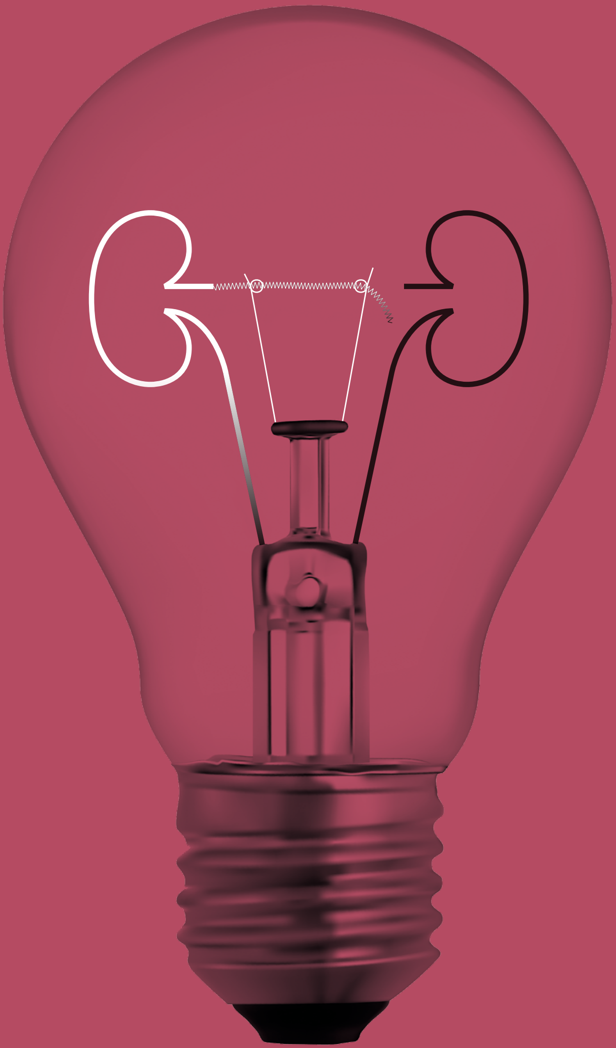
Exploring the mental health of living kidney donors



Lotte Timmerman

Exploring the

Onderzoek naar de

mental health

geestelijke gezondheid

# of living

van levende nierdonoren

kidney donors

Lotte Timmerman

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Exploring the Mental Health of Living Kidney Donors

Onderzoek naar de geestelijke gezondheid van levende nierdonoren

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Introduction

Living kidney donation has become an important treatment option for patients with chronic kidney disease. Chronic kidney disease is defined as either kidney damage or a decreased kidney functioning (indicated by glomerular filtration rate, GFR) for at least three months[1]. If a person has a GFR less than 15 the person is classified as being in the worst stage of chronic kidney disease labelled ‘kidney failure’, which is mostly accompanied with symptoms like fatigue, pruritus, and haematuria[1,2]. Such patients require renal replacement therapy, either dialysis or a kidney from a deceased or living person. Transplantation from a living person is the best option, as this treatment is associated with a higher survival rate[3], higher quality of life[4,5], and lowest costs[6,7] in comparison with dialysis and transplantation with a kidney from a deceased person.

Healthy persons who are motivated to donate one of their kidneys to an emotionally and/or genetically related person (specified donors) or to an anonymous and unknown person on the waiting list (unspecified donors) make living donor kidney transplantations possible[8]. Although some have argued that operating on a healthy person in order to help another person goes against the medical ethical principle of primum non nocere or ‘first do no harm’[9], it is justified for two reasons. Firstly, the benefits for the recipients as mentioned above are a justification and the presumed indirect benefits for the donors, i.e., a donor may benefit from the physical recovery of their loved one in terms of increased quality of life[10,11]. Secondly, donors’ choice for donation is justified by the right to autonomy, which stipulates that individuals have the right to determine what they do and what happens to their body[12].

In order to enhance the balance between risks and benefits for living kidney donors, it is important that the risks of negative medical and psychological consequences are minimized after donation. The short-term medical outcomes for living kidney donors are well documented: the overall mortality rate is 0.03%[13,14], and the morbidity rate (including minor complications) is < 10%[15]. Although two recent studies showed an increased risk of kidney failure and mortality among living kidney donors on the long term after donation[16,17], the majority of studies revealed that donors have a normal life span and an excellent quality of life many years after donation[15,18-20]. In addition, many medical risk factors have been identified which form the basis of medical screening guidelines[15,18,21,22].

In contrast to the physical outcomes, little is known about the psychological impact of living kidney donation and how potential and actual donors should be supported in order to enhance positive psychological outcomes. For example, in the past decades many psychosocial screening guidelines have been developed for potential donors (e.g. [23,24,25]), however the necessity for such a screening has not been demonstrated empirically. Research to date investigated the impact of living kidney donation on different aspects of mental health: quality of life, psychological distress, depression, anxiety, and personal benefit. The overall conclusion of these studies is that the different aspects of mental health of most donors appear unchanged after donation, while mental health increases or decreases in a small percentage of the donors [26-36]. However, a number of studies found mixed results. For instance, in two prospective studies depressive symptoms were found to decrease after donation [26,35], while two other studies found an increase in depressive symptoms over time [37,38]. These contradictory results could be the consequence of methodological limitations, such as the lack of a prospective design [29,32,36] and a suitable control group [26-36]. Another limitation of studies to date is measurement of individual facets of mental health, such as depression and anxiety [26-36], instead of overall mental health. The most comprehensive way to measure mental health is to include both positive and negative aspects, defined as wellbeing and psychological symptoms respectively [39], which is in line with the definition of 'mental health' of the World Health Organization [40]. Another question that remained unanswered is whether changes found in donors' mental health are due to the donation process or reflect fluctuations that are also observed in the general population. Methodologically stronger studies that investigate changes in donors' overall mental health between predonation and postdonation and compare variation over time with changes observed in the general population are warranted in order to give more insight into the psychological impact of living kidney donation and the necessity of a psychosocial screening.

Another gap in the literature relates to the factors that have an influence on change in donors' mental health during the donation process. In the past decades, many psychological factors were included in psychosocial screening guidelines, however the content of these guidelines differ. Moreover, none of the individual components are based on evidence regarding the relationship between each component and change in donors' mental health. A comparison of the various psychosocial screening guidelines that have been developed to date would be beneficial to get insight into the components that are most often proposed by professionals. Subsequently, it is important to know more about the predonation characteristics of donors who could be classified as at risk of negative psychological outcomes after donation. For instance, it would be beneficial to know which donors have extreme expectations prior to donation, as various professionals suggested that expectations should be included in the psychosocial screening of potential living donors[35,41]. A subsequent question is whether the screening criteria and donors' characteristics are related to change in donors' mental health. A limited number of studies have found that donors' mental health is related to the following components at one time-point in the donation process: expectations regarding personal consequences of the donation process[41], knowledge about living donation[42], social support[43], and coping style[44]. However, due to the cross-sectional design of these studies it is unknown whether these factors predict change in donors' mental health. In addition, these studies are not theoretically underpinned and therefore potentially important psychological concepts may have been missed. Factors such as appraisals or thoughts about the donation process and life events could also have an influence on donors' mental health, based on models that describe the factors that have an influence on the psychological impact of an event[45,46]. Other unanswered questions are whether the donors' and recipients' medical process and socio-demographic characteristics have an influence on change in donors' mental health and whether specified and unspecified donors differ in change in mental health. To summarize, more research is warranted to identify donors who are at risk of negative psychological outcomes during and after donation in order to optimize and tailor psychological support/screening for living kidney donors.

aims and outline of this thesis

There were two main aims of this thesis:

1 To examine whether there was a change in mental health between predonation and postdonation among living kidney donors.

2 To identify the socio-demographic, psychological, and medical factors that have an influence on (change in) living kidney donors' mental health.

The current thesis describes various studies that attempt to achieve the aforementioned aims:

Chapter 2 describes a review of the literature on psychosocial screening practices among living donors. This chapter also provides an overview of the gaps in literature on factors that influence donors' mental health.

Chapter 3 provides an exploration of donors who have extreme expectations before living kidney donation.

Chapter 4 describes whether prospective living kidney donors and recipients are sufficiently informed about dialysis, transplantation, and living donation one day before their surgery, and the characteristics of donors and recipients who lacked knowledge.

Chapter 5 describes a study that examined whether there was a change in psychological symptoms among unspecified living kidney donors between predonation and postdonation.

Chapter 6 includes a review of the literature on differences between specified and unspecified living kidney donors in psychological outcomes after donation and an elaboration on whether there is evidence for additional screening of unspecified living kidney donors.

Chapter 7 describes the changes in donors' mental health between predonation and one year postdonation and an examination of whether these changes differ from fluctuations observed in a matched-control group from the general population.

Chapter 8 describes whether the complexity of the medical process among living kidney donors and their recipients has an influence on donors' mental health.

Chapter 9 describes whether appraisals, expectations, knowledge, social support, coping, and life events have an influence on (change in) donors' mental health.

Chapter 10 provides a general discussion and clinical recommendations.

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2

Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review

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Transplant International 2014; 27: 2-18

abstract

Evaluating a person's suitability for living organ donation is crucial, consisting not only of a medical but also of a thorough psychosocial screening. We performed a systematic literature review of guidelines, consensus statements, and protocols on the content and process of psychosocial screening of living kidney and liver donor candidates. We searched PubMed, Embase, CINAHL, and PsycINFO until June 22, 2011, following the PRISMA guidelines, complemented by scrutinizing guidelines databases and references of identified publications. Thirty-four publications were identified, including seven guidelines, six consensus statements, and 21 protocols or programs. Guidelines and consensus statements were inconsistent and lacked concreteness for both their content and process, possibly explaining the observed variability in center-specific evaluation protocols and programs. Overall, recommended screening criteria are not evidence-based and an operational definition of the concept 'psychosocial' is missing, causing heterogeneity in terminology. Variation also exists on methods used to psychosocially evaluate potential donors. The scientific basis of predonation psychosocial evaluation needs to be strengthened. There is a need for high-quality prospective psychosocial outcome studies in living donors, a uniform terminology to label psychosocial screening criteria, and validated instruments to identify risk factors.

introduction

Although there are substantial benefits for living donor recipients (e.g., reduced waiting times, better survival)[1-2], the benefits of donating are less straightforward as this provides no direct physical benefit and may even carry certain peri- and postoperative risks for the donor's health and safety[3-4]. On the other hand, a donor might gain psychosocially from an increased self-esteem or a potentially improved relationship with the recipient[5,6]. Recent systematic reviews show that, once recovered from the immediate surgical effects, the donors' wellbeing is equal or even better when compared with the general population[5-7]. Yet, there is growing evidence that donors might also experience psychosocial difficulties post-donation, like depression (5-23%), anxiety (6-14%), stress (6-22%), and worries about health (6-50%) as reported in a systematic review[5]. In case of adverse recipient outcomes, single studies show that donors might also have feelings of waste (13%), guilt (5%), and even suicidal ideation (11%)[5]. Although these percentages are small, the burden of such events in otherwise healthy donors should not be underestimated and conflict with the nonmaleficence principle (Primum non nocere). Consequently, professionals always need to trade-off potentially positive and negative aspects of living donation by healthy persons. It is therefore clear that all efforts are needed to protect the donor from medical or psychosocial harm. A careful thorough predonation medical and psychosocial evaluation helps to balance the benefits and risks, and is indispensible to minimize undesirable outcomes postdonation.

An increasing number of medical evaluation protocols have been published, highlighting the importance of and growing consensus on the content of the predonation medical evaluation. Given the risk for adverse psychosocial outcomes[5], the transplant community agrees that, similar to the medical evaluation, the predonation psychosocial evaluation is also an essential component of the process to determine a person's suitability for donation. Despite this consensus, the format of this evaluation has been the subject of much debate, materialized in many different guidelines on the psychosocial evaluation of living organ donor candidates. However, no comprehensive systematic reviews exist on psychosocial screening processes in both living kidney and liver donor candidates including all types of relationships with the recipient. Kranenburg et al.[8] conducted a systematic review focusing solely on the psychosocial evaluation of living kidney donors donating to an anonymous or unspecified recipient. Tong et al.[9] focused primarily on the medical screening of living kidney donors and only briefly touched upon psychosocial screening.

We conducted a systematic review of published guidelines, consensus statements, and description of protocols or programs **[t1]** to identify the content and process of a psychosocial evaluation of living kidney and liver donor candidates.

[t1 definitions]

type of document	definition
guidelines	guidelines (also called clinical practice guidelines), as defined by the Institute of Medicine in 2011[46], include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options
consensus statements	according to the National Institutes of Health[47], consensus statements synthesize new information, largely from recent or ongoing medical research, that has implications for reevaluation of routine medical practices. Consensus statements are primarily based on the evidence-based or state-of-the-art knowledge of a representative group of experts
clinical protocols	clinical protocols are more detailed and provide specific instructions or algorithms for individual clinical decisions

[t2 detailed search string used in the electronic database PubMed*]

PubMed (565 results on June 22, 2011)
(living donors [MeSH terms] OR live donor OR living donation OR living donor OR living kidney donation OR living related kidney transplant* OR living donor kidney OR living unrelated kidney transplant* OR living liver donation OR living donor liver OR living related liver transplant* OR living unrelated liver transplant* OR Samaritan donor OR altruistic donor OR donor candidates) AND (screening OR assessment OR selection OR evaluation) AND (psych* OR mental OR social OR psychosocial OR smoking OR alcohol* OR substance abuse OR addiction OR depress*) AND (‘humans’[MeSH Terms] NOT ((child OR adolescent OR infant) NOT adult))

* Similar search strings were used for the other electronic databases (available upon request).

methods

The methodology and results of this systematic review are reported in line with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines[10].

search strategy

We searched the databases PubMed, Embase (via EMBASE.com), PsycINFO (via OvidSP), and CINAHL (via EBSCO) until June 22, 2011, using search strings developed during iterative brainstorming sessions with the co-authors **[t2]**, supplemented by screening the references from relevant studies, and by searching the National Guideline Clearinghouse, National Institute For Health And Clinical Excellence (NHS), Scottish Intercollegiate Guidelines Network (SIGN), and Trip database.

inclusion and exclusion criteria

To be included, publications had to meet all the following criteria: (i) guideline, consensus statement/report or description of protocol/program; (ii) description of the content or process of the predonation psychosocial evaluation; and (iii) evaluation of living kidney or liver donor candidates (as the most common types of living organ donation).

Exclusion criteria were as follows: (i) quantitation of predonation psychosocial variables without embedding these in a screening protocol or procedure; (ii) written in a language none of the research team understood (i.e., languages other than English, French, German, or Dutch); and (iii) full text could not be found.

study selection

Two researchers (ND and FD) independently screened all titles and abstracts for eligibility, followed by a full text analysis of potentially relevant abstracts, using ENDNOTE”X2 software (Thomson Reuters, New York, NY, USA).

data extraction

The following data were extracted if reported: first author, publication year, setting, living organ type (i.e., kidney or liver), type of living donor-recipient relationship and its definition, name of guideline/consensus statement/ protocol, the content (i.e., psychosocial screening criteria) and their evidence base, and all process-related information (e.g., for whom? how? when? where? by whom? presence of third parties? cooling-off period?). In case of multiple publications on the same program or protocol, data were extracted from the most recent report only. One reviewer extracted data (ND or LT), which was checked by a second reviewer (FD) for accuracy and completeness.

results

study selection

Thirty-four papers are included **[f1]**, consisting of seven guidelines (20.6%), six consensus statements or conference reports (17.6%), and 21 papers describing a living donor evaluation protocol or program (61.8%).

Papers were published between 1995 and 2011, of which 23 originated from North America (67.6%), seven from Europe (20.6%), two from Australia (5.9%), and two from Asia (5.9%) **[t3]**. Seventeen papers focused on living kidney (50.0%), eight on living liver (23.5%), four on both living kidney and liver donation (11.8%), and five did not specify organ type (14.7%). Seventeen papers (50%) did not specify for which donor-recipient relationship the guideline or protocol was intended [6,11-26]. Six [27-32] of these did not define this relationship.

content of the psychosocial evaluation

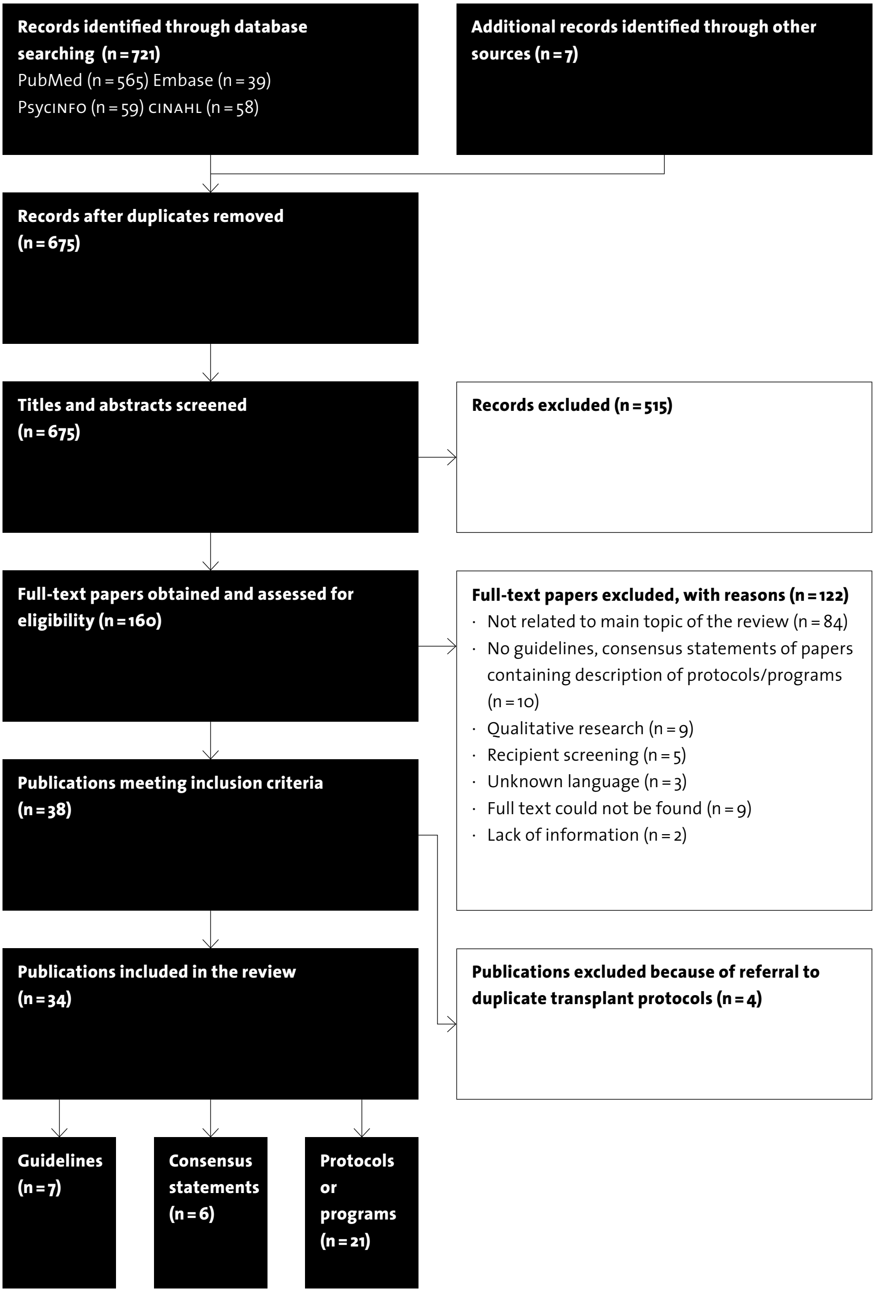
type of factors being considered

Across 34 publications, 197 different psychosocial factors were identified that can be clustered into 42 psychosocial domains, ordered from most frequently to least frequently reported **[t4]**. The screen procedures could be divided into initial simple screenings and extensive psychosocial evaluations. In case an initial screening is taking place before an extensive one, most frequently addressed factors were motivation to donate, social history, expectations about donation, basic knowledge about the risks involved in donation, relationship with recipient, and mental or emotional disorders.

definition of psychosocial criteria

The broad spectrum of psychosocial domains observed suggests that a clear definition or taxonomy of what ‘psychosocial evaluation’ entails is missing, making it unclear if certain behavioral factors need to be addressed during the psychosocial or medical evaluation. For instance, Rudow and Brown [20] and Gentil Govantes and Pereira Palomo [13] addressed behaviors like alcohol and drug use as well as sexual promiscuity, homosexuality, prostitution, incarceration, or having tattoos or body piercing as part of the medical screening as some of these might contain a potential risk of infectious disease transmission or postsurgical complications in general [27,33,34].

[f1 flow chart of the study selection process**]**



There was also much heterogeneity in terminology used (e.g., psychological wellbeing, psychosocial stability, psychopathology) and in the level of detail provided in defining each criterion: some authors only addressed broad ‘umbrella’ terms, like psychiatric disorders [13,29,33], whereas others specified these (e.g., mood disorders (depression, anxiety), personality disorder (schizophrenia, borderline)). Moreover, some authors just listed factors without any clarification, whereas others provided detailed descriptions, together with examples from clinical practice [21,30]. For example, Leo et al. [30] explained why employment status is important, as employers are a principal source of economic support by providing sick leave or vacation time during postsurgical recovery.

evidence base

Most factors were not supported by evidence or were at least not referenced, making it unclear if they indeed predict poor outcomes in donor candidates. Authors publishing their center’s protocol often refer to other guidelines or consensus statements, without explicitly listing all their center’s psychosocial factors. For example, Mark et al. [35] referred to the Live Organ Donor Consensus Group [36] and the National Conference on the Non-directed Live Organ Donor [37], but did not present which of the factors outlined in these publications are addressed within their own evaluation.

psychosocial contraindications

Contraindications for donation were specifically stipulated in 18 papers (52.9%) [15,19,20,23,25-30,32,34,35,37-41], of which only three indicated whether these were absolute or relative contraindications [19,25,26], and only one paper indicated that these were evidence-based [27]. Contraindications most frequently reported were as follows: motivation-related factors, some kind of coercion or pressure to donate, current or past psychiatric disorders, ambivalence, and unrealistic expectations. The level of detail of what these contraindications entail is again very heterogeneous. Some stated that contraindications to unspecified donation are the same as for other donation types, whereas Dew et al. [27] suggested additional contra-indications for ‘unrelated donors’. Jacobs et al. [40] proposed different contraindications for the initial screening than for the more detailed evaluation. Some state that the presence of risk

[t3 description of the included papers]

author, year published (setting)	organ type	type of donor-recipient relationship	name of guideline, consensus statement, or protocol/program
guidelines			
Delmonico et al. 2007[39] (USA)	Kidney	Related and unrelated	not specified
Dew et al. 2007[6] (USA)	not specified	not specified	not specified
Gentil Govantes et al. 2011[13] (Spain)	Kidney	not specified	not specified
Van Hardeveld et al. 2010[14] (Australia)	Kidney	not specified	CARI guidelines. Psychosocial care of living kidney donors
Kasiske et al. 1996[15] (USA)	Kidney	not specified	The evaluation of living renal transplant donors: clinical practice guidelines
Leo et al. 2003[30] (USA)	Kidney	Unrelated	not specified
Schroder et al. 2008[21] (USA)	not specified	not specified	not specified
consensus statements or conference reports			
Abecassis et al. 2000[36] (USA)	Kidney, liver, (pancreas, intestine, lung)	Directed + nondirected	Consensus statement on the Live Organ Donor
Adams et al. 2002[37] (USA)	Kidney	Nondirected	The nondirected live kidney donor: Ethical considerations and practice guidelines
Barr et al. 2006[11] (Canada)	Liver	not specified	A Report of the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas, and Intestine: Data and Medical Guidelines

definition provided	evidence base
Related = having at least some HLA identity with the recipient (genetically related) or having emotional bonds forged in marriage or friendship (emotionally related); *Unrelated* = individuals who have neither a genetic or longstanding emotional relationship with the transplant recipient (e.g., who come forward through internet solicitation and other public appeals) (also called nondirected)	Literature review
not specified	Literature review
not specified	Consensus statement of the Amsterdam Forum on the Care of the Live Kidney donor (2004)[42] and the CARI guidelines (2010)[14]
not specified	Literature review, Level III and IV evidence
not specified	Literature using MEDLINE, bibliographies in pertinent publications, personal experiences/opinions; Draft versions were reviewed by the Ad Hoc Clinical Practice Guidelines Subcommittee of the Patient Care and Education Committee and the Board Directors of the American Society of Transplant Physicians
not specified	Literature, cases from own clinical experience, the interview guideline has been adapted from the Structured Interview for Renal Transplantation, which is used to determine the psychological appropriateness of renal transplant recipients[48]
not specified	Literature review
Directed donation = donation to an identified recipient; *Nondirected donation* = donation to a candidate unknown to the potential donor (also referred to as a Good Samaritan donor)	Consensus
Donation to a complete stranger, no specification of an intended recipient or no direction for the selection	National expert opinion, clinical experience, open discussion
not specified	not specified

[t3 continued**]**

author, year published (setting)	organ type	type of donor-recipient relationship	name of guideline, consensus statement, or protocol/program
Canadian Council for Donation and Transplantation[12] (Canada)	Kidney, liver, (lung)	not specified	Enhancing living donation: A Canadian Forum: Report and Recommendations
Dew et al. 2007[27] (USA)	Kidney	Unrelated	Guidelines for the Psychosocial Evaluation of Living Unrelated Kidney Donors in the United States
Ethics Committee of the Transplantation Society, 2004[42] (Canada)	Kidney	not specified	The Consensus Statement of the Amsterdam Forum on the Care of the Live Kidney donor
protocols or programs			
Ben-Haim et al. 2005[38] (Israël)	Liver	Significant long-term relations with recipient, first or second degree familial relatives	not specified
Erim et al. 2010[34] (Germany)	Liver	Family members/persons who have obvious close relationships with the recipient	not specified
Fisher, 2003[28] (USA)	Kidney	Related + unrelated	not specified
Gilbert et al. 2005[29] (USA)	Kidney	Altruistic nondirected	not specified
Jacobs et al. 2003[40] (USA)	Kidney	Nondirected	not specified
Lopes et al. 2011[16] (Portugal)	Kidney	not specified	not specified
Mark et al. 2006[35] (USA)	Kidney	Nondirected	The organ procurement organization-based nondirected living kidney donation program
O'Dell et al. 2003[17] (Canada)	Kidney, liver, (lung)	not specified	not specified
Olbrisch et al. 2001[33] (USA)	Kidney, liver, (lung)	Genetically and emotionally related donors, Good Samaritan Donors (directed), Good Samaritan Donors (Nondirected)	not specified

definition provided	evidence base
not specified	Experts opinion, literature review, existing recommendations, current Canadian and international practice, discussion
not specified	Experience of experts in the field of the North American transplant community that met during a conference meeting, existing recommendations, evidence base in genetically and emotionally related donors
Donation to a potential recipient (known by the potential donor or not known in the circumstance of anonymous donation)	International experience of professionals and evidence-based recommendations
Significant long-term relations with recipient, first or second degree familial relatives	Inclusion and exclusion criteria and phases of evaluation followed recently published recommendations, algorithm is based on lessons learned from their experience
Family members/persons who have obvious close relationships with the recipient	Literature review on predictors facilitating a favorable psychosocial outcome
not specified	Literature review, guidelines from an ad hoc clinical practice guidelines subcommittee of the patient care and education committee of the American Society of Transplant Physicians developed in 1996
not specified	not specified
Volunteers who offer to donate to anyone waiting on the waiting list	Clinical experiences
not specified	not specified
Donation of a kidney to a stranger	Consensus statements [36,37]
not specified	Literature (both in living donors and transplant recipients), consensus statement of Abecassis et al. [36]
Genetically related donors: genetical relationship; *Emotionally related donors*: a relationship that has been built on reciprocal giving, relationships based on personal commitment to another person, love, affection, mutual interests; *Good Samaritan donors* (directed): a distant or no relationship with a specific recipient; *Good Samaritan donors* (nondirected): someone who wishes to donate an organ to be used by any recipient who needs it, without knowledge of the recipient's need or distress	Clinical experience, transplant team interactions, literature

[t3 continued]

author, year published (setting)	organ type	type of donor-recipient relationship	name of guideline, consensus statement, or protocol/program
Papachristou et al. 2010[18] (Germany)	Liver	not specified	not specified
Potts et al. 2009[19] (UK)	not specified	not specified	not specified
Reichman et al. 2010[31] (Canada)	Anonymous directed and nondirected	not specified	not specified
Renz et al. 1995[32] (USA)	Liver	related	not specified
Rudow et al. 2003[20] (USA)	Kidney	not specified	not specified
Shrestha et al. 2003[22] (USA)	Liver	not specified	not specified
Sites et al., 2008[23] (USA)	not specified	not specified	not specified
Smith et al. 2004[24] (Australia)	Kidney	not specified	not specified
Stagno et al. 2007[25] (Switzerland)	not specified	not specified	not specified
Sterner et al. 2006[43] (USA)	Kidney	related	not specified
Walter et al. Med Sci Monit, 2005[26] (Germany)	Liver	not specified	not specified
Zhao et al. 2010[41] (China)	Kidney	Related	not specified

definition provided	evidence base
not specified	Clinical experience, literature, consensus statement of Abecassis et al.[36]
not specified	not specified
not specified	
not specified	not specified
not specified	not specified
not specified	not specified
not specified	not specified
not specified	not specified
not specified	not specified
(The recipients are always children, as this protocol is described and used by The Children's Hospital of Philadelphia)	not specified
not specified	not specified
Relative	not specified

[t4 psychosocial domains and factors covered by guidelines, consensus statements, and protocols]

psychosocial domains	range of psychosocial factors to be addressed in evaluation of donors as reported in the included papers	*n* (%)
Motivation-related factors	Motivation/reasons for donation; Embedment of the donation into a meaningful context; A logic rationale for donation that is understandable for the team; Guilt; Ulterior motives (potential benefits, expectations, or perceived obligations on the part of either the donor or the recipient, to atone or gain approval, to stabilize self-image, media attention, to remedy psychological malady, to develop a personal relationship, desire for recognition, financial benefits, avoidance of military duty)	25 (73.5)
Some kind of coercion or pressure to donate	Coercion; Family pressures; Vulnerability to coercion/pressure; Level of autonomy; Risk for exploitation (by others for monetary or other personal gain); Financial inducements; Organ trade	23 (67.6)
Any kind of support before and after donation	Social support; Emotional support; Available psychological support after donation; Practical support; Available practical support after donation during recovery; Financial support; Tangible support; Physical support; Support networks; Significant relationships	22 (64.7)
Donor-recipient relationship	Relationship (if any) between donor and recipient; Nature of the relationship (strengths, past conflicts/difficulties); Subordinate relationship between donor and recipient (e.g., employer-employee); Donor-recipient interaction; Dynamics of the relationship between donor and recipient; Emotional quality of the relationship	20 (58.8)
Current or past psychiatric disorders	Specified: Substance abuse; Mood disorders (depressive or bipolar disorder); Anxiety disorder, panic, or needle phobias; Personality disorder (e.g., paranoid, schizophrenia, borderline, narcissistic, narcissistic self-organization, and self-regulation); Suicidality or self-harm; Eating disorders; Orientation issues, thought processing, thought disturbances (hallucinations, delusional thinking, or illusions); Other serious disorders (low self-image, body image disorder)	17 (50.0)
	Unspecified	11 (32.4)
Competence	Competence; Ability to solve conflicts; Ability to develop a realistic and logical plan for donation; Decision-making capabilities; Competence to comprehend information and to give informed consent for donation	16 (47.1)
Financial issues	Financial status; Availability of resources to cover (un)expected donation-related expenses; Ability to deal with the economic implications that may arise throughout the donation process; Status as a sole wage earner (may be relative contraindication for donation); Availability of disability and health insurance; Ability of the donor to subsequently obtain life insurance without additional cost; Financial hardship imposed on the donor and family as a results of the donation (including lost wages, out-of-pocket travel, inability to obtain sick leave, and lack of job security); Potential economic risks associated with donation; Potential hardships for the donor and his or her family because of donation	16 (47.1)

psychosocial domains	**range of psychosocial factors to be addressed in evaluation of donors as reported in the included papers**	***n* (%)**
Coping-related issues	Coping; Coping strategies/mechanisms/styles/behavior; Illness-coping strategies; Former psychological coping; Current psychological coping (with which coping styles does the candidate react to the operation); Ability of potential donor (and family) to cope effectively with stresses associated with transplantation (before and after donation); Nature of coping skills to manage current or past life- or health-related stressors; Coping with previous difficult life events; Emotional resources to cope with stressors related to the donation process; Ability to cope with adverse outcomes for recipients; Coping with pain after the transplant	15 (44.1)
Employment-related issues	Employment status; The interaction with the donor's employer; Potential occupational risks or implications for donor's current job and their future employability; Work- and/or school-related issues (arrangements with employer or school; financial resources); Able to withstand time away from work or established role, including unplanned extended recovery time	15 (44.1)
Family-related issues	Family context and relationships; Family dynamics and organization; Temporary change (limitations) in the donor's role within a family; Health issues of other family members; History of family's mental health issues; The necessity of making alternative arrangements for child care when the donor is the primary care provider; Outside assistance required when the transplant is between spouses; Feelings, perspectives, or reactions of family members or another significant about donation and the donation decision of the donor; The degree to which potential donors have discussed the plan for donation with their own significant family members	14 (41.2)
Ambivalence; resoluteness regarding the decision of donation		13 (38.2)
Socio-demographic characteristics	Socio-demographic characteristics; Race or ethnicity; Educational level; Social situation or history; Living situation or arrangements	13 (38.2)
Psychological status	Psychological functioning; Psychological stability; Psychological wellbeing; Psychological fitness; Psychological complaints	13 (38.2)
Decision-making process (how the decision to donate was made)		11 (32.4)
(Unrealistic) Expectations (e.g., about the process, health expectations for the recipient, expectations regarding the effect of the donation on the relationship with the recipient)		11 (32.4)

[**t4** continued]

psychosocial domains	**range of psychosocial factors to be addressed in evaluation of donors as reported in the included papers**	***n* (%)**
Comprehension/knowledge/awareness/understanding of the recipient process (including risks, benefits, health outcomes, recovery process, …)		11 (32.4)
Cognitive status	Cognitive status; Learning disability or other cognitive impairments; Intelligence level	10 (29.4)
Values, (religious) beliefs, sense of charity, and community/community activities		9 (26.5)
Memory (short-term, remote, and long-term)		8 (23.5)
Health behavior*	Life style; Regular physical activities; Weight/obesity; Substance use; Compliance (medication compliance, nonattendance at appointments)	8 (23.5)
Current stressors (e.g., relationships, home, work, financial, health) or stress level		7 (20.6)
Altruism	Altruism; History of altruistic acts; History of volunteerism or charitable deeds; Voluntariness	6 (17.6)
Marital situation	Marital status; Stability of marriage/relationships; Marital stress	6 (17.6)
Current or past use of therapeutic interventions (counseling, medication)		5 (14.7)
Legal issues	Legal situation; Legal history; Legal offense history and citizenship, incarceration or imprisonment	4 (11.8)
Comprehension/knowledge/awareness/understanding of the recipients' illness or availability of alternative treatments for the TX candidate		4 (11.8)
Victim of physical, psychological, or sexual abuse		3 (8.8)

factors does not necessarily rule out donation, but that the goal of an evaluation is to identify areas for additional support or therapeutic interventions to optimize outcomes[6,13,21,30,36].

process of psychosocial evaluation

for whom is psychosocial evaluation necessary?

Nineteen papers (55.9%) did not specify which candidates need to undergo psychosocial evaluation[6,11,15,16,21-26,28-33,37,38,42]. Other papers widely differed whether all[12-14,17,18,20,34, 36,39,41,43] or specific subgroups need to be screened (e.g., anonymous donors)[19,27,35,40]. Eleven out of these 15 papers (73.3%) recommended to screen all potential donors, yet, given that they focused on a specific donor-recipient relationship, it remained unclear whether they really meant all candidates (i.e., irrespective of their relationship with the recipient). Zhao et al.[41], for example, recommended to evaluate all donor candidates, yet, they only describe donation between relatives. Of note, the group of Ben-Haim[38] reported that screening is also necessary in case of urgent transplantation.

how should psychosocial evaluation be performed?

There was agreement among nine papers (26.5%) that the evaluation should take place in two phases, i.e., an initial (often combined with medical screening questions and providing information about the donation process) and a more extensive evaluation[13,27,29,34,35,37-40]. Some indicated that psychosocial questions need to be integrated in the initial screening to rule out persons with obvious contraindications, such as poor motivation, unrealistic expectations about donation, or severe mental illnesses[13,37,40].

For the more extensive evaluation phase, 14 papers (41.2%) recommended using an interview, either a standardized structured one (5/14 (35.7%)), which might also be helpful to retrieve comparable information from a relative[28], or a semi-structured format[12,14,18,24,26,30,34,37] (8/14 (57.1%)), providing a framework for comprehensive assessment, but allowing room for flexibility[30]. Only one paper (7.1%) preferred an open dialog using an unstructured interview[29].

Ten papers (29.4%) proposed additional psychometric testing[18,22,24,26,28,29,34,40,41,43], although one paper did not specify which tools

[**t5** psychometric instruments]

psychometric instruments	**concepts measured**
Berlin Mood Questionnaire (BMQ) [18,22,26]	Psychological wellbeing
Giessen Complaint Questionnaire (GBB) [18,22,26]	Physical complaints
36-Item Short Form Health Survey Evaluation (SF-36) [22,24]	Quality of life (physical and psychosocial functioning)
Anamnestic Comparative Self-Assessment scale (ACSA) [18,22]	Quality of life
(Modified) Beck depression Inventory (BDI/MBDI) [22,41]	Depressive symptoms
Minnesota Multiphasic Personality Inventory (MMPI) [22,40]	Personality traits
Narcicissm Inventory (NI) [18,26]	Narcissistic self-organization and self-regulation
Symptom checklist-90-Revised (SCL-90-R) [22,43]	Psychosomatic complaints
Transplant Evaluation Rating Scale (TERS) [24,34]	Past and present psychiatric symptoms and personality, compliance, coping behavior, and social support (as in Smith et al. (2004)) [24] Mental stability and social functioning (as in Erim et al. (2010)) [34]
22-item questionnaire developed by the TX center (unpublished) [41]	Unknown
Addiction Severity Index (ASI) [28]	Substance abuse problems
Alltagsfragebogen (ALL) [18]	Daily functions
Brief Mental Status Exam (MSE) [28]	Mental status, cognitive functioning
COPE (COPE-28) [18]	Coping behavior
Drug Abuse Screening Tool (DAST) [28]	Substance abuse
Freiburg Illness-Coping Questionnaire (FKV) [18]	Illness-coping strategies
Generalized Anxiety Disorder Questionnaire (GAD 7) [18]	Anxiety
Hopkins Symptom Checklist [22]	Anxiety and depression symptoms
Medical Outcomes Survey (MOS) Social Support Survey [43]	Different types of social support and positive social interactions
Michigan Alcohol Screen Tool (MAST) [28]	Social, vocational, and family problems frequently associated with heavy drinking
Quality of Life Questionnaire (WHOQOL BREF) [18]	Health-related quality of life
Patient Health Questionnaire (PHQ/PHQ-15) [18,24]	Depression, panic, psychosocial functioning (as in Papachristou et al. (2010)) [18] Somatic complaints, depression, anxiety, eating disorders, alcohol use (as in Smith et al. (2010)) [24]
Perceived Available Support from the Berlin Social Support Scale (PAS) [18]	Social support
Perceived Stress Questionnaire (PSQ) [18]	Subjective stress (stressors and stress reactions)
Questionnaire on Self-Efficacy, Optimism, and Pessimism/ Selbstwirksamkeit Optimismus, Pessimismus (SWOP) [18,22]	Self-efficacy, optimism, pessimism
Self-rating anxiety scale [41]	Anxiety
Wechsler Adult Intelligence Scale (WAIS) [41]	Intelligence

should be used[29]. **[t5]** shows that there is quite some variability on type, number, and content of instruments.

With regard to record keeping, O'Dell and Wright[17] were the only ones recommending using an electronic assessment tool, providing a time-saving, efficient, and standardized method of information gathering.

when should psychosocial evaluation be performed?

There is no agreement on the timing of the evaluation. Eighteen papers (52.9%) did not specify an exact time point[6,12,14,16,17,21,23,25,28,30,31,33,35-39,42], whereas some others presented a detailed algorithm with all sequential steps of the evaluation[15,43]. Most authors, however, recommended that the psychosocial evaluation should take place after a minimum set of medical tests (e.g., laboratory tests, viral studies)[11,15,20,40], but early in the process, to avoid invasive and expensive medical tests if clear psychosocial contraindications are present[11,13,15,19,20,22,24,26,27,32,40,41]. Nine percent state that it can also depend on the situation, e.g., characteristics of the donor (fear, emotional instability), a hospital's facilities, or the urgency of the procedure depending on the recipient's health[13,15,18]. The contact frequency was never documented.

where should psychosocial evaluation take place?

The majority (82%) did not specify the location. Others recommended following options: in the center where donor surgery will take place (5.9%)[27,29], at the hospital's psychosocial unit (5.9%)[33,34], in the transplant center (2.9%)[40], or at the center of choice (2.9%)[35]. Six papers (17.6%) reported that the initial screening can be done by telephone[27,29,35,37,39,40], especially for donor candidates living far away[35].

who should perform the psychosocial evaluation?

In the 27 papers (79.4%) documenting who should perform the evaluation, there was considerable agreement among 14 papers (51.9%) that this person should be a healthcare professional or a team not involved in the recipient's care, and thus allowing independent decision-making[12,17,20,22-24,27,29,34,36,39-41,43], including social workers (59.3%), psychiatrists (59.3%), (external) psychologists (57.1%), psychiatric nurses/nurse specialists (14.8%), physicians (7.4%), or other specialists in psychosomatic medicine (3.7%). Also, organ procurement organization (OPO) coordinators (7.4%)[29,35] and transplant coordinators (3.7%)[40] are sometimes entitled to perform an initial screening. Abecassis et al.[36] added that when a potential donor is undergoing mental health treatment at the time of candidacy, their mental health professional should also contribute to the evaluation process. Olbrisch et al.[33] stated that the evaluation needs to be viewed as a multidisciplinary team approach, yet, did not clarify this statement. Some papers underlined that psychosocial evaluators should be well informed on, or should have prior clinical experience in transplantation[13,15,18,34]. Erim et al.[34], who gave detailed descriptions of the psychosocial evaluator's profile, noted that they should have a positive attitude toward living donation, based on their ethical convictions or personal life experience.

Along the same lines, 11 papers (32.4%) explicitly recommended the use of an independent donor advocate or team[12,20,22,23,31,32,34,35,37,38,43], defined as a professional who is not involved in the recipient's care, who advocates the welfare of the potential donor, and ensures safe evaluation and protection of the donor's rights. However, their role is not always explained and varies between centers, ranging from providing education, monitoring policies and procedures to safeguard donors, or actively participating in the evaluation[23].

can third parties be present?

In 10 papers (29.4%), the presence of a relative, significant other or even a collateral interview of this person was mentioned[16,18,20,24,27-30,33,40,43], e.g., for support[40], to ensure trustworthiness of information provided[28,43], to help understanding family dynamics (e.g., available support, coercion, family conflicts)[34,43], and to inform them about the need for tangible support during the donor's recovery[43]. Papachristou et al.[18] also suggested to involve the recipient during a second interview. Other authors prefer third parties not being present during the confidential part of the interview[43].

Erim et al.[34] were the only ones that reported organizing a second psychosomatic evaluation in which both the donor and recipient and their respective evaluators meet, with the purpose to investigating the dynamics of the donor-recipient relationship and the expectations with respect to their relationship postdonation.

Only one paper (2.9%) mentioned the use of professional interpreter services in case of language differences, and to forbid friends or relatives to translate to avoid bias, coercion, or conflict of interest[43].

need for a cooling-off period?

Once accepted as a donor, a cooling-off period or waiting interval (i.e., period between consent and donation) is recommended in nine papers (23.5%), ranging from minimally one week to as much time the donor needs[12,23,27,29,31,35,40-42], to ensure that the decision to donate has been adequately considered and to allow time to withdraw their consent.

discussion

This study is the first of its kind as guidelines, consensus statements, and protocols on psychosocial evaluation of living donor candidates have not been previously studied to this extent. Compared to the systematic review of Tong et al.[9] that only limitedly focused on the content of a psychosocial evaluation of living kidney donor candidates, we focused on both kidney and liver donors, addressed the psychosocial screening issues in much more detail, and also gained interesting insights in process-related factors.

At present, there is no consensus, nor strong evidence or concrete guidance on what to screen for, how to handle identified psychosocial problems, and how to perform the screening, leading to huge variability in screening practices, the risk that important psychosocial factors might be overlooked or that unnecessarily time-consuming and costly procedures are being undertaken. Although we did not include gray literature, we supplemented our searches by screening reference lists and reviewing databases specifically devoted to guidelines. Second, psychosocial evaluation protocols could have been wrongly judged by the authors, as many papers only briefly and imprecisely addressed psychosocial screening, yet, the risk of bias was minimized using a systematic approach.

Several reasons might exist why there is no uniform set of psychosocial criteria for living donor selection, of which the most important one is the lack of evidence underpinning these risk factors. Criteria seem to have been established based on opinions and individual center experiences rather than on empirical evidence. Consequently, there is the risk that relevant psychosocial aspects may be missed or that many efforts are being put in measuring psychosocial factors that might be irrelevant. Up to today, few studies have investigated predonation psychosocial risk factors for poor postdonation outcomes prospectively[5], highlighting a definite need for prospective cohort studies to help identifying those psychosocial risk factors that are indeed predictive for poor outcomes. In that way, persons who may be less ideal donors or who might benefit from postoperative psychosocial care can be identified. A second reason for the lack of uniform criteria lays in the variable terminology used to label psychosocial factors across papers. This is probably caused by the lack of a universally accepted definition of the concept ‘psychosocial screening’. The development of such a definition might be an important first step in creating a common language between investigators and healthcare professionals, using consistent terminology and classification on psychosocial factors. Third, specific guidance is missing on how to measure these factors, which is in line with the observations outlined in the systematic review of Tong et al.[9]. Some papers did not report whether and which instruments they used, or recommended widely varying instruments. Although standardized measures might have several benefits, including ensuring a comprehensive assessment, providing a basis for prospective monitoring, and allowing comparisons of psychosocial risk factors and outcomes between centers, further investigation is needed into which tests, in addition to a semi-structured or structured interview, are the most suitable in the context of living donor psychosocial evaluation. Fourth, there is still much debate on who needs to be screened psychosocially. There are an increasing number of ways persons can donate their kidney or liver, as shown by the recently published taxonomy on donor-recipient relationships[44]. Subsequently, it can be questioned if all donor candidates or only specific subgroups require psychosocial assessment (e.g., if one wants to donate to a complete stranger or has psychosocial problems). This necessitates setting up comparing the prevalence and incidence of psychosocial problems between various types of donor-recipient relationships. Fifth, no optimal process for evaluation seems to exist. Yet, given that psychosocial screening is an expensive and time-consuming process, most agree to apply a stepwise process, beginning with the least expensive and least invasive tests. In case of rapid deterioration of the recipient’s health, urgency should not exclude a psychosocial evaluation. Sixth, with regard to the psychosocial evaluator, a wide range of healthcare professionals have been suggested. Although we cannot determine who is best placed to perform the evaluation, we believe that this person should at least be familiar with transplantation medicine or should have prior clinical transplant experience, and needs to be trained to administer and interpret psychological tests. Seventh, the involvement of a donor advocate or advocacy team was reported by only a few of the included reports. It is possible that this is not described, as donor advocacy might not be seen as an exclusive part of the psychosocial evaluation, but rather as essential throughout the overall donor process. There is also much debate whether the donor advocate should be a donor-appointed advocate, a member of the transplant team not caring for the recipient, a hospital employee outside the transplant team, an OPO, or a team of advocates[45]. Next, we agree with Sterner et al.[43] that an independent translator should be involved in case of language problems to avoid coercion or conflict of interest if a family member is interpreting. Finally, although a cooling-off period seems to be of utmost importance to give donors sufficient time to adequately consider their decision to donate, it was mentioned in only eight papers (24%) and the time period varied tremendously. Qualitative research may help to reveal how (future) donors, and perhaps also professionals perceive the importance and nature of this cooling-off period.

This systematic review hence reveals that there are many opportunities to further improve the quality and safety of living organ donation from a psychosocial viewpoint and underscores the need for a line of research working toward the development of uniform, standardized, and evidence-based psychosocial evaluation criteria for living donor candidates:

1 A conceptual framework of 'psychosocial' in the practice of screening living organ donors needs to be developed to enhance the use of a uniform language between transplant professionals.

2 We recommend giving priority to prospective cohort studies to identify those psychosocial risk factors that are predictive for poor outcomes in living organ donors before considering the development of new guidelines. Also the differences in psychosocial problems between various types of donor-recipient relationships should receive more attention in this regard. While awaiting results of these prospective cohort studies, we see that motivation to donate, social history, expectations about donation, basic knowledge about the risks involved in donation, relationship with recipient, and mental or emotional disorders are most common reported factors. As there is, however, heterogeneity in how to assess these factors, consensus is needed on psychometric instruments to be used, allowing for comparisons between different transplant centers.

3 As it remains unclear what the influence is of ruling out individuals for donation on the basis of psychological reasons, knowledge about psychosocial risk factors should be used not necessarily to rule out donation, but to help clinicians to identify those individuals who are most at need of additional support or therapeutic interventions pre or postdonation.

4 Efforts to standardize the process are needed internationally, and each center should have a clear protocol on all process-related aspects of a predonation psychosocial evaluation (i.e., who, what, how, by whom, when). These recommendations, however, should be tailored to fit individual needs.

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3

Who has extreme expectations of donation? Exploring the psychological profile of living kidney donors

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abstract

background
Assessing extreme expectations regarding personal consequences of donation (e.g., personal growth) is often one of the components in the psychosocial screening of living kidney donors. Little is known about who has extreme expectations; therefore we explored the relationship between the psychological and socio-demographic profile of potential donors and their expectations.

methods
One-hundred and thirty-six potential living kidney donors, both specified and unspecified, completed the Living Donation Expectancies Questionnaire (LDEQ) and questionnaires that measure mental health, stress, coping, and social support before donation. The LDEQ measures both positive and negative expectations regarding the donation process. To assess mental health both psychological wellbeing and complaints were measured.

results
Psychological complaints were significantly associated with expectations, psychological wellbeing was not. Greater negative affect, depression, deficiency in social support, and a less active coping style were related to more extreme positive and negative expectations, while greater social support and less anxiety were related to more extreme positive expectations only. A close relationship with the recipient was associated with more extreme positive and negative expectations.

conclusions
Greater negative affect and a close relationship with the recipient were particularly related to more extreme expectations of living donation. Whether expectations relate to subsequent mental health after donation is a question for future research.

introduction

The current literature on living kidney donation suggests that the majority of the donors show no change or an improvement in mental health while a small percentage show a deterioration in mental health after donation[1]. One of the many unanswered questions about the impact of living donation is what factors contribute to an improvement, no change, or a deterioration in mental health. Expectations regarding personal consequences of donation may have an influence on the mental health of the donor. A systematic review by Duerinckx and colleagues[2] showed that unrealistic expectations is one of the most frequently reported components in psychosocial screening guidelines, consensus statements, and protocols for living kidney and liver donor candidates. Virzì and colleagues[3] have suggested that the post-donation mental health of living kidney donors is related to expectations of the long-term result of the transplantation. Finally, a study by Rodrigue and colleagues revealed that more extreme positive and negative expectations regarding the donation process were found among donors who had psychosocial contraindications for donation[4].

Despite the suggested importance of expectations of living donation, little is known about the profile of donors with extreme expectations and what the potential consequences of these expectations might be. In this cross-sectional analysis of data from the first wave of a prospective study, we explored the relationship between the psychological and socio-demographic profile of living kidney donors and their expectations of personal consequences before donation.

methods

participants

All potential living kidney donors who underwent medical screening for living kidney donation at Erasmus Medical Center between July 2011 and September 2012 received a Patient Information Form for this study after the intake procedure with a transplant coordinator. This cohort included both potential specified and unspecified donors[5]. One week before the final appointment of the screening process with the nephrologist, a researcher (LT) called the potential donor and asked if he/she had questions about the study and would like to participate if he/she was approved for donation.

Between 5th July 2011 and 13th September 2012, 212 potential living kidney donors were approved for donation. Sixteen potential donors were excluded from this study, because they did not speak the Dutch language sufficiently or did not live in the Netherlands. Sixteen potential donors refused participation: 5 did not have time, 2 were too strained, 6 did not wish to participate, and 3 gave no reason. Due to logistical issues such as screening in another hospital, we were unable to approach 19 donors for participation. One-hundred and sixty-one potential donors approved participation for this study which consisted of a face-to face interview and completion of self-report questionnaires. Of the participants, twelve donors refused to participate in the interview but completed the questionnaires. Thirteen donors participated in the interview, however did not return the questionnaires. Consequently, 136 donors completed both questionnaires and interview and were included in these analyses.

procedure

The participants were asked to complete questionnaires and participate in an interview immediately after the final appointment with the nephrologist in which the results of the medical screening were discussed. Expectations were measured in the interview, the other concepts were measured using questionnaires. The interview was conducted by a psychologist (LT, ML, or EM) and took place at the outpatient clinic of Erasmus Medical Center 0 to 16 (median 2) months before donation. One-hundred and four

(64.2%) participants completed the questionnaires at home and 32 (35.8%) at the outpatient clinic.

measures

socio-demographic characteristics & relationship with the recipient

The following socio-demographic characteristics were obtained from medical records: age, gender, employment status, marital status, native country, highest level of education completed, religious affiliation, and co-habitation with the recipient. Finally, we categorized the relationship between donor and recipient in 5 groups: unspecified donors, partners, children, parents, siblings, and others (such as: friends, neighbors, cousins). See **[t1]** for details.

expectations

Outcome expectancies were measured using the Living Donation Expectancies Questionnaire (LDEQ)[4], which consists of 42 items. This questionnaire measures the level of positive and negative expectations regarding personal consequences of the donation process. Four subscales measure positive expectations: Interpersonal Benefit ($\alpha = 0.81$), Personal Growth ($\alpha = 0.93$), Spiritual Benefit ($\alpha = 0.79$), Quid Pro Quo ($\alpha = 0.67$). Two subscales measure negative expectations: Health Consequences ($\alpha = 0.86$) and Miscellaneous Consequences ($\alpha = 0.73$)[4]. 'Quid pro quo' refers to expectations of getting something in return for the donation, for example to get a preferential treatment by the recipient after donation. A sample item of a positive expectation is: 'As an organ donor, I expect to be respected and admired by family and friends'. A sample item of a negative expectation is: 'As an organ donor, I expect to experience a great deal of pain and discomfort'. The questionnaire was constructed by Rodrigue and colleagues[4]. A back translation procedure was used: the questionnaire was translated from English into Dutch by a native Dutch speaker; subsequently a native English speaker translated the Dutch questionnaire back into English, and concluded that the last English version resembled the original English version. The items were read out by a psychologist and the participant answered to what extent he/she agreed with the items on a 5-point scale from *totally disagree* to *totally agree* by choosing the best answer option from a response sheet. The scores on the items were summed per subscale.

mental health

Psychological complaints: the Brief Symptom Inventory (BSI)[6,7] was used to measure the presence of psychological complaints. The 53 items of the BSI can be grouped into 9 subscales: Somatization, Cognitive Problems, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism. The participant rated the extent to which he/she experienced the symptom in the past two weeks on a 5-point scale from *totally not* to *very much*. The scores on the items were summed per subscale. Negative affect was measured using the Positive And Negative Affect Schedule (PANAS)[8,9]. The questionnaire consists of 10 positive and 10 negative affective states. The participant rated the extent to which he/she experienced the affective states in the past two weeks on a 5-point scale from *very little or not at all* to *very much*. The mean of the scores on the negative affective states was used.

Psychological wellbeing: the Mental Health Continuum-Short Form (MHC-SF)[10,11], the Satisfaction With Life Scale (SWLS)[12], and the Positive Affect subscale of the PANAS were used to measue psychological wellbeing. The MHC-SF consists of 14 items that measure various feelings of wellbeing. The participant rated how often he/she experienced the feeling in the past month from never to every day. The SWLS assesses global life satisfaction with 5 items on a 7-point scale from *totally disagree* to *totally agree*.

stress

The total score of the stress subscale of the short-form version of the Depression Anxiety Stress Scale (DASS-21) was used to measure distress level[13]. The participant rated the extent to which he/she experienced 7 stress symptoms on a 5-point scale at that moment from *totally not applicable* to *certainly applicable*.

generic coping

Generic coping was measured using the Dutch version of the COPE-Easy[14] which consists of 32 items. The participant rated the use of the coping style on a 4-point scale from *not at all* to *a lot*. The scores on the items were summed and grouped into 3 main dimensions:

1. active problem-oriented coping,
2. social support seeking coping,
3. avoidant behaviour.

generic social support

The Social Support List – Interactions (SSL-I)[15] and the Social Support List – Discrepancies (SSL-D)[15] were used to measure the amount of social interactions experienced and the deficiencies experienced in social interactions respectively. On the SSL-I the participants rated the extent to which they experienced social interactions on a 4-point scale from *seldom or never* to *very often*. On the SSL-D the participants rated the extent to which they experienced discrepancies in social interactions on a 4-point scale from '*I miss this, I would like to experience this more*' to '*This happens too often, I prefer to happen this less often*'. Both scales consist of 34 items. The scores on the 2 scales were summed into 2 separate total scores.

statistical analyses

Univariate analyses (correlation for continuous variables and independent t-tests or one-way ANOVA's for the categorical variables) were carried out to select the predictors that had a potential relationship with the 6 different kinds of expectations ($p < 0.10$). Subsequently, we conducted 6 multiple linear regression analyses with these predictors and the 6 expectations subscales as outcomes. In each step, factors that were not significantly associated with the outcome variable were removed from the model using the backward elimination method. Dummy variables were used for the categorical variable 'relationship with the recipient' in the regression analyses with 'partner' as reference group.

results

socio-demographic characteristics and relationship with the recipient

[t1] shows the socio-demographic characteristics and the relationship with the recipient. The gender distribution was almost equal. Over half of the participants were married or living together, were in paid employment, were well educated, had been born in the Netherlands, had no religious affiliation, and did not live in the same house as the recipient. The most common relationship with the recipient was partner.

factors associated with positive expectations

[t2] gives an overview of the final multiple linear regression analyses which show the socio-demographic and psychosocial factors that were associated with positive expectations. Expectations regarding Interpersonal Benefit were positively related to depression, negative affect, and social support, but negatively related to anxiety. They were higher if the donor and recipient lived in the same house. Expectations regarding Personal Growth were positively related to negative affect, social interactions experienced, deficiency in social support, but negatively related to anxiety. They were also higher if the donor and recipient lived in the same house. Expectations regarding Spiritual Benefit were higher if the donor had a religious affiliation, if the donor and recipient lived in the same house, and were positively related to negative affect. Expectations regarding Quid Pro Quo were positively related to negative affect and negatively related to use of an active coping style. The type of relationship with the recipient was also associated with expectations of Quid pro Quo: partners had more extreme expectations of Quid pro Quo than parents and the 'other' relationships with the recipient.

factors associated with negative expectations

[t3] gives an overview of the final multiple linear regression analyses which show the socio-demographic and psychosocial factors that were associated with negative expectations.

Expectations regarding Health Consequences were positively related to negative affect and negatively related to use of an active coping style.

Further, partners had more extreme expectations regarding negative Health Consequences than unspecified donors, children, siblings, and the 'other' relationships. Finally, expectations regarding Miscellaneous Consequences were positively related to negative affect.

[t1 participants' socio-demographic characteristics and the relationship with the recipient**]**

participants (N = 136)	**n**	**%**
median age (range)		55 (18–83)
gender		
men	61	44.9
marital status		
married/living together	88	64.7
single/divorced/widowed	47	34.6
missing	1	0.7
employment status		
paid employment	78	57.4
retired/voluntary work/unemployed	56	41.2
missing	2	1.5
highest level of education completed		
primary/secondary school	48	35.3
further education	84	61.8
missing	4	2.9
native country		
the Netherlands	120	88.2
other country	15	11.0
missing	1	0.7
religious affiliation		
yes	59	43.4
no	73	53.7
missing	4	2.9
co-habitation with recipient		
yes	56	41.2
no	80	58.8
relationship with recipient		
unspecified	17	12.5
partner	44	32.4
child	20	14.7
parent	11	8.1
sibling	24	17.6
other	20	14.7

[**t2** factors associated with positive expectations]

	B	SE B	ß	p
factors associated with expectations of interpersonal benefit				R² = 0.35
constant	–0.40	2.09		
depression	3.77	1.10	0.30	0.00
anxiety	–2.82	1.30	–0.26	0.03
negative affect	4.01	1.21	0.43	0.00
social support (interactions)	0.07	0.02	0.21	0.01
co-habitation (yes/no)	2.49	0.63	0.29	0.00
factors associated with expectations of personal growth				R² = 0.25
constant	2.15	5.06		
anxiety	–4.75	2.32	–0.26	0.04
negative affect	8.24	2.28	0.47	0.00
social support (interactions)	0.13	0.05	0.24	0.01
deficiency in social support	0.14	0.07	0.19	0.03
co-habitation (yes/no)	3.33	1.18	0.23	0.01
factors associated with expectations of spiritual benefit				R² = 0.20
constant	2.06	1.35		
co-habitation (yes/no)	1.73	0.78	0.18	0.03
negative affect	3.18	0.92	0.28	0.00
religious affiliation (yes/no)	3.20	0.76	0.35	0.00
factors associated with expectations of quid pro quo				R² = 0.31
constant	6.23	1.58		
negative affect	2.35	0.61	0.34	0.00
problem-oriented coping	–1.38	0.40	–0.29	0.00
deficiency in social support	0.05	0.03	0.17	0.07
relationship with recipient:				
· partner vs. child	–1.12	0.70	–0.15	0.11
· partner vs. parent	–2.32	0.92	–0.23	0.01
· partner vs. sibling	–1.15	0.66	–0.16	0.09
· partner vs. other	–2.37	0.72	–0.30	0.00

[t3 factors associated with negative expectations**]**

	B	**SE B**	***ß***	***p***
factors associated with expectations of health consequences				$R^2 = 0.32$
constant	8.93	1.24		
negative affect	2.43	0.60	0.32	0.00
problem-oriented coping	–1.64	0.39	–0.33	0.00
relationship with recipient:				
· partner vs. unspecified	–2.49	0.81	–0.26	0.00
· partner vs. child	–2.35	0.73	–0.28	0.00
· partner vs. parent	0.84	0.94	0.07	0.37
· partner vs. sibling	–1.89	0.70	–0.24	0.01
· partner vs. other	–1.53	0.75	–0.17	0.04
factors associated with expectations of miscellaneous consequences				$R^2 = 0.08$
constant	2.07	0.94		
negative affect	1.02	0.49	0.19	0.04
problem-oriented coping	0.04	0.02	0.16	0.07

discussion

In the present study, we found that donors' mental health, social support, and generic coping as well as the relationship with the recipient were associated with more extreme positive and negative expectations of personal consequences of donation. On the one hand we found that the positive component of mental health, i.e., psychological wellbeing was not related to the level of expectations. On the other hand, the negative component of mental health, psychological complaints, was significantly related to expectations. This is in line with the finding of Rodrigue and colleagues that lower scores on the mental component of the SF-36 were related to more extreme positive and negative expectations[4]. We found that particularly negative affect was associated with more extreme positive and negative expectations. Depression, deficiency in social support, and less use of an active coping style were also independently related to at least one of the positive expectation subscales. Less use of an active coping style was also related to more extreme expectations of negative health consequences. Research has shown that depression, deficiency in social support, and less use of an active coping style are generally related to a higher negative affect[16-18]. Therefore the direction of the relationship between negative affect and expectations is the same as the relationship between depression, social support, coping style, and expectations. These findings suggest that more depressed and potentially isolated potential donors expect greater personal consequences of living donation.

Since the current study had a cross-sectional design, it remains unclear whether the mental health status of the potential donors influenced their expectations or vice versa. We can only speculate about the causality of the associations found. It is possible that anxiety contributed to less positive expectations, since studies in other settings also revealed that anxious persons have less positive expectations than non-anxious persons[19]. Similarly, it is possible that higher negative affect contributed to more extreme negative expectations. This is in line with studies in other situations in which individuals with a higher negative affect have a tendency towards hopelessness and have more extreme negative expectations of situations[20]. In contrast, we found that a higher negative affect was also related to more extreme positive expectations. This could be a compensation for the negative expectations and take away the cognitive dissonance that could be the consequence of the negative expectations. Cognitive dissonance refers to discomfort that arises when a person has two or more conflicting cognitions and the cognitive mechanisms that arise to reduce the discomfort[21]. In this case, potential donors could experience discomfort as result of their negative expectations and their wish to continue with the donation procedure. The positive expectations could be the consequence of a cognitive mechanism to justify their choice. Another possible explanation is that some people tend to have unrealistic high expectations about events in their lives which may lead to discrepancies between expectations and outcomes[22]. These discrepancies make them vulnerable for a negative affect[22]. Donors with more extreme expectations also appear to have a less positive psychological profile and possibly hope to gain more from their donation.

Finally, we found that factors that denote a close relationship with the recipient were associated with more extreme positive and negative expectations. Earlier research of Rodrigue and colleagues revealed that genetically unrelated donors expected less interpersonal benefit and had more extreme negative expectations[4,23]. However, since the unrelated group included also emotionally related relationships, such as partners and friends, comparisons with these results are not possible. The finding that those close to the recipient had more extreme positive expectations could be the consequence of the impairments in quality of life that these individuals experience before donation as result of the kidney disease of the recipient. The finding that partners had more extreme expectations of negative health consequences than unspecified donors, children, siblings and the ‘other’ relationships, could be the due to the double role of donor and caregiver of the recipient which could impede a speedy recovery from surgery.

A limitation of the current analysis is that only comparisons between partners and the other categories were made and no comparisons between the other five relationship categories, because we chose the group that represents the majority of participants as reference group[24]. Given the sample size further comparisons were not possible. A second limitation is that five items of the LDEQ concern the recipients and therefore are not applicable for unspecified donors. Due to the large number of items concerning recipients in the Quid Pro Quo subscale, no scores were calculated for the unspecified donors. Therefore the findings for this outcome cannot be generalised to unspecified donors.

The results of the current study offer many challenging questions for future research. The main question is whether expectations relate to subsequent mental health after donation. On the one hand, one would expect that an optimistic view (i.e., extreme positive expectations) of a situation predicts more positive experiences. On the other hand, if positive expectations are not fulfilled after donation, disappointment could follow. Rodrigue and colleagues have suggested that there may be an optimal level of expectations[4]. Further research is needed to clarify when expectations are too high or too low and whether these expectations have consequences for the mental health of the donor. In order to answer these questions, prospective cohort studies are needed in which mental health, predonation expectations and postdonation expectation fulfilment are measured.

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4

Exploring knowledge about dialysis, transplantation, and living donation among patients and their living kidney donors

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abstract

background

In order to make a well-considered decision and give informed consent about renal replacement therapy, potential living kidney donors and recipients should have sufficient understanding of the options and risks.

purpose

We aimed to explore knowledge about Dialysis & Transplantation (DT) and Living Donation (LD) among prospective living kidney donors and recipients.

methods

Eighty-five donors and 81 recipients completed the Rotterdam Renal Replacement Knowledge-Test (R3K-T) 1 day before surgery. The questionnaire was available in various languages.

results

Recipients knew significantly more about DT than donors ($p < 0.001$); donors knew more about LD than recipients ($p < 0.001$). A minority of donors (15%) and recipients (17%) had a score that was comparable to the knowledge level of the naïve general population. Recipients and donors knew less about DT and LD if their native language was not Dutch. In addition, recipients knew less about DT if they were undergoing pre-emptive transplantation.

conclusions

We conclude that recipients and donors retain different information. The decision to undergo living donation appears to be not always based on full knowledge of the risks. We recommend that professionals assess knowledge of prospective donors and recipients during the education process using the R3K-T, and extra attention is required for non-native speakers.

introduction

Live donor kidney transplantation is the best option for extending and improving the lives of patients with end-stage renal disease (ESRD)[1,2]. For the living donor, the short term medical outcomes are well documented: the overall mortality rate is 0.03%[3,4] and the morbidity rate (including minor complications) is <10%[5]. Two recent studies showed an increased risk of ESRD among living kidney donors on the long term after donation[6,7]; however, the majority of studies revealed that donors have a normal life span and an excellent quality of life many years after donation[8-11].

Although some have argued that the living donation procedure goes against the medical ethical principle of primum non nocere or 'first do no harm'[12], it is justified for two reasons. Firstly, the benefits for the donor are a justification, such as an increased quality of life[13]. Secondly, the right to autonomy[14], which comprises that individuals have the right to determine what they do and what happens to their body.

In order to make a well-considered autonomous decision regarding living kidney donation, it is important that the potential donor is fully informed about the consequences of the donation/transplantation procedure and other renal replacement therapies (RRT) and the decision is consistent with the person's values[15]. In addition, the potential donor should be willing to donate, medically and psychosocially suitable, and free from coercion[16]. These components constitute the 'informed consent'[16]. For every medical treatment, informed consent is important in order to guarantee a patient's autonomy[17]. Informed consent is particularly important among living donors since the right to autonomy is one of the justifications of this procedure as mentioned above[14].

However, two studies have shown that some living kidney donors do not completely consider the risks versus the benefits of the donation[18,19]. Moreover, a retrospective study by Valapour and colleagues[20] revealed that a substantial percentage of donors reported after donation that they had not completely understood the psychological, financial, and long-term medical risks of donation at the time of their surgery. What is yet unknown is the actual level of knowledge on dialysis, transplantation, and living donation among prospective living kidney donors at the time of the donation and the factors that are associated with their knowledge. This question is relevant to examine whether professionals should make extra efforts (in particular cases) to ensure that the prospective donor makes a well-informed decision.

Like potential donors, patients with ESRD need appropriate knowledge about dialysis, transplantation, and living donation to make a fully informed treatment decision[21]. Therefore, we also investigated the knowledge level of prospective recipients. This examination is also relevant as a lack of knowledge among ESRD patients is probably related to concerns regarding living donation[22] and a barrier to pursuing live donor kidney transplantation[23-25]. In reaction to this, various educational interventions have been developed to increase knowledge and indirectly to promote live donor kidney transplantations[23]. Insight into the current gaps in recipients' knowledge and the factors that are associated with knowledge are relevant for improving such interventions.

In the present study, we explored the level of knowledge about dialysis, transplantation, and living donation among prospective living kidney donors and recipients using the Rotterdam Renal Replacement Knowledge-Test (R3K-T)[26-28]: at a moment in time when they should be fully informed yet still be unbiased by the experience. Our aim was to examine whether there were gaps in knowledge among prospective donors and recipients. We also aimed to examine whether knowledge differed between donors and recipients and the socio-demographic and medical factors that are associated with knowledge.

methods

participants & procedure

In our center, all donors and recipients have consultations with a nephrologist, a nurse practitioner, a transplant coordinator, and a social worker, in which written and verbal information about the donation/transplantation process and accompanying risks and consequences is provided. The written information is provided in the native language of the donor/recipient when possible. Subsequently, the prospective donors and recipients sign an informed consent form for the donation/transplantation procedure.

Between 19 April 2011 and 28 February 2012, all prospective living kidney donors and living donor kidney recipients who were hospitalized for living donation or transplantation at Erasmus Medical Center in Rotterdam were invited to participate in this study on the day of admission into the hospital (1 day before donation/transplantation). The participants were informed about the study and were asked to complete a written questionnaire in their native language (see below). Under Dutch law, simple questionnaire-based investigations do not need approval of a medical ethical committee.

In addition, we used data from Ismail et al.[26] consisting of R3K-T scores of a representative sample from the general Dutch population (n = 515) that completed the questionnaire in an online survey. For more details about this sample see Ismail et al.[26]

measurements

socio-demographic characteristics

The following socio-demographic characteristics were obtained from medical records: age, gender, marital status, employment status, highest level of education completed, native country, native language, religious affiliation, and registration in the Dutch organ donation register. Finally, we assessed co-habitation by asking if the donor and recipient lived in the same house (yes/no). Co-habitation was included as indicator for the closeness of the relationship between donor and recipient that could influence the knowledge level of the participants. See **[t1]** for details.

knowledge level

The Rotterdam Renal Replacement Knowledge-Test (R3K-T)[26-28] was used to measure knowledge about dialysis, transplantation, and living donation. The items of the questionnaire were based on literature as well as on contributions of experts and patients who were involved during the item generation process[26]. The questionnaire consists of 21 items and takes 10-15 min to complete. The scale comprises two subscales: the first subscale is *dialysis and transplantation* (DT) and consists of 11 items, and the second subscale is *living donation* (LD) and consists of 10 items. The test is available in nine languages: Dutch, English, French, Spanish, Arabic, Turkish, Papiamento, Portuguese, and Modern Hindi, which are the most commonly spoken languages in the Rotterdam region. In cases of doubt about an answer, the participants were asked to answer with 'I do not know'; this was scored as an incorrect answer. Correct answers were assigned a score of one and summed per subscale. The scores on the subscales were summed to calculate a total score.

The R3K-T has been validated in 187 patients on dialysis, 82 patients who were undergoing live donor kidney transplantation the following day, and the Dutch (n = 515) and American general population (n = 550)[26]. In the present study, we explored the knowledge of the same population of 82 patients who were undergoing live donor kidney transplantation the following day with their associated living donors. We excluded one recipient of this population for our analysis, because this person did not meet our criterion of completion of 70% of the questionnaire.

medical factors

Medical factors that are indicators of experience with ESRD and RRT were obtained from the recipients' medical records: whether the cause of kidney failure was an inherited disease (yes/no), whether the patient was on dialysis prior to transplantation (yes/no), and whether this transplantation was the first transplantation or a re-transplantation. Transplantation without previous dialysis is called 'pre-emptive transplantation'. See **[t1]** for details.

statistical analyses

Firstly, we examined whether socio-demographic characteristics differed between participants versus non-participants (donors and recipients who refused to participate or were not approached due to logistical issues) using independent t-tests for continuous data and chi-square tests for categorical data.

Secondly, to examine whether there were gaps in knowledge among prospective living kidney donors and recipients, their scores were compared with knowledge scores of the general Dutch (naïve) population. Boxplots were made for the three groups on the two subscales. Then, we examined how many donors and recipients had scores that resemble the knowledge of the naïve population better than the knowledge of their own population. We classified the scores of donors and recipients using cutoff points as calculated by the c-formula of Jacobson and Truax[29]. We calculated the cutoff point for the donor population using the means and standard deviations of the donor population and the naïve population on the R3K-T, resulting in a cutoff point $c = 12$. If a donor has a R3K-T score lower than 12, his/her knowledge level is more comparable with the knowledge level of the naïve population rather than the donor population. Cutoff points for the recipient population reported by Ismail et al.[26] were used for the recipients: the cutoff point between the naïve population and dialysis patients is $c = 11$, the cutoff point between dialysis patients and the recipient population is $c = 14$.

Thirdly, to investigate which items were not well understood by the donors and recipients, we calculated the percentages of the donors and recipients who answered the question incorrectly or did not know the answer.

Finally, we conducted a multivariate analysis of variance (MANOVA) to examine whether recipients and donors had different knowledge levels on the two subscales, and to examine whether socio-demographic variables and medical factors were associated with the scores on the two subscales. Before conducting the MANOVA, three steps were taken. In the first step, we screened the donors' and recipients' knowledge scores for outliers on the total score: z-score > 3.29[30]. In the second step, the scores were reversed and subsequently transformed using a square root transformation, as the donors' and recipients' knowledge scores were not normally distributed. We note that all data reported in this article is transformed back and can be interpreted as the original scores. The final step were univariate analyses (Pearson's correlations for the continuous variables and independent t-tests for the categorical variables) to select the covariates that had a potential relationship with knowledge on DT and LD ($p < 0.10$). In a primary analysis, a MANOVA was conducted with knowledge on DT and LD as dependent variables, and the group factor (donors vs. recipient) as well as the selected socio-demographic variables as independent variables. In a secondary analysis among recipients only, the selected medical factors were added as covariates. Significant covariates in the MANOVA were followed up using univariate ANOVA's.

results

participants

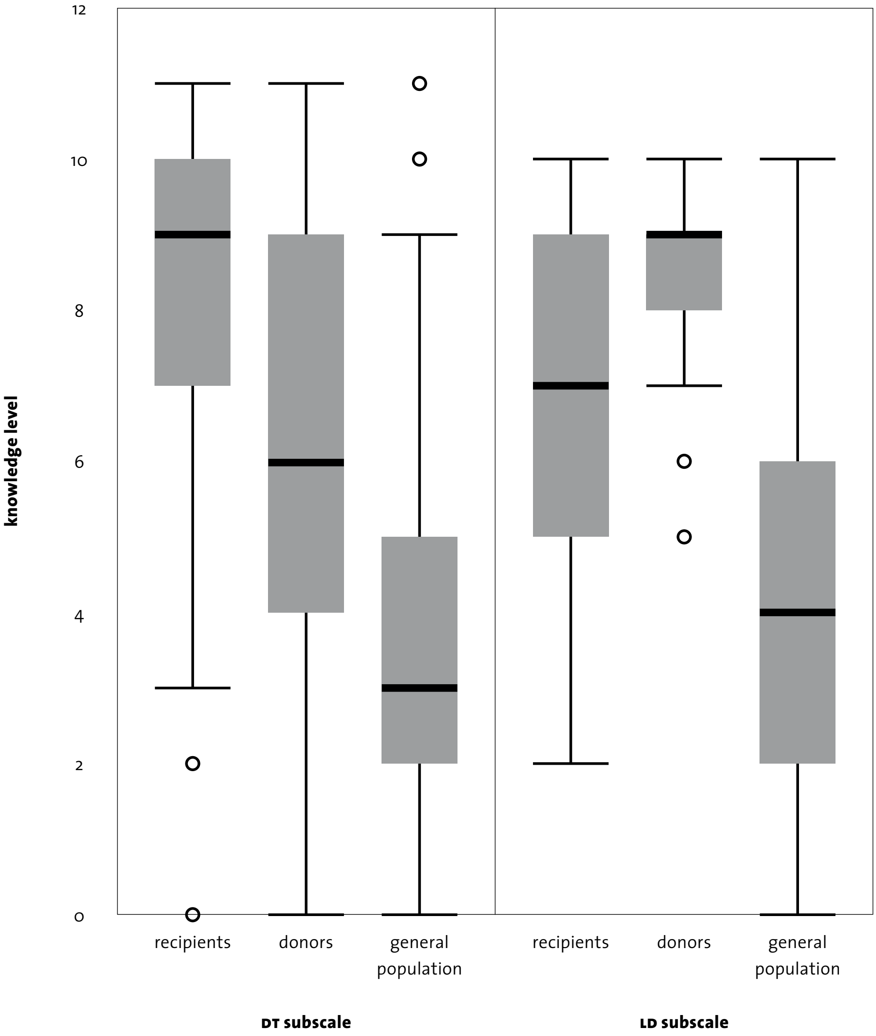
Between 19 April 2011 and 28 February 2012, 115 living kidney donors and 115 living donor kidney recipients were hospitalized for living donation or transplantation. Two recipients were children and were excluded from this study. One recipient was re-transplanted within the research period and was only approached for participation at the first transplantation. Due to logistical issues such as last minute changes in theater planning, we were unable to collect data from 25 recipients and 22 donors. Seven donors refused participation: three donors gave no reason and four donors reported that they were too strained because of their hospitalization. This last reason was also mentioned by five recipients who refused participation. One recipient and one donor completed less than 70% of the questionnaire (15 items or less) and were excluded from the analyses. Consequently, 81 living donor kidney recipients and 85 living kidney donors were studied.

socio-demographic and medical characteristics

[t1] shows the socio-demographic characteristics and medical factors of the 81 prospective living donor kidney recipients and the 85 living kidney donors who participated in this study. Most recipients were male, and over half of the donors were female. Over half of the recipients and donors were married or living together, were well educated, had been born in the Netherlands, had Dutch as their native language, had a religious affiliation, and were not registered in the Dutch organ donation register. Over half of the donors and recipients did not live in the same house. Non-inherited diseases were the most common cause of kidney failure. Most recipients were on dialysis before their transplantation and were about to undergo primary transplantation.

[t1] also shows the socio-demographic and medical characteristics of the non-participants and a comparison of these characteristics with the participants' characteristics. Recipients and donors who participated in this study did not differ from recipients and donors who did not participate on all socio-demographic characteristics and medical factors. We concluded

[f1 the boxplots for the knowledge scores of the recipients, donors, and the general population**]**



that our study population was a representative sample of the donor and recipient population at Erasmus Medical Center.

The participants completed the questionnaire in their own language: one donor completed the questionnaire in English and one recipient in Turkish, the remaining participants completed the questionnaire in Dutch.

gaps in knowledge

The boxplots for the knowledge scores of the recipients, donors, and the general population **[f1]** confirm our finding that donors and recipients differed on their knowledge level. In addition, the boxplots make clear that within the three groups, participants varied widely in their knowledge, except for donors' scores on LD.

Thirteen of the 85 donors (15.3%) had a total score lower than 12, the cutoff point between the naïve population and the donor population. That means that 15.3% of the donors had a score that is comparable with the knowledge level of the naïve population. Fourteen of the 81 recipients (17.3%) had a total score lower than 11, the cutoff point between the naïve population and the dialysis patient population. That means that 17.3% of the recipients had a score that is comparable with the knowledge level of the naïve population rather than that of the patient populations. Nine of the 81 recipients (11.1%) had a total score between 11 (the cutoff point between the naïve population and the dialysis patient population) and 14 (the cutoff point between the dialysis patient population and the recipient population). That means that 11.1% of the recipients had a score that resembles the knowledge of the dialysis patient population better than the knowledge of the recipient or the naïve population.

[t2] and **[t3]** show the percentages of donors and recipients who answered the items incorrectly or did not know the answer. The percentages reveal that donors scored the lowest on items relating to peritoneal dialysis. Recipients scored the lowest on items relating to the health consequences of donation for donors. A substantial minority of donors and recipients answered items concerning the consequences of living kidney donation incorrectly or did not know the answer (item 12-17).

[t1 participants’ socio-demographic characteristics and medical factors]

median age (range)
gender
men
marital status
married/living together
single/divorced/widowed
missing
employment status
paid employment
retired/voluntary work/unemployed
missing
highest level of education completed
primary/secondary school
further education
missing
native country
the Netherlands
other country
native language
Dutch
non-Dutch
missing
religious affiliation
yes
no
missing
registered in Dutch organ donation register (deceased donation)
yes
no
missing
co-habitation
yes
no
missing
cause of kidney failure
inherited disease
non-inherited disease
missing
pre-emptive transplantation
yes
number of transplants
first transplantation
re-transplantation (>1)

recipients			donors		
participants (n = 81)	**non-participants (n = 31)**	***p***	**participants (n = 85)**	**non-participants (n = 30)**	***p***
55 (19–77)	55 (22–79)	0.894	49 (21–86)	53 (21–83)	0.588
		0.640			0.985
56 (69.1)	20 (64.5)		37 (43.5)	13 (43.3)	
		0.075			0.562
58 (71.6)	17 (54.8)		60 (70.6)	20 (66.7)	
22 (27.2)	14 (45.2)		23 (27.1)	10 (33.3)	
1 (1.2)	0		2 (2.4)	0	
		0.439			0.366
37 (45.7)	11 (35.5)		50 (58.8)	15 (50.0)	
43 (53.1)	18 (58.1)		34 (40.0)	15 (50.0)	
1 (1.2)	2 (6.5)		1 (1.2)	0	
		0.786			0.964
33 (40.7)	14 (45.2)		36 (42.4)	13 (43.3)	
45 (55.6)	17 (17.6)		48 (56.5)	17 (56.7)	
3 (3.7)	0		1 (1.2)	0	
		0.641			0.119
62 (76.5)	25 (80.6)		73 (85.9)	22 (73.3)	
19 (23.5)	6 (19.4)		12 (14.1)	8 (26.7)	
		0.558			0.131
69 (85.2)	25 (80.6)		74 (87.1)	23 (76.7)	
12 (14.8)	6 (19.4)		10 (11.8)	7 (23.3)	
–	–		1 (1.2)	0	
		0.265			0.837
50 (61.7)	15 (48.4)		53 (62.4)	19 (63.3)	
31 (38.3)	15 (48.4)		28 (32.9)	11 (36.7)	
0	1 (3.2)		4 (4.7)	0	
		0.072			0.230
26 (32.1)	11 (35.5)		32 (37.6)	6 (20.0)	
50 (61.7)	15 (48.4)		50 (58.8)	22 (73.3)	
5 (6.2)	5 (16.1)		3 (3.5)	2 (6.7)	
		0.222			0.677
29 (35.8)	15 (48.4)		33 (38.8)	10 (33.3)	
52 (64.2)	16 (51.6)		52 (61.2)	19 (63.3)	
–	–		0	1 (3.3)	
		0.967			
20 (24.7)	9 (29.0)				
37 (45.7)	17 (54.8)				
24 (29.6)	5 (16.1)				
		0.117			
31 (38.3)	7 (22.6)				
		0.475			
69 (85.2)	28 (90.3)				
12 (14.8)	3 (9.7)				

[t2 percentages of the donors/recipients who answered items incorrectly or did not know the answer on the subscale 'dialysis and transplantation'**]**

subscale DT	item	correct answer	recipients	donors
1	Peritoneal dialysis is a form of dialysis for treating patients with end-stage renal disease. Which part of the body makes this treatment possible?	the peritoneum	18.5	52.9
2	Peritoneal dialysis is a form of renal replacement therapy that can be used as an alternative for hemodialysis. An advantage of peritoneal dialysis is:	that you have more freedom of movement in between the in and out flow of the dialysis fluid	38.3	64.7
3	During peritoneal dialysis, fluid is brought into the abdominal cavity through a catheter. What happens with the fluid after that?	the fluid stays in the abdominal cavity, after a couple of hours it is removed	44.4	64.7
4	Peritonitis is an infection of the peritoneum. This is one of the biggest problems with patients with peritoneal disease.	true	42.0	58.8
5	Certain vitamins are lost during dialysis. If you are on dialysis you are therefore prescribed extra vitamins.	true	23.5	60.0
6	How many hours a day is a hemodialysis patient connected to the machine?	3-8	12.3	29.4
7	Renal replacement therapy is necessary if kidney function is only 50%.	false	25.9	34.1
8	To be connected to the hemodialysis machine, there must be permanent access to the bloodstream.	true	13.6	32.9
9	Kidneys from living donors have a longer graft survival rate than kidneys from deceased donors.	true	17.3	23.5
10	Kidney transplantation is generally preferred to dialysis for the treatment of end-stage renal disease.	true	11.1	18.8
11	Immunosuppressive drugs are administered to transplant patients for:	prevention and treatment of rejection of the kidney	13.6	23.5

[t3 percentages of the donors/recipients who answered items incorrectly or did not know the answer on the subscale ‘living donation’**]**

subscale LD	**item**	**correct answer**	**recipients**	**donors**
12	Surgical complications after donation are common in living kidney donors.	false	35.8	11.8
13	Donating a kidney increases the risk of developing a kidney disease.	false	18.5	7.1
14	Most living kidney donors remain in the hospital for 2 weeks after surgery.	false	32.1	4.7
15	Very few living kidney donors have long-term health problems after donation.	true	46.9	31.8
16	Kidney donation may affect a woman’s chance of getting pregnant.	false	59.3	47.1
17	Most living kidney donors can participate in sports and work within 4–6 weeks after donation.	true	22.2	14.1
18	When the kidney of a living donor does not match the recipient, living donation is no longer an option with this donor.	false	38.3	27.1
19	A living kidney donor has to be younger than 50 years old.	false	21.0	9.4
20	Only direct family members (brothers, sisters, parents, or children) can donate a living kidney.	false	13.6	1.2
21	All the hospital costs of a living kidney donation are paid for by the recipient’s health insurance and not by the donor’s insurance.	true	19.8	9.4

MANOVA's

primary analysis

The donors' and recipients' scores were screened for outliers on the total score, and one donor was deleted. The following socio-demographic variables had a potential relationship with knowledge on DT and LD and were entered into the MANOVA ($p < 0.10$): group, marital status, employment status, religious affiliation, and native language. Using the Pillai's trace, there was a significant group effect on knowledge, $V = 0.30$, $F(2,151) = 31.85$, $p < 0.001$. There was also a significant association between native language and knowledge on DT and LD, $V = 0.04$, $F(2,151) = 3.14$, $p < 0.05$. Marital status, employment status, and religious affiliation were not related to knowledge on DT and LD. Univariate ANOVA's showed that donors and recipients differed on both subscales **[t4]**: recipients knew more about DT than donors ($F(1,152) = 24.03$, $p < 0.001$) and donors knew more about LD than recipients ($F(1,152) = 19.32$, $p < 0.001$). Univariate ANOVA's also showed that participants whose native language was Dutch knew more about DT than participants whose native language was not Dutch ($F(1,152) = 4.01$, $p < 0.05$). The same effect was found on knowledge about LD ($F(1,152) = 4.36$, $p < 0.05$).

A sensitivity analysis with the outlier included in the MANOVA revealed the same results. The MANOVA was also repeated with interactions between 'group' and the remaining covariates as independent variables to examine whether the effects differed across donors and recipients; however, none of these covariates were significant.

[t4 univariate ANOVA's of significant covariates in the primary MANOVA**]**

	subscale DT (estimates) CI				**subscale LD (estimates) CI**			
	lower bound	**upper bound**	***F***	***p***	**lower bound**	**upper bound**	***F***	***p***
group			24.03	< 0.001			19.32	< 0.001
recipients	6.62	8.06			5.38	6.54		
donors	4.21	6.13			6.72	7.74		
native language			4.01	0.047			4.36	0.038
Dutch	6.53	7.52			6.78	7.43		
non-Dutch	4.12	6.94			5.17	7.01		

secondary analysis

Only the medical factor 'pre-emptive transplantation' had a potential relationship with knowledge and was added into the MANOVA ($p < 0.10$). In the MANOVA, pre-emptive transplantation was also associated with knowledge, $V = 0.25$, $F(2,72) = 11.95$, $p < 0.001$. Univariate ANOVA's showed that this relationship was only significant for knowledge about DT ($F(1,73) = 12.37$, $p < 0.01$) and not for LD, $F(1,73) = 1.48$, $p = 0.23$ **[t5]**. However, as the univariate ANOVA of DT violated the homogeneity of variance assumption, the test was repeated with a Welch's test and showed the same results, $F(1,53.61) = 6.69$, $p < 0.05$. The relationship found included that recipients knew less about DT is they were undergoing pre-emptive transplantation. We note that the relationship between knowledge and native language was not significant in this MANOVA, $V = 0.05$, $F(2,72) = 1.76$, $p = 0.18$.

[t5 univariate ANOVA's of significant covariates in the secondary MANOVA**]**

	subscale DT (estimates) CI				**subscale LD (estimates) CI**			
	lower bound	**upper bound**	***F***	***p***	**lower bound**	**upper bound**	***F***	***p***
pre-emptive transplantation			12.37	0.001			1.48	0.227
yes	4.93	7.34			5.35	7.35		
no	7.30	8.84			4.82	6.62		

discussion

The results of the present study give insight into how informed prospective living kidney donors and living donor kidney recipients are when they completed the informed consent procedure. We found that a number of donors and recipients did not retain all the information they were given as they had incomplete knowledge about dialysis, transplantation, and living donation at the time of their surgery. Furthermore, donors and recipients retained different information: recipients knew significantly more about dialysis and transplantation than donors, and donors knew significantly more about living donation than recipients. Finally, recipients and donors knew less about DT and LD if their native language was not Dutch and recipients knew less about DT if they were undergoing pre-emptive transplantation.

It appears that, even though prospective living kidney donors and recipients are informed and go through the donation process together, they retain different information. This might stem from selective attention for personally relevant information during information gathering. Psychological research has shown that selective attention for personally relevant information strengthens the encoding and retrieval of this information[31].

In addition, we found that 15% of the donors and 17% of the recipients had a score that resembles the knowledge of the naïve general population better than their own population, i.e., they had a significantly lower knowledge level than one would expect. Moreover, we found that a substantial minority of donors and recipients lacked knowledge about the risks of living donation (items 12-17). Results consistent with these findings were found among living liver donors[32]. Valapour and colleagues found in a retrospective study that living kidney donors reported after donation that they lacked knowledge about the risks of donation if they were asked how informed they were at the time of their surgery[20]; however, subsequent experiences could have biased their answers. We found consistent results using an objective measure and at a moment in time when donors are still unbiased by the experience, and subsequently, we add that this is also the case for prospective recipients. Valapour and colleagues[20] concluded that the motivation of potential living kidney donors for donating their kidney is based mostly on a ‘wish to help’[18] rather than on their understanding of the risks and benefits of donation[20,33,34]. A study by Papachristou and colleagues[19] revealed consistent motivations for donation among prospective living liver donors, and also found that a proportion of donors avoided later reconsideration or confrontation with donation-related issues. These studies indicate that the motivations of prospective living kidney donors may lie more in emotional considerations than in rational ones which may influence information retention. It is also possible that some recipients avoid confrontation with donation-related issues. We speculate that this could be the consequence of an avoidant coping style of prospective recipients who have some difficulties in accepting a kidney from their potential donor[35].

These findings raise the question of the potential consequences of a lack of knowledge about the risks of donation/transplantation. Accurate knowledge about a prospective event contributes to realistic expectations and may prevent potential disappointment[36]. Johnson et al.[9] found some indication for this relationship among living kidney donors by showing that donors who experienced the least amount of stress reported that they were well informed and knew what to expect before and after donation. Whether incomplete objective knowledge about the consequences of the donation/transplantation contributes to disappointment and/or stress after donation/transplantation among donors and recipients, needs further research.

Our results show that donors' and recipients' knowledge levels were particularly lower if their native language was not Dutch and therefore deviated from the professional's native language. This result is probably not the consequence of linguistic barriers, as most participants in our study speak the Dutch language fluently: only one donor and one recipient completed the R3K-T in another language than Dutch. It is possible that cultural factors played a role. A review by Schouten et al.[37] showed that if doctors and patients have different cultural and ethnic backgrounds, doctors interact less affectively with the patient and the patients are less assertive and affective during the medical consultations than in case of equal backgrounds. This phenomenon could be the consequence of factors like differences in beliefs about illness and values across cultures, e.g., the perceived appropriateness to talk about illness and ask questions. It is possible that difficulties in the doctor-patient communication contributed to lower knowledge among ethnic minorities in our study; however, this requires further research. As earlier studies also revealed that patients from ethnic minorities are less likely to pursue with live donor kidney transplantation[38], our findings highlight that even if these patients proceed with live donor kidney transplantation, extra care must be taken to ensure full comprehension of information that forms the basis of informed consent. We recommend that if the donor's or recipient's native language deviates from the professional's native language regardless of speaking a common language, extra efforts should be made to ensure that they understand the information they are given and professionals should be sensitive for the potential influence of cultural differences during medical consultations.

A striking result of this study is that native language was associated with knowledge in the primary analysis with donors and recipients included, but not in the secondary analysis with only recipients and the covariate 'pre-emptive transplantation' included. As we found no difference between donors and recipients in the association between native language and knowledge, we conclude that 'pre-emptive transplantation' is probably more strongly associated with knowledge about DT than native language.

Although this study has several strengths, a number of limitations have to be noted. Firstly, knowledge was measured on the day of admission into the hospital, which is a stressful day for some donors and recipients. Possibly a number of participants experienced stress at the time of completing the questionnaire that influenced the recall of knowledge; however, this requires further research. Secondly, as the education process of potential living kidney donors may differ across transplant centers and countries, our findings may not be generalizable to other settings and requires similar research in other countries.

A practical contribution of the present study is the norm scores of actual donors on the R3K-T. The boxplots and cutoff points can be used to determine how a donor scored relative to other donors, recipients, or a naïve population. These insights can be used to determine whether a potential donor or recipient needs extra education. The questionnaire could also be used to examine whether knowledge of potential donors who decided not to donate differ from knowledge of actual donors. The results of such studies could clarify whether a lack of knowledge is a barrier to pursuing living kidney donation, which has been found among potential recipients of live donor kidney transplantation[23].

In conclusion, potential living kidney donors and living donor kidney recipients retain different information during the information process of living donation/transplantation. The decision to undergo living donation/transplantation appears to be not always based on full knowledge of the risks. We recommend that professionals assess knowledge and information needs of prospective donors and recipients using the R3K-T in order to tailor educational efforts to the informational needs of these individuals, and extra attention is required for non-native speakers.

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5

Psychologic functioning of unspecified anonymous living kidney donors before and after donation

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abstract

background
There has been discussion regarding the psychologic functioning of living donors who donate their kidney to an unrelated and unknown patient (‘unspecified living donors’). This is the first prospective study to investigate group- and individual-level changes in psychologic functioning among a large group of unspecified donors.

methods
Forty-nine medically and psychologically screened unspecified living kidney donors completed the Symptom Checklist before and after donation.

results
Group-level analysis showed that overall psychologic symptoms increased after donation ($p = 0.007$); the means remained within the average range of the normal population. Individual-level analysis showed that 33 donors showed no statistically significant change, 3 donors showed a statistically significant decrease, and 13 donors showed a statistically significant increase in psychologic symptoms. Two of the latter donors showed a clinically significant increase.

conclusions
We found more increases in psychologic symptoms than decreases, particularly if follow-up time was longer. However, for almost all donors, these increases were not clinically significant and the clinically significant changes found are comparable with natural fluctuations in psychologic symptoms in the general population. Possibly, the donors underreported their psychologic symptoms before donation to pass the screening. Due to the low level of predonation symptoms reported, regression to the mean could also explain the results. Although we found that changes were not associated with donation-related factors, it is possible that other donation-related factors or other life events not measured have an influence on psychologic functioning. Therefore, further research is needed to investigate whether the fluctuations are related to the donation process.

introduction

Over the past decade, an increasing number of individuals have donated their kidney to an unknown recipient with whom they are not genetically related or emotionally bonded[1]. This type of donor is classified as an 'unspecified donor' and has previously been referred to as an altruistic, anonymous, Good Samaritan, or living unrelated donor[2]. This procedure is performed in only a limited number of countries[3] and the number of these donations is relatively small in comparison with specified donations[1]. Within the transplant community, there has been debate regarding the psychologic functioning of unspecified donors[4,5]. Some professionals questioned whether the motivations of these donors (e.g., 'to help an unknown person without direct benefit') were a sign of psychologic dysfunction[4,6]. A study by Henderson et al.[4] revealed that a significant number of the individuals who were interested in unspecified donation were psychologically stable. However, we know little about whether the donation has an influence on the psychologic functioning of the donors. To gain more insight into this question, it is important to investigate the psychologic functioning of unspecified donors before and after donation.

Until now, a limited number of studies have investigated psychologic outcomes of unspecified living kidney donors after donation[7-10]. These studies concluded that most donors reported no psychologic problems after donation, although a few donors reported unexpected stress or that the donation contributed to depression or anxiety[7,8,10].

A study by Massey et al.[9] investigated the psychologic functioning of the first 24 unspecified living kidney donors in their center using a pre-post design. The results of this study showed few group-level changes in psychologic symptoms after living kidney donation. Although this study reported on one of the largest groups of unspecified donors at that time, the sample size was relatively small for statistical analysis. In addition, a few individuals who donated to a known recipient with whom they had no previous genetic or emotional relationship were included and group-level analyses were used rather than individual-level analyses.

Building upon this previous study[9], we performed a prospective study to investigate group- and individual-level changes in psychologic functioning among unspecified living kidney donors. We used the method of 'clinical significant change' described by Jacobson and Truax[11] to investigate individual-level changes. Although the group-level analysis describes whether the means of the pretest and posttest statistically differ from each other, the clinical significant change method provides information about the variability in changes from person to person and whether these changes are clinically relevant. Further, we included only unspecified donors in the analysis: therefore, the present research population is a homogenous group of unsolicited, unspecified living kidney donors. Finally, we investigated whether socio-demographic characteristics, procedural characteristics of the donation, and self-reported experiences of the donation were associated with changes in psychologic functioning.

methods

participants

Between April 2000 and October 2011, 70 unspecified donors donated their kidney in the Erasmus Medical Center (Rotterdam, the Netherlands) and were invited to participate in the study. One donor did not wish to participate. Thirteen donors without a predonation measurement were excluded from the analysis. Of the remaining 56 donors, 7 donors were already patients themselves before donation: 2 donors had a medical indication for nephrectomy and 5 donors had a chronic disease (2 patients with Huntington's disease, 1 with ependymoma, 1 with oligodendroglioma, and 1 with progressive chronic obstructive pulmonary disease). These donors were excluded from the analyses, because their physical symptoms and the disease progression may influence their psychologic functioning. The 49 remaining donors were included in the analyses.

procedure

In addition to the standard medical and psychosocial screening for every living kidney donor[12], prospective unspecified donors have a consultation with a clinical psychologist (RE). In an in-depth interview, he explores the risk of potential psychologic harm to the donor. The interview covers the following topics: motives, voluntariness, expectations, psychiatric background, emotional resilience, understanding of the associated risks, perception of reality, earlier hospital experience, anticipated regret, and practical and emotional social support. Furthermore, the potential donor completes the SCL-90 using a pen-and-paper test (see *measurements*). The predonation SCL-90 measurement was used as the baseline in the current study.

After donation, the SCL-90 was administered by a psychologist (LT) via the telephone or completed by the donor at the outpatient clinic.

measurements

socio-demographic characteristics

The following socio-demographic characteristics were obtained from medical records: age (years), gender, ethnicity, employment status, marital status, highest level of education completed, number of children, religious affiliation, and whether the person was registered in the Dutch organ donation register **[t1]**.

psychologic functioning

The Dutch version of the SCL-90[13] was used to measure psychologic functioning. The SCL-90 consists of 90 items that measure self-reported psychologic symptoms of the past 2 weeks. Each item is rated on a five-point Likert scale ranging from *not at all* to *extremely*. The total score of the questionnaire (psychoneuroticism) gives an indication of current general psychologic functioning (potential range, 90-450). A higher score indicates greater psychologic symptoms. The SCL-90 also comprises eight subscales: agoraphobia, anxiety, depression, somatization, inadequacy in thought and action, interpersonal sensitivity, hostility, and sleep problems. Scores for each subscale were summed.

The internal consistency (Cronbach's α) for the total score is 0.97 for the general Dutch population, which represents excellent reliability. The internal consistency of the eight subscales varies between good and excellent (α = 0.76-0.91). Because of the high reliability the SCL-90 can be used to draw conclusions on an individual level and it is a valid instrument to distinguish between the normal population and psychiatric populations[13].

procedural characteristics and experiences of the donation

The following procedural characteristics of the donation were obtained from medical records: type of donation (donation directly to a person on the waitlist or a domino-paired procedure[14]) and length of hospital admission (days) and the occurrence of minor medical complications (e.g., wound infection) within 3 months after donation (yes/no). None of the donors experienced a major complication. At Erasmus Medical Center, unspecified donors are asked if they want to donate in a domino-paired procedure or directly to the waitlist. Time between the date of donation and postdonation measurement (months) was recorded as 'time since donation'.

Self-reported physical health before donation (1 = very bad and 10 = very good) was obtained from a self-constructed questionnaire that was administered by the transplantation coordinator before donation. Finally, the following self-reported experiences of the donation were obtained from self-reported questionnaires that were administered by the transplant coordinator 3 months after donation: physical health (1 = very bad and 10 = very good), whether donation fulfilled one's expectations (1 = disappointed and

10 = exceeded one's expectations), and after how many weeks the donor felt completely recovered. The administration of these self-constructed questionnaires is part of standard procedure for donors at Erasmus Medical Center.

statistical analyses

First, we computed the averages of the predonation and postdonation SCL-90 total scale and the subscales. These averages were compared with the norm scores of the Dutch general population, which are classified into seven categories ranging from very low to very high psychologic symptoms. Paired t-tests were carried out to examine whether the predonation and postdonation means differed.

Second, to investigate the individual-level changes in psychoneuroticism, we used the method of 'clinical significant change'[11]. To our knowledge, this is the most appropriate method to describe individual changes in psychologic symptoms. We used the method as described in the Dutch manual of the shortened version of the SCL-90, the Brief Symptom Inventory[15].

The method of 'clinical significant change' consists of two criteria. The first criterion is statistical significance, which is measured using the Reliable Change Index (RCI). Using the RCI, one can determine whether an individual change in symptoms is more than one can expect based on measurement error. An individual change is considered to be statistically significant if the individual change exceeds the RCI. We calculated the RCI for the psychoneuroticism score with the RCI formula described by Jacobson and Truax[11]. We used the internal consistency (Cronbach's $\alpha = 0.97$) and the SD's of the general Dutch population (SD = 32.38) and the outpatient psychiatric patients (SD = 61.60) that are described in the Dutch manual of the SCL-90[13]. These calculations result in a RCI = 16 for the functional range and RCI = 30 for the dysfunctional range.

The second criterion is clinical significance, a cutoff point between the functional and the dysfunctional range. We calculated this cutoff point for the psychoneuroticism score with the c-formula reported by Jacobson and Truax[11]. We used the Dutch general population norms (mean = 118.28, SD = 32.38) and the outpatient psychiatric patients norms (mean = 203.55, SD = 61.60)[13], resulting in a cutoff point of C = 148. All participants with a score lower than the cutoff point were categorized in the functional range, and all participants with a score above this point in the dysfunctional range. A statistically significant change is a requirement for a clinically significant change[16].

The third question is whether socio-demographic characteristics, procedural characteristics, and self-reported experiences of the donation were related to changes in the psychoneuroticism score. Univariate analyses (correlation for continuous variables and independent t-tests for the categorical variables) were carried out to select the predictors that had a potential relationship with psychoneuroticism difference scores ($p < 0.15$). Subsequently, we carried out a saturated multilevel regression with time (predonation vs. postdonation), these predictors, and their interactions with time as covariates. Using Wald tests, nonsignificant covariates were removed step by step until a parsimonious model was reached. Cohen's d was calculated for the difference between pre- and post-test estimates.

[t1 socio-demographic characteristics of participants**]**

	***n* (%)**
gender	
male	28 (57.1)
ethnicity*	
caucasian	47 (95.9)
asian	1 (2.0)
employment	
paid employment	30 (61.2)
retired / voluntary work / unemployed	18 (36.7)
marital status	
married / living together	27 (55.1)
single / divorced / widowed	22 (44.9)
children*	
yes	29 (59.2)
highest level of education	
high school	21 (42.9)
further education	28 (57.1)
religious*	
yes	26 (53.1)
registered in Dutch organ donation register (deceased donation)*	
yes	40 (81.6)
type of donation	
directly to person on the waitlist	14 (28.6)
to a recipient of an incompatible couple (domino-paired)	35 (71.4)

* one missing

results

socio-demographic characteristics

Forty-nine unspecified donors completed the Symptom Checklist (scl-90) before (median: 9, range: 2-13 months) and after (median: 19, range: 3-36 months) their donation. **[t1]** shows the socio-demographic characteristics of the participants. Age at donation ranged between 31 and 84 years (median: 59 years). The participants were all Caucasians, except for one; more than half of the participants were male, in paid employment, well educated, religious, married or living together, and a parent.

psychologic symptoms

Twenty-five donors completed the self-reported questionnaire scl-90 via the telephone and 24 donors completed the questionnaire at the outpatient clinic. Postdonation psychologic symptoms did not differ according to method of completion ($t(47) = -0.52$; $p = 0.61$).

group-level analyses

[t2] gives an overview of the means and standard deviations (sd) of the predonation, postdonation, and difference scores. A higher score on the scl-90 refers to a greater number of symptoms and thus lower psychologic functioning. These mean scores were compared with the Dutch norm scores of the general population[13]. **[t2]** shows that the means of the predonation and postdonation total and subscales fall into the average range for the general Dutch population, with the exception of the mean of ‘sleep problems’, which falls into the high range after donation.

Paired t-tests revealed significantly higher postdonation scores than predonation scores for the total score (psychoneuroticism) and the subscales: anxiety, depression, somatization, hostility, and sleep problems **[t2]**. Agoraphobia, inadequacy in thought and action, and interpersonal sensitivity did not significantly change.

[t2 psychologic symptoms (N = 49)**]**

subscales	average ranges of general Dutch population[12]	predonation mean (SD)	postdonation mean (SD)	difference scores mean (SD)	paired-samples t-test t	*p*
anxiety	12-14	11.53 (1.77)	12.31 (2.64)	0.78 (2.48)	−2.19	0.03
agoraphobia	7-8	7.67 (1.48)	7.47 (0.89)	−0.20 (1.22)	1.17	0.25
depression	20-23	20.24 (4.59)	22.47 (7.17)	2.22 (5.17)	−3.01	0.004
somatization	15-18	15.10 (3.19)	16.45 (5.12)	1.35 (3.38)	−2.79	0.008
inadequacy in thought and action	11-14	12.45 (3.77)	13.16 (4.02)	0.71 (3.22)	−1.55	0.13
interpersonal sensitivity	22-26	23.63 (5.88)	23.63 (6.33)	0.00 (4.96)	0.00	1.00
hostility	7-8	6.98 (1.30)	7.61 (2.31)	0.63 (1.72)	−2.58	0.01
sleep problems	4-5	4.59 (1.79)	5.31 (2.83)	0.71 (2.51)	−1.99	0.05
total score: psychoneuroticism	113-123	112.63 (19.89)	119.47 (25.89)	6.84 (17.06)	−2.81	0.007

[t3 final multilevel linear model with psychoneuroticism as outcome**]**

	b	SE b	95% CI	*p*
intercept	112.632	3.24	[106.16 – 119.11]	< 0.001
time (pre-post)	6.839	2.32	[2.18 – 11.49]	0.005
time since donation (months)	−0.085	0.30	[−0.68 – 0.51]	0.78
time × time	0.431	0.21	[0.01 – 0.86]	0.05

individual-level analyses

[f1] and **[f2]** show the classification of the predonation and postdonation scores of the participants based on the two criteria of clinical significant change. All individuals in sections A to D had a predonation score that fell into the functional range (n = 45). The individuals in section A showed a statistically significant decrease in symptoms (n = 3). The individuals in section B showed no statistically significant change and were thus ‘unchanged’ (n = 30). The individuals in section C showed a statistically significant increase in psychologic symptoms; however, their postdonation score remained in the functional range and was thus not clinically significant (n = 10). The individuals in section D also showed a statistically significant increase and their postdonation score shifts to the dysfunctional range and was thus clinically significant (n = 2).

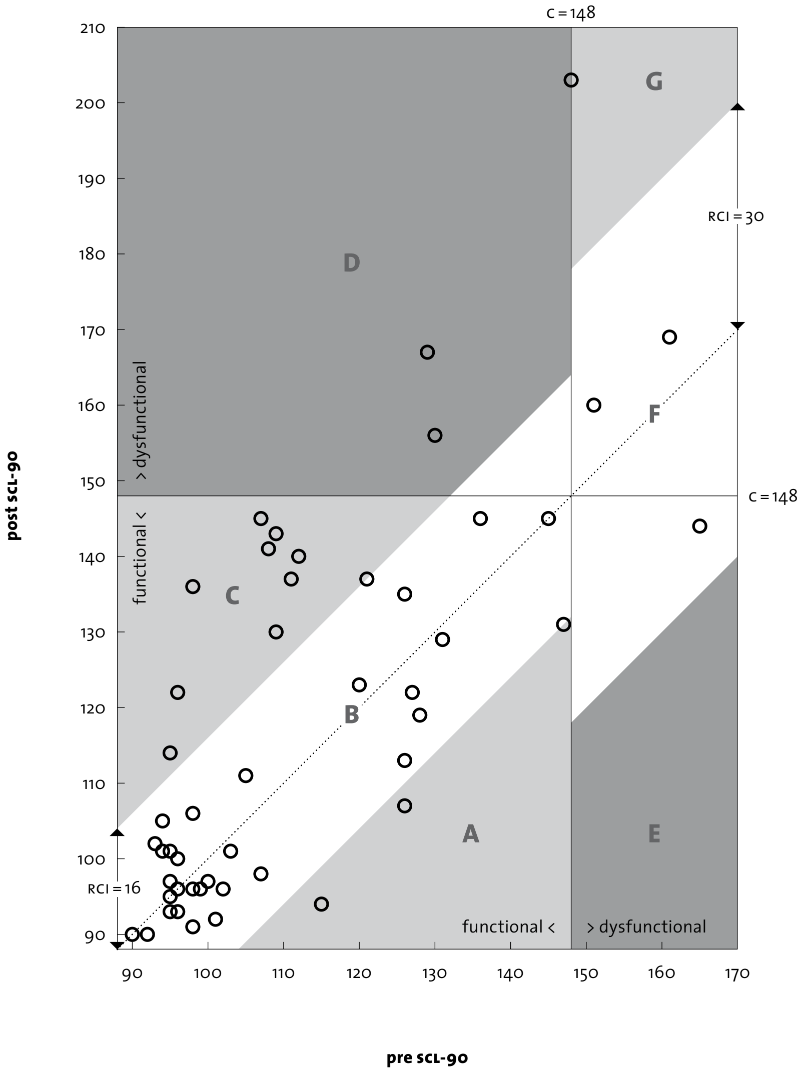
All individuals in sections E to G had a predonation score that fell into the dysfunctional range (n = 4). There are no individuals in section E, which shows a clinically significant decrease in symptoms. The individuals in section F showed no statistically significant change and were thus ‘unchanged’ (n = 3). The individual in section G showed a statistically significant increase in symptoms (n = 1).

factors associated with change in psychologic symptoms

association with socio-demographic characteristics, procedural characteristics, and self-reported experiences of the donation

The following factors that had a potential predictive relationship with psychoneuroticism difference scores were entered into the model ($p < 0.15$): time since donation, whether donation fulfilled one’s expectations, and marital status. The final model retained time (predonation vs. postdonation) and ‘time since donation’ and their interaction as co-variates **[t3]**. We centered ‘time since donation’ to facilitate the interpretation. This model implies that participants with a mean time since donation (19.3 months) had a predonation psychoneurotic estimation of 112.6 and a postdonation score of 119.5 (d = 0.30, a small effect). Participants who had a year longer time since donation had about the same predonation score, but their postdonation score was estimated at 124.6 (d = 0.53, a medium effect). Participants with a year shorter time since donation (i.e., ~ 7 months) had a marginal increase in psychoneuroticism score (114.2; d = 0.07).

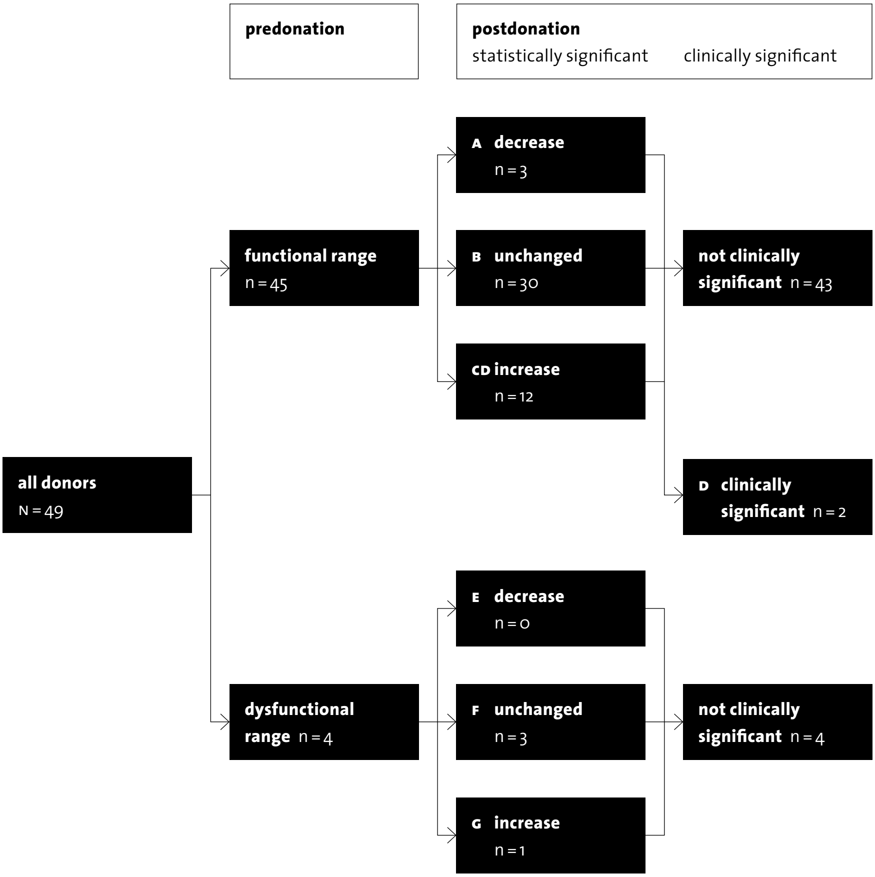
[f1 scatter plot of distribution total scores]



A-D **predonation score in the functional range**
A statistical significant decrease
B no statistically significant change
C statistically significant increase but not clinically significant
D statistically and clinically significant increase

E-G **predonation score in the dysfunctional range**
E statistically and clinically significant decrease
F no statistically significant change
G statistically significant increase

[**f2** distribution of the donors following the two criteria of clinical significant change]



A-D predonation score in the functional range

A statistical significant decrease
B no statistically significant change
C statistically significant increase but not clinically significant
D statistically and clinically significant increase

E-G predonation score in the dysfunctional range

E statistically and clinically significant decrease
F no statistically significant change
G statistically significant increase

discussion

In the present study, we investigated both group- and individual-level changes in psychologic functioning among unspecified living kidney donors between predonation and postdonation. We note that the sample size is relatively small; however, because unspecified donation is not a common procedure, we describe the psychologic functioning of the largest group of unspecified donors to our knowledge. On a group level, we found an increase in overall psychologic symptoms, anxiety, depressive symptoms, somatization, hostility, and sleep problems between predonation and postdonation. However, the means of these scales remained within the average range compared with Dutch norm scores after donation, with the exception of sleep problems. These findings are consistent with the study of Massey et al.[9] On an individual level, most donors (n = 33) showed no statistically significant change, whereas a minority showed a statistically significant decrease (n = 3) or increase (n = 13) in psychologic symptoms. However, 2 of those 13 donors showed a clinically significant increase. This number corresponds with the percentage of donors who reported that being a donor contributed to anxiety or depression in the earlier mentioned study of Rodrigue et al.[10] Also, among specified donors, most studies reveal that a small percentage of the donors show an increase in psychologic symptoms, although the results are, to some extent, conflicting[17]. Our results highlight the importance of long-term psychologic follow-up of unspecified living kidney donors and psychosocial support upon indication. A subsequent question is whether the fluctuations found are attributable to the donation process.

A first consideration is that the predonation measurement was part of the psychosocial screening. It is plausible that some donors underreport their psychologic symptoms before donation to pass the screening. A study by Hurst et al.[18] also indicated that living kidney donors have the tendency to respond in a socially desirable manner and try to appear psychologically healthy during a psychologic evaluation before the donation. Repressed predonation scores could account for the change in symptoms over time.

A second consideration is that, as a consequence of the low level of symptoms reported before donation, ‘regression to the mean’ could explain the results. Regression to the mean refers to the phenomenon that, in the case of an extreme score on a first measurement, the score will tend to be closer to the mean on the second measurement[19]. The donors successfully passed the screening partly because they had low scores on the SCL-90 (**[f1]** shows that the predonation scores are relatively low). Subsequently, the chance of scores closer to the mean at the second measurement point is greater than the chance of the same extreme scores. Similarly, because most donors had a predonation score in the functional range, it was not possible to show a clinically significant decrease in psychologic symptoms, and it was only possible to remain stable or increase.

A third consideration is the question whether the two cases of clinically significant increase in psychologic symptoms are comparable with observed variation in psychologic symptoms in the general population. The incidence rate of first onset of any mental disorder in the general population is 5.7 per 100 person-years at risk in the Netherlands[20] and 6.6 per 100 person-years at risk in the United States[21]. In our study, we found that 4% shifted from a functional to a dysfunctional range in a median time of 26 months (range, 6-46 months). Comparing this percentage with the incidence rates in the general population, the fluctuations found in our study appear to be comparable with natural fluctuations in psychologic symptoms in the general population. We note that the SCL-90 gives an indication of the level of psychologic symptoms and is not a tool for making a clinical diagnosis. Nevertheless, the SCL-90 does successfully discriminate between psychiatric patients and healthy individuals[22].

A fourth consideration is that more time after donation was correlated with a larger increase in psychologic symptoms. This association could have different explanations. First, it is possible that donors experience a boost in self-esteem and life satisfaction as result of feelings of pride and positive reactions from the environment right after donation. This was also found in the study by Rodrigue et al.[10]. This boost could suppress or outweigh psychologic symptoms in the first months after donation. However, these positive effects might diminish over time, through which psychologic symptoms come to the fore. A second possible explanation is that the fluctuations are not related to the donation process but are affected by other life events in the intervening time. The data of this current study cannot clarify whether one of the explanations is true, because we did not register other life events during the research period and time between donation and postdonation measurement varied per donor.

A final consideration is that if the changes in psychologic symptoms were associated with the donation, one would expect that donors with a less positive experience of the donation (e.g., who experienced a minor medical complication) would show a greater increase in psychologic symptoms. Because we did not find associations between change in psychologic functioning and procedural characteristics of the donation and self-reported experiences of the donation, this suggests that the fluctuations in psychologic symptoms are independent of the donation. However, it is possible that other donation-related factors not measured in this study (e.g., pain) have an influence on psychologic functioning.

To get more insight into the question whether the fluctuations in psychologic functioning are attributable to the donation process, prospective cohort studies are needed in which psychologic functioning is measured at several and consistent time intervals for every donor and comparisons could be made with the changes in psychologic functioning of specified donors. Multicenter or international studies would allow greater generalizability of the results. Other life events and other donation-related factors (e.g., pain and expectations regarding the donation) not measured in this study should be taken into account. In addition, positive aspects of mental health (e.g., self-confidence) should be measured to evaluate the potential occurrence of a boost in mental health after donation.

In conclusion, we found fluctuations in psychologic symptoms over time that were more often increases than decreases, particularly if the time since donation was larger. However, for almost all donors, these increases were not clinically significant and the clinically significant changes found are comparable with natural fluctuations in psychologic symptoms in the general population. Repressed predonation scores as consequence of underreporting before donation and regression to the mean might have contributed to the change in symptoms over time. Based on the current data, it remains unclear whether the fluctuations are attributable to the donation process or not; therefore, further research is needed. Additionally, the results of this study highlight the importance of long-term psychosocial follow-up of unspecified living kidney donors and psychosocial support upon indication.

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6

An argument to abolish legal restrictions on unspecified living kidney donation

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Increasingly more individuals came up with a wish to donate a kidney to an unknown and arbitrary patient from the kidney transplant waiting list. This type of donation is called ‘unspecified donation’ and implies that the donor and recipient are genetically and emotionally unrelated. It is only performed in a few countries because most countries have legal restrictions against unspecified donation. If unspecified donation would be more widely accepted, it could be a good solution for decreasing the gap between kidney demand and available donors.

However, a number of professionals doubted the motivations of unspecified donors, and some even wondered whether their wish to donate could be an indicator for mental instability[1]. Similarly, they questioned whether these donors are fully aware of the risks and would regret their decision. These questions are especially sensitive as the cost benefit ratio for unspecified donors is less evident in comparison with specified donors who witness the recovery of their recipient. Therefore, research on the psychologic outcomes after unspecified living kidney donation is essential.

Two studies revealed that most unspecified living kidney donors were satisfied with the donation process and did not regret their decision[2,3]. Subsequently, in our own study, we found that the majority of donors showed no change in psychologic symptoms after donation, whereas a small minority of donors showed an increase or decrease after donation[4]. However, these changes seemed comparable to changes in psychologic symptoms observed in the general population. In conclusion, these studies show reassuring results on the psychologic outcomes after unspecified donation.

However, a subsequent question is whether psychologic outcomes of unspecified donors are equivalent to the outcomes for specified donors. This question is important because it is unknown what the impact is if the donor cannot witness the recovery process of the recipient. Rodrigue et al.[5] compared unspecified and specified donors after donation and found no differences between these two groups on motives, psychologic benefits, and health-related quality of life.

Now in the present issue of Transplantation, Maple et al.[6] build on the latter study and performed a comprehensive retrospective study that included the largest number of unspecified donors until now. In this study, 110 unspecified living kidney donors and 90 specified donors completed questionnaires after their donation. The merits of this study are a high response rate and the inclusion of many different outcomes: physical outcomes, both positive and negative aspects of mental health, and donation-related outcomes. Because the results of this study show that specified and unspecified donors do not differ on the mentioned outcomes, the conclusion is that the absence of a relationship with the recipient has no negative effect on psychologic outcomes after donation. Possibly, unspecified donors get sufficiently satisfied from the awareness that someone benefited from their donation, which is in line with their motivations to donate and their altruistic lifestyle.

We note that a limitation of the study by Maple et al.[6] is the retrospective design. It is possible that unspecified donors were psychologically more healthy before donation than specified donors. This potential difference is conceivable because unspecified donors received a more rigorous psychosocial screening than specified donors. Prospective cohort studies are needed to examine whether changes in psychologic outcomes are equivalent for specified and unspecified donors.

Another point we would like to discuss is the psychologic screening of potential donors. Maple et al.[6] concluded that their psychologic screening of unspecified donors was satisfactory as psychologic outcomes were not different between specified and unspecified donors. However, we note that there is no data on the content and necessity for psychologic screening for both specified and unspecified donors. For instance, it is unclear whether the decisions based on current psychologic screening guidelines are accurate. A first question that has to be answered is whether changes in mental health found among a minority of donors reflect normal fluctuations that are also found in the general population or not. To answer this question, prospective cohort studies are needed that compare changes in the donors' mental health with a representative control group from the general population.

In conclusion, Maple et al.[6] revealed that the absence of a relationship with the recipient does not impair psychologic outcomes of living kidney donors after donation. These results are encouraging for the current practice of unspecified donation in countries that accept this type of donation and an argument to abolish legal restrictions on unspecified living kidney donation in the remaining countries.

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7

Mental health among living kidney donors: a prospective comparison with matched controls from the general population

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abstract

The impact of living kidney donation on donors' mental health has not been sufficiently nor comprehensively studied. Earlier studies demonstrated that mental health did not change in the majority of donors, however they often lacked a suitable control group and/or had other methodological limitations. Consequently, it remains unclear whether changes in mental health found among a minority of donors reflect normal fluctuations. In this study we matched 135 donors with individuals from the general Dutch population on gender and baseline mental health and compared changes in mental health over time. Mental health was measured using the Brief Symptom Inventory and Mental Health Continuum Short Form. Primary analyses compared baseline and 6 months follow-up. Secondary analyses compared baseline and 9 (controls) or 15 months (donors) follow-up. Primary multilevel regression analyses showed that there was no change in psychological complaints ($p = 0.20$) and wellbeing ($p = 0.10$) over time and donors and controls did not differ from one another in changes in psychological complaints ($p = 0.48$) and wellbeing ($p = 0.85$). Secondary analyses also revealed no difference in changes between the groups. We concluded that changes in mental health in the short term after donation do not significantly differ from normal fluctuations found in the Dutch general population.

introduction

Living kidney donors undergo surgery primarily for the benefit of another person. This has been suggested to be in conflict with the medical ethical principle of nonmaleficence[1], however proponents of living donation highlight that refusing this gift would be paternalistic and disrespecting of the individual's autonomy. Therefore, in order to justify living donation, it is imperative that negative medical and psychological outcomes are minimized. Previous research on living kidney donors showed that mental health did not change among the majority of donors 6 weeks to 5 years after donation, while a small minority showed a positive or negative change in their mental health[2-13]. However, these studies were hampered by the lack of a prospective design[7,12], suitable control group[2-13], and/or measurement of overall mental health[2-13]. As a result, it remains unclear whether the changes found were provoked by the donation process or reflect normal fluctuations in mental health that can also be observed in the general population.

First, a prospective design is necessary as it allows comparison of predonation and postdonation mental health levels so as to establish whether change has taken place. Studies without a baseline measurement are unable to establish change. Second, a suitable control group is necessary as psychological complaints and wellbeing in the general population also fluctuate over time[14,15], which raises the question whether fluctuations found among donors reflect such normal fluctuations or not. To date a number of studies compared donors' scores on quality of life or psychological complaints to norm scores from the general population[5,16-21]. Three other studies used a control group from the general population that was matched on socio-demographic variables[22-24]. However, since living kidney donors are medically and psychologically screened before donation, they are relatively physically and psychologically healthier than the general population. Therefore a suitable control group should be selected that is equally healthy at baseline[25]. Clemens et al[26] responded to this problem by using a control group of physically healthy individuals and comparing their quality of life to donors' quality of life after donation retrospectively. However, in order to study the psychological impact of living kidney donation the most suitable control group would be equally psychologically healthy as the donors at baseline. A study that had such a control group and had a prospective design was still lacking.

Third, in order to examine the impact of living kidney donation, it is preferable to examine overall mental health rather than individual facets such as depression, anxiety, and quality of life[2-13]. In earlier studies, possible positive outcomes were often neglected as only negative outcomes such as psychological complaints were measured. The most complete way to measure mental health is to include both negative and positive aspects[27]. This is in line with the view of the World Health Organization that mental health is more than the absence of psychological complaints, but also includes the presence of positive mental health or ‘wellbeing’[28]. Whereas mental illness incorporates psychological complaints, wellbeing incorporates emotional, psychological, and social wellbeing. Emotional wellbeing is the presence of positive affect, the absence of negative affect, and satisfaction with life[29]. Psychological wellbeing contains factors that contribute to realizing one’s personal potential, such as personal growth and autonomy[30]. Social wellbeing is the appraisal of one’s circumstances and functioning in society, such as social contribution and social integration[31].

The present study is a reaction to the need for methodologically stronger, prospective cohort studies on all aspects of mental health after living kidney donation[32,33]. To our knowledge this is the first prospective study to explore whether changes in positive and negative aspects of mental health are different from normal fluctuations observed in a matched-control group from the general population.

methods

participants and procedure: living donors

All potential living kidney donors who underwent medical screening for living kidney donation at Erasmus Medical Center between July 2011 and September 2012 received a Patient Information Form for this study after the initial consultation with a transplant coordinator. This cohort included both directed and nondirected donors. One week before the final appointment with the nephrologist, a researcher (LT) called the potential donor and asked if he/she would like to participate if he/she was approved for donation. Potential donors who did not speak the Dutch language sufficiently or did not live in the Netherlands were not eligible for this study.

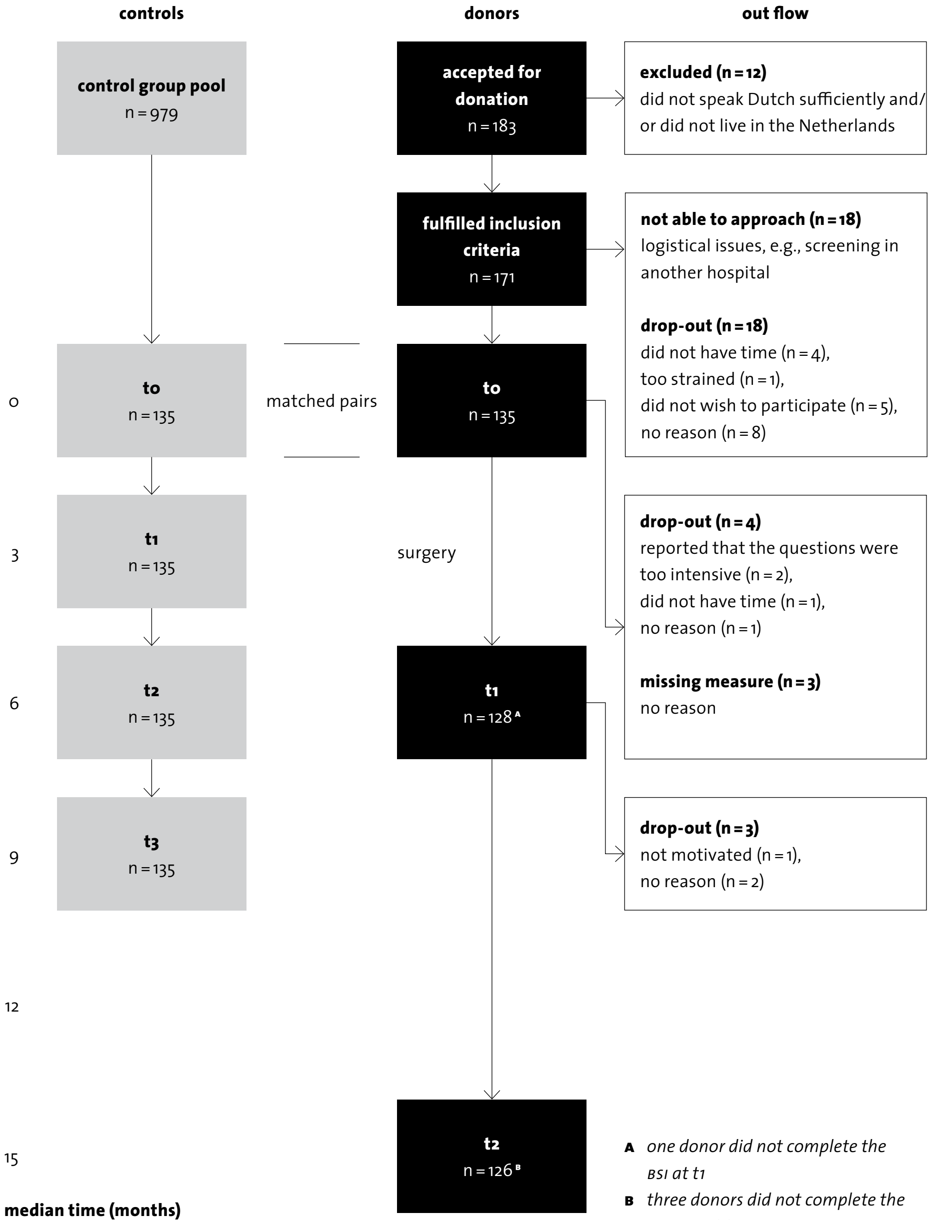
All donors approved for donation were asked to complete questionnaires immediately after the appointment with the nephrologist in which the final results of the medical screening were discussed (baseline measurement). Subsequently, all donors underwent laparoscopic nephrectomy. Participants were asked to complete the same questionnaires immediately after evaluation at the outpatient clinic 3 months (second measurement) and 1 year after donation (third measurement), respectively. The questionnaires were explained by a psychologist (LT, ML, EKM, or DKB) and were either completed in a private room at the outpatient clinic or at home and returned by post.

This study was approved by the institutional review board of Erasmus Medical Center (MEC-2011-271). All participants signed an Informed Consent before participation and they were assigned a unique code to anonymize the data.

participants and procedure: control group

A matched-control group was selected from the Longitudinal Internet Studies for the Social sciences (LISS) panel data[34,35] as administered by CentERdata (Tilburg University, the Netherlands). The LISS panel is a representative sample of the Dutch general population who participated in Internet surveys. Individuals who did not have Internet access were lent a computer and an Internet connection was provided. We used data from the Mental Health study of the LISS panel that comprises 1663 participants.

[f1 flow diagram of inclusion of the donors and matching with the controls**]**



A *one donor did not complete the BSI at t1*

B *three donors did not complete the MHC-SF at t2*

Participants completed the Brief Symptom Inventory (BSI) and Dutch Mental Health Continuum Short Form (MHC-SF) four times in December 2007, March 2008, June 2008 and September 2008. The data on all four measurements were used in our analyses. Of the participants, 979 completed all questionnaires (59%). Controls were selected (1:1) from this pool to match actual donors who completed the first measurement (n = 135). They were matched hierarchically: first on gender, then on baseline BSI and finally on baseline MHC-SF. See **[f1]** for an overview of the measurements.

measures

socio-demographic characteristics and relationship with the recipient:

The following socio-demographic characteristics of the donors were obtained from medical records: age, gender, employment status, marital status, highest level of education completed, religious affiliation, native country, native language, and number of children. We categorized the relationship between donor and recipient into five groups: nondirected donors, partners, children, parents, siblings, and others (such as friends, neighbors, cousins). Socio-demographic characteristics of the controls were obtained from the LISS panel database[34]. See **[t1]** for details.

mental health

psychological complaints

The Dutch version of the BSI[36,37] was used to measure the presence of psychological complaints, which has been shown to be a reliable instrument ($\alpha = 0.96$)[36]. The scale consists of 53 items and measures psychological complaints such as depressive mood and anxiety complaints. The total score can be used to indicate psychoneuroticism. Participants rated the extent to which they experienced each symptom in the past week (controls) or 2 weeks (donors) on a 5-point scale from *totally not* to *very much*. A higher score indicates more complaints. The mean score of the total scale was calculated (range: 0-4).

wellbeing

The Dutch MHC-SF[38,39] was used to measure wellbeing, which has been shown to be a reliable instrument ($\alpha = 0.89$). The MHC-SF consists of 14 items

[t1 socio-demographic characteristics and mental health outcomes of donors and controls**]**

	donors (n = 135)		controls (n = 135)		donors vs. controls
socio-demographic characteristics	**n**	**%**	**n**	**%**	***p***
median age (range)	56 (21-83)		52 (18-84)		0.06
gender					1
men	63	46.7	63	46.7	
employment status					0.20
paid employment	79	58.5	68	50.4	
retired/voluntary work/unemployed	56	41.5	68	48.9	
missing	0	0	1	0.7	
marital status					0.38
married	87	64.4	80	59.3	
never been married/divorced/widowed	48	35.6	55	40.7	
highest level of education					0.24
primary/secondary school	43	31.9	51	37.8	
further education	89	65.9	78	57.8	
missing	3	2.2	6	4.4	
religious					
yes	64	47.4	n.a.	n.a.	
missing	5	3.7			
native country					0.14
the Netherlands	120	88.9	125	92.6	
other country	15	11.1	8	5.9	
missing	0	0	2	1.5	
native language					< 0.001
Dutch	122	90.4	133	98.5	
other language	13	9.6	0	0	
missing	0	0	2	1.5	
children					0.09
yes	108	80	96	71.1	
relationship with recipient					
nondirected donors	15	11.1	n.a.	n.a.	
partner	46	34.1	n.a.	n.a.	
child	17	12.6	n.a.	n.a.	
parent	10	7.4	n.a.	n.a.	
sibling	24	17.8	n.a.	n.a.	
other	23	17.0	n.a.	n.a.	

n.a.: *these data are not available or not applicable.*

	donors (n = 135)		controls (n = 135)	
mental health outcomes	**M**	**SD**	**M**	**SD**
Brief Symptom Inventory				
baseline	0.19	0.24	0.19	0.24
3 months follow-up			0.21	0.25
median 6 months follow-up	0.26	0.38	0.20	0.24
9 months follow-up			0.22	0.29
median 15 months follow-up	0.27	0.37		
Mental Health Continuum Short Form				
baseline	3.07	1.02	3.06	0.88
3 months follow-up			3.07	0.98
median 6 months follow-up	2.95	1.01	2.95	0.94
9 months follow-up			3.07	0.95
median 15 months follow-up	2.93	1.04		

and measures the three components of wellbeing: emotional, psychological, and social wellbeing. An example item is: ‘In the past month, how often did you feel satisfied.’ Items are rated on a 6-point scale indicating how often they experienced the feeling in the past month from *never* to *every day*. A higher score indicates higher wellbeing. The mean score of the total scale was calculated (range: 0-5).

statistical analyses

First, we examined whether socio-demographic characteristics differed between donors versus controls and participants versus nonparticipants using independent t-tests for continuous data and chi-square tests for categorical data. We also examined whether scores on the BSI and MHC-SF differed according to method of completion (in the clinic vs. at home) using independent t-tests.

Second, for our primary analyses we carried out two saturated multilevel regression models for the BSI and MHC-SF with all available measurements at baseline and 6 months follow-up. For the donors the first and second measurements were included and for the controls the first and third measurements. The advantage of multilevel analyses is that these analyses can efficiently handle missing and unbalanced time points[40]. In addition, the model corrects for the bias of missing time points.

Our models had two levels: the participant was the upper level, their repeated measures the lower level. We checked the assumptions of multilevel regression analyses and found that the residuals of the BSI model were not normally distributed and therefore we transformed the BSI scores using logistic transformation[41]. The deviance statistic[42] using restricted maximum likelihood[43] was applied to determine the covariance structure.

Both models had three covariates. The first covariate was ‘group’ to examine whether donors and controls differed in the outcomes. The second covariate was ‘time (months)’ to examine whether donors and controls together showed a linear increase or decrease in the outcomes over time. The third covariate was the interaction between ‘time’ and ‘group’ to examine whether donors and controls differed in change in the outcomes over time.

Third, in the secondary analyses the two multilevel regression models were repeated with all measurements of donors and controls included. The last follow-up measurement was 9 months for the controls and median 15 months for the donors. Despite the fact that a multilevel regression model is a good analysis to take variation in time into account[40], it is preferable that the variation in time is independent of the group variable, which was not the case in our analyses. In these analyses we were able to include quadratic functions due to the inclusion of more than two measurements per participant. This could be valuable as changes in donors' quality of life have been shown to be quadratic rather than linear in previous studies[44,45]. The first extra covariate was the quadratic function of time to examine whether there was an initial decrease in the outcomes followed by an increase over time (positive quadratic function) or the other way around (negative quadratic function). The interaction between the quadratic function of time and 'group' was also included as covariate, to examine whether donors and controls differed in a quadratic change in the outcomes over time. Subsequently, we plotted the predicted values and their confidence intervals based on the two multilevel regression models on the same time points as our measurements. We examined whether the 95% confidence intervals of the donors and controls overlapped or not. Non-overlapping confidence intervals indicate that the two groups are significantly different from each other on the outcome[46].

Fourth, we examined how many donors and controls showed an increase, decrease, and no change in their mental health over time based on the reliable change indexes (RCI's)[47]. Using the RCI one can determine whether an individual change score on a measure is large enough that it is unlikely that this change is the consequence of measurement error and can therefore be considered as a 'real change'[47]. We calculated the RCI's with the RCI formula described by Jacobson and Truax[47]. To calculate the RCI's for the BSI and MHC-SF we used the standard deviations of the BSI for men (SD = 0.30) and women (SD = 0.39) and the internal consistency ($\alpha = 0.97$) of the Dutch general population[48] and the standard deviation (SD = 0.85) and internal consistency ($\alpha = 0.89$) of the MHC-SF of the Dutch general population[49]. Difference scores on the BSI and MHC-SF were calculated between baseline and the third measurement for the controls (6 months after baseline) and the second measurement for the donors (median 5.6 months after baseline), as this was the most comparable follow-up period for donors and controls and the RCI analyses cannot take into account variation in time. Subsequently, donors and controls were divided into three categories: if a difference score (follow-up score – baseline score) was smaller than the RCI, the person was assigned to the 'no change' category; if a difference score was positive and greater than the RCI, the person was assigned to the 'increase' category; and if a difference score was negative and greater than the RCI, the person was assigned to the 'decrease' category. Finally, using Mann-Whitney tests we examined whether RCI changes differed between donors and controls.

For all analyses we used SPSS version 21.0 (IBM Corporation, Armonk, NY) and a p-value less than 0.05 was considered statistically significant.

results

participants: living donors

Between July 5, 2011, and September 13, 2012, 183 potential living kidney donors were approved for donation and subsequently donated their kidney. Twelve donors were excluded due to language or living abroad, therefore 171 were invited to participate. See **[f1]** for the number of participants and nonparticipants at the three measurements. One hundred thirty-five donors completed the baseline measurement (response rate was 79%). Seven donors dropped out during the study (5%) and three donors did not complete the second measurement (2%). One donor did not complete the BSI at the second measurement and three donors did not complete the MHC-SF at the third measurement.

socio-demographic characteristics

[t1] shows the socio-demographic characteristics of the donors and controls. Donors and controls did not differ on any socio-demographic characteristic, except for native language: controls' native language was more often Dutch than donors' native language ($\chi^2(1) = 13.46$, $p < 0.001$).

We examined whether participants (n = 135) and non-participants (donors who refused to participate or were not approached due to logistical issues) (n = 36), differed on socio-demographic characteristics. Participants did not differ from nonparticipants on gender ($p = 0.81$), employment status ($p = 0.78$), marital status ($p = 0.36$), highest level of education ($p = 0.68$), and religion ($p = 0.11$). However, participants were significantly older than non-participants ($t(169) = -2.48$, $p = 0.01$) and more participants had been born in the Netherlands than non-participants ($\chi^2(1) = 4.54$, $p = 0.03$).

descriptive statistics

Donors' scores on the BSI and MHC-SF did not differ according to method of completion (in the clinic vs. at home) at all measurements, BSI: $t(280.84) = 1.22$, $p = 0.23$ and MHC-SF: $t(384) = 0.05$, $p = 0.96$.

Donors donated their kidney a median of 2.4 (range 0.1–16.4) months after baseline. Median time between the first and second measurement was 5.6 (range 2.9–20.4) months and between the second and third measurement 9.2 (range 6.0–12.2) months.

[t2 primary analyses: multilevel regression models with baseline and 6 months follow-up included**]**

	b	SE b	95% CI	*p*
psychological complaints				
intercept	−3.60825	0.11715	[−3.83865 – −3.37784]	< 0.001
time (months)	0.01839	0.01434	[−0.00982 – 0.04661]	0.20
group (donor-control)	0.01694	0.16764	[−0.31272 – 0.34660]	0.92
time × group	−0.01577	0.02217	[−0.05942 – 0.02788]	0.48
wellbeing				
intercept	3.05968	0.08155	[2.89925 – 3.22010]	< 0.001
time (months)	−0.01488	0.00899	[−0.03257 – 0.00282]	0.10
group (donor-control)	0.00269	0.11646	[−0.22636 – 0.23175]	0.98
time group	−0.00263	0.01387	[−0.02992 – 0.02467]	0.85

[t3 secondary analyses: multilevel regression models with all measurements included**]**

	b	SE b	95% CI	*p*
psychological complaints				
intercept	−3.61051	0.11271	[−3.83214 – −3.38888]	< 0.001
time (months)	0.02129	0.02008	[−0.01813 – 0.06071]	0.29
group (donor-control)	0.04072	0.16009	[−0.27409 – 0.35552]	0.80
time × group	0.00201	0.03860	[−0.07381 – 0.07782]	0.96
time × time	−0.00001	0.00115	[−0.00226 – 0.00224]	0.99
time × time × group	−0.00224	0.00367	[−0.00945 – 0.00497]	0.54
wellbeing				
intercept	3.06974	0.08317	[2.90621 – 3.23327]	< 0.001
time (months)	−0.02719	0.01380	[−0.05430 – −0.00009]	0.05
group (donor-control)	0.00985	0.11806	[−0.22229 – 0.24198]	0.93
time × group	−0.00092	0.02636	[−0.05268 – 0.05085]	0.97
time × time	0.00120	0.00080	[−0.00038 – 0.00277]	0.14
time × time × group	0.00153	0.00252	[−0.00343 – 0.00648]	0.55

multilevel models

primary analyses: 6 months follow-up

The model with the best fit for the BSI scores and MHC-SF scores had a random intercept but did not have a random slope. Time (months), group (donors vs. controls), and interaction between time and group did not significantly predict psychological complaints and wellbeing over time **[t2]**. This means that psychological complaints and wellbeing did not change over time and donors and controls did not differ on psychological complaints and wellbeing over time.

secondary analyses: 9 or 15 months follow-up

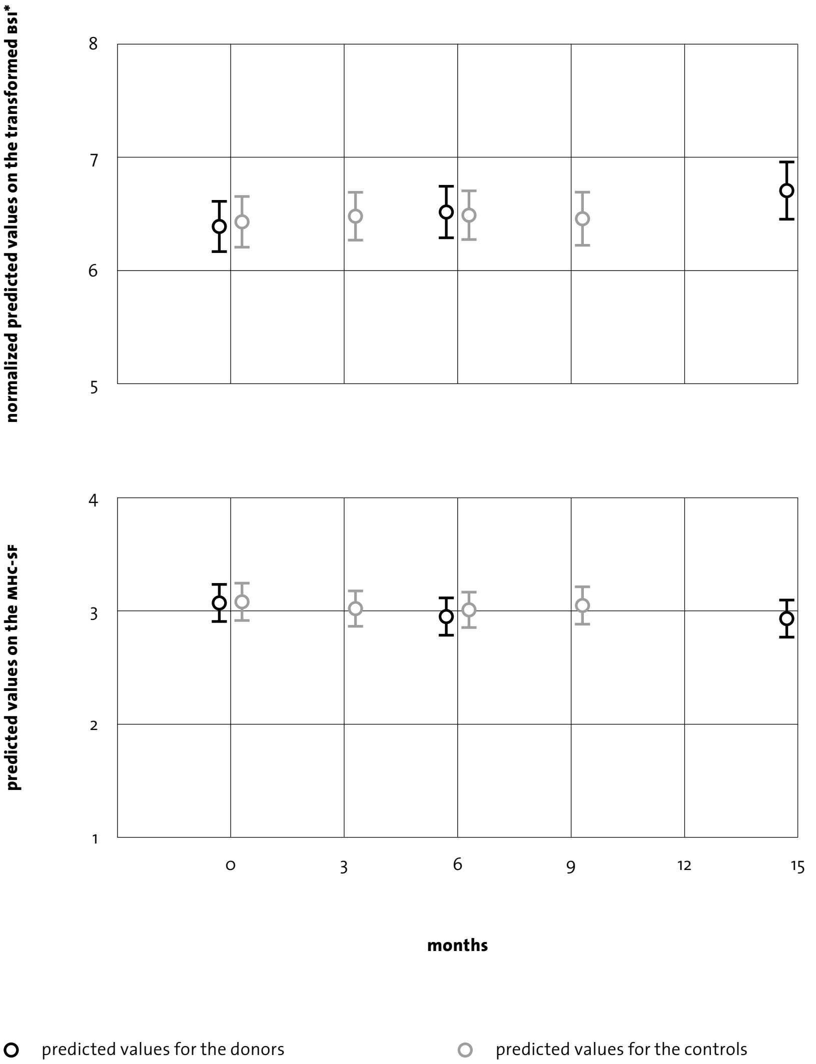
The model with the best fit for the BSI scores had a random intercept and a random slope. The model with the best fit for the MHC-SF scores had a random intercept but did not have a random slope. There was a significant effect of time for wellbeing: wellbeing decreased linearly among both donors and controls over time (t(678.28) = –1.97, $p < 0.05$). None of the other covariates significantly predicted wellbeing over time **[t3]**. This means that donors and controls did not differ on wellbeing over time. In addition, none of the covariates significantly predicted psychological complaints over time **[t3]**. This means that psychological complaints did not change over time and donors and controls did not differ on psychological complaints over time.

[f2] shows that the confidence intervals of the predicted values on the BSI and MHC-SF of the donors and controls overlap. This figure visually confirms the conclusion that donors and controls did not significantly differ on psychological complaints and wellbeing over time.

reliable change indexes

We examined whether individual change scores of donors who completed the first and second measurement (n = 128) and their controls (n = 128) were greater than the RCI of the BSI and MHC-SF between baseline and 6 months follow-up. The RCI calculation of the BSI resulted in RCI = 0.14 for men and RCI = 0.19 for women. The RCI calculation of the MHC-SF resulted in an RCI = 0.78. The number of donors and controls who increased, decreased, or remained the same on psychological complaints and wellbeing based on the RCI's are depicted in **[t4]**.

[f2 predicted values on the BSI and the MHC-SF of donors versus controls and their 95% confidence intervals based on the multilevel regression model of [t3] **]**



*A constant of 10 was added to the transformed BSI scores, as the transformed BSI scores were negative.
We note that the scores on the Y-axis are not interpretable as a result of the transformation.
Only the direction on the Y-axis is interpretable: a higher score indicates more psychological complaints.

There was no significant difference in the distribution of donors and controls who showed a decrease, no change, or an increase in psychological complaints between baseline and follow-up (U = 7604.50, z = −1.06, *p* = 0.29). There was also no significant difference for wellbeing (U = 7951.00, z = −0.52, *p* = 0.60).

[t4 number of participants who showed changes in psychological complaints and wellbeing based on the reliable change indexes (RCI's) between baseline and a median of 6 months follow-up**]**

	changes in psychological complaints using the RCI [A]		**changes in wellbeing using the RCI [B]**	
	n	**%**	**n**	**%**
donors				
decrease	12	9.4	18	14.1
no change	93	73.2	98	76.6
increase	22	17.3	12	9.4
controls				
decrease	12	9.4	25	19.5
no change	101	79.5	88	68.8
increase	14	11.0	15	11.7

A RCI = 0.14 for men and RCI = 0.19 for women

B RCI = 0.78

discussion

This is the first prospective cohort study to examine the psychological impact of living kidney donation by comparing fluctuations in mental health over time between donors and a representative control group from the general population up to 1 year after donation. In addition, this is the first study in which overall mental health was measured including both positive and negative components. In line with earlier research [2-13] we found that there was no change in mental health after donation among the majority of donors, while a minority of donors showed either a deterioration or an improvement. Our primary analyses showed that donors did not differ from controls in changes of mental health within the first few months after donation. Secondary analyses confirm this conclusion for a follow-up period of 1 year after donation. We conclude that both positive and negative changes in donors' mental health in the short term after donation do not differ from changes observed in the general Dutch population. These findings compliment research which showed that medical outcomes of donors were similar to those of the general population [50].

The findings raise the question whether fluctuations in mental health among a small minority of living donors could be related to the donation process. Since donors and matched controls, who did not undergo this life event, did not differ in mental health over time, we conclude that there is no evidence that these fluctuations were triggered by the donation process in the short term after donation. We note that this study does not give insight into the factors that may have contributed to changes in mental health among donors and controls. In general, fluctuations in mental health correlate with the occurrence of life events [51,52]. It is possible that for some donors the donation process was also experienced as a life event, defined as: 'an occurrence in a person's life, which requires adjustment of the person' [53 p.291]. Future research is necessary to explore whether living donation is experienced as a life event, whether this is positive or negative, and what the relative impact of donation is in comparison with other life events. Such research could clarify whether the subjective impact of the donation process is related to fluctuations in mental health. Medical outcomes of the donor and recipient should also be taken into account [54] as these may influence both subjective impact of the donation process and subsequent psychological outcomes. Finally, we recommend that future prospective studies have a longer follow-up, as the psychological impact of living donation after 1 year is still unknown[13] and there is some indication that psychological symptoms increase as time since donation increases among nondirected donors[10].

Our findings are also relevant to the issue of psychological screening of living kidney donors. The content of the psychosocial screening differs across transplant centers[55]. In our center, we perform a minimal psychosocial anamnesis during the medical screening that consists of consultations with a nephrologist, a nurse practitioner, a transplant coordinator, and a social worker. Only in case of doubts about the psychological ability of a potential donor to cope with the donation procedure, will he/she be referred to a psychologist. Potential nondirected donors are always screened by a clinical psychologist, using an in-depth interview and a self-report questionnaire measuring psychological complaints[10]. However, as none of the potential donors were rejected for psychological reasons during the research period of the present study, there was no selection bias in this sample. The reassuring results of the present study suggest that it could be possible that our standard limited psychosocial screening method is sufficient for the majority of potential donors and that more in-depth screening is only needed on indication. In the past decade, many extensive psychosocial screening guidelines have been developed and used by transplant centers, however the effectiveness of these screening criteria in preventing adverse psychological outcomes has yet to be investigated[55]. Likewise, the impact of being rejected as a living donor for psychological reasons is not known[56]. Therefore, we would like to encourage a discussion and more research on the necessity of extensive psychosocial screening of potential living kidney donors.

A striking result of the present study is that both donors and controls showed a significant decrease in wellbeing over time. A plausible explanation could be ‘regression to the mean’, which refers to the phenomenon that extreme scores on a first measurement tend to be closer to the mean on a subsequent measurement[57]. In the present study, donors and controls scored relatively high on wellbeing at the first measurement.

Despite the strengths of this study such as the matched-control design and a high response rate, a number of limitations should be taken into consideration. First, the mental health scores of controls were available for a shorter follow-up period than for donors. As a consequence, the last follow-up measurement of the donors could not be included in all analyses. Therefore, future research is necessary with longer and corresponding follow-up times for donors and controls. Second, as the psychosocial screening of living donors differs between transplant centers and countries, the findings may not be generalizable to other settings. Therefore, we would like to encourage similar prospective matched-control studies in other countries. Third, despite our high response rate of 79%, our participants were older and more likely to have been born in the Netherlands than nonparticipants. Extra efforts should be made to recruit younger and nonnative donors into future follow-up studies. Finally, subgroup analyses by relationship were not investigated and requires further research.

In conclusion, changes in mental health in the short term after living kidney donation are comparable to changes seen in the general population in the Netherlands. Similar studies in other settings are needed to confirm these findings. In addition, we would like to encourage discussion on the necessity of extensive psychological screening of living kidney donors and further research into the long-term impact of living kidney donation on psychological outcomes.

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8

The impact of the donors' and recipients' medical process on living kidney donors' mental health

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abstract

A minority of living kidney donors have poor psychological outcomes after donation. There is mixed evidence as to the influence of the medical process on these outcomes. We examined whether complexity of the medical process among donors and recipients predicted changes in donors' mental health (psychological symptoms and wellbeing) between predonation and one year postdonation. One-hundred forty-five donors completed questionnaires on mental health predonation and 3 and 12 months post-donation. Number of recipient re-hospitalizations and donor complications (none; minor; or severe) were obtained from medical records at 3 and 12 months after surgery. Multilevel regression analyses were used to examine whether these indicators predicted changes in donors' mental health over time after controlling for socio-demographic characteristics. We found that donor complications (p=0.003) and recipient re-hospitalizations (p=0.001) predicted an increase in donors' psychological symptoms over time. Recipient re-hospitalizations also predicted a decrease in wellbeing (p=0.005) over time, however this relationship became weaker over time. We conclude that a more complex medical process experienced by either the donor or recipient is a risk factor for deterioration in donors' mental health after living kidney donation. Professionals should monitor donors who experience a complex medical process, and offer additional psychological support when needed.

introduction

Many studies have shown that a minority of living kidney donors experience suboptimal psychological outcomes after living kidney donation[1-6]. It is important to identify these donors and anticipate by support and guidance needs. Various studies highlight the influence of complexity of the medical process among donors and recipients on donors' mental health, but the results are mixed and limited by methodological issues.

Two studies showed that donors who had a longer recovery period[7] or complications after donation[7,8], had a lower score on the mental component of quality of life postdonation. Minz et al.[9] also found that donors' self-reported health is related to depressive symptoms postdonation. Contrary to these results, two other studies did not find a relationship between the number of donors' hospitalization days or occurrence of medical complications and psychological outcomes after donation[5,10].

Mixed results were also found on the relationship between complexity of the medical process among recipients and donors' mental health postdonation. While various studies found no association between recipients' medical outcomes and donors' quality of life[7,10-12] or satisfaction with life[13], Giessing et al.[8] found an association between unfavourable recipient outcomes and a lower quality of life among donors. Two other studies found similar results whereby donors who perceived the health status of their recipients as worse, had more psychological problems than other donors[14,15].

The contradictory findings might be partly explained by the different aspects of mental health that were measured in the studies, for instance measuring quality of life is not the same as measuring psychological symptoms. Research would benefit from measuring overall mental health, instead of just separate aspects of mental health as measured in earlier studies. Models of overall mental health such as that of Keyes et al.[16] stipulate the importance of both positive and negative aspects of mental health, defined as wellbeing and psychological symptoms respectively. Wellbeing consists of factors like satisfaction with life, personal growth, and social contribution[16].

Moreover, the results of most earlier studies were hampered by a retrospective design[7,8,11-13,17]. Consequently, it is possible that donors who reported negative medical experiences already had a lower mental health score predonation and their score postdonation is unrelated to the medical process. Furthermore, a number of aforementioned studies[9,14,15] based their conclusions on donors' perceptions of the medical process and thus offer insight into the association between the donors' subjective interpretation of the medical process and donors' mental health. A potential bias in such studies is that a person's mood and mental health status can have an influence on the frequency and intensity of reported physical complaints[18]. Therefore, in order to explore the causal relationship between the donors' and recipients' medical process and donors' mental health a prospective study is necessary in which the medical process is measured with objective measures.

Furthermore, it is important to control for the potential influence of socio-demographic characteristics, as earlier research revealed that these characteristics are related to donors' mental health postdonation[7,11]. Knowledge of the relationship between such characteristics and mental health can also help to identify donors who may need extra monitoring and psychological support.

To summarize, we investigated the extent to which objectively measured indicators of donors' and recipients' medical process were related to the absolute level and change in donors' overall mental health between predonation and postdonation after controlling for socio-demographic characteristics.

methods

participants

All potential donors who underwent medical screening for living kidney donation at Erasmus Medical Center between July 2011 and September 2012 received a patient information form about the study. This cohort included both specified and unspecified donors[19]. One week before the final appointment of the screening process with the nephrologist, the researcher (LT) called the potential donor to ask whether he/she would participate if he/she was approved for donation. Potential donors who did not speak the Dutch language sufficiently or did not live in the Netherlands were not eligible for this study.

procedure

All those approved for donation were asked to complete questionnaires immediately after the final appointment with the nephrologist (baseline measurement). Participants were asked to complete the same questionnaires immediately after evaluation at the outpatient clinic three months (second measurement) and one year after donation (third measurement). The questionnaires were explained by a psychologist (LT, ML, EM, or DB) and were either completed in a private room at the outpatient clinic or at home and returned by post. Indicators of complexity of the medical process among donors and recipients and donors' socio-demographic characteristics were obtained at 3 and 12 months after the operation from medical records.

This study was approved by the institutional review board of Erasmus Medical Center (MEC-2011-271). All participants signed an Informed Consent form prior to participation.

measures

socio-demographic characteristics

Donors' socio-demographic characteristics are depicted in **[t1]**. We categorized the relationship between donor and recipient into two groups: unspecified and specified donors. The specified donors were subdivided into five categories: partners, children, parents, siblings, and others (e.g., friends, neighbours).

[t1 socio-demographic characteristics and mental health outcomes of participants (N = 145)]

socio-demographic characteristics	n	%
median age (range)		56 (20–83)
gender		
men	70	48.3
employment		
paid employment	87	60.0
retired/voluntary work/unemployed	58	40.0
marital status		
married/living together	96	66.2
single/divorced/widowed	49	33.8
highest level of education		
primary/secondary school	47	32.4
further education	95	65.5
missing	3	2.1
religious		
yes	74	51.0
missing	5	3.4
native country		
the Netherlands	129	89.0
other country	16	11.0
native language		
Dutch	131	90.3
other language	14	9.7
children		
yes	114	78.6
relationship with recipient		
unspecified	16	11.0
partner	48	33.1
child	18	12.4
parent	12	8.3
sibling	28	19.3
other	23	15.9
co-habitation with recipient		
yes	60	41.4
not applicable (unspecified donors)	16	11.0

mental health outcomes	M	SD
Brief Symptom Inventory		
baseline	0.19	0.24
3 months after donation	0.27	0.40
1 year after donation	0.28	0.38
Positive and Negative Affect Schedule – Negative affect		
baseline	1.30	0.39
3 months after donation	1.34	0.52
1 year after donation	1.35	0.52
Mental Health Continuum – Short Form		
baseline	3.09	1.03
3 months after donation	2.94	1.05
1 year after donation	2.93	1.04
Positive and Negative Affect Schedule – Positive affect		
baseline	2.94	0.76
3 months after donation	2.79	0.79
1 year after donation	2.81	0.77

[t2 classification of minor versus severe complications of the donor and prevalence of complications]

	0-3 months after donation	4-12 months after donation	total
	n	n	n
no complications	53	85	138
minor complications	72	43	115
wound infection, wound was not opened	6		6
bleeding/hematoma, without blood transfusion	14		14
urinary tract infection: once	7	3	10
urinary retention, less than a week (during hospitalization)	2		2
pain without intervention	23	17	40
fatigue	15	11	26
itchiness	2	1	3
atrial fibrillation	1		1
incontinence	1	1	2
dyspnea		1	1
edema	1		1
LUTS / oliguria		7	7
scar correction (cosmetic reasons)		1	1
dizziness		1	1
severe complications	28	5	33
wound infection, wound had to be opened	15		15
bleeding/hematoma, with blood transfusion	4		4
urinary tract infection, more than once			
urinary retention, more than a week	1		1
epididymitis	1	1	2
nerve damage	3	2	5
neumonia/pneumothorax	2		2
re-hospitalization	1	1	2
respiratory infection	1		1
scar tissue surgically removed		1	1
missing	4	15	19

mental health

Psychological symptoms: the Brief Symptom Inventory (BSI[20,21]) ($\alpha = 0.96$) was used to measure the presence of psychological symptoms, such as depressive mood[20]. The participant rated the extent to which he/she experienced the 53 symptoms in the past two weeks on a 5-point scale from *totally not* to *very much*. The mean was calculated (range: 0-4), a higher score indicates more symptoms. Psychological symptoms was further operationalized as 'negative affect' as measured by the Negative Affect subscale of the 'Positive And Negative Affect Schedule' (PANAS-NA[22,23]) ($\alpha = 0.86$). The Positive And Negative Affect Schedule (PANAS) consists of ten positive and ten negative affective states. The participant rated the extent to which he/she experienced the affective states in the past two weeks on a 5-point scale from *very little or not at all* to *very much*. Mean scores were calculated (range: 1-5).

Wellbeing: the Dutch Mental Health Continuum-Short Form (MHC-SF[24,25]) was used to measure wellbeing ($\alpha = 0.89$)[25]. The participant rated how often he/she experienced 14 different feelings of wellbeing in the past month from *never* to *every day* on a 6-point scale. Mean scores were calculated (range: 0-5). Wellbeing was also operationalized using the 'positive affect' subscale of the PANAS (PANAS-PA: $\alpha = 0.89$)[22]. Mean scores were calculated (range: 1-5).

medical process

The occurrence of medical complications among donors was used as an indicator of complexity of the medical process among donors and was summed for 0-3 months and 4-12 months to align with the measures of psychological factors at 3 and 12 months. Complications were coded into categories by a nephrologist (WW): no complication, minor complication, or severe complication. Donors' medical information was anonymized before coding. The classification was inspired by the *Clavien-Dindo Classification of Surgical Complications*[26] and adapted to the situation of living kidney donors. We chose to use a dichotomous classification, as there was not much variation in complications and there were no life-threatening complications. See **[t2]** for details of the classification. Minor complications were assigned one point and severe complications two points, and in case of multiple complications the points assigned to each complication were summed.

Number of re-hospitalizations (at Erasmus Medical Center or another hospital) were used as indicator of complexity of the medical process among recipients and were summed for 0-3 months and 4-12 months after the operation. We chose to use number of re-hospitalizations as this is an indicator of recurrent medical problems among recipients. Due to the low incidence of graft failure (n=2) and death among recipients (n=2), it was impossible to use these events as indicators of complexity of the medical process. Nevertheless, the recipients who had a failing kidney or died in the research period were more often re-hospitalized than the median of the total group. As unspecified donors did not know their recipient, they had no data on this item.

statistical analyses

First, we examined whether participants (donors who completed at least one measurement) differed on socio-demographic characteristics from non-participants (donors who refused to participate or were not approached due to logistical issues). Independent t-tests were used for the continuous data and chi-square tests for categorical data.

Multilevel regression models were used to examine whether socio-demographic characteristics and complexity of the medical process among donors and recipients were related to (changes in) psychological outcomes. The advantage of multilevel analyses is that these analyses can efficiently handle missing and unbalanced time-points and corrects for the bias of missing time-points [27], therefore all available data points were included in the analyses. Furthermore, multilevel analyses have a higher power in finding effects than analyses like MANOVA [28,29]. Because the BSI and the PANAS-NA were not normally distributed these were transformed with logistic transformations [30].

In a first step, we conducted separate multilevel regression models for the four mental health outcomes, in order to select potentially relevant socio-demographic variables ($p < 0.01$). Covariates were: time, time to surgery, one of the socio-demographic characteristics, and its interaction with time.

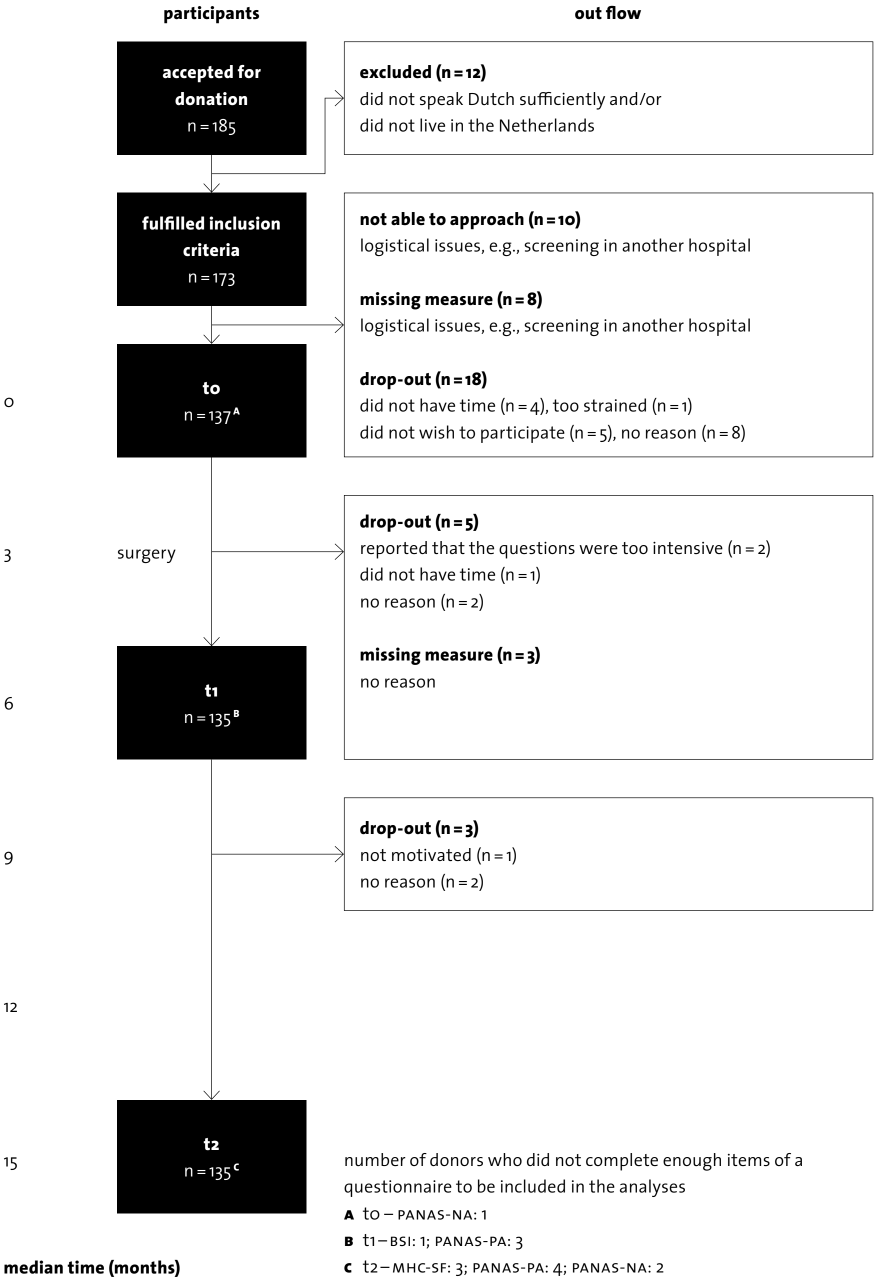
In a second step, we conducted final multilevel regression models for the four mental health outcomes. The covariates were: time, time to surgery, the selected socio-demographic variables from step 1 ($p < 0.01$), a medical process indicator (either complication score of the donor or number of recipient re-hospitalizations), and its interactions with time. Each model was conducted twice:

1. for donor complications
2. for recipient re-hospitalizations

The medical process indicators of the donor and recipient were not included in the same model, as unspecified donors have no data on the recipients' re-hospitalizations and would therefore automatically be excluded from all analyses. Therefore, in the second analyses only specified donors were included. Medical process indicators were time varying: all donors were assigned 0 at baseline, indicators of the medical process till 3 months after donation were added to the second measurement, and indicators between 4-12 months after donation were added to the third measurement. Consequently, the medical process covariate shows whether it was related to change in mental health after donation and the interaction with time indicates whether this relationship changed between 3 and 12 months. Non-significant covariates were removed step by step until a parsimonious model was reached. Figures were made for the models of mental health outcomes that had a significant relationship with either donor complications or recipient re-hospitalizations.

For all analyses we used SPSS version 21.0 (IBM Corporation, Armonk, NY, USA). In the univariate analyses a *p*-value less than 0.05 was considered statistically significant, while in the multilevel regression models a *p*-value less than 0.01 was considered statistically significant due to multiple testing.

[f1 flow diagram of participants**]**



number of donors who did not complete enough items of a questionnaire to be included in the analyses

A t0 – PANAS-NA: 1

B t1 – BSI: 1; PANAS-PA: 3

C t2 – MHC-SF: 3; PANAS-PA: 4; PANAS-NA: 2

results

participants

Between 5th July 2011 and 13th September 2012, 185 potential living kidney donors were approved for donation and subsequently donated their kidney. All donors underwent laparoscopic nephrectomy. Twelve donors were excluded from participation due to language or living abroad. Eighteen donors were not approached for the first measurement due to logistical issues, e.g., screening in another hospital. Six of these donors participated from the second measurement and two donors only participated at the third measurement. One-hundred forty-five donors completed at least one measurement (response rate was 84%) who are referred as ‘participants’. See **[f1]** for the number of participants and non-participants at the three measurements. Eight donors dropped out during the study (6%) and three donors completed the first and third but not the second measurement (2%).

descriptive statistics

Participants’ socio-demographic characteristics are depicted in **[t1]**. We found that participants did not significantly differ from non-participants on socio-demographic characteristics except for native country and religious affiliation: more participants were born in the Netherlands ($\chi^2(1) = 6.04$, $p = 0.01$) and were less likely to have a religious affiliation ($\chi^2(1) = 7.79$, $p = 0.01$) than non-participants.

Donors’ scores on the questionnaires did not differ according to method of completion (in the clinic versus at home) at all measurements, BSI: $t(399) = 0.04$, $p = 0.97$, PANAS-NA: $t(397) = 0.50$, $p = 0.62$, MHC-SF: $t(399) = 0.19$, $p = 0.85$, and PANAS-PA: $t(393) = 1.28$, $p = 0.20$.

Donors donated their kidney a median of 2.5 (range 0.1-21.7) months after baseline. Median time between the first and second measurement was 5.6 (range 2.9-24.2) months and between the first and third measurement 15.1 (range 11.7-29.2) months.

medical process

Eighty-eight donors (61%) experienced at least one complication till 3 months after donation, 45 donors (31%) experienced at least one complication between 4 and 12 months after donation. A minority had missing data: 4 donors (3%) till 3 months after donation and 15 donors (10%) between 4 and 12 months after donation. The remaining donors did not experience a complication. See **[t2]** for the prevalence of each complication.

Fifty-five recipients (43%) were re-hospitalized at least once till 3 months after transplantation, 68 recipients (53%) were at least once re-hospitalized between 4 and 12 months after transplantation. Four recipients (3%) had missing data on both measurements. The remaining recipients were not re-hospitalized. See **[t3]** for details on the occurrence of recipient re-hospitalizations.

[t3 prevalence of recipient re-hospitalizations till 3 and 12 months after transplantation**]**

	0-3 months after transplantation	**4-12 months after transplantation**
number of recipient re-hospitalizations	**n**	**n**
0	70	57
1	28	25
2	15	14
3	5	12
4	6	9
5		3
6	1	
7		2
8		2
9		1
missing	4	4
not applicable (unspecified donor)	16	16

influence of donors' medical process on change in donors' mental health

See **[t4]** for the final models with donor complications included as predictor.

psychological symptoms

Psychological symptoms (BSI) increased significantly over time. More severe complications among donors were related to an increase in psychological symptoms over time (see **[f2]** for a visual representation of this relationship). Age was negatively related to psychological symptoms: younger donors had a higher level of psychological symptoms across the donation process.

Negative affect (PANAS-NA) increased significantly over time. Donor complications were not related to change in negative affect over time. Age was negatively related to negative affect: younger donors had a higher negative affect score across the donation process. The interaction between time and marital status was negatively related to negative affect over time: a greater increase in negative affect over time was found among donors who did not have a partner.

wellbeing

Wellbeing (MHC-SF) did not change over time, and donor complications were not related to change in wellbeing over time. Religious affiliation was positively related to wellbeing: religious donors had a higher wellbeing across the donation process than non-religious donors.

Positive affect (PANAS-PA) did not change over time, and donor complications were not related to change in positive affect over time. Unemployment was negatively related to positive affect: employed donors had a higher positive affect during the donation process than unemployed donors.

influence of recipients' medical process on change in donors' mental health

See **[t5]** for the final models with recipient re-hospitalizations included.

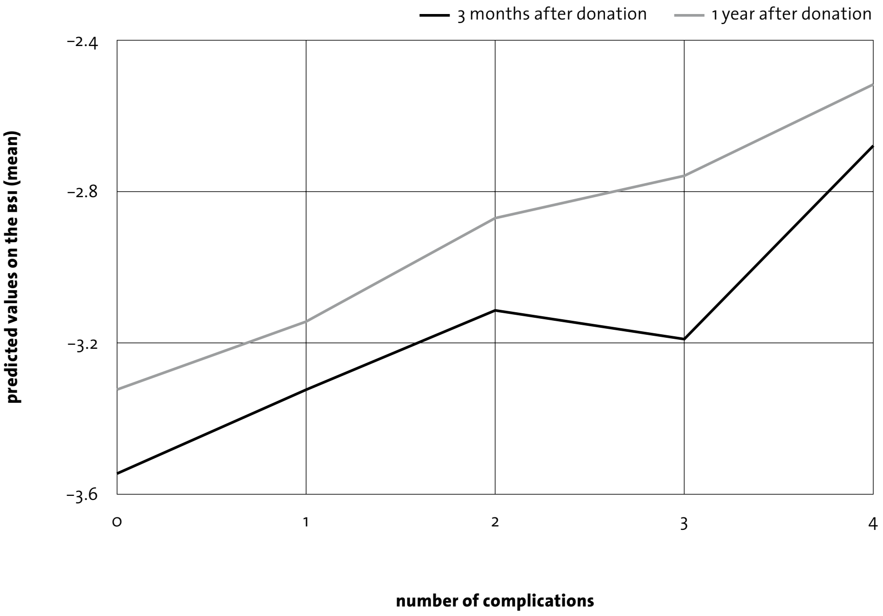
psychological symptoms

Psychological symptoms (BSI) did not change over time. A greater number of recipients re-hospitalizations was related to an increase in psychological symptoms over time (see **[f3]** for a visual representation of this relationship).

[t4 final models for the relationship between donors' medical process and donors' mental health (N=145)**]**

	b	SE b	*p*	95% CI
psychological symptoms (BSI)				
intercept	−2.620	0.404	< 0.001	[−3.420 – −1.821]
time (months)	0.024	0.008	0.005	[0.007 – 0.041]
complication score of the donor	0.208	0.069	0.003	[0.073 – 0.342]
age	−0.019	0.007	0.010	[−0.034 – −0.005]
negative affect (PANAS-NA)				
intercept	−1.750	0.361	< 0.001	[−2.462 – −1.037]
time (months)	0.036	0.013	0.005	[0.011 – 0.061]
age	−0.022	0.007	0.001	[−0.035 – −0.009]
marital status	0.062	0.207	0.765	[−0.346 – 0.470]
time × marital status	−0.048	0.015	0.002	[−0.078 – −0.018]
wellbeing (MHC-SF)				
intercept	2.801	0.108	< 0.001	[2.587 – 3.015]
religious affiliation	0.407	0.156	0.010	[0.099 – 0.715]
positive affect (PANAS-PA)				
intercept	3.033	0.067	< 0.001	[2.901 – 3.164]
unemployment	−0.436	0.105	< 0.001	[−0.644 – −0.229]

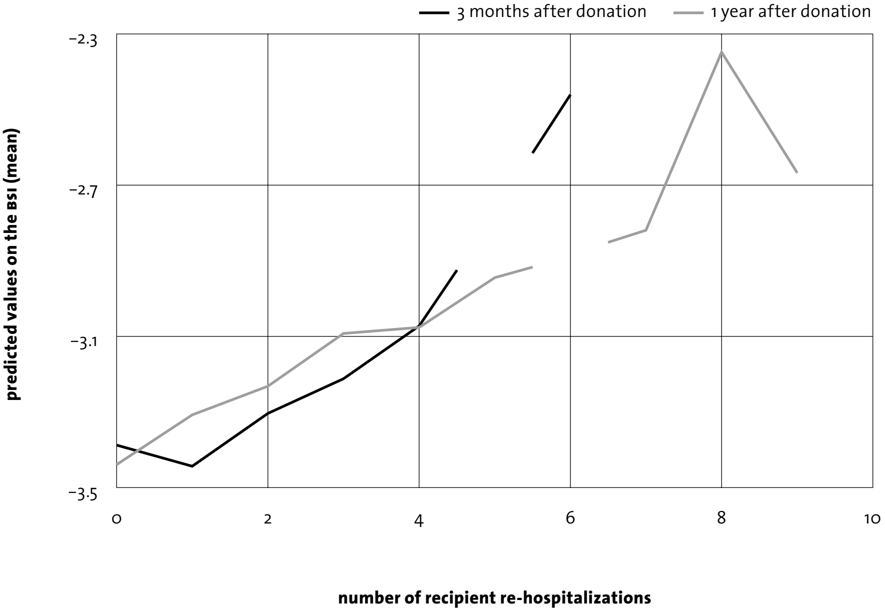
[f2 relationship between donor complications and psychological symptoms among donors**]**



[t5 final models for the relationship between recipients’ medical process and donors’ mental health (n=129)**]**

	b	SE b	*p*	95% CI
psychological symptoms (BSI)				
intercept	−2.374	0.422	< 0.001	[−3.208 – −1.539]
recipient re-hospitalizations	0.130	0.039	0.001	[0.053 – 0.207]
age	−0.021	0.008	0.008	[−0.037 – −0.006]
negative affect (PANAS-NA)				
intercept	−2.614	0.186	< 0.001	[−2.981 – −2.247]
time (months)	0.035	0.014	0.012	[0.008 – 0.063]
marital status	−0.303	0.224	0.178	[−0.746 – −0.139]
time × marital status	−0.048	0.017	0.004	[−0.082 – −0.016]
wellbeing (MHC-SF)				
intercept	3.001	0.088	< 0.001	[2.827 – 3.175]
time (months)	−0.011	0.006	0.097	[−0.023 – 0.002]
recipient re-hospitalizations	−0.147	0.053	0.005	[−0.251 – −0.044]
time × recipient re-hospitalizations	0.014	0.005	0.004	[0.005 – 0.023]
positive affect (PANAS-PA)				
intercept	2.976	0.068	< 0.001	[2.842 – 3.110]
unemployment	−0.360	0.110	0.001	[−0.576 – −0.143]

[f3 relationship between recipient re-hospitalizations and psychological symptoms among donors**]**



Consistent with the earlier model of the BSI, younger donors had a higher level of psychological symptoms.

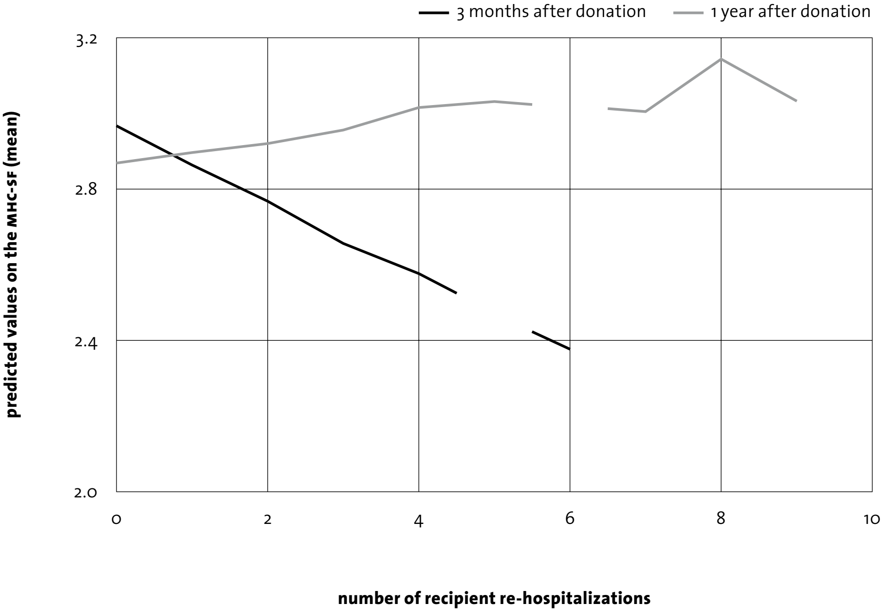
Recipient re-hospitalizations and its interaction with time did not significantly predict negative affect (PANAS-NA).

wellbeing

Wellbeing (MHC-SF) did not change over time. A greater number of recipient re-hospitalizations was significantly related to a decrease in wellbeing over time. The interaction between time and recipient re-hospitalizations was also significant, indicating that the negative relationship between recipient re-hospitalizations and negative affect is stronger the first months after donation and weaker one year after donation. See **[f4]** for a visual representation of this relationship.

Recipient re-hospitalizations and its interaction with time did not significantly predict positive affect (PANAS-PA).

[f4 relationship between recipient re-hospitalizations and wellbeing among donors**]**



discussion

In this study we provide new insights into the impact of the donors' and recipients' medical process on donors' mental health after living kidney donation by investigating this question in a prospective cohort study. Previous research was inconclusive, used mainly retrospective designs, relied often on subjective measures, and measured single components of mental health. We examined the medical process objectively and measured overall mental health. The results showed that a more complex medical process of the donor and/or recipient was related to a deterioration in donors' mental health over time. Furthermore, we found that a younger age, no religious affiliation, and unemployment were related to a stable lower mental health across the donation process and a greater deterioration in mental health over time was found among donors who did not have a partner.

On the basis of these results we recommend that professionals monitor the mental health of living kidney donors who experience complications themselves and/or recipient re-hospitalizations. We do not recommend that all donors who experience such unfavorable medical outcomes receive psychological support as standard, as routine psychological treatment after a life event is not effective and could even have a detrimental effect for some individuals[31]. We therefore recommend that professionals monitor the need for psychological support among these donors and refer them for additional psychological support when indicated. Extra attention is needed in case of extreme negative medical outcomes, such as graft failure or recipients' death, as earlier research revealed that these donors often have difficulties in expressing their need for additional psychological support[32].

A number of socio-demographic risk factors were identified that may characterize donors needing greater psychological support during the donation process. These were a lack of a partner, younger age, no religious affiliation, and being unemployed. These donors were more likely to have poorer mental health (changes) across the donation process.

Which psychological intervention techniques could be used to prevent deterioration in donors' mental health? To our knowledge, there are no guidelines or studies on effective psychological interventions that help donors to cope with a complex medical process. Our suggestions for appropriate psychological interventions are: supportive counseling, acceptance focused interventions[33,34], stress reducing techniques[35], or grief therapy[36]. Furthermore, we highlight the importance of educating potential living donors about the risks of medical complications after donation/transplantation and the potential impact on donors' mental health. This is in line with conclusions from earlier research that improving the informed consent process of donors will contribute to positive psychological outcomes after donation, for instance by increasing realistic expectations before donation[37], increasing knowledge about living donation/transplantation[38], and reducing ambivalence against donation[39]. These interventions should be performed by a clinical psychologist who is familiar with the interventions. We would like to encourage future research on the effectiveness of these interventions among donors.

It is likely that not all donors will react to medical complications (their own or those of the recipient) in the same way. Psychological processes are likely to influence the impact on mental health outcomes, for example some donors may cope more effectively or have more social support than other donors. It is feasible that such factors have an influence, as many studies revealed that the influence of an event is more influenced by psychosocial factors, rather than the physical characteristics[40,41]. The influence of these psychological factors on mental health outcomes among donors is yet to be investigated.

Despite the strengths of this study such as a high response rate and low attrition over time, a number of limitations should be taken into consideration. Firstly, more participants were born in the Netherlands and were less likely to have a religious affiliation than non-participants. Extra efforts should be made to recruit non-native and religious donors in future research to enhance the generalizability of our results. Secondly, the follow-up period of this study is limited to one year and therefore we were not able to examine the impact of kidney failure or recipient's death on psychological outcomes of the donor due to the low incidence of these events. Prospective studies with a longer follow-up period investigating the influence of medical factors on donor psychological outcomes could add important insights to this area.

We conclude that a more complex medical process experienced by either the donor or recipient is a risk factor for deterioration in donors' mental health after living kidney donation. This information should be added to education programs for potential living kidney donors. Furthermore, professionals should monitor the mental health of donors who experience complex medical processes, and offer additional support when needed. Future research is needed to explore which psychosocial factors such as personal resources are, in addition to the medical process, related to mental health after living kidney donation.

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9

Predicting mental health after living kidney donation: the importance of psychological factors

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Submitted

abstract

background

Living donor kidney transplantation offers advantages to the patient, however, involves risks to the donor. In order to optimize donors' mental health after donation we studied the influence of psychological factors on this outcome. Potential predictors were based on models of Lazarus (1999) and Ursin & Eriksen (2004) that describe predictors of mental health mediated by stress.

methods

Living kidney donors (N=151) were interviewed before donation and completed questionnaires 2.5 months before, and 3 and 12 months postdonation. Using multilevel regression models we examined whether appraisals, expectations, knowledge, social support, coping, life events, and sociodemographic characteristics predicted psychological symptoms and wellbeing; and whether these relationships were mediated by stress.

results

A greater increase in psychological symptoms over time was found among donors without a partner. Younger age, lack of social support, expectations of interpersonal benefit, lower appraisals of manageability, and an avoidant coping style were related to more psychological symptoms at all time-points. The latter three were mediated by stress. No religious affiliation, unemployment, history of psychological problems, less social support, expectations of negative health consequences, and less positive appraisals were related to lower wellbeing at all time-points.

conclusions

This study identified a risk profile for negative psychological outcomes among living kidney donors. Professionals should examine this profile before donation and the need for extra psychological support in relation to the number and magnitude of the identified risk factors. Interventions should be focused on the changeable factors (e.g., expectations), decreasing stress/psychological symptoms, and/or increasing wellbeing.

introduction

Living donor kidney transplantation is considered the best option for extending and improving the lives of patients with end-stage renal disease[1,2]. Healthy persons who are motivated to donate one of their kidneys to a known or unknown person make these transplantations possible. As these donors do not benefit directly from their surgery and medical ethical principles dictate to 'do no harm'[3], it is important that the risk of negative medical and psychological consequences are minimized after donation. Medical outcomes after living kidney donation are well-documented, including an overall mortality rate of 0.03%[4,5], and morbidity rate (including minor complications) of < 10%[6]. Furthermore, many medical risk factors have been identified which form the basis of medical screening guidelines[6,7]. However, little research has been done on the psychological outcomes and/or risk factors for postdonation deterioration in mental health.

Until now, research on psychological outcomes revealed that mental health remained the same for the majority of donors, while mental health improved or deteriorated for a minority after donation[8-11]. In reaction to these findings, many psychosocial screening guidelines have been developed for potential donors, however the components of these guidelines are based on professional opinions and experience rather than on longitudinal empirical data[12,13]. There is a lack of research that identifies which donors are at risk of poorer psychological outcomes after donation. Such studies are essential in order to tailor psychosocial support during the donation process.

In a recent study, we found that donors who experienced complications themselves and/or recipient re-hospitalizations and donors without a partner are at greater risk for developing psychological symptoms or a lower wellbeing after living kidney donation[14]. In addition, we identified a number of socio-demographic factors that were related to a stable lower mental health during the whole donation process: a young age, no religious affiliation, and unemployment. Besides the medical and socio-demographic factors, psychological processes are likely to have an influence on the psychological impact of living donation, as they are proved to have an influence on the psychological impact of other events[15,16]. For example some donors may cope more effectively or have more social support than other donors.

Identifying the psychological factors that have an influence on donors' mental health might also open the door to effective interventions: while socio-demographic and medical factors may be less amenable to change, psychological factors are modifiable and can therefore be influenced by psychological interventions.

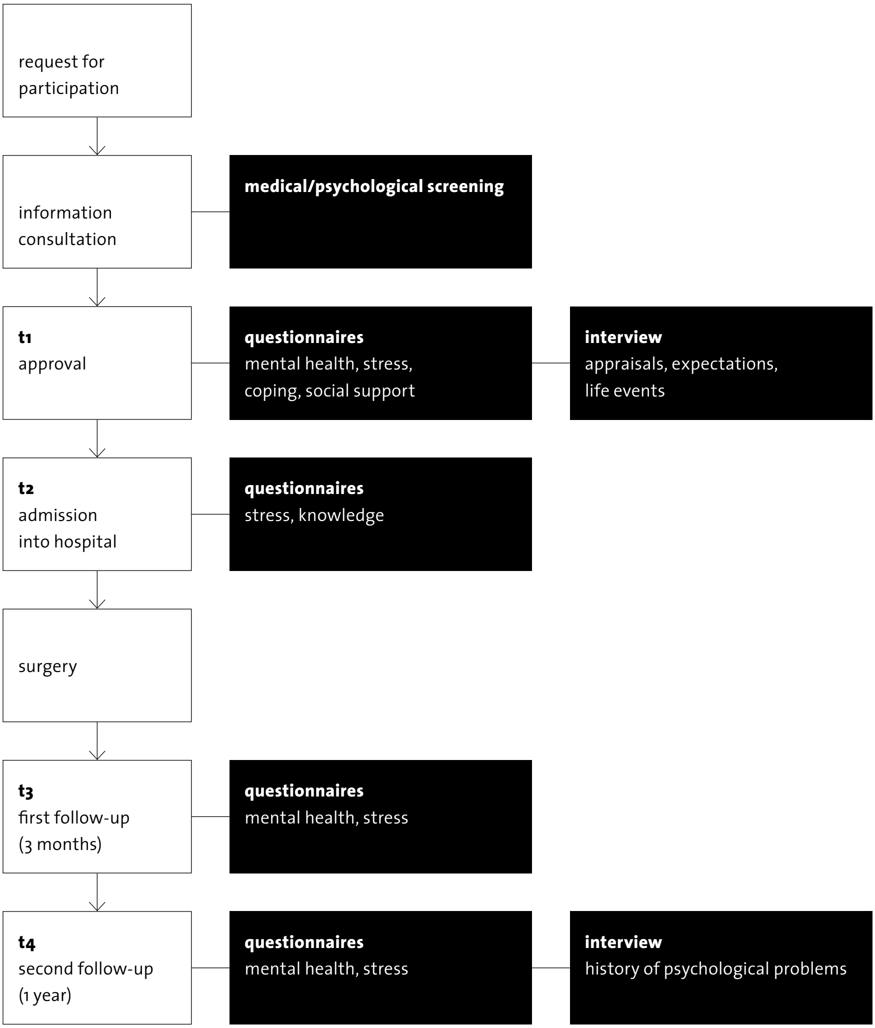
There are validated models that describe psychological factors predicting the psychological impact of an event, examples of which are the stress models of Lazarus[15] and Ursin and Eriksen[16]. These models describe that factors such as appraisals and expectations predict whether a situation is stressful for a person and subsequently the degree of stress predicts the impact of an event on the person's mental health. Stress is thus a mediator in the models. Various studies found support for these models among patients undergoing another kind of surgery[17,18], however the importance of these factors has yet to be investigated in the case of living kidney donation.

The first factor that has an influence on stress are appraisals, which refers to the subjective evaluation of a situation and consists of primary and secondary appraisals[15]. Primary appraisal is the evaluation of the nature and meaning of the event in relation to a person's wellbeing and includes appraisals of threat, harm, challenge, and centrality. Secondary appraisal is a subjective assessment of a person's coping resources and includes: perceived ability to change the situation and perceived ability to manage one's emotional reactions to the situation[19]. Expectations are another component of these models, as stress occurs when there is discrepancy between what is expected and what happens in reality[16]. Accurate knowledge about a situation contributes to realistic expectations and has therefore also an impact on a person's stress level[16]. The amount and deficiency in social support are also proposed as determinants of stress[15]. The final determinant of stress is coping, which can be divided into three broad dimensions, i.e., active problem-oriented, social support seeking, and avoidant coping[20], whereby avoidant coping is particularly related to stress[21].

In addition to the concepts in these models, life events that donors experience prior to the donation may also have an influence on their stress level and mental health[22,23]. Earlier studies revealed that the number of life events experienced can have a negative influence on a person's ability to cope with a subsequent event[24]. In other words, it is possible that donors who experienced many life events in the past year have a higher burden as a result of these events and are potentially less resilient to cope with the donation process.

The primary aim of the present study was to explore whether appraisals, knowledge, expectations, coping, social support, and life events have an influence on (change in) living kidney donors' overall mental health, which consists of both psychological symptoms and wellbeing as defined by the World Health Organization[25]. The secondary aim was to investigate whether these relationships were mediated by (change in) donors' stress level.

[f1 overview of measurements and content of interview and questionnaires**]**



methods

participants

All potential donors who underwent medical screening for living kidney donation at Erasmus Medical Center between July 2011 and September 2012 received a patient information form about the study. This cohort included both specified and unspecified donors[26]. One week before the final appointment of the screening process with the nephrologist, the researcher (LT) called the potential donor to ask whether he/she would participate if he/she was approved for donation. Potential donors who did not speak the Dutch language sufficiently or did not live in the Netherlands were not eligible for this study.

procedure

All those approved for donation were asked to participate in a structured interview and complete questionnaires immediately after the final appointment with the nephrologist (baseline measurement). Participants were asked to complete questionnaires on the day of admission into the hospital (1 day prior to donation, second measurement), 3 months (third measurement), and 1 year after donation (fourth measurement).

The structured interviews were conducted by a psychologist (LT, ML, EM, or DB). The items were read out by the psychologist and the participant answered to what extent he/she agreed with the items by choosing the best answer option from an answer booklet. The majority of the interviews took place at the outpatient clinic, however because of logistical reasons 5 interviews were conducted at the participants' home and 2 via the telephone. The instructions of the questionnaires were face-to-face explained by one of the psychologists. The questionnaires of the second measurement were completed on the hospital ward. The questionnaires of the other measurements were either completed in a private room at the outpatient clinic or at home and returned by post. In an earlier study with the same data we found that donors' scores on the questionnaires did not differ according to method of completion[14]. See **[f1]** for an overview of the measurements and the content of the interview and questionnaires.

This study was approved by the institutional review board of Erasmus Medical Center (MEC-2011-271). All participants signed an Informed Consent form prior to participation.

[t1 socio-demographic characteristics of participants (N = 151)**]**

	n	%
median age (range)		55 (20–83)
gender		
men	71	47.0
employment		
paid employment	90	59.6
retired/voluntary work/unemployed	61	40.4
marital status		
married/living together	99	65.6
single/divorced/widowed	52	34.4
highest level of education completed		
primary/secondary school	50	33.1
further education	98	64.9
missing	3	2.0
religious		
yes	71	47.0
missing	5	3.3
native country		
the Netherlands	132	87.4
other country	19	12.6
native language		
Dutch	136	90.1
other language	15	9.9
children		
yes	120	79.5
relationship with recipient		
unspecified	16	10.6
specified		
partner	51	33.8
child	19	12.6
parent	12	7.9
sibling	28	18.5
other	25	16.6
co-habituation with recipient		
yes	63	41.7
not applicable (unspecified donors)	16	10.6
history of psychological problems		
yes	52	34.4
missing	23	15.2

measures

socio-demographic characteristics & relationship with the recipient

Donors' socio-demographic characteristics are depicted in **[t1]**. We categorized the relationship between donor and recipient into two groups: unspecified and specified donors. The specified donors were subdivided into five categories: partners, children, parents, siblings, and others (such as: friends and neighbours).

mental health

Psychological symptoms: the Brief Symptom Inventory (BSI: $\alpha = 0.96$)[27,28] was used to measure the presence of psychological symptoms, such as depressive mood[27]. The participant rated the extent to which he/she experienced the 53 symptoms in the past two weeks on a 5-point scale from *totally not* to *very much*. The mean was calculated (range: 0-4), a higher score indicates more symptoms. Psychological symptoms was further operationalized as 'negative affect' as measured by the Negative Affect subscale of the 'Positive And Negative Affect Schedule' (PANAS-NA: $\alpha = 0.86$)[29,30]. The Positive And Negative Affect Schedule (PANAS) consists of 10 positive and 10 negative affective states. Participants rated the extent to which he/she experienced the affective states in the past two weeks on a 5-point scale from *very little or not at all* to *very much*. Mean scores were calculated (range: 1-5).

Wellbeing: the Dutch Mental Health Continuum-Short Form (MHC-SF)[31,32] was used to measure wellbeing ($\alpha = 0.89$)[32]. Participants rated how often he/she experienced 14 different feelings of wellbeing in the past month from *never* to *every day* on a 6-point scale. Mean scores were calculated (range: 0-5). Wellbeing was also operationalized using the 'positive affect' subscale of the PANAS (PANAS-PA: $\alpha = 0.89$)[29]. Mean scores were calculated (range: 1-5).

stress

The stress subscale of the Dutch short-form of the Depression Anxiety Stress Scale was used to measure donors' stress level (DASS-Stress: $\alpha = 0.85$)[33]. Participants rated the extent to which they experienced 7 stress symptoms at that moment on a 4-point scale from *totally not applicable* to *certainly applicable*. Sum scores were calculated (range: 0-21).

coping

Coping was measured using the Dutch version of the COPE-Easy[20]. Participants rated the use of 32 coping styles after setbacks in their lives on a 4-point scale from *not at all* to *a lot*. The scores on the items were summed and grouped into 3 main dimensions: (1) active problem-oriented coping, (2) social support seeking coping, and (3) avoidant behaviour[19]. The reliability of the subscales were calculated.

social support

The Social Support List-Interactions (SSL-I)[34,35] and the Social Support List-Discrepancies (SSL-D) were used to measure the amount and deficiencies in social interactions experienced respectively (SSL-I: $\alpha = 0.93$, SSL-D: $\alpha = 0.95$). On the SSL-I participants rated the extent to which they experienced 34 social interactions on a 4-point scale from *seldom or never* to *very often* and the scores were summed (range 34-136). Higher scores indicate a greater amount of social interactions. On the SSL-D participants rated the extent to which they experienced discrepancies of the same social interactions by choosing between 4 response options: *I miss this, I would like to experience this more* (3 points), *I do not really miss it, but it would be nice if it happened more* (2 points), *It is exactly right, I would not like it to be more or less frequent* (1 point), *This happens too often, I prefer to happen this less often* (1 point). The scores on all items were summed (range 34-102). Higher scores indicate deficiency in social support.

appraisals

Fourteen items were created to measure donors' primary and secondary appraisals of the donation process, based on the appraisal theory of Lazarus[15]. The Stress Appraisal Measure (SAM)[35] and the appraisal-scale of Power and Hill[37] were used for examples of items. Participants answered to what extent they agreed with the items on a 5-point scale from *totally disagree* to *totally agree* and the scores were summed (range 14-70). A factor analysis was conducted on the 14 items.

expectations

Expectations regarding personal consequences of the donation process were measured using the 42-item Living Donation Expectancies Questionnaire (LDEQ)[38]. Four subscales measure positive expectations: Interpersonal Benefit, Personal Growth, Spiritual Benefit, Quid Pro Quo; and 2 subscales measure negative expectations: Health Consequences and Miscellaneous Consequences. A forward-back translation procedure was used to translate the questionnaire from English into Dutch. The reliabilities of the subscales were calculated. The participant answered to what extent he/she agreed with the items on a 5-point scale from *totally disagree* to *totally agree*. Sum scores were calculated per subscale, higher scores indicate more extreme expectations.

life events

Donors were asked whether they had experienced life events that impacted their lives, either positive and negative, in the past year. A number of examples were announced, such as death of a family member or birth of a child. Participants completed two 10 centimetre VAS-scales for each event. Firstly, whether they experienced the event as negative or positive and secondly the impact of this event on their life from little impact to much impact. Based on the first VAS-scale the events were categorized in either a negative event category (0-5 cm) or positive event category (5.1-10 cm). The impact of all positive and negative life events were summed to two separate total scores.

statistical analyses

We conducted analyses to examine whether participants (donors who completed at least one measurement) differed on socio-demographic characteristics from non-participants (donors who refused to participate and donors who were not approached due to logistical issues). Independent t-tests were used for continuous data and chi-square tests for categorical data.

Multilevel regression models were used to examine whether socio-demographic and psychological factors were related to (change in) the four mental health outcomes and whether these relationships were mediated by stress. Each model had two levels: the participant was the upper level, their repeated measures the lower level.

Before conducting the analyses, we checked the assumptions of multilevel regressions analyses and found that the residuals of the BSI, PANAS-NA, and DASS-Stress were not normally distributed and were therefore transformed using a logistic transformation[39]. Then, a multilevel regression analysis was conducted for each mental health outcome in 4 steps, which are the prerequisites of mediation as presented in **[f2]**.

1 Determining path c. We conducted separate multilevel regression models for all socio-demographic/psychological variables as covariates and the mental health outcomes. All models had 4 covariates. The first covariate was 'time (since surgery)' to examine whether donors showed a linear increase/decrease in the outcome over time. Due to variation in time between baseline measurement and surgery, 'time to surgery' was entered as a second covariate. The third covariate was the socio-demographic/psychological variable to examine whether this factor was related to the overall score of the outcome. The last covariate was the interaction between time and the socio-demographic/psychological variable, to examine whether the variable was related to an increase/decrease in the outcome over time. The socio-demographic/psychological variables that had an univariate relationship with the mental health measure ($p < 0.01$) were entered in one multilevel model. A quadratic function of time was also included, to examine whether there was a non-linear change in mental health over time. Non-significant effects were removed step by step until a parsimonious model was reached.

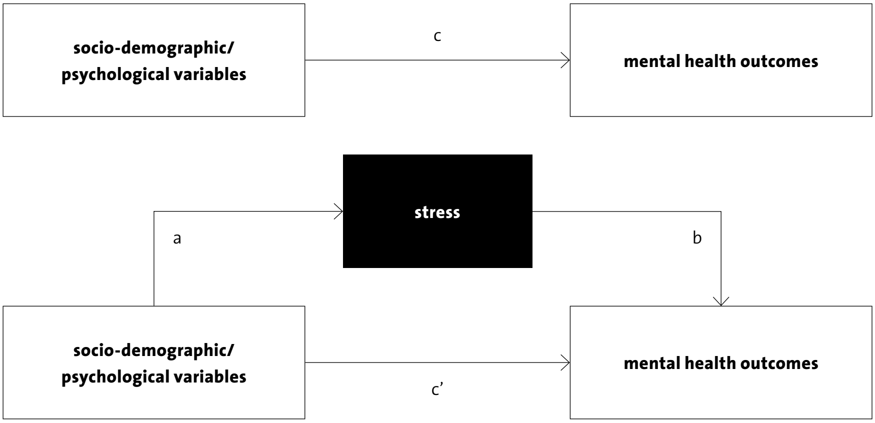
2 In order to investigate whether stress predicted mental health, we conducted a multilevel regression model with the mental health measures as outcome. The first two covariates were 'time' and 'time to surgery'. The third covariate was 'stress' to examine whether this factor was related to the overall score of the outcome. The last covariate was the interaction between time and stress, to examine whether the relationship between stress and the outcome differed over time.

3 Determining path a. We conducted separate multilevel regression models with the socio-demographic/psychological variables that predicted mental health (from step 1, path c) as covariates and stress as outcome. The models had the same covariates as the models in step 1: time, time to surgery, socio-demographic/psychological variable, and interaction between time and the socio-demographic/psychological variable. The socio-demographic/psychological variables that had an univariate relationship with stress ($p < 0.01$) were entered in one multilevel model. A quadratic function of time was also added. Non-significant effects were removed step by step until a parsimonious model was reached. The predicted values of the parsimonious model were saved and used in step 4.

4 Determining path c'. The final multilevel regression model of step 1 was repeated with the addition of the saved predicted values of the mediation model from step 3. We concluded that the influence of a covariate on the mental health outcome was mediated by stress, if the estimate of a covariate decreased significantly after the inclusion of the predicted values of stress from the mediation model of step 3 (path c' < path c)[40]. This significance was determined by evaluating the quotient of the difference in estimates and the pooled standard error as a z-score.

For all analyses we used SPSS version 21.0 (IBM Corporation, Armonk, NY, USA) and a p-value less than 0.01 was considered statistically significant due to multiple testing.

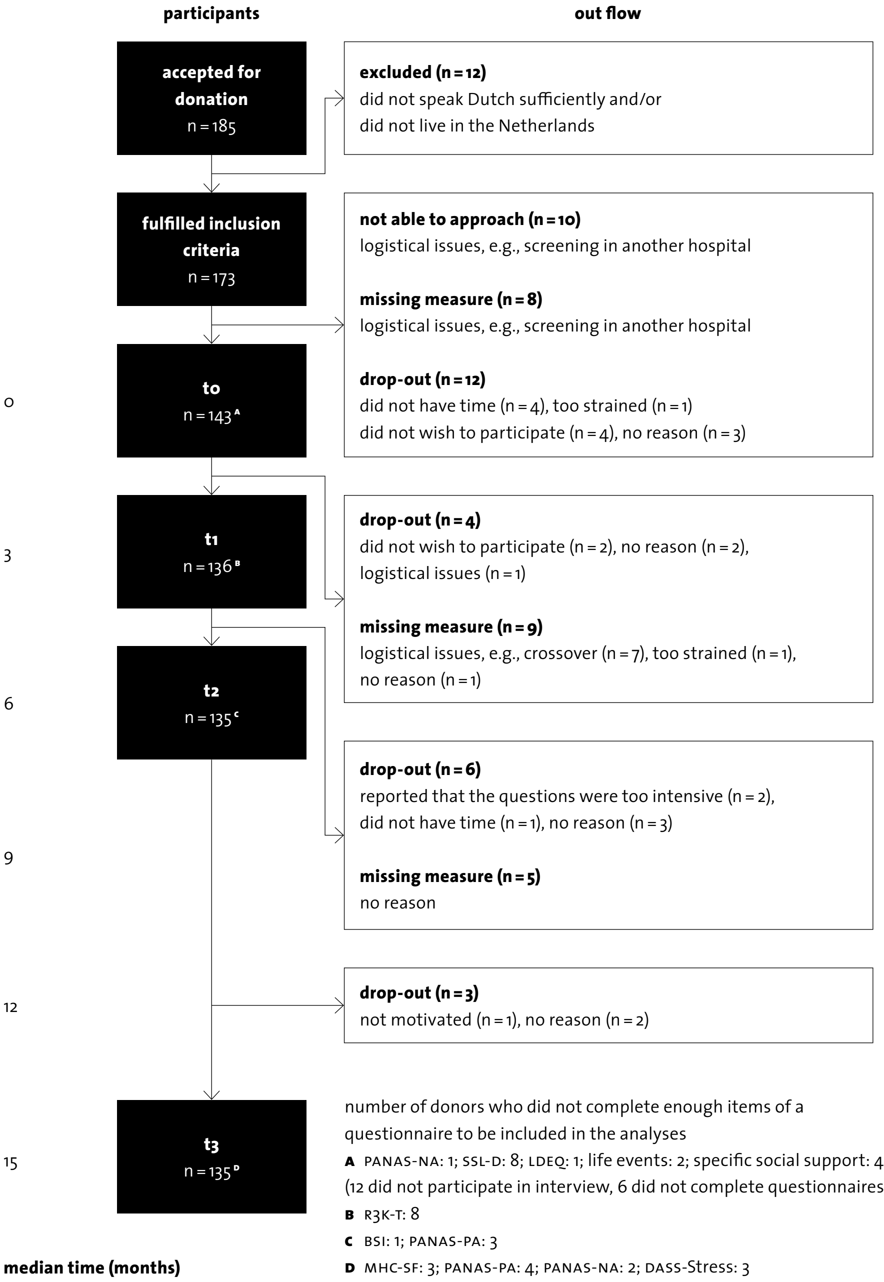
[f2 requirements for mediation**]**



a socio-demographic/psychological variable is mediated by stress if the following paths are significant:

- path c
- stress predicts mental health
- path a
- path c’ < path c

[f3 flow diagram of participants]



number of donors who did not complete enough items of a questionnaire to be included in the analyses

A PANAS-NA: 1; SSL-D: 8; LDEQ: 1; life events: 2; specific social support: 4; (12 did not participate in interview, 6 did not complete questionnaires)

B R3K-T: 8

C BSI: 1; PANAS-PA: 3

D MHC-SF: 3; PANAS-PA: 4; PANAS-NA: 2; DASS-Stress: 3

results

participants

Between 5th July 2011 and 13th September 2012, 185 potential living kidney donors were approved for donation and subsequently donated a kidney. Twelve donors were excluded from participation due to language or living abroad. Eighteen donors were not approached for the first measurement due to logistical issues, e.g., screening in another hospital. Six of these donors were subsequently included and participated from the second measurement, one from the third measurement, and one donor participated only in the fourth measurement **[f3]**. Nine donors did not complete the second measurement, however they all participated again in the third measurement.

One-hundred fifty-one donors completed at least 1 measurement (response rate was 87%), referred as the participants. Thirteen donors dropped out during the study (9%) and 22 donors missed 1 or 2 measurements (15%).

socio-demographic characteristics

Participants' socio-demographic characteristics are depicted in **[t1]**. Participants did not differ from non-participants on socio-demographic characteristics, except that participants were less likely to have a religious affiliation ($\chi^2(1)=4.90, p=0.027$) than non-participants.

descriptive statistics

Donors donated their kidney a median of 2.5 (range 0.1-21.7) months after baseline. Median time between the first and second measurement was 2.1 (range 0.03-20.4) months, between the first and third measurement 5.6 (range 2.9-24.2) months, and between the first and last measurement 15.0 (range 11.7-29.2) months.

psychometric properties of the questionnaires

coping

The internal consistencies of the subscales of the COPE-Easy ranged from high to respectable: active problem-oriented coping ($\alpha = 0.85$), social support seeking coping ($\alpha = 0.78$), and avoidant behaviour ($\alpha = 0.60$).

appraisals scale

A principal component analysis (PCA) was conducted on the 14 items with orthogonal rotation (varimax). The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis, KMO = 0.71 ('good' according to Field[41]), and all KMO values for the individual items were higher than the criterion of 0.5. The correlations between items were sufficiently large for PCA; Barlett's test of sphericity was significant, $\chi^2(91) = 563.83$, $p < 0.001$. We found that 5 components had eigenvalues higher than 1 (Kaiser's criterion) and explained 69.02% of the variance. See **[t2]** for the factor loadings on the 5 components after rotation, the labels of the components and its internal consistencies.

[t2 summary of exploratory factor analysis results for the appraisal scale**]**

items					**rotated factor loadings**
	negative: threat/harm	**centrality**	**ambiguity**	**manageability**	**positive**
threatening	0.861				
risky	0.835				
harmful	0.786				
negative impact	0.697				
important to me		0.904			
of high significance to me		0.897			
confusing			0.715		
complicated			0.692		
predictable			–0.628		0.409[A]
if something is going wrong, I will manage the problem				0.861	
if something is going wrong, I will manage my emotions				0.853	
challenge					0.814
beneficial					0.604
controllable			–0.473		0.567
eigenvalues	3.60	2.17	1.58	1.25	1.07
% of variance	25.72	15.48	11.27	8.93	7.62
α	0.84	0.82	0.52	0.76	0.56

[A] because of theoretical reasons item 'predictable' was included in the 'positive' component instead of the 'manageability' component, despite that this item loaded higher on the manageability component.

expectations

The internal consistencies of the subscales of the Living Donation Expectancies Questionnaire ranged from high to respectable: Interpersonal Benefit ($\alpha = 0.68$), Personal Growth ($\alpha = 0.83$), Spiritual Benefit ($\alpha = 0.79$), Quid Pro Quo ($\alpha = 0.57$), Health Consequences ($\alpha = 0.62$), and Miscellaneous Consequences ($\alpha = 0.59$). One item was deleted in the 'Miscellaneous Consequences' subscale as this item worsened the internal consistency of this subscale.

multilevel models

psychological symptoms (BSI)

1 Factors that had an univariate relationship with psychological symptoms at all time-points were: expectations of quid pro quo/negative health consequences, avoidant coping style, history of psychological problems, appraisals of centrality, impact of negative life events, expectations of interpersonal benefit, age, and deficiency in social support. After entering the covariates in one model, the latter three covariates remained significant (see **[t3]** path c).

2 More stress was related to more psychological symptoms ($t(392.63) = 11.93$, $p < 0.001$) at all time-points.

3 Expectations of interpersonal benefit was in addition to psychological symptoms related to stress at all time-points (see **[t3]** path a).

4 Path c' **[t3]** represents the final model from step 1 with the saved-predicted values from step 3 included.

5 As the estimate of expectations of interpersonal benefit decreased significantly after including the saved-predicted values from step 3 ($Z = (0.103-0.051) / \sqrt{((0.023^2 + 0.018^2) / 2)} = 2.59$, $p = 0.010$), we interpreted the model with path c': Psychological symptoms increased over time and younger age and a deficiency in social support were related to a higher level of psychological symptoms at all time-points. More expectations of interpersonal benefit were also related to a higher level of psychological symptoms and partly mediated by stress. See **[f4 A]** for a schematic representation of the final model.

negative affect (PANAS-NA)

1 Factors that had an univariate relationship with negative affect at all time-points were: expectations of interpersonal benefit/personal growth/quid pro quo/miscellaneous consequences, history of psychological problems, deficiency in social support, appraisals of centrality, impact of positive life events, appraisals of manageability, avoidant coping style, age, interaction between time and marital status, and impact of negative life events. After entering the covariates in one model, the latter five covariates remained significant (see **[t4]** path c).

2 More stress was related to higher negative affect ($t\,(397.67) = 11.25$, $p < 0.001$) at all time-points.

3 Appraisals of manageability and an avoidant coping style were in addition to negative affect related to stress at all time-points (see **[t4]** path a).

4 Path c’ **[t4]** represents the final model from step 1 with the saved-predicted values from step 3 included.

As the estimates of both appraisals of manageability ($Z = (-0.447 - 0.008) / \sqrt{(0.139^2 + 0.120^2) / 2} = -3.50$, $p < 0.001$) and avoidant coping style ($Z = (0.156 - 0.071) / \sqrt{(0.031^2 + 0.026^2) / 2} = 3.02$, $p = 0.003$) decreased significantly after including the saved-predicted values from step 3, we interpreted the model with path c’: Negative affect increased over time. A younger age was related to a higher negative affect at all time-points. Donors without a partner showed a greater increase in negative affect over time. Lower appraisals of manageability were almost completely mediated by stress, resulting in higher stress and consequently a higher negative affect at all time-points. An avoidant coping style was also related to a higher negative affect and partly mediated by stress. See **[f4 B]** for a schematic representation of the final model.

wellbeing (MHC-SF)

1 Factors that had an univariate relationship with wellbeing at all time-points were: deficiency in social support, expectations of negative health consequences, religious affiliation, history of psychological problems, social support (interactions), and positive appraisals. After entering the covariates in one model, the latter five covariates remained significant (see **[t5]** path c).

2 More stress was related to lower wellbeing ($t(348.36) = -5.53$, $p < 0.001$) at all time-points.

3 Expectations of negative health consequences were in addition to wellbeing related to stress at all time-points (see **[t5]** path a).

4 Path c' **[t5]** represents the final model from step 1 with the saved-predicted values from step 3 included. As the estimate of expectations of negative health consequences did not significantly change ($Z = (-0.088 - -0.059) / \sqrt{((0.025^2 + 0.026^2) / 2)} = -1.13$, $p = 0.26$) after including the saved-predicted values from step 3, we interpreted the model with path c: No religious affiliation, a history of psychological problems, less social support (interactions), more expectations of negative health consequences, and lower positive appraisals were related to a lower wellbeing at all time-points. No change in time was observed for wellbeing. See **[f4 c]** for a schematic representation of the final model.

positive affect (PANAS-PA)

1 Factors that had an univariate relationship with positive affect at all time-points were: appraisals of ambiguity, employment status, and social support (interactions). After entering the covariates in one model, the latter two covariates remained significant (see **[t6]** path c).

2 Stress was not related to positive affect ($t(348.36) = -5.53$, $p < 0.001$). Mediation in the positive affect model is therefore ruled out.

3 Not applicable.

4 Unemployment and lower social support (interactions) were related to lower positive affect at all time-points **[t6]**. No change in time was observed for positive affect. See **[f4 D]** for a schematic representation of the final model.

[t3 final model for psychological symptoms (bsi)**]**

	mediator (stress) as outcome			
	path a			
parameter	b	*se* b	*p*	ci 99%
intercept	–5.727	0.741	0.000	[–7.664––3.790]
expectations of interpersonal benefit	0.192	0.063	0.003	[0.028–0.356]
time				
age				
deficiency in social support				
mediator (predicted value of path a)				

[t4 final model for negative affect (panas-na)**]**

	mediator (stress) as outcome			
	path a			
parameter	b	*se* b	*p*	ci (99%)
intercept	–0.806	1.808	0.656	[–5.534––3.921]
appraisals of manageability	–1.430	0.397	0.000	[–2.469––0.392]
avoidant coping style	0.313	0.089	0.001	[0.081–0.545]
time				
age				
marital status				
time × marital status				
impact negative life events				
mediator (predicted value of path a)				

[t5 final model for wellbeing (mhc-sf)**]**

	mediator (stress) as outcome			
	path a			
parameter	b	*se* b	*p*	ci (99%)
intercept	–5.582	0.726	0.000	[–7.480––3.683]
expectations of health consequences	0.268	0.092	0.004	[0.028–0.508]
religious affiliation				
history of psychological problems				
social support (interactions)				
positive appraisals				
mediator (predicted value of path a)				

psychological symptoms as outcome							
path c				path c’			
b	*SE* b	*p*	CI 99%	b	*SE* b	*p*	CI 99%
–5.370	0.557	0.000	[–6.828––3.911]	–3.258	0.472	0.000	[–4.493––2.022]
0.103	0.023	0.000	[0.044–0.163]	0.051	0.018	0.005	[0.004–0.097]
0.026	0.009	0.003	[0.003–0.048]	0.025	0.009	0.004	[0.003–0.048]
–0.025	0.007	0.000	[–0.043––0.007]	–0.017	0.005	0.002	[–0.031––0.003]
0.050	0.011	0.000	[0.021–0.079]	0.030	0.009	0.001	[0.007–0.052]
				0.322	0.033	0.000	[0.235–0.409]

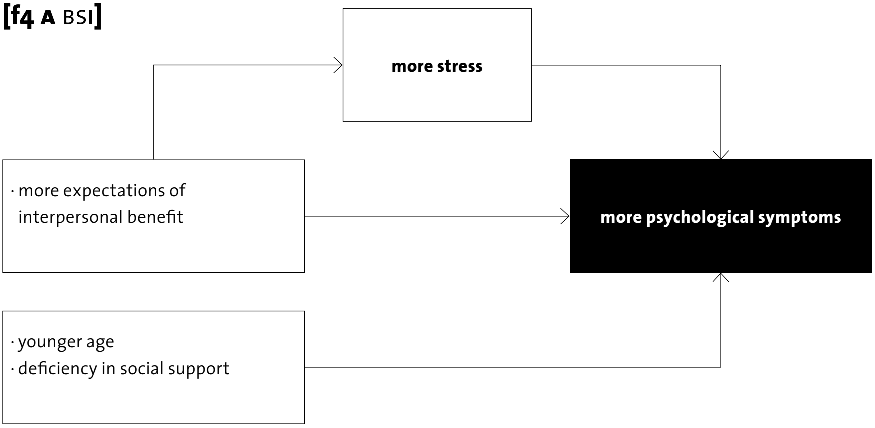
psychological symptoms as outcome							
path c				path c’			
b	*SE* b	*p*	CI (99%)	b	*SE* b	*p*	CI (99%)
–1.756	0.730	0.018	[–3.666–0.155]	–2.000	0.572	0.001	[–3.497––0.503]
–0.447	0.139	0.002	[–0.812––0.083]	0.008	0.120	0.946	[–0.307–0.323]
0.156	0.031	0.000	[0.076–0.236]	0.071	0.026	0.007	[0.004–0.138]
0.035	0.014	0.013	[–0.001–0.070]	0.036	0.014	0.009	[0.000–0.072]
–0.019	0.006	0.003	[–0.034––0.003]	–0.014	0.005	0.004	[–0.026––0.001]
–0.011	0.196	0.955	[–0.521–0.499]	0.155	0.163	0.343	[–0.269–0.578]
–0.047	0.017	0.006	[–0.091––0.003]	–0.049	0.017	0.004	[–0.092––0.005]
0.036	0.012	0.003	[0.005–0.067]	0.019	0.009	0.041	[–0.005–0.044]
				0.286	0.033	0.000	[0.201–0.372]

psychological symptoms as outcome							
path c				path c’			
b	*SE* b	*p*	CI (99%)	b	*SE* b	*p*	CI (99%)
0.812	0.487	0.098	[–0.464–2.089]	0.172	0.518	0.741	[–1.185–1.528]
–0.088	0.025	0.001	[–0.155––0.022]	–0.059	0.026	0.027	[–0.128–0.010]
0.365	0.135	0.008	[0.011–0.719]	0.376	0.130	0.005	[0.035–0.718]
–0.389	0.140	0.006	[–0.755––0.023]	–0.309	0.137	0.027	[–0.669–0.051]
0.021	0.005	0.000	[0.008–0.035]	0.024	0.005	0.000	[0.011–0.037]
0.400	0.095	0.000	[0.150–0.650]	0.359	0.093	0.000	[0.116–0.603]
				–0.091	0.031	0.004	[–0.173––0.010]

[**t6** final model for positive affect (PANAS-PA)]

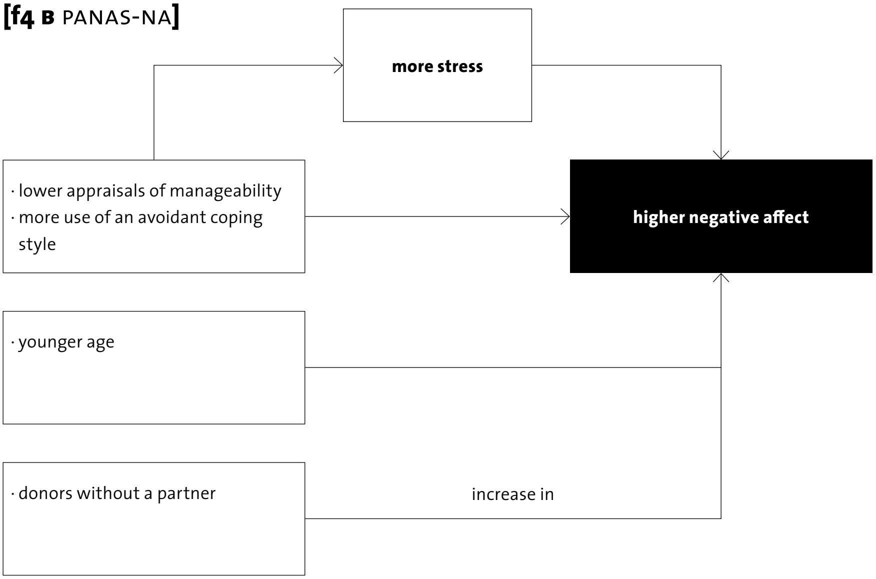
	path c			
parameter	b	SE b	*p*	CI (99%)
intercept	2.026	0.307	0.000	[1.223–2.829]
employment status	–0.369	0.107	0.001	[–0.647––0.090]
social support (interactions)	0.013	0.004	0.001	[0.003–0.023]

[f4 A BSI**]**



[f4 C MHC-SF**]**

[f4 B PANAS-NA]



[f4 D PANAS-PA]

discussion

This study fills the need for prospective studies on the risk factors for unfavourable mental health outcomes after living kidney donation. Many guidelines for the psychosocial evaluation of donor candidates have been developed, however there was little empirical evidence for the predictive value of each component. In the present study, we identified characteristics of donors who have lower mental health during the whole donation period: a history of psychological problems, expectations of interpersonal benefit and negative health consequences, an avoidant coping style, lack of social support, and appraisals of the donation process as an unmanageable and/or negative event. Of these factors, expectations, coping style, and appraisals of manageability caused greater stress which in turn caused greater psychological symptoms. Furthermore, we found that a younger age, no religious affiliation, and unemployment were also related to a lower mental health and psychological symptoms increased to a greater degree among donors who did not have a partner.

A number of findings are in line with previous cross-sectional research. Our findings on expectations are in line with Rodrigue et al.[38] who found that potential donors who had extreme expectations on negative health consequences and interpersonal benefit were more often classified in the category 'high risk for negative psychological outcomes' before donation by professionals. In addition, our finding that a lack of social support is related to unfavourable psychological outcomes is in line with an earlier study that found a comparable association for quality of life[42]. We expand upon these earlier studies by providing prospective evidence for these relationships up to one-year postdonation.

In this study we identified donors who have a low mental health prior to donation that remains stable up to one year postdonation. Many of the components that were related to a low stable mental health are also included in screening guidelines that have been developed to date[12]. Most guidelines indicate that in case of one or more of these factors potential donors should be rejected for donation, as many professionals presume that the factors are red flags of deterioration in donors' mental health. We however did not find any evidence that these factors are predictive of deterioration, nor increase, in mental health after donation, except for the lack of a partner. We therefore argue that potential donors should not be rejected for donation based on these risk factors, but the factors should be used to identify donors who might be in need for more psychological support. Such support will contribute to positive psychological outcomes for donors which may also have a positive influence on a person's recovery after surgery[43].

Characteristics of donors who potentially need additional psychological support can be divided into changeable and unchangeable factors. The unchangeable factors are a younger age, no religious affiliation, no partner, unemployment, and a history of psychological problems. The changeable factors that are modifiable by psychological interventions are expectations of negative health outcomes/interpersonal benefit, an avoidant coping style, lack of social support, and appraisals of the donation process as an unmanageable and/or negative event. We recommend that professionals assess the presence of risk factors among potential donors and in case of one or more factors, the professional should examine whether this donor needs extra psychological support during the donation procedure. In the case of only unchangeable risk factors, the intervention should focus on improving donors' mental health. For the changeable factors, such as expectations and coping behaviour, we recommend cognitive-behavioural techniques[44]. Stress-reducing techniques[45] are also a good option in all cases as a higher stress level contributed to negative psychological outcomes and the influence of expectations, coping style, and appraisals was mediated by stress.

We note that we do not have insight into what accurate cutoff points are for the different risk factors that indicate a potential need for additional psychosocial support. We would like to encourage future studies aiming to develop a tool on how risk factors could be measured in an effective way and what accurate cutoff points are for each risk factor.

Despite the strengths of this study, such as a prospective design, a number of limitations should be taken into consideration. First, two subscales from the appraisal questionnaire, one from the COPE-Easy, and three from the LDEQ did not have high reliabilities. We recommend that future research aiming to validate a screening tool should also take into consideration the reliability of the screening questions. Second, due to the sample size and associated power it was impossible to investigate the influence of interactions between different socio-demographic and psychological factors, which could be interesting. For instance, it is possible that the relationship between expectations and mental health is different for men and women.

To summarize, our findings provide many practical advices in order to strengthen the tailored psychosocial support of living kidney donors. Professionals should pay extra attention to certain characteristics of donors. Younger age, no religious affiliation, no partner, unemployment, and a history of psychological problems are unchangeable risk factors for lower mental health. Risk factors that are modifiable by psychological interventions are expectations of negative health consequences/interpersonal benefit, an avoidant coping style, lack of social support, and appraisals of the donation process as an unmanageable and/or negative event. Professionals should assess these risk factors and examine the need for extra psychological support in the case of one or more risk factors. Future research is needed on 'how' these risk factors should be measured effectively and what appropriate cutoff values are for each factor as well as on which interventions might effectively promote mental health among living donors.

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9 Predicting mental health after living kidney donation: the importance of psychological factors

10

Discussion

In the past decades many insights have been gained into the medical consequences of living kidney donation and the best-practices to prevent adverse medical outcomes[1-6]. However, many questions remained unanswered about the psychological impact of living kidney donation and the best-practices to promote positive psychological outcomes. Earlier studies found mixed results and had methodological limitations. Therefore, various methodologically stronger prospective studies were conducted that are described in this thesis. The aims of these studies were (1) to examine whether there was a change in mental health between predonation and one-year postdonation among living kidney donors and (2) to identify the socio-demographic, psychological, and medical factors that have an influence on (change in) living kidney donors' mental health.

main findings

changes in donors' mental health over time

Two studies are described in this thesis that investigated changes in donors' mental health. These studies revealed that mental health remained the same for the majority of donors, while mental health improved or deteriorated for a minority after donation (chapter 5 & 7). This conclusion is in line with earlier studies[7-17], however the studies described in this thesis give new insights by providing the percentages of donors who changed in overall mental health during the donation process as well as showing the changes in the various (positive and negative) components of mental health. The study described in chapter 7 found an improvement in wellbeing among 9% of the donors and a deterioration in wellbeing among 14% of the donors, which reflects the positive component of mental health, such as satisfaction with life, positive affect, and feelings of personal growth. The percentages of changes in psychological symptoms, the negative component of mental health, differed between the studies described in chapter 5 and 7. The study described in chapter 5 found that an improvement in psychological symptoms was observed among 6% of the donors and a deterioration among 27%, while the study described in chapter 7 found a higher percentage of donors who improved in psychological symptoms (9%) and a lower percentage of those who deteriorated in psychological symptoms (17%). A likely cause of the differences is that the predonation measurement of the study described in chapter 5 was part of the screening. Consequently, donors might have underreported their psychological symptoms in order to pass the screening. The predonation measurement of the study described in chapter 7 was not part of the screening and therefore may give a more accurate representation of donors' psychological symptoms at that moment in time.

A question that remained unanswered in earlier studies is whether changes in donors' mental health were provoked by the donation process or reflect fluctuations that can also be observed in a group of individuals from the general population who did not undergo living donation. This question was investigated in a study described in chapter 7. The results of this study showed that changes in psychological symptoms and wellbeing observed among donors are not significantly different from changes observed in the general Dutch population. These results indicate that the changes in mental health among the minority of donors are not triggered by the donation process.

factors that have an influence on donors' mental health

In this thesis we found evidence that a complicated medical process and not having a partner were related to a deterioration in donors' mental health. A complex medical process experienced by the recipient predicted a deterioration in donors' mental health after donation (chapter 8). Contradictory results were found on the influence of the donors' medical process. While the study described in chapter 8 showed that a more complex medical process experienced by the donor was a risk factor for a deterioration in donors' mental health among specified and unspecified donors, a study among unspecified donors did not find this relationship (chapter 5). However, the results of the study described in chapter 5 were hampered by methodological limitations. More specifically, there was a difference in measurement points between the medical indicators and donors' psychological symptoms: hospitalizations days and occurrence of medical complications were measured until 3 months after donation, while psychological symptoms were measured 3 to 36 months after donation. It is likely that the impact of the medical process on psychological outcomes diminished over time among these donors. The study described in chapter 8 is methodologically stronger and is therefore a better basis from which to draw conclusions. In this study we found that a complex medical process experienced by the donor is a risk factor for deterioration in donors' mental health.

A second risk factor of a deterioration in donors' mental health is the lack of a partner: a greater increase in negative affect over time was found among donors without a partner (chapter 8 & 9). It is possible that donors without a partner lacked social support during the donation process, which had an impact on their mood and mental health. However, the study described in chapter 9 showed that predonation social interactions and a deficiency in social support were not related to change in donors' mental health over time. It is possible that the need for social support among donors increases during the donation process and therefore becomes more important in a later stage of the donation process. The influence of social support during and after the donation process was not investigated in this thesis and warrants further research.

This thesis also describes whether expectations, appraisals, knowledge, coping, social support, and life events predict the absolute level or a change in donors' mental health (chapter 9). These factors are based on stress models of Lazarus[18] and Ursin and Eriksen[19] and have demonstrated predictive value on the psychological impact of other events. Moreover, many of these factors are included in psychosocial screening guidelines that have been developed to date to screen donor candidates (chapter 2). The results of the study described in chapter 9 showed that none of the factors predicted changes in donors' mental health over time. However, we found evidence that the following psychological risk factors were predictive of the absolute level of donors' mental health during the donation process: a history of psychological problems, expectations of interpersonal benefit and negative health outcomes, an avoidant coping style, lack of social support, and appraisals of the donation process as an unmanageable and/or negative event. In addition, a number of socio-demographic risk factors were identified that were related to a stable lower mental health among donors: a younger age, no religious affiliation, and unemployment.

clinical implications

The findings of this thesis have many implications for the psychosocial education, screening, and support of (potential) living kidney donors.

psychosocial education

Next to the medical consequences of living kidney donation, it is important that potential donors should be informed about the psychological consequences of donation. The conclusions of the current thesis should be included in the education process of living donors and can be described as follows:

There is no evidence that the donation process has an influence on donors' mental health up to one year after the donation. Some donors may need additional psychosocial support during the donation process, especially if the donor or recipient experiences medical complications and/or a re-hospitalization. Please do not hesitate to ask a healthcare processional for psychosocial support when needed. This information could also be included in the education process of prospective living donor kidney recipients.

In addition, professionals should be aware that a number of donors lacked knowledge on living donation one day before their surgery (chapter 4), which is probably the consequence of an emotional decision making process that is observed among living kidney donors[20]. Donors' knowledge did not have an influence on change in donors' mental health after donation (chapter 9), however, knowledge is important for a well-considered decision making and essential to give informed consent[21,22]. Therefore, it is recommended that professionals not only provide information but also assess processing and understanding, and subsequently tailor educational efforts to the informational needs of these potential donors. A useful and validated tool that can be used to measure potential donors' knowledge is The Rotterdam Renal Replacement Knowledge-Test (chapter 4).

psychosocial screening

In the past decades many guidelines have been developed by professionals on psychosocial screening of living donors. However, there was no evidence on whether these factors are predictive of mental health outcomes after living donation (chapter 2). There was therefore little evidence on the necessity of rejecting potential donors based on these psychological criteria. In this thesis, different arguments are provided that rejection for donation based on these psychosocial screening guidelines as described in the literature would be neither necessary nor helpful, with the exception of donors who are incompetent to give informed consent due to an impaired mental health status. Firstly, chapter 7 describes that changes in donors' mental health (up to one year) are not different from changes observed in the general population. The donors who participated in this study were screened with a minimal psychosocial anamnesis during the medical screening and unspecified donors were additionally screened by a clinical psychologist, using an in-depth interview and a self-report questionnaire measuring psychological symptoms. However, as none of the potential donors were rejected for psychological reasons during the research period, there was little to no selection bias. These results suggest that such a limited psychosocial screening as conducted in Erasmus Medical Center is sufficient. Secondly, the factors that are mostly included in psychosocial screening guidelines, i.e., a history of psychological problems, appraisals, expectations, knowledge, coping, social support, and life events, have no predictive value on change in donors' mental health (chapter 9). Thus, there is no evidence that factors such as extreme expectations regarding personal consequences of the donation process will contribute to a deterioration in donors' mental health and therefore there is no grounds for rejection for living donation on the basis of such components. Finally, an important question that is not yet investigated is what the psychological impact is of rejecting potential living donors because of psychological reasons.

psychosocial support

Although there is little evidence to reject donor candidates based on the idea of vulnerability to deterioration in mental health over time, there are likely to be individuals who come into the donation process with mental health issues and may need more attention that other donors. These donors have a low stable mental health during the donation process and could benefit from additional psychosocial support. There are different arguments for the importance of such support, even though the changes in donors' mental health and number of psychological symptoms are not extreme (chapter 7). A first argument is that improving positive changes in donors' mental health will contribute to a fair balance between risks and benefits after donation. Secondly, it is known that promoting perioperative mental health predicts a shorter recovery period, less complications[23], and faster wound healing[24] after a surgery and subsequently minimizes medical costs[25]. Maple et al.[26] found among living donors that greater positive psychological health predicts faster wound healing. Therefore promoting positive psychological outcomes among donors provides an opportunity for improving donors' postoperative recovery process. Thirdly, it is conceivable that a number of donors who show negative changes in their mental health after donation will attribute at least a part of the negative change in their mental health to the donation process. One could imagine that such attributions will enhance the likelihood of regret or difficulties in the donor-recipient relationship after donation. Finally from an ethical point of view, regardless of whether psychological symptoms are related to the donation, as health care professionals we have a duty to provide support and treatment when needed.

The risk factors for a negative change or a stable low mental health status among donors as described earlier would be used to identify the donors who probably need more psychological support during the donation process. It is recommended that professionals measure these risk factors prior to donation and in the case of one or more factors, the professional should examine whether this donor needs extra psychological support during the donation procedure. A number of predonation risk factors are changeable factors that are modifiable by psychological interventions and a number of factors are unchangeable factors. The changeable factors include expectations of interpersonal benefit and negative health consequences, an avoidant coping style, lack of social support, and appraisals of the donation process as an unmanageable and/or negative event (chapter 9). Other unchangeable risk factors are a younger age, no religious affiliation, no partner, unemployment, and a history of psychological problems (chapter 9). In addition to the predonation risk factors, professionals should also examine the need for additional psychological support in the case of a complex medical process among the donor or recipient after the operation, as this is another unchangeable risk factor (chapter 8).

Different psychological interventions are available if additional psychological intervention is indicated. In the case of unchangeable risk factors, such as a complex medical process or socio-demographic characteristics, the intervention could focus on improving the donors' mental health using cognitive-behavioral techniques[27]. In the case of complex medical outcomes, supportive counseling, acceptance focused interventions[28,29], or grief therapy could also be used[30]. For the changeable factors, such as expectations and appraisals, we recommend cognitive-behavioral techniques[27]. Stress-reducing techniques[31] are also recommended as a higher stress level contributed to negative psychological outcomes and the influence of expectations, coping style, and appraisals was mediated by stress.

differences between specified and unspecified donors

In reaction to the many concerns on the psychological stability of unspecified living kidney donors[32], three studies are described that investigated the differences in mental health between specified and unspecified donors or the general population after donation. A review of the literature to date showed that there are no differences in mental health outcomes between specified and unspecified donors after donation (chapter 6). In addition, two prospective studies described in this thesis found that changes in unspecified donors' mental health are not different from changes observed among specified donors (chapter 7) and the general population (chapter 5). These results indicate that the absence of a relationship with the recipient does not impair psychological outcomes after living kidney donation. However, it is possible that a number of psychologically unstable unspecified donor candidates were excluded from donation and therefore from the studies described in chapter 5 and 6, due to a more extensive psychological screening for unspecified donors in comparison with specified donors. In these studies it was not registered whether donor candidates were rejected because of psychological reasons, which would have biased the results. This is not a problem in the study described in chapter 7, as the rejections for donation in the research period were registered and no one was rejected because of psychological reasons. However, in the study described in chapter 7 only 15 unspecified donors were included. Therefore, this study should be replicated with a larger group of unspecified donors in order to improve the generalizability of these results. If such a study find similar results, there will be no indication that unspecified donors should be psychologically screened or supported during the donation process in a different way to specified donors.

limitations

Despite the strengths of the studies that are described in this thesis, such as prospective designs in most studies and a large sample size of donors in comparison with earlier studies, a number of limitations should be taken into consideration.

Firstly, most conclusions were based on self-reported questionnaires and interviews. It is possible that a number of donors answered the questions in a socially desirable manner that could have influenced their scores on the questionnaires. Earlier research has demonstrated that living kidney donors have a tendency to respond in a socially desirable manner and try to appear psychologically healthy during a psychological evaluation before the donation[33]. We do not know if social desirability played a role in the current studies and whether or not this is a particular problem prior to donation compared to postdonation measures. In order to avoid this effect, measures presented (with the exception of chapter 5) were not part of the psychosocial screening. In addition, the researchers highlighted to the donors that the study was not part of the screening and that they participated anonymously in the study. A suggestion for future research is to measure social desirability among donors prior to donation using the Social Desirability Scale-17[34] or the Short form of the Marlowe-Crowne Social Desirability Scale[35]. Such studies could give insight into whether social desirability is observed among a number of donors or not.

Secondly, the current findings are mainly based on single-center studies. Due to the differences in the psychosocial screening of living donors across centers and countries[36], similar prospective cohort studies among donors in other settings are necessary to generalize the current results. It is expected that the results will at least be as positive as the current findings, as the psychosocial screening process at Erasmus Medical Center is limited in comparison with other transplant centers. In other words, it is expected that the more psychologically vulnerable donors will have been excluded from donation in other transplant centers.

future directions

A number of future questions arise from the results of the studies described in this thesis. The first question is whether the changes in donors' mental health and the factors influencing mental health up to one year post-donation will be the same many years after donation. There is some indication that psychological symptoms increase as time since donation increases among unspecified donors (chapter 5). This question is yet to be investigated among specified and unspecified donors together in a methodologically stronger study that does not use the psychological screening as predonation measurement. It is recommended that the studies described in chapter 7, 8, and 9 are replicated with longer follow-up periods.

Secondly, there are many questions on the subjective psychological impact of living kidney donation. For instance, it is unknown whether the donation process is experienced as a life event, whether this is positive or negative, and what the relative impact of donation is in comparison with other life events. Furthermore, it is unknown if the changes found in donors' mental health correspond with the subjective impact of the donation process as reported by the donors. In-depth interviews among living donors predonation and postdonation would give insights into these questions.

Thirdly, it is unknown what the psychological impact is of rejection on psychological grounds for donation. Research investigating this question using both qualitative and quantitative measures is warranted, to give insight into the impact of rejection on ongoing psychological problems and the need to post-screening care in the case of rejection (or collaboration with the psychologist/psychiatrist treating these issues outside the transplant clinic).

A final question is how the risk factors such as expectations and coping as described in chapter 9 could effectively be measured and what cutoff points can be used to identify those in need of additional psychosocial support. Additionally, the effectiveness of psychological interventions such as cognitive-behavioral techniques[37] should be evaluated in the case of low mental health among donors as suggested in chapter 8 and 9. The results of such studies will contribute to the improvement of tailored psychosocial support of living kidney donors.

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11

Summary

Samenvatting

summary

Living donor kidney transplantation is the best option for extending and improving the lives of patients with end-stage renal disease. The benefits for the donor are less straightforward: a donor is a healthy person who undergoes a surgery in the first place for the benefit of another person. It is therefore of great importance to minimize negative medical and psychological outcomes after living kidney donation and optimize positive outcomes. In the past decades, many studies have been done on the medical outcomes after living kidney donation and the best-practices in order to prevent negative medical outcomes. However, there is little research on the psychological outcomes after living kidney donation and how donors should be supported in order to prevent negative psychological outcomes. Therefore the aims of this thesis were to examine whether there is change in mental health between predonation and postdonation among living kidney donors and to identify the socio-demographic, psychological, and medical factors that have an influence on (change in) living kidney donors' mental health.

This thesis starts with a general introduction to the topic of living kidney donation in **chapter 1**. **Chapter 2** is a review of the current practices of the psychosocial evaluation of potential living donors. This study revealed that many psychosocial screening guidelines have been developed, however the guidelines vary in their recommendations on how living donors should be screened and supported. More specifically, there is no consensus on whether all potential donors should be psychologically screened or not (or only specific sub-groups), what components should be included in such a screening, how this screening should be performed, and who should administer the screening. The diversity in guidelines is the consequence of many factors. The most important cause is the lack of studies on the psychological outcomes after living donation and factors that predict poor psychological outcomes.

The review described in **chapter 2** revealed that expectations regarding personal consequences of living donation were one of the most commonly reported criteria for donor psychosocial screening. Therefore in **chapter 3** a profile of living kidney donors was described who had extreme expectations regarding personal consequences prior to donation. In this study, 136 living kidney donors completed questionnaires and participated in a structured interview prior to donation. The most important finding is that more depressed and isolated donors expected greater positive and negative personal consequences of living donation. The fact that these donors expected more negative consequences is in line with studies in other situations in which depressed individuals have a tendency towards hopelessness and more extreme negative expectations of situations. It is possible that these donors had developed positive expectations about their donation to compensate their negative expectations in order to justify their choice for donation. Another possible explanation is that some people tend to have unrealistically high expectations about events in their lives which may lead to discrepancies between expectations and outcomes. These discrepancies make them vulnerable for a depressed mood.

In **chapter 4** knowledge on dialysis, transplantation, and living donation of prospective living kidney donors and recipients was explored. It is important that donors and recipients have enough knowledge on these topics in order to make a well-considered and informed decision on living donation. Furthermore, sufficient knowledge contributes to realistic expectations about the donation process. In this study, 85 donors and 81 recipients completed a questionnaire on knowledge about dialysis, transplantation, and living donation one day before their surgery. The most important finding is that a minority of donors (15%) and recipients (17%) lacked knowledge, e.g., about the risks of living donation. This finding suggests that the decision to donate is not always based on full knowledge of the risks. Donors and recipients had especially lower knowledge levels if their native language was not Dutch. On the basis of the results, we recommended that professionals assess knowledge and information needs of prospective donors and recipients during the education process in order to adapt educational efforts to the informational needs of each individual. Extra attention is required for non-native speakers, as they had lower knowledge levels.

Chapter 5 describes a study on the psychological functioning of living kidney donors who donated their kidney to a genetically and emotionally unrelated and unknown person, referred to as ‘unspecified living donors’. In this study, 49 unspecified living kidney donors completed a questionnaire on psychological symptoms before and after their donation. Examples of psychological symptoms are a depressive mood and anxiety symptoms. This study showed that psychological symptoms remained the same over time for the majority of donors (67%), while psychological symptoms decreased (6%) or increased (27%) among a minority of donors. The question whether these changes are the consequence of the donation process is difficult to answer on the basis of this study. A limitation of this study was that the predonation measurement was part of the screening. It is possible that donors underreported their psychological symptoms before donation in order to pass the screening which may explain the seemingly greater symptoms among 27% of the donors after donation. As a consequence of the low predonation scores it was only possible to increase in psychological symptoms and not to decrease. In addition, it is unclear whether the changes observed among donors would be comparable to those observed among the general population.

Chapter 6 includes a review of studies on differences between specified (donors who donate their kidney to a genetically and/or emotionally related person) and unspecified living kidney donors in psychological outcomes after donation. This comparison is important as a number of professionals doubted the motivations of unspecified donors, and some even wondered whether their wish to donate could be a sign of mental instability. This issue is sensitive as the benefits for unspecified living donors are less evident, because these persons do not know the recipient and therefore do not directly benefit from their recovery. As a result of these concerns, unspecified living kidney donation is only performed in a few countries while most countries have legal restrictions against unspecified donation. If unspecified donation would be more widely accepted, it could be a good solution for decreasing the gap between kidney demand and available donors. We concluded from the current literature that specified and unspecified donors do not differ on mental health and donation-related outcomes (such as regret) after donation. Therefore the absence of an emotional and genetic relationship with the recipient does not have a negative effect on psychological outcomes after donation. We use these findings to argue that unspecified living kidney donation is justified and legal restrictions on this type of donation should be removed.

Chapter 7 describes a study in which changes in donors' mental health between predonation and one year postdonation were compared with changes observed in a group individuals from the general Dutch population. As donors are on average psychologically healthier than the general population due to the screening prior to donation, individuals from the general population were selected for this study if they were equally psychologically healthy as the donors. In this study, 135 living kidney donors completed questionnaires on mental health predonation and three and twelve months postdonation. In addition, 135 individuals from the general population completed the same questionnaires at baseline, and three, six, and nine months follow-up. Donors included both specified and unspecified donors. The results of the study showed that mental health remained the same for the majority of donors, while mental health improved or deteriorated for a minority after donation. These changes were comparable to changes found in mental health among the general Dutch population, suggesting that the increases and decreases in mental health among the minority of donors are not triggered by the donation process.

Chapter 8 describes a study that examined whether complexity of the medical process among donors and recipients predicted changes in donors' mental health between predonation and postdonation. One-hundred forty-five donors completed questionnaires on mental health predonation, three and twelve months postdonation. Indicators of complexity of the medical process were complications among donors and number of recipient re-hospitalizations, which were obtained from medical records at three and twelve months after the operation. The results of the study showed that a more complex medical process experienced by either the donor or recipient is a risk factor for deterioration in donors' mental health after donation. Professionals should therefore monitor donors who experience a complex medical process, and offer additional psychological support when needed.

Chapter 9 describes a study that examined whether socio-demographic factors such as age and gender and psychological factors such as social support and expectations predicted donors' mental health during the donation process. One-hundred fifty-one living kidney donors were interviewed before donation and completed questionnaires predonation and three and twelve months postdonation. The results of this study showed that there was only one factor that predicted change in donors' mental health: a greater deterioration in mental health was observed among donors without a partner. A number of donors' characteristics were related to a stable lower mental health during the donation process: younger age, unemployment, no religious affiliation, history of psychological problems, lack of social support, and a tendency to not actively deal with problems. A number of donation-related factors measured prior to donation were also related to a stable lower mental health among donors: expectations of appreciation from the environment in reaction to the donation, expectations of negative health consequences, feelings that he/she will not be able to manage with setbacks during the donation, and negative thoughts about the donation process. Given that none of the predonation psychological factors were predictive of deterioration in mental health, we found little evidence for rejection of potential donors based on these factors. It is recommended that professionals assess these risk factors prior to donation, where appropriate intervene for example on unrealistic expectations of donation, and assess the need for additional psychological support in the case of one or more risk factors.

In the general discussion (**chapter 10**) the findings of all studies are integrated and a main conclusion and recommendations are given. The main conclusion is that mental health remained the same for the majority of living kidney donors till one year after donation, while mental health improved or deteriorated for a minority after donation. However, the changes among the minority of donors were not more or less than the changes found in mental health among the general population. This indicates that the changes among donors are not triggered by the donation process. Therefore, we did not find evidence to reject potential donors based on psychological reasons, except for donor candidates who are incompetent to give informed consent due to an impaired mental health status. In addition, we identified a number of donors who may benefit from additional psychological support during the donation process. Potential risk factors that are related to low mental health during the donation process should be examined prior to donation and include: expectations of appreciation from the environment in reaction to the donation or negative health consequences, feelings that he/she will not be able to manage with setbacks during the donation, negative thoughts about the donation process, history of psychological problems, lack of social support, a tendency to not actively deal with problems, younger age, unemployment, no religious affiliation, and the lack of a partner. Furthermore, the occurrence of donors' and recipients' medical complications is another risk factor that should be monitored. It is recommended that professionals examine the risk profile prior and during the donation process and the need for additional psychological support in the case of one or more risk factors. Interventions could be focused on decreasing stress/psychological symptoms, increasing wellbeing, and/or the risk factors, such as an intervention on unrealistic expectations. These recommendations will strengthen the psychosocial support of living kidney donors.

samenvatting

Transplantatie met een nier van een levende donor is de beste optie om het leven van mensen met eindstadium nierfalen te verlengen en te verbeteren. De voordelen voor de donor zijn minder duidelijk: een donor is een gezond persoon die een operatie ondergaat in de eerste plaats om het leven van iemand anders te verbeteren. Het is daarom belangrijk dat negatieve lichamelijke en psychologische gevolgen na nierdonatie bij leven voorkomen worden en positieve gevolgen zoveel mogelijk worden bevorderd. In de laatste decennia is er veel onderzoek gedaan naar de lichamelijke gevolgen van nierdonatie bij leven en de screening en begeleiding van donoren om negatieve lichamelijke gevolgen te voorkomen. Er is echter weinig onderzoek gedaan naar de psychologische gevolgen van nierdonatie bij leven en hoe donoren gescreend en begeleid moeten worden om negatieve psychologische gevolgen te voorkomen. Het doel van dit proefschrift is daarom om te bekijken in hoeverre donoren die bij leven hun nier afstaan een verandering laten zien in hun geestelijke gezondheid van vóór tot na de donatie en welke sociodemografische, psychologische en medische factoren van invloed zijn op (de verandering in) de geestelijke gezondheid van donoren.

Dit proefschrift begint met een algemene introductie over nierdonatie bij leven, welke beschreven staat in **hoofdstuk 1**. **Hoofdstuk 2** beschrijft een vergelijking van de screeningsinstrumenten die tot nu toe zijn ontwikkeld. Dit onderzoek laat zien dat er veel verschillende richtlijnen voor de screening van donoren zijn ontwikkeld, maar zij verschillen in hun aanbevelingen hoe donoren gescreend en begeleid moeten worden. Er is namelijk geen overeenstemming of alle donoren psychologisch gescreend zouden moeten worden (of alleen bepaalde subgroepen), uit welke componenten een dergelijke screening zou moeten bestaan, hoe de screening uitgevoerd zou moeten worden en wie de screening zou moeten uitvoeren. Er zijn meerdere oorzaken waardoor deze verschillen zijn ontstaan. De belangrijkste oorzaak is dat er weinig onderzoek is gedaan naar de psychologische gevolgen van nierdonatie bij leven en de factoren die negatieve psychologische gevolgen beïnvloeden.

In **hoofdstuk 2** is naar voren gekomen dat de verwachting dat de donatie veel persoonlijke gevolgen zal hebben vaak onderdeel is van psychologische screeningsinstrumenten die tot nu toe zijn ontwikkeld. In **hoofdstuk 3** wordt daarom bekeken welke donoren extreem veel persoonlijke gevolgen verwachtten na de donatie. Honderdzesendertig donoren hebben meegedaan aan deze studie en hebben vragenlijsten ingevuld en deelgenomen aan een interview voorafgaand aan hun donatie. De belangrijkste uitkomst van dit onderzoek is dat sombere en geïsoleerde donoren meer positieve en negatieve persoonlijke consequenties van hun donatie verwachtten dan andere donoren. In andere situaties is eerder ook aangetoond dat sombere mensen zich sneller hulpeloos voelen en vaak negatieve verwachtingen hebben van situaties. Mogelijk hebben donoren naast de negatieve verwachtingen ook positieve verwachtingen ontwikkeld om hun keuze voor de donatie voor zichzelf en anderen te kunnen rechtvaardigen. Een andere mogelijke verklaring voor de resultaten is dat er bepaalde mensen zijn die over het algemeen onrealistisch hoge verwachtingen hebben van situaties. Deze verwachtingen komen vervolgens niet uit, waardoor zij kwetsbaarder zijn voor sombere gedachten en gevoelens.

In **hoofdstuk 4** wordt de kennis van donoren en ontvangers over dialyse, transplantatie en nierdonatie bij leven beschreven. Het is belangrijk dat toekomstige donoren en ontvangers voldoende kennis hebben over deze onderwerpen zodat zij een weloverwogen en geïnformeerde beslissing kunnen nemen over de donatie. Daarnaast draagt voldoende kennis bij aan realistische verwachtingen over het donatieproces. In deze studie hebben 85 donoren en 81 ontvangers één dag voor hun operatie een vragenlijst ingevuld waarin hun kennis over dialyse, transplantatie en nierdonatie bij leven werd gemeten. De belangrijkste uitkomst van dit onderzoek is dat een klein gedeelte van de donoren (15%) en ontvangers (17%) weinig kennis had, o.a. over de risico's van nierdonatie bij leven. Deze uitkomsten laten zien dat de beslissing voor nierdonatie bij leven niet altijd wordt gebaseerd op voldoende kennis over de voordelen en risico's. Professionals moeten daarom het kennisniveau en de informatiebehoefte van toekomstige donoren en ontvangers meten tijdens het voorlichtingsproces en hun voorlichting aanpassen aan de behoefte van een persoon. Professionals moeten extra letten op het begrip van donoren en ontvangers die niet in hun moedertaal worden voorgelicht, omdat hun kennisniveau over het algemeen lager is.

Hoofdstuk 5 beschrijft een studie waarin het psychologisch functioneren in kaart wordt gebracht van donoren die een nier hebben gedoneerd aan iemand waar ze geen emotionele of genetische band mee hebben en ook niet kennen. Dit type donoren wordt ook wel 'niet-gerichte donoren' genoemd. In deze studie hebben 49 niet-gerichte donoren meegedaan die een vragenlijst hebben ingevuld voorafgaand en na hun donatie over psychologische klachten. Voorbeelden van psychologische klachten zijn een sombere stemming en angstklachten. De resultaten van deze studie laten zien dat de meeste donoren (67%) geen verandering in hun psychologische klachten lieten zien. Een minderheid van de donoren liet een afname (6%) of toename (27%) in klachten zien over tijd. De vraag of de veranderingen in psychologische klachten toegeschreven kunnen worden aan het donatieproces is niet te beantwoorden op basis van deze studie. Een beperking van deze studie is namelijk dat de voormeting onderdeel was van de screening. Het is mogelijk dat donoren bij de voormeting psychologische klachten niet gerapporteerd hebben, zodat zij door de screening zouden komen. Dit zou verklaren waardoor 27% een toename in psychologische klachten ondervond na de donatie. Doordat zij heel weinig klachten rapporteerden op de eerste meting, was het alleen nog maar mogelijk om een toename in klachten te laten zien na de donatie. Daarnaast is het ook niet duidelijk of de veranderingen die donoren lieten zien in psychologische klachten vergelijkbaar zijn met veranderingen in psychologische klachten die in de algemene populatie worden gezien.

In **hoofdstuk 6** wordt een onderzoek beschreven waarin studies worden vergeleken die verschillen in psychologische gevolgen tussen gerichte donoren (mensen die hun nier afstaan aan iemand waar ze een emotionele en/of genetische band mee hebben) en niet-gerichte donoren hebben onderzocht. Deze vergelijking is belangrijk, omdat een aantal professionals twijfelt aan de motieven van niet-gerichte donoren. Sommige professionals vermoeden dat de wens om een nier af te staan aan een onbekend persoon kan duiden op psychologische instabiliteit. Het is belangrijk om onderzoek te doen naar de psychologische gevolgen van niet-gerichte donatie, omdat deze donoren hun ontvanger niet kennen en daarom geen voordeel hebben aan het herstel van de ontvanger. Omdat verschillende professionals vraagtekens zetten bij niet-gerichte donatie is dit type donatie in slechts een aantal landen toegestaan en bij wet verboden in de meeste landen. Als niet-gerichte donatie vaker geaccepteerd zou worden, zou het een goede oplossing zijn om het gat tussen vraag en aanbod van beschikbare donornieren te verkleinen. Op basis van het onderzoek concludeerden wij dat er geen verschil is in de geestelijke gezondheid van gerichte en niet-gerichte donoren na de donatie en donatie-gerelateerde uitkomsten (zoals spijt). Het ontbreken van een emotionele of genetische band heeft dus geen negatieve invloed op het psychologisch functioneren van de donoren na de donatie. Deze resultaten zijn een argument om door te gaan met niet-gerichte donatie waar dit is toegestaan en om het type donatie toe te staan in de landen waar het op dit moment verboden is.

Hoofdstuk 7 beschrijft een studie waarin de veranderingen die donoren laten zien in hun geestelijke gezondheid van voor tot één jaar na de donatie worden vergeleken met de veranderingen die een groep mensen uit de algemene Nederlandse populatie laat zien. Omdat donoren psychologisch gezien gezonder zijn door de screening, mochten mensen uit de algemene populatie alleen meedoen in deze studie als zijn psychologisch gezien even gezond waren als de donoren. In het onderzoek deden 135 donoren mee die vragenlijsten hebben ingevuld over hun geestelijke gezondheid voorafgaand aan de donatie, drie maanden na hun donatie en één jaar na hun donatie. Daarnaast hebben 135 mensen uit de algemene populatie dezelfde vragenlijsten ingevuld en na drie, zes en negen maanden nog een keer. In het onderzoek deden zowel gerichte als niet-gerichte donoren mee. De resultaten van het onderzoek laten zien dat de meeste donoren geen veranderingen lieten zien in hun geestelijke gezondheid en een klein gedeelte liet een positieve of negatieve verandering zien. De veranderingen zijn echter vergelijkbaar met de veranderingen in geestelijke gezondheid die de groep mensen uit de algemene Nederlandse populatie liet zien. Deze resultaten suggereren dus dat de veranderingen in geestelijke gezondheid die een minderheid van de donoren laat zien niet door de donatie veroorzaakt worden.

Hoofdstuk 8 beschrijft een studie waarin onderzocht werd in hoeverre het medisch proces van de donor en ontvanger van invloed is op veranderingen in de geestelijke gezondheid van donoren van voor tot na de donatie. In deze studie deden 145 donoren mee die vragenlijsten hebben ingevuld over hun geestelijke gezondheid voor hun donatie, drie maanden na hun donatie en één jaar na hun donatie. Het medisch proces werd in kaart gebracht door bij donoren te kijken of zij een complicatie hadden meegemaakt en bij de ontvangers het aantal heropnames in het ziekenhuis op te tellen tot drie maanden na de operatie en één jaar na de operatie. De resultaten van het onderzoek laten zien dat complicaties bij de donor en heropnames bij de ontvanger een negatieve invloed hadden op de geestelijke gezondheid van donoren. Professionals moeten daarom de donoren in de gaten houden die negatieve medische uitkomsten hebben meegemaakt en extra psychologische hulp aanbieden als zij dat willen.

Hoofdstuk 9 beschrijft in hoeverre socio-demografische factoren zoals leeftijd en geslacht en psychologische factoren zoals sociale steun en verwachtingen de geestelijke gezondheid van donoren beïnvloeden. Honderdeenenvijftig donoren werden geïnterviewd voorafgaand aan hun donatie en zij vulden vragenlijsten in voorafgaand aan de donatie en drie maanden na de donatie en één jaar na de donatie. De resultaten van deze studie laten zien dat er slechts één factor was die verandering in de geestelijke gezondheid van donoren voorspelde: donoren zonder partner lieten vaker een verslechtering zien in hun geestelijke gezondheid. Daarnaast was er een aantal factoren gerelateerd aan een stabiel slechtere geestelijke gezondheid: een jongere leeftijd, geen werk hebben, geen religie aanhangen, een geschiedenis van psychologische problemen hebben, weinig sociale steun ervaren en de neiging hebben om problemen niet actief aan te pakken. Ook was er een aantal donatie-gerelateerde factoren die vaker voorkwamen bij donoren met een stabiel slechtere geestelijke gezondheid: verwachtingen van veel waardering vanuit de omgeving na de donatie, de verwachting dat de donatie veel negatieve gezondheidsgevolgen met zich mee zal brengen, het gevoel niet in staat te zijn om met tegenslagen om te gaan tijdens de donatie en negatieve gedachten over de donatie. Aangezien de psychologische factoren geen veranderingen in geestelijke gezondheid voorspelden, zien wij geen reden om donoren af te wijzen op basis van deze factoren. Het wordt wel aangeraden dat professionals de risicofactoren voorafgaand aan de donatie meten en waar nodig een interventie toepassen. Een professional kan bijvoorbeeld ingaan op onrealistische verwachtingen van donoren. Daarnaast moeten professionals psychologische begeleiding aanbieden als een donor risico loopt op een slechtere geestelijke gezondheid en hij/zij behoefte heeft aan begeleiding.

In **hoofdstuk 10** zijn de bevindingen van alle studies samengevoegd en wordt de hoofdconclusie van de studies beschreven. De hoofdconclusie is dat de meeste donoren geen veranderingen laten zien in hun geestelijke gezondheid tot één jaar na de donatie. Een klein gedeelte laat een positieve of negatieve verandering zien. De veranderingen die de minderheid van donoren laat zien is echter niet meer of minder dan in de algemene populatie wordt gevonden. Dit suggereert dat de veranderingen in geestelijke gezondheid die een minderheid van de donoren laat zien niet door de donatie veroorzaakt worden. Er is daarom geen reden om potentiële donoren af te wijzen op basis van psychologische redenen, met uitzondering van potentiële donoren die niet wilsbekwaam zijn om met een behandeling in te stemmen als gevolg van hun psychologische/psychiatrische stoornis. Daarnaast is er een aantal donoren dat baat zou hebben bij extra psychologische begeleiding. Er zijn verschillende risicokenmerken geïdentificeerd die samenhangen met een stabiel slechtere geestelijke gezondheid: verwachtingen van veel waardering vanuit de omgeving na de donatie, de verwachting dat de donatie veel negatieve gezondheidsgevolgen met zich mee zal brengen, het gevoel niet in staat te zijn om met tegenslagen om te gaan tijdens de donatie, negatieve gedachten over de donatie, een geschiedenis van psychologische problemen, weinig sociale steun ervaren, de neiging hebben om problemen niet actief aan te pakken, een jongere leeftijd, geen werk hebben, geen religie aanhangen en geen partner hebben. Donoren die zelf een complicatie hebben gehad of waarvan de ontvanger heropgenomen is geweest, hebben ook meer kans op een verslechtering in hun geestelijke gezondheid. Professionals moeten monitoren of de risicofactoren aanwezig zijn bij (potentiële) donoren voor en tijdens het donatieproces en inventariseren of een persoon in dat geval behoefte heeft aan extra begeleiding. De interventies kunnen gericht zijn op het verminderen van stress/psychologische klachten, het verbeteren van welzijn en/of de risicofactoren, zoals een interventie gericht op onrealistische verwachtingen. Deze aanbevelingen zullen bijdragen aan een verbeterde psychologische ondersteuning van donoren die bij leven hun nier afstaan of hebben afgestaan.

12

Appendices

PhD portfolio
list of publications
curriculum vitae
dankwoord

PhD portfolio

phd-training	**year**	**hrs**	**ECTS**
general courses			
· CPO Minicursus: methodologie van patiëntgebonden onderzoek en voorbereiding van subsidieaanvragen	2011	7	
· Conceptual foundation of Epidemiologic Study Design (NIHES)	2011		0.7
· Cohort studies (NIHES)	2011		0.7
· Courses for the Quantitative Researcher (NIHES)	2012		1.4
· Repeated Measurements in Clinical Studies (NIHES)	2012		1.4
· English Biomedical Writing and Communication	2012		4.0
seminars and workshops			
· Endnote and PubMed workshops	2011	4	
· various workshops of Promeras, VENA, and Postdoc Network	2011–2015		1
conferences attended (without a presentation)			
· Bootcongres Amsterdam, the Netherlands	2011		1
· European Health Psychology Conference Hersonissos, Greece	2011		1
presentations			
· American Transplant Congress Boston, United States: *poster*	2012		1
· International Congress of The Transplantation Society Berlin, Germany: *poster*	2012		1
· Bootcongres Maastricht, the Netherlands: *oral*	2012		1
· European Transplant Coordinators Organization congress Dubrovnik, Croatia: *oral/poster*	2012		2
· Bootcongres Duiven, the Netherlands: *oral/poster*	2013		2
· Ethical, Legal and Psychosocial Aspects of Transplantation Congress Rotterdam, the Netherlands: *three orals*	2013		3
· Congress of the European Society for Organ Transplantation Vienna, Austria: *oral/poster*	2013		2
· European Conference on Positive Psychology Amsterdam, the Netherlands: *oral/poster*	2014		2
· World Transplant Congress San Francisco, United States: *two posters*	2014		2
· European Health Psychology Society Conference Innsbruck, Austria: *oral/poster*	2014		2
· Joint British Transplantation Society & Nederlandse Transplantatie Vereniging Congress Bournemouth, England: *oral*	2015		1
teaching			
lecturing			
· lectures for medical/psychology students	2011–2014		1
· lectures at the department of Dialysis (Erasmus Medical Center / Maasstadziekenhuis)	2011–2014		1
· lectures at meetings for patients, donors, and professionals	2011–2014		1
supervising/tutoring			
· supervision of 2nd year medical students at the minor 'organ transplantation': writing a review	2012–2014		1
· supervision of a psychology student: writing a Master's thesis	2013–2014		1
· tutor at the minor 'medical psychology'	2013		1
· moderator at a discussion meeting about anonymity in living kidney donation	2013	4	
other activities			
· member of ELPAT (Ethical, Legal and Psychosocial Aspects of Transplantation) 'Psychological Care' working group	2011–2015		
· part-time internship as psychologist at the department of Psychiatry	2014		
· member of the SWON (landelijk werkgroep Sociaal Wetenschappelijk Onderzoek Nefrologie)	2011–2015		

list of publications

1

Timmerman L, Zuidema WC, Erdman RA, Kranenburg LW, Timman R, IJzermans JN, Busschbach JJV, Weimar W, Massey EK. Psychologic functioning of unspecified anonymous living kidney donors before and after donation. *Transplantation* 2013; 95: 1369-74

2

Timmerman L, Laging M, Zuidema WC, IJzermans JNM, Betjes MGH, Busschbach JJV, Weimar W, Massey EK. Who has extreme expectations of donation? Exploring the psychological profile of living kidney donors. In: Weimar W, Bos MA, Busschbach JJV, editors. *Organ transplantation: Ethical, legal and psychosocial aspects. Global issues, local solutions*. Lengerich, Germany: Pabst Science Publishers, 2014; p. 230-239

3

Timmerman L, Weimar W. An argument to abolish legal restrictions on unspecified living kidney donation. *Transplantation* 2014; 98: 1145-1146

4

Timmerman L, Laging M, Westerhof GJ, Timman R, Zuidema WC, Beck DK, IJzermans JNM, Betjes MGH, Busschbach JJV, Weimar W, Massey EK. Mental health among living kidney donors: a prospective comparison with matched controls from the general population. *American Journal of Transplantation* 2015; 15: 508-517.

5

Timmerman L, Ismail SY, Luchtenburg AE, Zuidema, WC, IJzermans, JNM, Busschbach JJV, Weimar W, Massey EK. Exploring knowledge about dialysis, transplantation, and living donation among patients and their living kidney donors. *International Journal of Behavioral Medicine* 2015 (in press)

6

Timmerman L, Laging M, Timman R, Zuidema WC, Beck DK, IJzermans JNM, Betjes MGH, Busschbach JJV, Weimar W, Massey EK. The impact of the donors' and recipients' medical process on living kidney donors' mental health. *Submitted*

7
Timmerman L, Timman R, Laging M, Zuidema WC, Beck DK, IJzermans JNM, Busschbach JJV, Weimar W, Massey EK. Predicting mental health after living kidney donation: the importance of psychological factors. *Submitted*

8
Ismail SY, Timmerman L, Timman R, Luchtenburg AE, Smak Gregoor PJ, Nette RW, van den Dorpel RM, Zuidema WC, Weimar W, Massey EK, Busschbach JJV. A psychometric analysis of the Rotterdam Renal Replacement Knowledge-Test (R3K-T) using item response theory. *Transplant International* 2013; 26: 1164-1172

9
Duerinckx N, Timmerman L, Van Gogh J, Busschbach JJV, Ismail SY, Massey EK, Dobbels F, on behalf of the ELPAT Psychological Care for Living Donors and Recipients working group. Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review. *Transplant International*. 2014; 27: 2-18

10
Ismail SY, Duerinckx N, Van der Knoop MM, Timmerman L, Weimar W, Dobbels F, Massey EK, Busschbach JJV, on behalf of the ELPAT Psychological Care for Living Donors and Recipients Working Group. Towards a conceptualization of the content of psychosocial screening in living organ donors: an ELPAT consensus. *Transplantation* (in press)

curriculum vitae

Lotte Timmerman was born on 18th March 1987 in Zierikzee. After finishing secondary education (VWO) at Buys Ballot College in Goes in 2005, she began studying psychology at Erasmus University in Rotterdam. She wrote her Bachelor's thesis on the impact of stress on somatoform disorders among children and adolescents. In 2009 she completed her clinical internship at GGZ Delfland in Naaldwijk and Delft. Under the supervision of Dr. C. van der Heiden and Prof. dr. P. Muris she wrote her Master's thesis on metacognitive group therapy for the generalized anxiety disorder.
In 2010 she received her Master's degree in Clinical Psychology. After her graduation, she spent two months in Ghana and visited and participated in various projects of the Onyame Foundation, which aims to improve health, education, and agriculture. In January 2011 she started her PhD concerning the mental health of living kidney donors at the department of Internal Medicine at Erasmus Medical Center in Rotterdam. During her PhD she also worked as a trainee psychologist at the department of Psychiatry at Erasmus Medical Center and she was member of the ELPAT (Ethical, Legal and Psychosocial Aspects of Transplantation) 'Psychological Care' working group. Currently, she is continuing her research on the mental health of living kidney donors on a part-time basis at Erasmus Medical Center. In May 2015 she began working as a psychologist at Top Clinical Center Body, Mind, and Health of GGZ Breburg in Tilburg.

dankwoord

Promoveren kan je alleen als anderen het jou gunnen om dit tot stand te brengen. In de afgelopen 4,5 jaar zijn er veel mensen belangrijk voor mij geweest die er mede voor hebben gezorgd dat mijn proefschrift nu in jouw/uw handen ligt. Sommigen hebben mij geholpen door mooie kansen te bieden, anderen door mij inhoudelijk te helpen of te (blijven!) zeggen dat het goed komt en soms ook door simpelweg te begrijpen dat ik even geen tijd had. Wat ben ik jullie dankbaar! Omdat de eeuwige discussie is in welke volgorde een dankwoord geschreven zou moeten worden en ik geen idee heb wat de juiste volgorde is, beschrijf ik iedereen zo veel mogelijk in een chronologische volgorde van wanneer een persoon in mijn leven is gekomen.

Ten eerste wil ik mijn ouders bedanken voor het vertrouwen dat ze altijd in mij hebben en de steun die ze mij geven. Zij hebben vanaf het begin af aan geloofd dat mijn proefschrift af zou komen, ook al had ik daar soms zelf mijn twijfels over. Ook wil ik mijn broer en zusje, Arne en Evi, bedanken dat jullie er altijd voor mij zijn. En Sanne en Joren natuurlijk ook!

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Na de middelbare school ben ik naar de Erasmus Universiteit in Rotterdam gegaan. In deze periode heb ik een aantal vriendinnen gekregen die ik niet meer uit mijn leven kan wegdenken. Eva, Rianne, Sabine, Ingrid, Nancy, Esther en Annelot, super bedankt voor al jullie aanmoedigingen en gezelligheid tijdens mijn promotietraject. Hoe had ik mijn promotie vol kunnen houden zonder jullie koffietjes in de stad, eetdates, weekendjes weg enzovoorts?

Tijdens mijn studietijd heb ik in een studentenhuis gewoond, waar ik het eerste jaar van mijn promotie ook nog heb gewoond. Wat was dit een toptijd! Sharon, Sanne, Erik, Leon, Tim, Tom, Peter (+aanhang), wat zijn jullie toch altijd goed in mij oppeppen en wat zorgen jullie toch altijd weer voor een goede afleiding.

Tijdens mijn studententijd heb ik als onderzoeksassistente gewerkt op de afdeling Maatschappelijke gezondheidszorg van het Erasmus MC. Daar heb ik Rianne, Farsia en Sanne leren kennen. Ik vind het echt super leuk dat we elkaar nog steeds zien en bedankt voor alle steun en gezelligheid tijdens mijn promotie.

In Januari 2010 ben ik met mijn promotietraject begonnen. Beste projectteam, prof. Willem Weimar, prof. Jan van Busschbach, Emma en Willij, bedankt voor het vertrouwen dat jullie in mij hebben en de kansen die jullie mij hebben gegeven. Ik ben blij dat onze samenwerking efficiënt en goed is verlopen, ondanks dat onze standpunten vanuit de medische en psychologische wereld soms lijnrecht tegenover elkaar stonden. Ik hoop dat we onze goede samenwerking ook nu nog verder kunnen voortzetten. Beste Willij, ik wil jou bedanken dat je altijd met veel enthousiasme mee hebt gedacht en gewerkt in de projecten. Emma, ik vind het heel bijzonder hoe jij mij hebt begeleid en mij altijd hebt kunnen motiveren. Ik heb ontzettend veel van je geleerd en ben trots op onze samenwerking. Ik vind het knap hoe geduldig je bent, zelfs als ik voor de zoveelste keer dezelfde Engelse fout maak. Prof. van Busschbach, beste Jan, dank voor je gastvrijheid op de afdeling Medische psychologie & Psychotherapie. Ook wil ik je bedanken voor al je adviezen en je persoonlijke begeleiding die je mij hebt gegeven. Prof. Weimar, beste Willem, ik wil je bedanken voor je duidelijke en doortastende begeleiding. Ik heb veel van je geleerd en ben je dankbaar voor de kansen die je me hebt gegeven.

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In het derde jaar van mijn promotietraject heb ik een werkervaringsplek gehad als psycholoog bij de afdeling psychiatrie van het Erasmus MC. Beste Gerrit, Joke, Tilleke, Hennie, Sohal en Renée, bedankt dat jullie mij deze mogelijkheid hebben gegeven en bedankt voor de leerzame en gezellige periode!

Sinds mei 2015 ben ik werkzaam als psycholoog bij GGZ Breburg. Beste nieuwe collega's, bedankt dat jullie mij zo gastvrij hebben ontvangen en jullie steun bij de laatste loodjes van mijn proefschrift.

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Lotte, mei 2015

Stellingen behorende bij het proefschrift

Exploring the mental health of living kidney donors

1 Nierdonatie bij leven heeft geen negatieve invloed op de geestelijke gezondheid van nierdonoren. (*dit proefschrift*)

2 Er zijn veel psychologische screeningsinstrumenten ontwikkeld voor potentiële levende nierdonoren, zonder dat er bewijs is voor de noodzaak en effectiviteit van een dergelijke screening. (*dit proefschrift*)

3 Het is beter om levende nierdonoren aanvullende psychologische begeleiding aan te bieden, dan hen af te wijzen om psychologische redenen. (*dit proefschrift*)

4 Levende nierdonoren die het meeste baat kunnen hebben van psychologische begeleiding zijn donoren die zelf of waarvan hun ontvanger tegenslag hebben ervaren in de postoperatieve fase. (*dit proefschrift*)

5 De begeleiding van levende nierdonoren kan verbeterd worden door te monitoren op verwachtingen en gedachten over de donatie, psychologische problemen, sociale steun en coping. (*dit proefschrift*)

6 Het is belangrijk dat huisartsen eerder psychologische hulp inzetten bij patiënten die vaak langskomen met somatisch onvoldoende verklaarde lichamelijke klachten. (*Kroenke, 2006*)

7 Het belang van wetenschappelijk onderzoek binnen de geestelijke gezondheidszorg wordt door professionals van deze discipline onderschat.

8 Een persoon met een verstandelijke beperking in de naaste omgeving kan een verrijking zijn in je leven.

9 Veel werkgevers onderschatten het effect van een prettige werkplek op het verhogen van de productiviteit en het voorkomen van werkgerelateerde stress bij hun werknemers. (*Roelofsen, 2002*)

10 Mensen die af en toe een glaasje alcohol drinken zijn gelukkiger dan geheelonthouders. (*Veenhoven, 2007*)

11 Wie zichzelf overwint is sterker dan wie een stad overwint. (*Joka Timmerman*)

Lotte Timmerman

2 december 2015

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