

## 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.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Exploring the developmental tasks of emerging adults after pediatric heart transplantation- a cross-sectional case control study
<b>AUTHORS</b>	Sepke, Maria; Ferentzi, Hannah; Disselhoff, Vera; Albert, Wolfgang

## VERSION 1 – REVIEW

<b>REVIEWER</b>	Pirooz Eghtesady Washington University in St Louis, USA
<b>REVIEW RETURNED</b>	18-Jun-2018

<b>GENERAL COMMENTS</b>	<p>This is a report on the QOL assessment among a cohort of patients who underwent pediatric transplantation. The paper is well written. I have only two concerns:</p> <ol style="list-style-type: none"><li>1. The "experimental" cohort (PTXP) have a rather wider range of age distribution (16-35) than the controls (23 +/- 2 years). I would have liked to have seen specifically the data comparison among the similar age group and not included those that are late teens or early 30s. That could lead to a skewed representation.</li><li>2. This is rather a small sample size and there can be bias in participation unless the authors believe they overcame that limitation somehow. Otherwise, they should share some data to suggest how the cohort that participated is similar (or not) to those who did not.</li><li>3. I think the limitations noted in part 2 and other limitations deserve their own paragraph.</li></ol>
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<b>REVIEWER</b>	Josef Jenewein University Hospital Zurich, Switzerland
<b>REVIEW RETURNED</b>	30-Jun-2018

<b>GENERAL COMMENTS</b>	<p>Review Manuscript ID: bmjopen -2018-022461 Submitted to Journal: BMJ open Title: Exploring the developmental tasks of emerging adults after pediatric heart transplantation- a cross-sectional case control study</p> <p>This is an interesting paper relating to the long-term psychosocial well-being of young adult patients after heart transplantation (PHTX). This cross-sectional study compared 38 young adults who underwent PHTX and 46 healthy controls regarding sociodemographic factors, physical and mental QoL, and well-being. The authors found an overall fairly good psychosocial adjustment</p>
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	<p>after PHTX across time compared to the controls in many important sociodemographic and health related factors.</p> <p>Strengths of this paper include an important topic of both clinical and research interest; careful attention to measurement-related and statistical issues; and on the whole, the paper is clearly written. However, there are some methodological shortcomings that should be addressed. Further, there are some grammar errors and the manuscript should be revised by a native speaker.</p> <p>Introduction/Background: on the whole clearly written.</p> <ul style="list-style-type: none"> <li>• P5, line 14: description of measures and scales can be omitted because they are already provided in Table 1.</li> </ul> <p>Methods:</p> <ul style="list-style-type: none"> <li>• It would be helpful for the reader to have a more proper description regarding the strategy of selecting the control group: for instance matching regarding age and gender....additionally: inclusion criteria regarding age of the controls are reported differently (between 19 and 26 or 16 and 35 years, p8, 3rd line and 23rd line, respectively)</li> <li>• I wonder why the authors did not a comparison with data from the age and gender matched general population, which should be available in Germany. This probably would allow a much more better estimation of the health and sociodemographic state of the PHTX patients.</li> <li>• Did the authors consider corrections because for multiple testing?</li> </ul> <p>Discussion:</p> <ul style="list-style-type: none"> <li>• I wonder if there is not more literature existing regarding transplantation in children and adults, probably in the field of lung-transplantation, which could be compared to the authors' findings.</li> </ul> <p>Table 4: not very reader-friendly, should be re-organized.</p>
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### VERSION 1 – AUTHOR RESPONSE

Dear Dr Eghtesady,

Thank you very much for taking the time to read the manuscript and for your valuable comments.

**Re 1st concern:** Thank you for pointing out this issue. We agree about the wide range of age distribution. The exclusion of PHTX patients who fall outside the age range of the control group would be an improper exclusion of subjects. Therefore, we have decided on the following procedure: In order to proceed methodologically correctly, we have replaced all t-tests by ANOVAs. ANOVAs have the advantage that they take into account the variances of the groups. By using the Levene test for homogeneity of variances, it was possible to explicitly address a deviation. The corresponding analyses have thus been corrected.

**Re 2nd concern:** Thank you for this suggestion. We agree with the limitation of a small sample size. Unfortunately, according to the European general Data Protection Regulation (German: EU-DSGVO), the use, processing and/or publication of Personal Data without prior written consent of the data subjects is prohibited. Therefore, we are not able to report on the characteristics of patients who declined participation in our study. However, we are very satisfied with the response rate of 73% (38 participants out of 52 who met the inclusion criteria, see page 7, line 44). Baruch & Holtom (2008) report an average response rate in clinical trials of about 50%, which we were able to exceed.

Accordingly, we consider the bias not to be higher than in other clinical studies, especially considering that this is a very specific and rare patient cohort.

**Re 3rd concern:** We agree that the above mentioned and other limitations deserve their own paragraph. Accordingly, we have now listed the limitations separately, on page 18.

Again, thank you very much for your valuable comments! We hope to have clarified the issues you mentioned to your satisfaction.

**Reference:**

Baruch Y, Holtom BC. Survey response rate levels and trends in organizational research. Human Relations. 2008, Vol. 61 Issue 8, p1139-1160. 22p.

Dear Prof Dr Jenewein,

Thank you very much for taking the time to read the manuscript and for your valuable comments.

**Re 1st suggestion (introduction):** Thank you for pointing out this error. We have deleted the description of measures and scales on P5, line 14 because they are already provided in Table 1.

**Re 2nd suggestion (methods):** Thank you for this suggestion. To have a better description regarding the strategy of selecting the control group, we have changed the relevant paragraph in the method section:

*'We ensured that the control group had the same mean age and gender distribution as the PHTX group. Eligible participants were recruited via social network and personal contacts and, if interested in participation, were contacted by phone, e-mail or personally. Informed consent of each participant was obtained; participants then received the questionnaires via e-mail, mail (together with a stamped envelope), or in person.'*

We have also subdivided the section on participants into the subsections "participants of the PHTX group" and

"participants of the control group", to give better orientation for the readers.

**Re 3rd suggestion (methods):** Thank you for this interesting question. Indeed, for all of the instruments used, data of representative normative samples are available. Our concern was mainly based on the mostly outdated data:

Bullinger M, Kirchberger I. **SF-36**. Fragebogen zum Gesundheitszustand. Handanweisung. Göttingen: Hogrefe; **1998**;

Ravens-Sieberer U, Gosch A, Rajmil L, Erhart M, Bruil J, Duer W, et al. **KIDSCREEN-27** quality-of-life measure for children and adolescents. Expert Rev Pharmacoecon Outcomes Res. **2005** Jun;5(3):353-64;

Fydrich T, Sommer G, Brähler E. **F-SoZU** - Social support questionnaire. Brähler E, Schumacher J, Strauß B, editors. Göttingen: Hogrefe; **2002**;

Brähler E, Scheer J. Der Gießener Beschwerdebogen (**GBB**). Bern: Hogrefe; **2001**;

Additionally, the age groups of the normative samples vary greatly from instrument to instrument. E.g., the age groups for the SF-36 are '18-19 years', '20-29 years', '30-39 years' and so on. The age groups for the F-SoZu are 'up to 60 years' and 'older than 60 years'. In order to achieve an

appropriate age group for comparison to the PHTX patients, and also in order to avoid comparison with outdated norm groups, we decided to recruit a control group that had comparable mean age and gender distribution.

**Re 4th suggestion:**

We had considered correcting for multiple testing at length, but eventually decided against it. As our study is exploratory, rather than confirmatory, our goal is to generate hypotheses rather than to test them. Any of our 'findings' should therefore be taken as starting points for future research. Although correction for multiple testing is not unheard of in exploratory studies, this is still a subject of controversy, see for instance Streiner & Norman (2011), Bender & Lange (2000), or Glickman, Rao & Schultz (2014). It is out of the scope of our project to settle this debate here, but we have added the following clause to our "Limitations" paragraph to explicitly address this matter:

*"No correction for multiple testing was applied, as this study is exploratory and hypothesis-generating. Our results need to be interpreted accordingly and replicated in a confirmatory manner."*

**Re 5th suggestion (discussion):** Thank you for this interesting idea of using lung transplantation studies for comparison. We also considered publications in this area. After a current literature search we found an excellent article by Grady et al. 2018. Due to the early submission of our manuscript in February 2018, we missed this article. We now have the opportunity to compare their results with our results in the discussion section. For this purpose we have added the following passages:

*'These findings are similar to those of a recent study by Grady and colleagues, who examined 88 young adults after pediatric heart transplantation in their early twenties (35). About 50% of the patients reported working for income, compared to 51% in our study (part time work, full time work and apprenticeship taken together).'*' *'The results differ somewhat from those of the study by Grady and colleagues, in which only 9% of the patients reported having a partner, compared to the 32% in our study.'*

**Re 6th suggestion (table 4):** Thank you for this valuable suggestion. We have re-organized table 4 to make it more reader-friendly: We have separated the variable "marital status" more clearly into the subgroups 'single', 'divorced' and 'married' and changed the variable 'partnership' into 'having a partner', with the subgroups 'yes' and 'no'.

**References:**

Grady KL et al. Pediatric Heart Transplantation: Transitioning to Adult Care (TRANSIT): Baseline Findings. *Pediatr Cardiol* (2018) 39:354–364, <https://doi.org/10.1007/s00246-017-1763-x>

Streiner DL & Norman GR. Correction for multiple testing: Is there a resolution? *Chest* 2011; 140: 16–18.

Bender R, Lange S. Adjusting for multiple testing – when and how? *J Clin Epidemiol* 2001;54:343–9.

Glickman ME, Rao SR, Schultz MR. False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *J Clin Epidemiol* 2014;67:850–7.

Again, thank you very much for your valuable comments! We hope to have clarified the issues you mentioned to your satisfaction.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Josef Jenewein Clinic Zugersee, Department of Psychiatry and Psychotherapy, Switzerland and University of Zurich, Switzerland
<b>REVIEW RETURNED</b>	07-Aug-2018
<b>GENERAL COMMENTS</b>	The authors have addressed all reviewer's concers.