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Health-Related Quality of Life in Kidney Donors From the Last Five Decades: Results From the RELIVE Study

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Live donation benefits recipients, but the long-term consequences for donors remain uncertain. Renal and Lung Living Donors Evaluation Study surveyed kidney donors (N = 2455; 61% women; mean age 58, aged 24–94; mean time from donation 17 years, range 5–48 years) using the Short Form-36 Health Survey (SF-36). The 95% confidence intervals for White and African-American donors included or exceeded SF-36 norms. Over 80% of donors reported average or above average health for their age and sex ($p < 0.0001$). Donors' age–sex adjusted physical component summary (PCS) scores declined by half a point each decade after donation ($p = 0.0027$); there was no decline in mental component summary (MCS) scores. White donors' PCS scores were three points higher ($p = 0.0004$) than non-Whites'; this difference remained constant over time. Nine percent of donors had impaired health (PCS or MCS score >1 SD below norm). Obesity, history of psychiatric difficulties and non-White race were risk factors for impaired physical health; history of psychiatric difficulties was a risk factor for impaired mental health. Education, older donation age and a first-degree relation to the recipient were protective factors. One percent reported that donation affected their health very negatively. Enhanced predonation evaluation and counseling may be warranted, along with ongoing monitoring for overweight donors.

Keywords: Kidney, kidney donor, living donor, organ donation, quality of life

Abbreviations: AAHP, African-American Health Project; HRQOL, health-related quality of life; MCS, mental component summary; NHMS, National Health Measurement Survey; PCS, physical component summary; RELIVE, Renal and Lung Living Donors Evaluation Study; SF-36, Short Form-36 Health Survey

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Introduction

The benefits of living kidney donation to the recipient are well-established (1–2), but uncertainty remains regarding the long-term impacts on living donors (3). Studies have confirmed that surgical complication rates are low, and serious psychiatric sequelae are rare (4–6). Reports suggest that the majority of living donors experience levels of health-related quality of life (HRQOL) similar to or exceeding that of the general population (7–9). Nevertheless, it has been consistently shown that some donors (<5%) experience significant psychological distress or retain highly negative attitudes about donation (10,11). Information on the predictors and correlates of poor HRQOL outcomes is extremely limited (5), particularly for minority donors or the growing number of overweight donors (3,6,12–14).

The Renal and Lung Living Donors Evaluation Study (RELIVE) provided a unique opportunity to investigate the long-term HRQOL of living donors. RELIVE conducted an extensive chart review to identify all living donor surgeries performed from 1963 to 2005 at three large US transplant centers (15). Where possible, donor current address and phone contact information were derived from these records, and surviving donors requested to complete HRQOL questionnaires. The Short Form-36 Health Survey (SF-36) health survey (16) was included in this questionnaire because it is a standardized instrument with norms for US adults overall and grouped by

age and sex. SF-36 results from the African-American Health Project (AAHP) (17) provided nondonor comparison data for African-American donors. The study objectives were to provide a comprehensive analysis of the HRQOL of a large and representative sample of living kidney donors, and to identify predictors of poor long-term HRQOL outcomes. We hypothesized that donors' current HRQOL would be influenced by factors known at the time of donation, and also influenced by perceptions regarding the donation experience such as expected recovery time, time to resumption of usual activities and comfort with decision to donate, among other factors.

Methods

The RELIVE study was designed to evaluate the medical and HRQOL outcomes of living kidney donors at three large US transplant centers. Details about RELIVE have been published elsewhere (15).

Study design and population

An observational, cross-sectional survey of living kidney donors at least 5 years from time of donation was conducted. Enrollment is detailed in Figure 1. Medical records from all living kidney donor surgeries conducted at the three study sites (N = 8951) were reviewed. Surgeries performed after July 1, 2005 and known deaths were excluded, leaving 6909 potentially eligible donors (donation years 1963–2005). A study invitation letter was sent to each donor. If no response was received, a follow-up letter and at least two telephone calls were made by study coordinators. Although a fee-based Internet service was used to update address and phone numbers, current address and phone information could not be found for 13.6% (n = 938). Thirty-six percent overall (n = 2501) did not respond to any study contact attempts. This varied by race: 34% of White donors, 58% of African-American donors and 27% of donors of other or unknown race did not respond to any study contacts (Table S1). The true status of these donors is unknown; it is likely that some were passive refusals and others were never contacted. Fifty percent (n = 3470) of the potentially eligible donors were contacted: 2455 consented and completed a study questionnaire; 931 refused consent; 79 consented but failed to return the questionnaire and five were unable to participate due to a language barrier. Among those

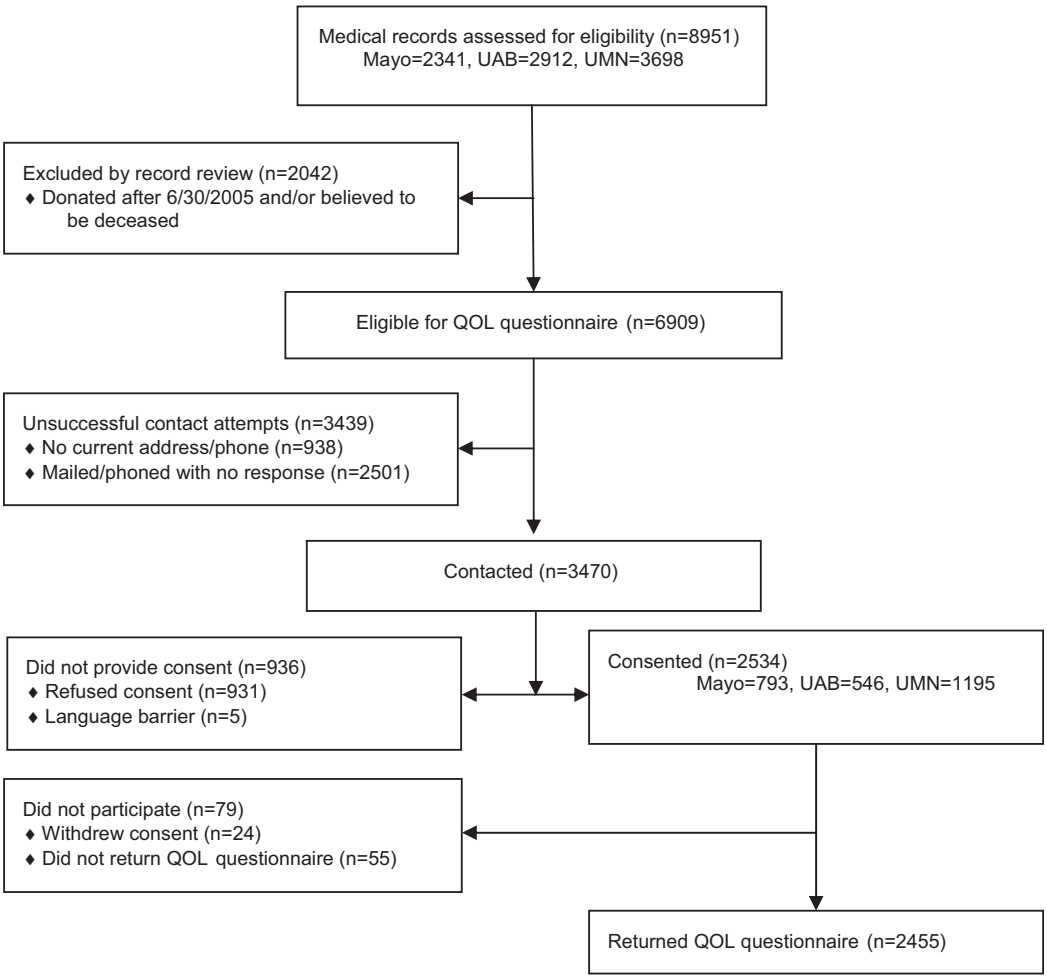


Figure 1: Enrollment flow diagram. This diagram describes how the sample of living organ donors who completed quality-of-life (QOL) questionnaires for this study (N = 2455) was derived from a comprehensive review of the medical records of all live donor kidney transplants conducted at three large clinical sites: University of Minnesota (UMN); The Mayo Clinic—Rochester, MN and University of Alabama, Birmingham (UAB).

contacted, rates of questionnaire completion were similar across transplant centers (67–76%) and for White and African-American donors (71% and 72%, respectively), and somewhat lower (65%) for donors of other or unknown race (Table S1). Participation rates diminished with increasing time from donor surgery, from 79% for procedures done since January 2000 to 55% for those done in the 1960s.

This study was approved by the institutional review boards of the transplant (UAB: IRB approval number X070604010; UMN: IRB approval number 0905M66501; Mayo: IRB approval number 09-001345) and data coordinating centers (IRB approval number CR00032674 and protocol number HUM00004345). Informed consent was given by each participant.

Data collection

HRQOL questionnaires were mailed, self-administered and returned in postage-paid envelopes. Questionnaires included the SF-36, version 2 (16,18), a self-assessment of day-to-day function and well-being over the previous 4 weeks in eight domains of HRQOL. Domain scores are standardized to the age and sex distribution of the US adult population and combined to form physical and mental component summary (PCS and MCS) scores. Higher scores indicate better health. SF-36 results were compared to the National Health Measurement Survey (NHMS) (19). Table S2 provides additional details about scoring and interpreting the SF-36.

Statistical analyses

Differences between respondents and nonrespondents by demographic characteristics, and differences among donors grouped by race, were examined using chi-square or Fisher's exact tests and one-way analyses of variance or rank tests for categorical and continuous predictors, respectively. Donors' SF-36 scores were compared to norms and other samples using t-tests and rank tests. Quantile regression estimated the impact of race, procedure (laparoscopic or open) and time from donation on sex-by-age adjusted PCS and MCS scores. Multivariable logistic regression analyses identified factors that predicted a poor HRQOL outcome. Factors known prior to the time of donation surgery were used to fit an initial prediction model using a best subsets approach. Additional models tested whether donation experience variables were associated with poor HRQOL, after adjustment for the initial model. Missing data were imputed using IVEware (20) and analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC). See the online supplement for statistical methodology details. A meaningful difference was defined as three points on the SF-36 MCS or PCS. Statistical significance was determined using a threshold of $p < 0.01$ to control Type I error and to focus on results where differences were most likely to be both statistically significant and clinically meaningful.

Results

RELIVE donors ($n = 2455$) were 15–74 years old at time of donation and 24–94 years old at time of study. The mean age at donation was 41 years, and women outnumbered men (61%). On average, 17 ± 10 years had elapsed since donation surgery. The majority of donors were White (93%), married (75%), educated beyond high school (77%) and working full (52%) or part-time (12%) (Table 1). Most were biologically related to their recipient as a sibling (41%), parent (18%) or child (13%). Nine percent were spouses. Seven percent were a friend of the recipient, and 6% were not a relative or friend of the recipient. Five percent of donors identified themselves as Black or African-American ($n = 113$), and 1% as Hispanic or Latino ($n = 31$). White donors were older than African-American donors, and were more likely to be currently married. Weight at time of donation, measured by body mass index (BMI), did not differ by race.

Compared to donors who declined study participation, RELIVE donors were slightly younger at donation (mean ages 40.5 vs. 41.5), donated more recently (16.3 vs. 19.5 years), had higher educational attainment at time of donation (56% vs. 39% educated beyond high school), and were more likely to be unrelated to their recipient (13% vs. 6%, all $p < 0.01$) (see Table S1).

To investigate the representativeness of our sample, we compared the demographics of RELIVE donors to 2009 US kidney donors, using data published in the OPTN/SRTR 2010 Annual Report (see Table S3). Although the mean age at donation was very close (about 41 years) and the percent of women (61%) was the same, substantially fewer RELIVE donors were African-American (5% vs. 12%) or Hispanic/Latino (1% vs. 14%) compared to the 2009 US donor data. Moreover, most of the African-American RELIVE donors (81%) had donated at a single site: the University of Alabama at Birmingham. Thus, the RELIVE donors are less ethnically diverse than current donors.

Donor HRQOL profile

Donors' SF-36 profile scores are shown in Figure 2. Donors reported significantly better function and well-being relative to the US adult population in all domains (Table 2, $p < 0.0001$ all). Overall physical and mental health were also higher (PCS scores, 51 ± 9, $p < 0.0001$; MCS scores, 53 ± 9, $p < 0.0001$). Compared to expected SF-36 profiles for people of their own sex and age, donors' scores were significantly higher ($p < 0.0001$, for all). Between 80% and 87% of donors' domain scores and 84% of their MCS and PCS values were in the average or above average range for their sex and age (Table 2).

The HRQOL profiles of White and African-American donors are shown in Figure 3. The 95% confidence intervals (CIs) for both White and African-American donors either included or exceeded US norms. White donors reported higher levels of social functioning than African-American donors ($p = 0.0007$); there were no other differences. Norms for people aged 55–64 are five points lower (worse health) on the PCS (unadjusted) than norms for those aged 35–44, yet these donors (current mean age 58) reported higher PCS values than the younger US population (1998 US census population: 51% women, mean age 35 years).

Comparisons to other US populations

Donor SF-36 scores are shown at the bottom of Figure 3, along with results from the NHMS and the AAHP (17,19). Most NHMS profile scores are higher than the SF-36 norms. Despite this, donors' profiles compared favorably with NHMS results. Donors' PCS, MCS and scores on 7 of 8

Table 1: Characteristics of donors, overall and grouped by self-reported race

	(n = 2455)	White or European American (n = 2282)	Race Black or African-American (n = 113)	Other or unknown (n = 60)
All donors	M (SD)	M (SD)	M (SD)	M (SD)
Age at donation*	41 (11)	41 (11)	36 (11)	38 (11)
Age at survey*	58 (11)	58 (11)	52 (10)	53 (12)
Years since donation	17 (10)	17 (10)	15 (8)	15 (8)
BMI at donation	26 (5)	26 (5)	27 (5)	26 (4)
	N (%)	N (%)	N (%)	N (%)
Female	1505 (61)	1403 (61)	71 (63)	31 (52)
Hispanic/Latino	31 (1)	18 (1)	0 (0)	13 (22)
Relationship of donor to recipient				
Parent	450 (18)	422 (18)	17 (15)	11 (18)
Child	316 (13)	283 (12)	21 (19)	12 (20)
Sibling	1011 (41)	942 (41)	50 (44)	19 (32)
Other relative	130 (5)	116 (5)	9 (8)	5 (8)
Spouse	219 (9)	208 (9)	8 (7)	3 (5)
Friend	173 (7)	165 (7)	4 (4)	4 (7)
Other unrelated	149 (6)	140 (6)	3 (3)	6 (10)
Missing	7 (0)	6 (0)	1 (1)	0 (0)
BMI at donation				
Less than 25	1092 (44)	1021 (45)	42 (37)	29 (48)
25–29.9	883 (36)	823 (36)	42 (37)	18 (30)
30–34.9	329 (13)	296 (13)	21 (19)	12 (20)
35 or higher	102 (4)	95 (4)	6 (5)	1 (2)
Missing	49 (2)	47 (2)	2 (2)	0 (0)
Type of surgical procedure				
Open	1630 (66)	1514 (66)	81 (72)	35 (58)
Laparoscopic	822 (33)	765 (34)	32 (28)	25 (42)
Unknown	3 (0)	3 (0)	0 (0)	0 (0)
Educational attainment at survey				
Less than high school	66 (3)	59 (3)	5 (4)	2 (3)
High school	497 (20)	468 (21)	16 (14)	13 (22)
Some college or tech school	920 (37)	846 (37)	50 (44)	24 (40)
College degree	510 (21)	477 (21)	22 (19)	11 (18)
Graduate degree	449 (18)	421 (18)	20 (18)	8 (13)
Missing	13 (1)	11 (0)	0 (0)	2 (3)
Marital status at survey*				
Married or living together	1852 (75)	1750 (77)	63 (56)	39 (65)
Separated, divorced or widowed	449 (18)	408 (18)	30 (27)	11 (18)
Never married	141 (6)	113 (5)	20 (18)	8 (13)
Missing	13 (1)	11 (0)	0 (0)	2 (3)
Employment at survey*				
Working full-time	1272 (52)	1181 (52)	67 (59)	24 (40)
Working part-time	299 (12)	280 (12)	7 (6)	12 (20)
Not working for pay	770 (31)	729 (32)	27 (24)	14 (23)
Unemployed	80 (3)	63 (3)	10 (9)	7 (12)
Missing	34 (1)	29 (1)	2 (2)	3 (5)
Transplant center*				
Mayo Clinic	773 (31)	748 (33)	6 (5)	19 (32)
University of Alabama	544 (22)	442 (19)	92 (81)	10 (17)
University of Minnesota	1138 (46)	1092 (48)	15 (13)	31 (52)
Recipient vital status (according to donor)				
Alive	1467 (60)	1368 (60)	67 (59)	32 (53)
Deceased	952 (39)	882 (39)	46 (41)	24 (40)
Unknown or missing	36 (1)	32 (1)	0 (0)	4 (7)
Recipient graft status (according to donor)				
Functioning	1060 (43)	997 (44)	41 (36)	22 (37)
Functioning, but with problems	98 (4)	87 (4)	7 (6)	4 (7)
Not functioning	307 (13)	283 (12)	19 (17)	5 (8)
Unknown or missing	990 (40)	915 (40)	46 (41)	29 (48)

*Significant differences between White and African-American donors, $p < 0.01$. Eight donors were missing information about ethnicity. Individuals not working for pay include homemakers, seasonal workers, retirees and students.

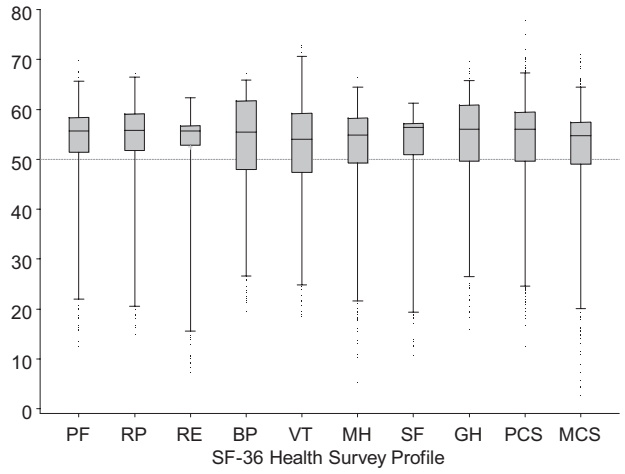


Figure 2: SF-36 profile of RELIVE donors. Boxplots display donor scores for all the scales in the Short Form-36 Health Survey (SF-36) profile. Higher scores indicate better health states. All SF-36 scales are standardized to have a mean of 50 and standard deviation of 10 in the US general population. A dotted line indicates the population mean on the y-axis. Boxes extend from the 25th to 75th percentiles; whiskers (vertical lines) extend from the 1st to the 99th percentiles. Physical component summary (PCS) score, mental component summary score (MCS), physical functioning (PF), impact of physical health on role functioning at home and at work (RP), bodily pain (BP), vitality (VT), general health perceptions (GH), social functioning (SF), impact of mental health on role functioning (RE) and mental health (MH).

domains were significantly higher or not different than NHMS results, and when the NHMS mental health score was higher, the difference was less than 1.2 points, below the SF-36 threshold for a clinically meaningful difference. HRQOL reports from African-American donors compared favorably to AAHP results, with donors reporting better general health perceptions ($p < 0.0001$), and no other differences.

Time from donation and HRQOL

Sex- and age-adjusted PCS and MCS scores are depicted against time from donation in Figure 4. In general, the most recent donors reported the highest PCS, while donors furthest away from donation reported the lowest scores. PCS declined by half a point with each decade after donation (slope [SE] = −0.54 [0.18] per decade, $p = 0.0027$). For comparison, a change in the PCS score from 51 (mean of this sample) to 50.5 (drop of half a point) represents moving from the 47th to the 45th percentile score in the US general population. There was not a statistically significant decline in MCS over time at the 0.01 level (slope [SE] = −0.32 [0.15] per decade, $p = 0.03$). White donors' PCS scores were three points higher than non-White donors' (beta [SE] = 3.02 [0.85], $p = 0.0004$), the threshold for a minimally important difference (16). This difference did not change over time (race by time interaction, $p = 0.11$). Race did not influence the trajectory of MCS scores over time (beta [SE] = 1.31 [0.81], $p = 0.11$). Procedure (laparoscopic vs. open) did not influence the trajectory of either PCS ($p = 0.31$) or MCS ($p = 0.73$) scores over time.

Donor self-rated health status

When donors were asked to rate their current health, the common responses were good (31.3%), very good (44.2%) or excellent (18.5%). Few donors selected fair (5.2%) or

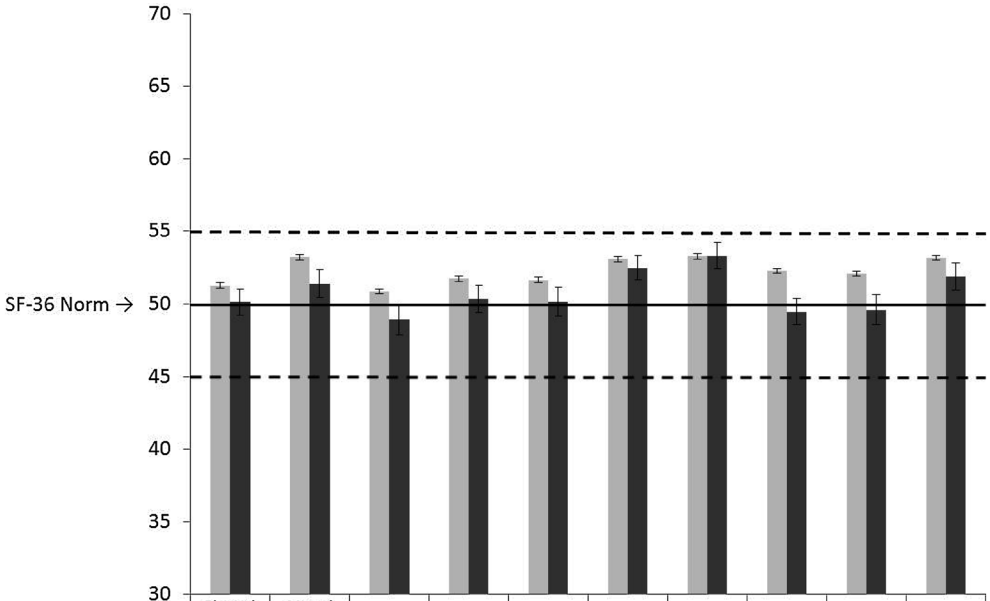
Table 2: RELIVE donors' Short Form-36 Health Survey (SF-36) profile and distribution of scores relative to US norms

SF-36 scores			Percent of donors with above or below average scores based on their sex and age (in 10-year categories)		
Scale	Mean[1,2]	SD	Below average (>5 points below), %	Average (within 5 points), %	Above average (>5 point above), %
PCS (N = 2415)	51	9	16	28	56
MCS (N = 2415)	53	9	16	37	47
PF (N = 2450)	51	9	14	29	57
RP (N = 2433)	52	9	14	23	63
BP (N = 2435)	52	10	20	30	50
GH (N = 2437)	53	9	15	32	54
VT (N = 2439)	53	9	19	31	49
SF (N = 2441)	52	9	14	19	68
RE (N = 2434)	52	8	13	26	61
MH (N = 2439)	53	9	17	33	50

Physical component summary (PCS) score and mental component summary (MCS) score, physical functioning (PF), impact of physical health on role functioning at home and at work (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), impact of mental health on role functioning (RE) and mental health (MH).

[1]Scores were transformed to have a mean of 50 and standard deviation of 10 in the general US population. Higher scores indicate better health states for all scales. All donor means are significantly different from SF-36 version 2 norms for the US general population: one-sample t-tests, p-values <0.0001, all.

[2]N = between 2415 for PCS and MCS and 2450 for PF. Missing values ranged from 5 (for PF) to 40 (for MCS and PCS).



RELIVE and other studies	Physical component score (N=2415)	Mental component score (N=2415)	Physical functioning (N=2450)	Role - physical (N=2433)	Bodily pain (N=2435)	General health (N=2437)	Vitality (N=2439)	Social functioning (N=2441)	Role - emotional (N=2434)	Mental health (N=2439)
NHIS study[18] (N=3,828)	49.22	53.78	50.68	49.47	50.66	50.10	53.71	51.37	51.44	54.27
RELIVE White (N=2,246)	51.28	53.23	50.87	51.75	51.67	53.11	53.30	52.29	52.10	53.18
RELIVE African American (N=111)	50.13	51.41	48.93	50.37	50.15	52.51	53.35	49.47	49.60	51.92
AAH project[15] (N=988)			48.95	47.14	48.26	46.62	52.13	48.53	48.96	51.82

Figure 3: SF-36 profiles of RELIVE White and African-American donors. Mean unadjusted Short Form-36 Health Survey (SF-36) scores of White and African-American donors are shown as bars. Race data were obtained by self-report. The horizontal solid line marks the population norm, and dotted lines mark ±0.5 SD (the range for average scores). White donors had higher scores for social functioning than African-American donors ($p = 0.0007$); other SF-36 scores were not significantly different at $p = 0.01$. Mean scores for RELIVE donors and two comparison groups are presented below the chart. Results from the National Health Measurement Survey (NHMS), a representative telephone survey of US adults 35–89 years old conducted in 2005–2006 (19), are shown in the first line. RELIVE donors' (all races combined) SF-36 scores were significantly higher than NHMS results for the PCS, role physical, bodily pain, general health perceptions and social functioning (p's from 0.006 to <0.0001); scores for physical functioning, vitality, role emotional, and the MCS did not differ; and NHMS mental health results were higher than RELIVE donors' scores ($p < 0.0001$). Results from the African-American Health Project (AAHP), a population-based, in-home survey of 998 African-American adults aged 49–65 living in Missouri conducted 2000–2001 (17), are shown in the bottom line beneath the chart. SF-36 overall and domain scores of African-American donors and AAHP participants were not significantly different, except for general health perceptions, where African-American donors reported higher scores ($p < 0.0001$).

poor (1%). Reports of fair or poor health are more common in the US population, 12.1% and 3.4%, respectively (19). Figure 5 shows the proportions of RELIVE donors with excellent or very good self-rated health by race and education (used here as a surrogate for socioeconomic status), and comparable rates for US White and African-American adults. After adjustment for education, White donors remained more likely to report excellent or very good health than either African-American donors ($p = 0.0034$) or donors of other races ($p = 0.0004$). Education was strongly correlated with self-rated health among US adults, White donors and donors of other or unknown race, but not among African-American donors.

Most donors reported that donation had no impact on their general health (73%). The remaining donors reported very positive (10%), somewhat positive (6%), somewhat negative (10%) or very negative (1%) impacts. Perceived impact of donation on health was related to race and to self-rated health ($p < 0.0001$, both). Donors of other or unknown race perceived a very negative health impact more often than White or African-American donors (6.8% vs. 0.8% and 2.7%, respectively). Despite perceiving a very negative impact of donation on their health, these donors rated their current health as reasonably good: excellent (4%), very good (8%), good (52%), fair (20%) or poor (12%), with missing data for one donor. In response to questions about their donation experience, about half ($n = 11$ of 25) reported medical complications and/or emotional, psychological or substance abuse difficulties as a result of donation, and five reported that they never recovered from donor surgery. The others (14 of 25) did not report these problems; they resumed usual daily activities (e.g. driving, shopping for groceries) less than 3 months after donor surgery, and reported no medical complications or emotional, psychological or substance abuse difficulties as a result of donation.

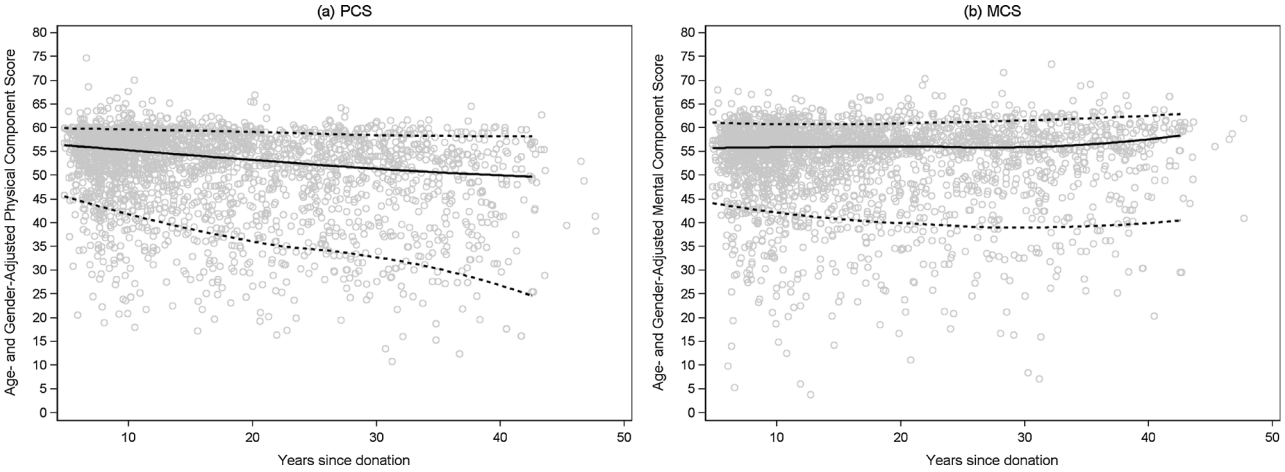
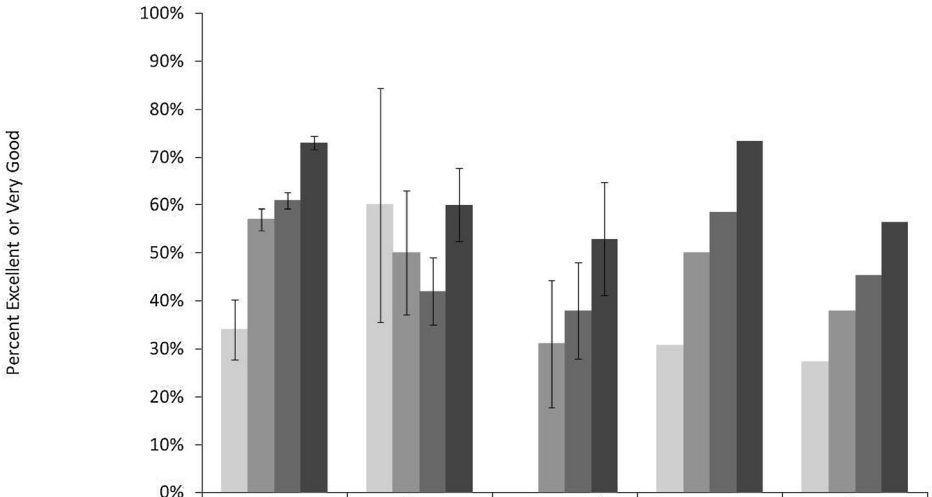


Figure 4: Sex- and age-adjusted PCS and MCS scores of RELIVE donors by time from donor surgery. Each donor's sex- and age-adjusted physical and mental component summary (PCS and MCS) score is plotted by time from donor surgery in years in this scatterplot. Data points above the norm mean (50) on the y-axis indicate donors with better health and functioning than peers of the same age and sex. The solid line is a loess curve fitted to the observed median score, and the dotted lines follow the 5th and 95th percentiles at each point in time. The overall adjusted PCS and MCS scores are 54 ± 9 (range 13–78) and 52 ± 9 (range 3–71), respectively. RELIVE, Renal and Lung Living Donors Evaluation Study.



	White Donors (n=2282)	African American Donors (n=113)	Donors of Other Race (n=60)	US White Adults	US African-American Adults
Less than high school	34%	60%	0%	31%	27%
High school graduate	57%	50%	31%	50%	38%
Some college	61%	42%	38%	59%	45%
4-yr college degree	73%	60%	53%	73%	56%

Figure 5: Proportions of donors reporting ''excellent'' or ''very good'' health, according to race and education and comparable data for US White and African-American adults. Bar heights indicate the proportion of donors reporting excellent or good health within four categories of educational attainment: less than high school, high school graduate, some college or 4-year college graduate. Vertical lines atop the bars indicate ± 1 standard error. The last eight bars are comparable data on self-reported health by educational attainment for US White and African-American adults aged 25–74 from the 2005 to 2007 Behavioral Risk Factor Surveillance Systems as reported by Braveman et al (24). Standard errors are not provided for the US population estimates because they have been weighted to reflect the entire population. Sixteen donors with missing values for education or self-rated health status were omitted. After adjustment for education, White donors were more likely to report excellent or very good health than either African-American donors or donors of other races ($p = 0.0034$ and $p = 0.0004$, respectively). Overall, patterns of self-rated health status are similar for donors and US adults.

Predictors of impaired HRQOL

Nine percent of donors (n = 211) had significantly impaired physical HRQOL, scoring more than 10 points below their sex-by-age adjusted PCS norm (see Table S2). These individuals would typically be unable to do vigorous activity, have difficulty working and/or have pain or other chronic conditions. Nine percent of donors (n = 233) had significantly impaired mental HRQOL based on the MCS. These individuals would typically have depressed or anxious moods some or most of the time, impacting their ability to socialize and function at work or home.

Predonation obesity, history of psychiatric difficulties and race were independent risk factors for impaired physical HRQOL, after adjustment for time since donation (Table 3). The influence of excess body weight is supported by evidence of a dose–response relationship. Donors with a BMI of 35 or higher at time of donation had more than four times the risk (OR = 4.32), donors with a BMI of 30–34.9 had nearly triple the risk (OR = 2.85), and donors with a BMI of 25–29.9 had almost double the risk (OR = 1.84) of impaired physical HRQOL compared to other donors. History of psychiatric difficulties predonation more than doubled (OR = 2.46) the risk of being in the impaired group. Non-White donors were also about twice as likely (OR = 2.05) to be in the impaired group. Although the likelihood of impaired physical HRQOL was associated with race, this risk was stable over time from donation. On the other hand, higher educational attainment at time of donation and first-degree relationship to the recipient were independent protective factors. For each additional level of education, the odds of having significant physical HRQOL impairment decreased by about 25% (OR = 0.77). First-degree relatives were half as likely as more distant relations or unrelated donors to have significant physical HRQOL impairment.

After adjustment for the factors listed above, the following aspects of the donation experience were associated with increased risk of impaired physical HRQOL: estimated time to recover from surgery, longer than expected recovery time, longer time to resumption of usual activities, feeling depressed or ignored and medical or psychological difficulty after donation. With each increment of time to resumption of usual activities, the adjusted risk of impaired physical HRQOL increased threefold (OR = 3.05). Perceptions of strong support from health providers, family and friends throughout the donation process were protective. Donors who reported positive impacts of donation on their health were also less likely to have impaired physical HRQOL.

History of psychiatric difficulties prior to donation more than tripled the risk of impaired mental HRQOL (OR = 3.82), after adjustment for time (Table 3). Being older at time of donation and having more education were protective. After adjustment for these predictors, increased risk of impaired mental HRQOL was associated with: time to recovery from surgery, time to resumption of usual activities, feeling depressed or ignored and medical or psychological difficulty after donation. Factors associated with reduced risk were positive perceptions of the donation experience, support from health providers, family and friends, comfort with decision to donate, positive impacts of donation on health and current education and marital status. Factors not associated with impaired HRQOL are listed in Table S4.

Discussion

The kidney donors in the present study reported better physical and mental functioning and well-being than their counterparts in the general US population. With a larger sample and longer-term follow-up (average 17 years), these results confirm and extend earlier reports from single-center series (5,8,21) and recent international studies (7,9). Worldwide, about 27 000 living kidney donations are performed each year (22). In Norway, Mjoen et al (9) surveyed 1414 donors who were on average 12.6 years from donation. These donors reported better HRQOL on all SF-36 domains compared to a population-based sample of adult Norwegians. An international collaborative (7) compared the HRQOL of nondonor controls to donors (N = 203) who were on average 5.5 years from donation and found no differences in SF-36 scores.

This study presents new information on the outcomes of African-American kidney donors. African-American donors' SF-36 scores compared favorably to norms and results from a population-based sample of African-American adults (17), and were generally similar to White donors' scores. After adjustment for age and sex, White donors had better overall physical functioning than non-White donors, but trends over time from donation did not differ by race, indicating that non-White donors did not have an accelerated decline in function or well-being in the decades following donation compared to White donors. These findings are reassuring, given evidence from administrative databases that African-American and Hispanic donors have higher risks of developing hypertension, diabetes and chronic kidney disease after donation than White donors, although not higher rates than minority nondonors (23).

It has been shown that differences in self-rated health are closely linked to socioeconomic status (24), and therefore, we expected donors with greater educational attainments to rate their current health higher than those with less education. This was true for White donors, but not for African-American donors. Reasons for this are unknown, but we are mindful that the majority of the RELIVE African-American donors hail from a single center and may differ from African-American donors elsewhere in ways we were unable to assess.

A novel finding from our work is the long-term HRQOL impact of excess body weight in otherwise healthy adults. We did not have current BMI information, and could not determine if donor BMIs increased or decreased in the years

Table 3: Multivariable logistic regressions predicting significantly impaired physical HRQOL[1] and mental HRQOL[2]

	Physical HRQOL impairment (n = 211 out of 2455)			Mental HRQOL impairment (n = 233 out of 2455)		
	OR	95% CI	p-Value	OR	95% CI	p-Value
(1) Model based on predonation characteristics						
Age at donation, per 10 years[3]	–	–	–	0.74	(0.65, 0.86)	<0.0001
10 years after donation[3,4]	4.38	–	*	2.86	–	**
20 years after donation[3,4]	11.30	–	–	5.47	–	–
30 years after donation[3,4]	17.14	–	–	6.97	–	–
40 years after donation[3,4]	15.29	–	–	5.92	–	–
Non-White (ref: White)	2.05	(1.27, 3.30)	0.0034	–	–	–
First-degree relative of recipient (ref: extended relation or not related)	0.54	(0.36, 0.80)	0.0025	–	–	–
BMI 25–29.9 (ref: <25)[4]	1.84	(1.31, 2.65)	0.0005	–	–	–
BMI 30–34.9 (ref: <25)[4]	2.85	(1.84, 4.42)	<0.0001	–	–	–
BMI ≥35 (ref: <25)[4]	4.32	(2.37, 7.87)	<0.0001	–	–	–
Education at donation (continuous, 5 levels)[4]	0.77	(0.64, 0.91)	0.0027	0.81	(0.70, 0.95)	0.0092
History of psychiatric difficulties prior to donation (ref: no history or unknown)[3,4,5]	2.46	(1.57, 3.84)	<0.0001	3.82	(2.61, 5.60)	<0.0001
Model 1 plus the following, entered one at a time						
Overall donation experience (poor – excellent)	0.79	(0.68, 0.92)	0.0024	0.67	(0.59, 0.77)	<0.0001
Recovery time compared with expected (shorter – longer)	1.26	(1.10, 1.44)	0.0008	–	–	–
Overall recovery time (<3 months – never)	1.63	(1.31, 2.02)	<0.0001	1.87	(1.53, 2.28)	<0.0001
Recovery time for daily activities (<3 months – never)[3,4]	3.05	(2.26, 4.12)	<0.0001	2.81	(2.11, 3.75)	<0.0001
I felt depressed for a while after the surgery	1.38	(1.22, 1.56)	<0.0001	1.49	(1.33, 1.67)	<0.0001
Once surgery was over, no one paid attention	1.31	(1.15, 1.49)	<0.0001	1.51	(1.34, 1.69)	<0.0001
There was support available to me from the healthcare providers	0.80	(0.71, 0.89)	0.0001	0.72	(0.65, 0.80)	<0.0001
My family or friends supported me throughout the donor surgery	0.78	(0.67, 0.90)	0.0007	0.69	(0.61, 0.79)	<0.0001
Comfort now with the decision to donate	–	–	–	0.64	(0.52, 0.78)	<0.0001
Self-reported complication (ref: no, unknown)	1.92	(1.39, 2.64)	<0.0001	2.26	(1.68, 3.03)	<0.0001
How did your donation affect your general health? (Very negatively – very positively)[3]	0.68	(0.55, 0.84)	0.0002	0.52	(0.42, 0.64)	<0.0001
Married or partnered at questionnaire completion	–	–	–	0.64	(0.47, 0.86)	0.0032
Educational attainment at questionnaire completion[3]	–	–	–	0.60	(0.48, 0.76)	<0.0001

HRQOL, health-related quality of life; MCS, mental component summary; PCS, physical component summary.
Data were missing for less than 5% of donors for all variables except educational attainment at donation (missing for 19%); missing values were multiply imputed using the sequential regression imputation method.
[1]Significantly impaired physical HRQOL was defined as a PCS >−1 SD below sex-by-age norms (n = 211 out of 2455) 9% of the sample.
[2]Significantly impaired mental HRQOL was defined as an MCS >−1 SD below sex-by-age norms (n = 233 of 2455) 9% of the sample.
[3]These variables remained significant ($p < 0.01$) when all variables in this table were simultaneously included in the mental HRQOL model (c-statistic = 0.760). Mental HRQOL base model c-statistic = 0.660. Additional model c-statistics for mental HRQOL with covariates were = 0.670–0.705.
[4]These variables remained significant ($p < 0.01$) when all variables in this table were simultaneously included in the physical HRQOL model (c-statistic = 0.762). Base Model Physical HRQOL c-statistic = 0.704. Additional model c-statistics for Physical HRQOL with covariates were 0.715–0.741.
[5]History of psychiatric difficulties was ascertained from medical records from the time of donation and included mentions of depression, anxiety, bipolar disorder, posttraumatic stress disorder and other psychiatric diagnoses.
*Physical HRQOL: time since donation, $p < 0.0001$; time since donation squared, $p = 0.0010$.
**Mental HRQOL: time since donation, $p = 0.0003$; time since donation squared, $p = 0.0095$.

since donation, but *obesity at time of donation* increased risk of significant physical impairment (PCS) between 5 and 48 years later. The credibility of this finding is supported by a graded relationship: the higher the BMI category, the greater the risk. When BMI and the SF-36 are measured concurrently, worse physical HRQOL (PCS) is consistently reported by the obese and overweight, compared to those in the normal weight range (25,26). Bodily pain and mobility are

most often negatively affected by obesity. The relationship between weight and mental HRQOL is more nuanced. Longitudinal cohort studies and weight loss trials generally find that gaining weight diminishes physical HRQOL, and losing weight improves both physical and mental HRQOL. Our findings for overweight and obese donors may have important implications for the future HRQOL of all adults who are currently overweight, but otherwise healthy (e.g. have no major comorbidities).

The association of predonation obesity (BMIs >30) with adverse long-term HRQOL is also notable in light of recent trends to accept heavier donors in the United States. Although the proportion of very obese donors (BMIs >35) changed little between 1999 and 2009 (from 2% to 3.1%), the proportion of obese donors (BMIs >30–35) more than doubled (from 8% to 21.8%) during this interval (3). Increased follow-up and study of these donors is warranted. Our findings also add support to current practices of excluding very obese donors, given higher surgical complication rates, the natural history of metabolic syndrome and recent evidence of poor long-term medical outcomes (14). Nogueira et al (14) found 42% of obese kidney donors (N $=36$, average 7 years postdonation) were hypertensive and 47% had compromised renal function.

Donor experience of long recovery time, complications and low donor support and attention were associated with impaired function and well-being many years after donation. These associations suggest that initiatives to improve the donor experience should be seriously considered.

In the past, it has been difficult to identify robust predictors of poor HRQOL among donors (5), and center differences, small sample sizes and limited follow-up have been identified as contributing to this problem. Varying definitions of HRQOL may also contribute, as we found differences in the predonation factors that predicted physical versus mental HRQOL impairment. Notably, obesity and non-White race were risk factors specifically for impaired physical HRQOL and older age at donation was specifically associated with reduced risk of impaired mental HRQOL. Donor history of psychiatric difficulties (donor chart documentation of history or treatment for depression, anxiety, posttraumatic stress disorder or other disorders), which has been regularly identified as a risk factor for poor outcomes (5,27,28), was a risk factor for both poor physical and mental HRQOL in our sample.

The main strength of RELIVE is its size, multi-center collaboration and length of follow-up. Limitations include the absence of predonation HRQOL data, and substantial under-representation of minority donors. Although 9.6% of donors in our study eligibility window were African-American, proportionately fewer African-Americans than White donors responded to study contacts, and as a result, African-Americans comprised only 5% of the RELIVE donor sample. Fewer than 2% of the donors in our eligibility window were Hispanic or Latino, and these donors were also less likely than White donors to respond to study contacts. In retrospect, greater efforts should have been made to devise more effective approaches for contacting minority donors. Overall, only 50% of the donors whose surgeries were identified from medical records responded to study contact attempts. No current contact information was available for over 900 donors, despite use of a fee-based Internet search service to locate current addresses and phone numbers. These limitations reflect the ambitious nature of securing follow-up as long as 50 years after donation. Finally, it should be kept in mind that RELIVE donors are from three centers, and are not a representative national sample.

A number of factors, in addition to race, differed between donors who did and did not participate in RELIVE, including age, education, time from donation and relationship to the recipient. Because our primary HRQOL results were age-adjusted and effects of all these factors were estimated in multivariate analyses, we do not believe that these factors served to bias our findings.

In conclusion, the majority of living kidney donors maintain average or above average HRQOL over the long term. Findings suggest potential donors who are overweight or obese, less educated, have prior psychiatric difficulties, are not White, or not first-degree relatives of the recipient represent groups at risk for poor HRQOL. New or enhanced efforts of predonation counseling and education, particularly weight loss counseling, and postdonation monitoring efforts could improve outcomes of these donors.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

References

1. Matas AJ, Payne WD, Sutherland DE, et al. 2,500 living donor kidney transplants: A single-center experience. Ann Surg 2001; 234: 149–164.
2. OPTN. 2012; Survival of kidney recipients by donor type—Living or cadaveric. Available at: http://optn.transplant.hrsa.gov/latestData/rptStrat.asp. Accessed June 18, 2012.

3. Leichtman A, Abecassis M, Barr M, et al. Living kidney donor follow-up: State-of-the-art and future directions, conference summary and recommendations. Am J Transplant 2011; 11: 2561–2568.
4. Abecassis M, Adams M, Adams P, et al. Consensus statement on the live organ donor. JAMA 2000; 284: 2919–2926.
5. Dew MA, Switzer GE, DiMartini AF, Myaskovsky L, Crowley-Matoka M. Psychosocial aspects of living organ donation. In: Tan HP, Marcos A, Shapiro R, eds. *Living donor transplantation*. New York: Informa Healthcare USA, Inc., 2007, pp. 7–26.
6. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. JAMA 2010; 303: 959–966.
7. 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: 463–469.
8. Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of kidney donation. N Engl J Med 2009; 360: 459–469.
9. Mjoen G, Stavem K, Westlie L, et al. Quality of life in kidney donors. Am J Transplant 2011; 11: 1315–1319.
10. Simmons RG, Marine SK, Simmons RL, eds., *Gift of life: The effect of organ transplantation on individual, family and societal dynamics*. 2nd ed. New Brunswick, NJ: John Wiley & Sons, 1987.
11. Feltrin A, Pegoraro R, Rago C, et al. Experience of donation and quality of life in living kidney and liver donors. Transpl Int 2008; 21: 466–472.
12. Gibney EM, King AL, Maluf DG, Garg AX, Parikh CR. Living kidney donors requiring transplantation: Focus on African Americans. Transplantation 2007; 84: 647–649.
13. Nogueira JM, Weir MR, Jacobs S, et al. A study of renal outcomes in African American living kidney donors. Transplantation 2009; 88: 1371–1376.
14. Nogueira JM, Weir MR, Jacobs S, et al. A study of renal outcomes in obese living kidney donors. Transplantation 2010; 90: 993–999.
15. Taler SJ, Messersmith EE, Leichtman AB, et al. Demographic, metabolic, and blood pressure characteristics of living kidney donors spanning five decades. Am J Transplant 2013; 13: 390–398.
16. Ware JE, Kosinski M, Bjorner JB, Turner-Bowker DM, Gandek B, Maruish ME. *User's manual for the SF-36v2 Health Survey*. 2nd ed. Lincoln, RI: QualityMetric Incorporated, 2007.
17. Wolinsky FD, Miller DK, Andresen EM, Malmstrom TK, Miller JP. Health-related quality of life in middle-aged African Americans. J Gerontol B Psychol Sci Soc Sci 2004; 59: S118–S123.
18. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30: 473–483.
19. Maglinte GA, Hays RD, Kaplan RM. US general population norms for telephone administration of the SF-36v2. J Clin Epidemiol 2012; 65: 497–502.
20. Raghunathan TE, Solenberger P, Van Hoewyk J. *IVEware: Imputation and variance estimation software users guide*. Ann Arbor, MI: Institute for Social Research, University of Michigan, 2002.
21. Clemens KK, Thiessen-Philborrk H, Parikh CR, et al. Psychosocial health of living kidney donors: A systematic review. Am J Transplant 2006; 6: 2965–2977.
22. Horvat LD, Shariff SZ, Garg AX. Global trends in the rates of living kidney donation. Kidney Int 2009; 75: 1088–1098.
23. 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.
24. Braveman PA, Cubbin C, Egerter S, Williams DR, Pamuk E. Socioeconomic disparities in health in the United States: What the patterns tell us. Am J Public Health 2010; 100 (Suppl 1): S186–S196.
25. Fontaine KR, Barofsky I. Obesity and health-related quality of life. Obes Rev 2001; 2: 173–182.
26. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity (Silver Spring) 2013; 21: E322–E327.
27. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. Transplantation 2006; 81: 1268–1273.
28. Rowley AA, Hong BA, Martin S, et al. Psychiatric disorders: Are they an absolute contraindication to living donation? Prog Transplant 2009; 19: 128–131.

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1: Characteristics of donors eligible for RELIVE and demographic comparisons between participating and nonparticipating donors, among those with confirmed study contact

Table S2: Scoring and Interpretation the SF-36 version 2 Health Profile based on the User's Guide by Ware et al (16)

Table S3: Comparisons between RELIVE Donors and US 2009 Kidney Donors

Table S4: Variables tested but not included in the HRQOL models because they were not significant