, 2018.
25. Organ Procurement and Transplantation Network. Adult Recipient Transplants By Donor Type, Center. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed January 20, 2016.
26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613.
27. Mercer SW, Maxwell M, Heaney D, Watt GC. The consultation and relational empathy (CARE) measure: development and preliminary validation and reliability of an empathy-based consultation process measure. *Fam Pract*. 2004;21(6):699-705.
28. Growing Older in America. *The Health and Retirement Study. National Institute on Aging*. Karp F, ed. https://hrsonline.isr.umich.edu/. Accessed September 1, 2016.
29. Health and Retirement Study. AHEAD 1993 (Wave 1) Documentation. Module 9: Financial Pressures. https://hrsonline.isr.umich.edu/modules/meta/1993/core/codebook/codb-modtxt.htm#V2212. Accessed November 15, 2016.
30. Strauss A, Corbin J. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*, 2nd edn. Thousand Oaks: Sage Publications; 1997.
31. Bernard HR, Wutich A, Ryan GW. *Analyzing Qualitative Data: Systematic Approaches*, 2nd edn. Thousand Oaks, CA: SAGE publications; 2017.

32. Reese PP, Boudville N, Garg AX. Living kidney donation: outcomes, ethics, and uncertainty. *Lancet*. 2015;385(9981):2003-2013.
33. Hanson CS, Ralph AF, Manera KE, et al. The lived experience of "Being Evaluated" for organ donation: focus groups with living kidney donors. *Clin J Am Soc Nephrol*. 2017;12(11):1852-1861.
34. Agerskov H, Ludvigsen MS, Bistrup C, Pedersen BD. Living kidney donors' experiences while undergoing evaluation for donation: a qualitative study. *J Clin Nurs*. 2015;24(15-16):2258-2267.
35. Agerskov H, Ludvigsen MS, Bistrup C, Pedersen BD. Relieved or disappointed-experiences of accepted and rejected living kidney donors: a prospective qualitative study. *J Clin Nurs*. 2015;24(23-24):3519-3527.
36. Conrad NE, Murray LR. The psychosocial meanings of living related kidney organ donation: recipient and donor perspectives–literature review. *ANNA J*. 1999;26(5):485-490.
37. Simmons RG, Hickey K, Kjellstrand CM, Simmons RL. Family tension in the search for a kidney donor. *JAMA*. 1971;215(6):909-912.
38. Lennerling A, Forsberg A, Meyer K, Nyberg G. Motives for becoming a living kidney donor. *Nephrol Dial Transplant*. 2004;19(6):1600-1605.
39. Joint Working Party of the British Transplantation Society and the Renal Association. United Kingdon Guidelines for living donor kidney transplantation. Third Edition. May 2011. https://bts.org.uk/wp-content/uploads/2016/09/19_BTS_RA_Living_Donor_Kidney-1.pdf. Accessed August 1, 2018.
40. Walter JK, Ross LF. Relational autonomy: moving beyond the limits of isolated individualism. *Pediatrics*. 2014;133(Suppl 1):S16-S23.
41. Mackenzie C, Stoljar N, eds. *Relational Autonomy: Feminist Perspectives on Autonomy, Agency, and the Social Self*. New York, NY: Oxford University Press; 2000.
42. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*, 5th edn. New York, NY: Oxford University Press; 2013.
43. Lentine KL, Kasiske BL, Levey AS. et al. KDIGO clinical practice guideline on the evaluation and care of living kidney donors. *Transplantation*. 2017;101(8S Suppl. 1):S1-S109.
44. Allen MB, Reese, PP. The ethics of promoting living kidney donation using nonargumentative influence: applications, concerns, and future directions. *Am J Transplant*. 2016;16(12):3378-3384.
45. Garonzik-Wang JM, Berger JC, Ros RL, et al. Live donor champion: finding live kidney donors by separating the advocate from the patient. *Transplantation*. 2012;93(11):1147-1150.
46. Grams ME, Sang Y, Levey AS, et al. Kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med*. 2016;374(5):411-421.
47. Lentine KL, Schnitzler MA, Xiao H, et al. Racial variation in medical outcomes among living kidney donors. *N Engl J Med*. 2010;363:724-732.
48. Halverson CM, Wang JY, Poulson M, Karlin J, Crowley-Matoka M, Ross LF. Living kidney donors who develop kidney failure: excerpts of their thoughts. *Am J Nephrol*. 2016;43(6):389-396.
49. Fehrman-Ekholm I, Brink B, Ericsson C, Elinder CG, Duner F, Lundgren G. Kidney donors don't regret: follow-up of 370 donors in Stockholm since 1964. *Transplantation*. 2000;69(10):2067-2071.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Reese PP, Allen MB, Carney C, et al. Outcomes for individuals turned down for living kidney donation. *Clin Transplant*. 2018;32:e13408. https://doi.org/10.1111/ctr.13408