PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Living kidney donor and recipient perspectives on their relationship: longitudinal semi-structured interviews
AUTHORS	Ralph, Angelique; Butow, Phyllis; Craig, Jonathan; Wong, Germaine; Chadban, Steve; Luxton, Grant; Gutman, Talia; Hanson, Camilla; Ju, Angela; Tong, Allison

VERSION 1 – REVIEW

REVIEWER	Jessica Ruck Johns Hopkins University School of Medicine, U.S.A.
REVIEW RETURNED	08-Oct-2018

GENERAL COMMENTS	Ralph et al. interview living kidney donor transplantation donor-recipient pairs to assess the effects of donation and transplantation on their relationship. The piece offers insights into the expectations of donors and how they are likely undermanaged by current practice. Additionally, the paper highlights the broad range of experiences of donor-recipient dyads. Such information would be useful for potential donors and their recipients and would be an important part of revising how transplant professionals set expectations pre-donation.
	Abstract: - "Particularly in recipients attributed to immunosuppression" – please clarify what this is supposed to mean.
	Introduction: - Page 6, line 18 – the word "characterized" appears unintentionally split across two lines - Page 6, line 26 – should this read "post-transplant depression", since it is referring to the recipient?
	Methods: - Further information about how patients were selected is needed to ensure that selection bias was minimal - Why was the donor-recipient relationship limited to spouses, siblings, and parents? Even if 70% of live donations were from these relationships in the cited studies, other types of donor-recipient relationships are on the rise, particularly in the United States.
	 - Was thematic saturation achieved? - Were all transcripts reviewed and coded by two investigators (AFR and AT) or just by one (AFR) with periodic discussions with a second investigator (AT)? Kappa statistics for investigator agreement should be reported. - Were donors and recipients interviewed at the same time or individually?

- What was the protocol for contacting donors and recipients for interviews? How many attempts were made, and by what means?

Results

- Were the characteristics of the donors and recipients who declined participation similar to those of the donors and recipients who agreed to participate? (assessment of selection bias)
- The results section would be clearer if donors' and recipients' general thoughts about relationships with each other versus their specific relationship were separated or clearly demarcated in some way. For example, you state that recipients refused to accept donations from specific family members (general feeling about relationship with donor) as well as reporting findings about the specific donor-recipient relationship.

Discussion:

- For some of the citations in the discussion, it is unclear from the text what the findings were in the cited text (e.g. "For some donors, this was a key motivation for donating a kidney, which may explain why spousal couples were focused on psychosocial impacts of LKDT [15]."). Please revise the text so that the cited literature is directly compared and contrasted with your findings and/or provides clear context for your research.
- The discussion of dyad pairs struggling with the side effects of immunosuppression is particularly interesting, as such coping strategies could benefit all recipients, not just those who received a live donor transplant from a spouse. This is a definite strength of the paper.
- An additional strength of this paper is the discussion of potential interventions based on the findings, including appropriate expectation-setting, psychological counseling post-donation, and adaptation of existing follow-up tools to encompass additional domains (e.g. sexual health) that are important to donors and recipients.
- The following article discusses donors who are "interdependent" with their recipients and would provide additional context and comparison for the authors' findings:

Val Pilsum Rasmussen, SE et al. Considering Tangible Benefit for interdependent Donors: Extending a Risk-Benefit Framework in Donor Selection. Am J Transplant. 2017 Oct; 17(10):2567-2571.

Limitations:

- The authors highlight the greatest limitation of this study: the generalizability of these findings to all donor-recipient dyads given that they were unable to assess the effect on the relationship of pairs who chose not to participate due to concerns about their relationship stability. The experiences of those dyads might differ significantly.
- An additional limitation of this study is an inability to assess relationships when either the donor or recipient (almost certainly the recipient) is a minor at the time of research. This would be an interesting area for future research, with possible interviews at later time points when the recipient is no longer a minor to facilitate informed consent by all parties.

REVIEWER	Dr Paul Gill Cardiff University, Wales, UK
REVIEW RETURNED	18-Oct-2018

GENERAL COMMENTS General comments:

I really enjoyed reading this paper, which makes a meaningful contribution to knowledge. It offers a novel insight into some of the wider issues associated with live (related) transplantation issues that have largely been inadequately explored in existing research; notably decision making issues beyond simply the live donor and the complexity of the decision making process (and post-transplant relationship issues) for recipients. There are, however, several areas that would benefit from further refinement.

Specific comments:

- Abstract, design it would be helpful to indicate to the reader the methodology (not just the methods) used to conduct the study. Grounded theory is alluded to in the data analysis section, although I'm not sure if this was the methodology used to conduct the study. It would, however, be useful to frame your study within a particular methodological framework (e.g. GT or descriptive qualitative?).
- Abstract, results it might be helpful (this is merely a suggestion for you to consider) for the reader, if you outlined what your key findings were, as opposed to providing an overview of your key themes
- Article summary, strengths and limitations 'all participants were English speaking and.... education'; this would benefit from a so what statement here relating to wider representativeness/transferability of findings.
- Materials, methods as per abstract, this would benefit from clarity re overarching methodology used to conduct the study.
- Participant selection please clarify how prospective participants were actually identified, approached and recruited into the study.
- Data collection please clarify why the specific timeframes for data collection (notably 11-14 months post-transplant) were chosen.
- Analysis 'the themes were reviewed by authors....'; please clarify, was this a form of peer review/validation to protect against lone researcher bias and further inform theme/theory development? The rationale provided is a little unclear re what purpose this process served.
- PPI was there any reason for not involving patients in the study design? This isn't a criticism by the way, I'm just curious as to why, having made the statement, patient's weren't involved, some clarity would help.
- Results, p7, line 50-52; '53 (87%) of interviews were conducted in person' how were the others conducted?
- Results, gaining a deeper appreciation, p9, line 28-31; 'some viewed the donation akin to marriage...'; was this in spousal donors only?
- Results, stronger empathy for each other, p9, line 48; 'recipients viewed... but helped concerns about their donor's health'; such as? Did they stipulate what aspects they were concerned about? If so, some examples would add further insight into this finding.
- Results, dissatisfaction over..., p12 the issue of recipients increased vitality and wanting to lead a more fast paced lifestyle etc. was this related to recipients re-evaluating life post-transplant in relation to potential improved health, QoL etc? This might benefit from further clarity to add additional insight into your findings (if appropriate).

- Potential study limitations, p15; as per abstract the issue of language and education would benefit from a 'so what' statement re wider representativeness/transferability of findings.
- Discussion, p16, lines 1-24; you make some excellent points here but they would benefit from further specificity, where appropriate, re potential timeframes of such interventions e.g. pre transplant or in first year post transplant etc?
- Participant illustrative Quotes; I suspect this is a journal presentation issue, but the incorporation of participant quotes into appropriate section of the findings are absolutely essential in qualitative research, as they add depth, meaning and insight to the study findings. Placing them in a box, separate to the findings themselves, adversely affects the presentation of qualitative findings. I would urge you (and the journal editors) to meaningful incorporate quotes into the findings if this is possible.
- The diagram provided on page 29 is interesting and I wonder if this to illuminate your findings or whether it is a key component of your 'grounded theory' (if this is your espoused methodology)? Either way, it would be helpful to provide some supporting narrative somewhere in the paper to this. However, if this forms the basis of your 'grounded theory' (again, if that is methodology used for this study) then your discussion may need to be revised accordingly, to demonstrate to the reader what this emergent theory actually means.

I hope these suggestions help

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

Abstract:

1. "Particularly in recipients attributed to immunosuppression" – please clarify what this is supposed to mean.

As noted, we have modified this sentence to clarify the meaning. The sentence now reads: "Donor-recipient relationships may be improved through increased empathy, appreciation, and ability to participate in life together, however unfulfilled expectations and behavioural and emotional changes in recipients (a side-effect related to immunosuppression), remain unresolved consequences of living kidney donor transplantation." (Abstract – marked copy) Introduction:

- 2. Page 6, line 18 the word "characterized" appears unintentionally split across two lines We have checked this and it appears to be a journal formatting issue. This will be corrected once the manuscript has been copy edited by BMJ Open.
- 3. Page 6, line 26 should this read "post-transplant depression", since it is referring to the recipient? As noted, we have amended this error. (Page 5, paragraph 2 marked copy)

 Methods:
- 4. Further information about how patients were selected is needed to ensure that selection bias was minimal

In accordance with the recommended approach for qualitative research[1, 2], we clarify that we used purposive sampling to obtain a diverse sample as possible based on demographic (including age, gender, donor relationship) and clinical (including dialysis modality, comorbidities) characteristics to capture a broad range of perspectives (Page 6, paragraph 1 – marked copy). Selection bias usually refers to a type of bias caused by non-random data for statistical analysis and therefore does not apply in our study. However, we have acknowledged that we did not include non-English speaking participants and minors (less than 18 years of age)(Page 16, paragraph 3 - marked copy)

5. Why was the donor-recipient relationship limited to spouses, siblings, and parents? Even if 70% of live donations were from these relationships in the cited studies, other types of donor-recipient relationships are on the rise, particularly in the United States.

Of note, spouses, siblings and parents comprise the majority (66%) of living kidney donors in Australia[1], where this study was carried out. Our explicit inclusion criteria was to include spouses, siblings, and parents (Page 6, paragraph 1 – marked copy) and would be beyond the scope of our study to include other donor-recipient relationships. However, we have suggested that future research could include other donor-recipient relationships given the rise of other types of donor-recipient relationships (e.g. friends, aunts, uncles) in countries such as the United States [3]. (Page 16, paragraph 3 – marked copy)

6. Was thematic saturation achieved?

There were no new concepts raised within the last three interviews, thus we achieved data saturation. (Page 6, paragraph 2 – marked copy).

7. Were all transcripts reviewed and coded by two investigators (AFR and AT) or just by one (AFR) with periodic discussions with a second investigator (AT)? Kappa statistics for investigator agreement should be reported.

Investigator AFR reviewed the transcripts line-by-line and coded the emerging concepts. AFR met frequently with AT to discuss the developing themes and refine the coding structure. Investigator AT did not code the transcripts. Investigators TG, CSH and AJ all read the transcripts and reviewed the themes developed by AFR to ensure the findings reflect the full range and depth of the data. (Page 7, paragraph 1 – marked copy). The kappa statistic for inter-rater reliability is only used for the deductive form of content analysis when the code/themes are defined apriori and there is a meaningful denominator [4]. It does not apply to the inductive form of thematic analysis, and where our aim was to describe the range and depth of concepts/themes identified.

- 8. Were donors and recipients interviewed at the same time or individually? As suggested, we have now clarified that donors and recipients were interviewed individually: One author (A.F.R) conducted two longitudinal, individual semi-structured interviews with each participant individually, during the month prior to their donation/transplant, and 11-14 months post-donation/transplant. (Page 6, paragraph 2 marked copy)
- 9. What was the protocol for contacting donors and recipients for interviews? How many attempts were made, and by what means?

Donors and recipients were recruited by transplant coordinators and nephrologists. Author AFR contacted consenting participants via phone (up to three attempts) and e-mail (one attempt) to schedule a pre-transplant interview. We have amended the methods to include this information. (Page 6, paragraph 1– marked copy)

Results:

10. Were the characteristics of the donors and recipients who declined participation similar to those of the donors and recipients who agreed to participate? (assessment of selection bias)

For ethical reasons, we were unable to collect or access data on donors and recipients who declined participation. However, donors and recipients who declined participation provided reasons for non-participation including lack of time and avoiding the risk of jeopardising the stability of their relationship prior to the transplant. (Page 7, paragraph 3 – marked copy)

11. The results section would be clearer if donors' and recipients' general thoughts about relationships with each other versus their specific relationship were separated or clearly demarcated in some way. For example, you state that recipients refused to accept donations from specific family members (general feeling about relationship with donor) as well as reporting findings about the specific donor-recipient relationship.

The results are arranged in the order of the "donation/transplantation trajectory" in the thematic scheme (Figure 1). One theme "Analytical decision making to mitigate regret" refers to donors' and recipients' perspectives about the donor-recipient relationship more broadly. As advised, we have

now moved this theme so that it is presented first and is thus separate from the remaining themes that focus solely on their individual donor-specific relationship. (Page 8, paragraph 2 – marked copy) Discussion:

12. For some of the citations in the discussion, it is unclear from the text what the findings were in the cited text (e.g. "For some donors, this was a key motivation for donating a kidney, which may explain why spousal couples were focused on psychosocial impacts of LKDT [15]."). Please revise the text so that the cited literature is directly compared and contrasted with your findings and/or provides clear context for your research.

As requested, we have amended the text in the discussion so that the cited literature is directly compared and contrasted.

For example:

"For some donors, enhanced combined quality of life was a key motivation for donating a kidney, which may explain why spousal couples in our study were focussed on psychosocial impacts of living kidney donor transplantation. This finding is in accordance with previous research whereby related donors prioritised psychosocial outcomes, namely the donor-recipient relationship and family life.[5]" (Page 14, paragraph 2 – marked copy)

And

"All sibling recipients in our study were either married and/or resided in another state to their donor, thus, unlike spousal and parent donors, the donor was less present in the recipient's day-to-day life and did not hold a caregiving role. This finding provides a more nuanced picture and extends previous research that has found that related donors with close relationships to their recipients give less consideration to the risks of donation and their long term health outcomes than those who with more distant relationships.[6]" (Page 15, paragraph 1 – marked copy)

13. The discussion of dyad pairs struggling with the side effects of immunosuppression is particularly interesting, as such coping strategies could benefit all recipients, not just those who received a live donor transplant from a spouse. This is a definite strength of the paper.

We agree with this comment and have suggested "incorporating education on strategies to cope with emotional lability for both recipients and family members prior to transplantation." (Page 16, paragraph 4 – marked copy).

14. The following article discusses donors who are "interdependent" with their recipients and would provide additional context and comparison for the authors' findings: Val Pilsum Rasmussen, SE et al. Considering Tangible Benefit for interdependent Donors: Extending a Risk-Benefit Framework in Donor Selection. Am J Transplant. 2017 Oct; 17(10):2567-2571.

We thank the reviewer for this suggestion and have now included discussion of "interdependent" donors from the above article. (Page 14, paragraph 1 – marked copy) Limitations:

15. The authors highlight the greatest limitation of this study: the generalisability of these findings to all donor-recipient dyads given that they were unable to assess the effect on the relationship of pairs who chose not to participate due to concerns about their relationship stability. The experiences of those dyads might differ significantly.

We confirm that we discussed this limitation.

16. An additional limitation of this study is an inability to assess relationships when either the donor or recipient (almost certainly the recipient) is a minor at the time of research. This would be an interesting area for future research, with possible interviews at later time points when the recipient is no longer a minor to facilitate informed consent by all parties.

As suggested, we have amended the discussion to include the reviewer's point: "All participants were English-speaking, over 18 years of age and the majority had attained a tertiary level of education. While this reflects the majority of the donor population in Australia, the transferability of these findings to other contexts is uncertain. Additionally, donor-recipient dyads where the recipient is under 18 years of age may have unique experiences not captured in this study. Of note, in Australia, donors must be of legal age (18 years) to be a living donor." (Page 16 paragraph 3 – marked copy)

Reviewer #2

Abstract

1. It would be helpful to indicate to the reader the methodology (not just the methods) used to conduct the study. Grounded theory is alluded to in the data analysis section, although I'm not sure if this was the methodology used to conduct the study. It would, however, be useful to frame your study within a particular methodological framework (e.g. GT or descriptive qualitative?).

We have amended the abstract to include this information. "Following the principles of grounded theory and thematic analysis, transcripts were analysed." (Abstract – marked copy) We confirm that this is a qualitative study and we did not adhere to a methodological framework. We followed a systematic and transparent process to elicit and describe the range and depth of data relevant to the aim of the study.

2. It might be helpful (this is merely a suggestion for you to consider) for the reader, if you outlined what your key findings were, as opposed to providing an overview of your key themes.

We thank the reviewer for this suggestion, however would prefer to retain the overview of key themes. We have discussed the key findings in the Discussion.

Article summary, strengths and limitations

3. 'all participants were English speaking and.... education'; this would benefit from a so what statement here relating to wider representativeness/transferability of findings.

As advised, we have added to this statement as follows: "All participants were English-speaking and the majority had attained a tertiary level of education, thus transferability of these findings to other contexts remains unclear." (Article Summary – marked copy)

Materials, methods

4. As per abstract, this would benefit from clarity re overarching methodology used to conduct the study.

As noted in in our Response #1 (Reviewer 2) above, we use principles of grounded theory (e.g. memoing to record initial concepts, constant comparison) and thematic analysis. We did not adhere strictly to an overarching qualitative methodology. However, we followed a systematic and transparent process, to ensure that our findings reflect the full range and depth of participant perspectives. Participant selection

5. Please clarify how prospective participants were actually identified, approached and recruited into the study.

As advised, we have clarified the participant selection process: They were purposively selected by nephrologists and transplant/donation coordinators to ensure a range of demographic (including age, gender, donor relationship) and clinical (including dialysis modality, comorbidities) characteristics. Participant pairs were eligible if they comprised a spousal, sibling, or parent living kidney donor (as approximately 70 percent of live donations in the U.S., Canada, Australia and New Zealand are from spouses or biologically related donors[7-9]) and a recipient with a confirmed transplant date. Transplant/donation coordinators and nephrologists invited eligible participants and those who provided initial consent were contacted via phone (up to three attempts) and/or e-mail (one attempt) by author A.F.R. to provide written consent. (Page 6, paragraph 1 – marked copy)

6. please clarify why the specific timeframes for data collection (notably 11-14 months post-transplant) were chosen.

Participants were eligible to participate in the study if they had a confirmed transplant date. Once their transplant was confirmed, the coordinator invited them to participate and if they gave verbal consent, author A.F.R contacted the participant to schedule an interview prior to their transplant. For all participants, their transplant date was confirmed approximately a month (or less) in advance, thus there was no opportunity to interview participants more than a month prior to donation/transplantation. The investigators decided on the target of 12 months as previous research has found that at 12 months post donation/transplantation, quality of life for many donors returns to pre-donation levels

[10] and quality of life for recipients' plateaus after improving in the first year.[11-16] The researcher scheduled interviews based on participants' availability and attempted to conduct as many face-to-face interviews as possible. It was not always feasible to conduct the second interview exactly at 12 months for all participants.

Analysis

7. 'the themes were reviewed by authors....'; please clarify, was this a form of peer review/validation to protect against lone researcher bias and further inform theme/theory development? The rationale provided is a little unclear re what purpose this process served.

We have clarified this in our paper and now stated: "As a form of investigator triangulation, authors T.G, C.S.H and A.J also read the transcripts and reviewed the themes to ensure that the findings reflect the full range and depth of the data and enhance the analytical framework." (Page 7, paragraph 1 – marked copy)

8. PPI – was there any reason for not involving patients in the study design? This isn't a criticism by the way, I'm just curious as to why, having made the statement, patient's weren't involved, some clarity would help.

We have made this statement as it is a journal requirement to state the level of public and patient involvement in the design of the study. They were not involved in the design of this particular study. However, given the aim and design of the study, we have elicited the perspectives of patients (and donors) on their relationship in the context of living kidney donation. Results

9. p7, line 50-52; '53 (87%) of interviews were conducted in person' – how were the others conducted?

We have stated in the "Data Collection" section that "The interviews were conducted face-to-face in their home, office or dialysis unit, or via telephone if this was not possible." (Page 6, paragraph 2 – marked copy)

10. Gaining a deeper appreciation, p9, line 28-31; 'some viewed the donation akin to marriage...'; was this in spousal donors only?

We have clarified this was in spousal donors: "Some spousal dyads viewed the commitment of donation akin to marriage and became more aware of how their partner "treasured them". (Page 9, paragraph 3 – marked copy)

11. Stronger empathy for each other, p9, line 48; 'recipients viewed... but helped concerns about their donor's health'; such as? Did they stipulate what aspects they were concerned about? If so, some examples would add further insight into this finding.

As requested, we have provided some examples: "...held concerns about their donor's health (e.g. kidney function, fatigue, potential cancers)" (Page 10, paragraph 2 – marked copy).

12. Dissatisfaction over..., p12 – the issue of recipients increased vitality and wanting to lead a more fast paced lifestyle etc. was this related to recipients re-evaluating life post-transplant in relation to potential improved health, QoL etc? This might benefit from further clarity to add additional insight into your findings (if appropriate).

Participants who wanted to lead a "more fast-paced lifestyle" want to return to activities they had engaged in prior to becoming unwell. We have now amended this sentence to add further clarity: "In some spousal pairs, the recipient's vitality increased and surpassed that of their donor, shifting the relationship dynamic and causing relationship tension as the recipient wanted to engage in activities (e.g. running, dancing, socialising) they had enjoyed prior to becoming unwell and to lead a more fast-paced and active lifestyle than their partner." (Page 12, paragraph 2 – marked copy) Discussion

13. Potential study limitations, p15; as per abstract the issue of language and education would benefit from a 'so what' statement re wider representativeness/transferability of findings.

As advised, we have elaborated on this limitation. This section now reads: "All participants were English-speaking and the majority had attained a tertiary level of education. While this reflects the majority of the donor population in Australia, the transferability of these findings to other populations and contexts is uncertain." (Page 16, paragraph 3 – marked copy)

14. p16, lines 1-24; you make some excellent points here but they would benefit from further specificity, where appropriate, re potential timeframes of such interventions – e.g. pre transplant or in first year post transplant etc?

We have now incorporated potential timeframes for the interventions suggestions on page 16. (Paragraph 4 – marked copy)

Participant illustrative Quotes;

15. I suspect this is a journal presentation issue, but the incorporation of participant quotes into appropriate section of the findings are absolutely essential in qualitative research, as they add depth, meaning and insight to the study findings. Placing them in a box, separate to the findings themselves, adversely affects the presentation of qualitative findings. I would urge you (and the journal editors) to meaningful incorporate quotes into the findings if this is possible.

After copy editing and formatting by the publisher, the table of quotations will be embedded in the results sections of the main manuscript for ease of reference.

Figure

16. The diagram provided on page 29 is interesting and I wonder if this to illuminate your findings or whether it is a key component of your 'grounded theory' (if this is your espoused methodology)? Either way, it would be helpful to provide some supporting narrative somewhere in the paper to this. However, if this forms the basis of your 'grounded theory' (again, if that is methodology used for this study) then your discussion may need to be revised accordingly, to demonstrate to the reader what this emergent theory actually means.

We have provided the supporting narrative in the Figure 2 legend. This figure will appear in the results section after copy-editing/type-setting. The purpose of this is to describe how the themes relate to each other. We have termed this as a thematic schema. (Page 28, Figure legend – marked copy) FORMATTING AMENDMENTS (if any)

1. Please provide an 'Article summary' section consisting of the heading: 'Strengths and limitations of this study', and containing up to five (5) bullet points that relate specifically to the study reported. This should be placed after the abstract.

We have included an "Article Summary" (Page 4).

2. Please provide another copy of your figures with better qualities and please ensure that Figures are of better quality or not pix-elated when zoom in. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi and 90mm x 90mm of width. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.

We have provided an enhanced figure with this submission.

Again, we appreciate the editorial and review comments that have helped to strengthen and improve the clarity of the manuscript. Thank you in advance for reviewing our revised manuscript and we look forward to hearing from you.

Kindest regards

Dr Angelique Ralph on behalf of all named authors

References

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VERSION 2 - REVIEW

REVIEWER	Dr Paul Gill
	School of Healthcare Sciences, Cardiff University, UK
REVIEW RETURNED	18-Dec-2018
GENERAL COMMENTS	Many thanks for submitting this revised manuscript. The paper