Author’s response to reviews

Title: Psychological adjustment and quality of life in children and adolescents following open-heart surgery for congenital heart disease: a systematic review

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Author’s response to reviews: see over
Dear Editor

After receiving your editorial letter and the reviews of our paper, we have revised our manuscript entitled "Psychological adjustment and quality of life in children and adolescents following open-heart surgery for congenital heart disease: a systematic review" according to the suggestions of the reviewers. Please note that we have changed the order of authorship because of the different involvement of the authors in revising the manuscript.

We would like to thank the reviewers very much for their extremely valuable and helpful comments. The concerns of the reviewers have been addressed as follows:

Reviewer 1 (Marijke Miatton):

#1 Reviewer: "Abstract: In the results section: (c) 'the studies on QOL suggest no impairments'. Since further on in the article the authors mention that QOL can be rated by both the patients and a proxy, they should mention in the abstract whether the results are on self- or proxy reports."

Revisions made: The wording has been changed according to the suggestion of the reviewer (p. 2; paragr. 3).

#2 Reviewer: "p 6: proxy-reported psychological functioning: 'seven studies observed significantly lower parent-reported overall functioning'. This result is confusing. According to table 1 all the studies mentioned, used the CBCL. The word "lower" suggests fewer problems; however in the next sentence more internalizing symptoms are mentioned, which will lead to misinterpretation."

Revisions made: The wording has been changed to clarify the results obtained with the CBCL (p. 8; paragr. 3).

#3 Reviewer: "p. 7: 'In contrast, four studies did not detect…' Are the results in these studies also parent-reported?"

Revisions made: Yes, they were all parent-reported. We have clarified this point (p.8; last paragraph).

#4 Reviewer: "Discussion: Can the authors elaborate a bit further on the reasons why, according to them, many results are contradictory, despite the good methodological quality of many studies? This holds for psychological functioning as well as for QOL and risk factors."
Revisions made: We have discussed the contradictory results in more detail throughout the discussion of the manuscript. (p. 13-18)

#5 Reviewer: Discussion: The authors use the word “cyanotic defects” only in the conclusion of their manuscript. There are two options: mention the distinction (cyanotic-acyanotic) earlier in the study and describe the outcome for both groups separately or keep the conclusion more general.

Revisions made: We agree with the reviewer and have kept the conclusion more general. (p. 18, paragraph “conclusions”.

#6 Reviewer: Table 2a: adjustment is typed incorrectly.

Revisions made: We have corrected this typo in Table 2a.

Reviewer 2 (Hedwig Hoevels-Guerich):

#1a Reviewer: Page 4, bottom: terms with *asterix as “p*ediatrics or behavio*r” are not clear. What does the asterix stand for?“

Revisions made: This is a very common search strategy. We have used asterix in the words „p*ediatrics“ and „behavio*r“ to include the American and British way of spelling these words (e.g., „pediatrics“ and „paediatrics“). No revisions were done.

#1b Reviewer: Page 8, line 9: “relationship” is correct.“

Revisions made: We have corrected this typo. (p. 10; first paragraph).

#1c Reviewer: Page 17, ref. 19: “psychosocial” is correct.“

Revisions made: We have corrected this (p. 20; reference 19).

#1d Reviewer: Page 18, ref. 30: “Fontan operation” is correct.“

Revisions made: We have corrected this (p. 21; now reference 29).

#2a Reviewer: Abstract (Results): ……except for children with transposition of the great arteries‘: this statement is not sufficiently supported by the literature and should be modified (look at d.). Even in children after homogeneous neonatal arterial switch operation, parental ratings are inhomogeneous across the studies (ref. 24 and 28 versus 31, 32 and 35 from the Boston circulatory arrest study group). This should be considered in the abstract.”

Revisions made: The reviewer is correct. We have therefore modified our statement in the abstract (p. 2; paragr. 3).

#2b Reviewer: Methods, page 4: “… period between 1990 and Jan. 2007…“: During the last time, a considerable body of current literature has been published with respect to the subject of the manuscript, comprising long-term follow-up studies in homogeneous patient groups other than TGA patients. The variance of outcomes due to time-dependent advances in surgical techniques is not augmented by considering long-time studies. The studies considered in this work should comprise at least all the year 2007!“

Revisions made: We have now included all studies until July 2008. This lead to the inclusion of 6 new studies assessing psychological adjustment and 4 new studies assessing quality of life (cf. Table 2a and Table 2b, see also abstract, p. 5; paragr. 1, p. 13; paragr. 1).
Reviewer: „Results, page 6: “…with surgically corrected transposition of the great arteries [18] and children with severe cyanotic defects after surgery [19]…”: Ref. 18 deals with patients after atrial switch (Senning or Mustard procedure), a physiological rather than anatomical “corrective” surgical procedure from the era of the 1970 and 1980s. In general, if TGA patients are mentioned, the kind of surgical procedure must be described (in the whole manuscript). Patients after atrial redirection therapy compared to those after anatomically corrective arterial switch operation mostly undergo a different follow-up with respect to neurodevelopment, cardiac health and exercise capacity. Ref. 19 deals with adolescents (mean age 16 years), not with children.”

Revisions made: We thank the reviewer for his helpful comment and agree with the reviewer. We have noted this in Tables 2a and 2b in the section „time/type of surgery). We have clarified this issue whenever possible throughout the manuscript (p. 7, paragr. 2; p. 9, paragr. 1; p. 11, paragr. 2).

Reviewer: „Page 6-7 (proxy-reported psychological functioning): As already mentioned for the abstract (a.), studies for TGA patients after arterial switch operation show different results (worse in ref. 24, 28; equal in ref. 23, 31; better in ref. 32) with respect to normal children.”

Revisions made: This point has now been clarified in the revised manuscript (p. 9; paragr. 1).

Reviewer: „Page 8, bottom (quality of life): Ref. 38: It should be mentioned that these were patients with TGA independent of the surgical procedure (as well after atrial as after arterial switch).“

Revisions made: This point has now been clarified in the revised manuscript (p. 11; paragr. 2).

Reviewer: „Discussion, page 10 (proxy-reported long-term outcome): “…In the same line, studies assessing… … As an exception, parents of children with …”: Again, it should be discussed that in TGA patients after arterial switch operation, parental ratings are different (ref. 24, 28 versus ref. 31, 32, 35).“

Revisions made: We thank the reviewer for his comment, however, we feel that we have stated this in the discussion section, citing the studies performing ASO for repair (p. 13; paragr. 2).

Reviewer: „Discussion, page 12, top: ….As current data are scarce…’. More systematic studies with respect to cardiac defects other than TGA exist, e.g. for VSD or Fallot patients, and should be considered.”

This sentence was not correctly written and we have deleted it.

Reviewer: „Discussion, page 14, top: …. no such scale exists for the assessment…’: Recently, a specific pediatric cardiac QoL instrument has been developed (by B. Marino, Qual. Life Res., 2008). This should be additionally considered.”

Revisions made: The pediatric cardiac QoL instrument by Marino et al. (2008) is now mentioned in the revised manuscript (p. 18; first paragraph).

Reviewer: „Conclusions, page 14: ….and children with cognitive impairment…’: Not only children with cognitive, but in general, with neurodevelopmental impairment, are at risk.”

Revisions made: The wording has been changed according to the suggestion of the reviewer (p. 18; paragr. „conclusions”).
Reviewer 3 (Lutz Goldbeck):

#1 Reviewer: „The background information is too short. There is no explanation available why the review was conducted or why it is considered to be necessary at the moment.“  
Revisions made: We have elaborated our introduction further in order to consider the suggestions by the reviewer (p. 3; last paragr.).

#2 Reviewer: „In general, as the authors state in their discussion, based on the available cross-sectional studies it is almost impossible to distinguish between effects of the disease itself, of the consequences of living with the disease, and of surgery. Therefore it should be clearly justified, why the authors focus on CHD patients after surgical interventions. Moreover, this inclusion criterion is in fact not consequently applied, because according to figure 1 only for at least 50% of the samples under study a history of surgery is required, so this review is in fact based on mixed populations of children with CHD.“  
Revisions made: This point has been clarified in the revised manuscript. We have now mentioned the reasons for selection of our specific inclusion and exclusion criteria in more detail The reason for inclusion of studies is now listed (p. 6; paragr. 1).

#3 Reviewer: „There are quite a few very specific inclusion and exclusion criteria for selecting papers for this review, but unfortunately there is no description available why particularly those were chosen. The cut-off follow-up period of at least two years after the first surgical intervention seems arbitrary.“  
Revisions made: see # 2 above.

#4 Reviewer: „The approach to examine a variety of risk factors for psychosocial outcome is very important, however the authors select only few factors. Developmental and family aspects of adaptation to chronic conditions and the socio-economical background of the patients are very important. Therefore, age at the time of heart surgery, age at the time of assessment of psychosocial functioning, and family/socio-economical factors should be considered more rigorously. For example, it would be important not only to report mean ages of the samples under study, but also age ranges or standard deviations.“  
Revisions made: As mentioned in the manuscript we have searched all reviewed papers for examined risk factors. The data are presented in Table 2a and 2b. We have not included age ranges or standard deviations in the tables, because we feel that the tables are already very dense.

Revisions made: The above mentioned studies were not included because of missing data regarding percentage of open-heart surgeries and length of follow-up time. In the meantime we have contacted the author who could provide additional informations on the population. Therefore, we have now included the paper published in Qual Life Res in our review. Data of this study are provided in the text and in Table 2b.
Reviewer: "Additionally, in the discussion section a recently developed and validated CHD-specific QoL instrument should be mentioned: the Pediatric Cardiac Quality of Life Inventory (PCQLI) by Marino et al. (Qual Life Res 2008, epub ahead)."

Revisions made: C.f. Reviewer 2, #2h.

Reviewer: "Besides the overlap with mental retardation due to syndromal/genetic diseases such as Down syndrome, there might be an overlap with a difficult family background, because a considerable proportion of congenital heart defects is due to a fetal alcohol syndrome. Did the authors find any studies regarding this aspect?"

Response: We appreciate this important comment. We did not find a study that specifically addressed this important confounder. Many studies excluded children with a syndrome associated with mental retardation or psychological dysfunction. Among those, fetal alcohol syndrome would be one and thus probably excluded. In our database, we only have one child with the full clinical picture of fetal alcohol syndrome out of over 300 study patients.

Reviewer: "The type of heart surgery might not be as relevant as the severity of CHD and the impact of surgery regarding correction of heart dysfunction. Again, the association between characteristics of the CHD and method and outcome of surgical intervention requires specific attention."

Response: The type of heart surgery may be a less detailed classification if one considers the type as cyanotic versus acyanotic. However, when going into more detail (e.g. univentricular versus biventricular CHD) this correlates strongly with the severity of CHD. We thus did not specifically discriminate between these two terms.

Reviewer: "The difference between clinically significant psychological maladjustment and proxy-reported psychological functioning is not clear, both sections refer to studies based on the Achenbach scales, so these are proxy measures according to the authors' definition. Both sections of the results might be better integrated."

Revisions made: The reviewer is correct. We now report the studies referring to the CBCL in the same section (p. 8; paragr. 1-3).

Reviewer: "As QoL was measured differently across studies, the analysis of associations with any risk factors across studies has a very weak methodological basis. The conclusion that QoL is not impaired in children after heart surgery, is for my opinion not justified, due to a probable sample effect of the studies with unclear selection biases. Moreover, disease specific QoL measures have not been applied so far, and a normative approach of comparing QoL of chronic patients with healthy individuals is always restricted to generic QL measures, thus there is a high probability of missing disease-specific problems with these measures."

Revisions made: The reviewer is correct. We have therefore extended our discussion and now mention all of the points mentioned by the reviewer (see discussion).

Reviewer: "How would the authors distinguish between behavioral symptoms related to the disease or to the consequences of the disease (p 14 first sentence)"

Revisions made: As cited in our manuscript (Perrin et al., 1991) screening measures that were developed for the assessment of psychopathology in somatically healthy children and adolescents, such as the CBCL, may not be able to distinguish between behavioral symptoms and the consequences of the disease. The problem is that somatic symptoms, such as headaches, are interpreted as a sign of psychopathology. In fact, they may be a consequence of the illness. Therefore, as discussed in our manuscript, screening measures for psychopathology that are used in ill children may overestimate
rates of maladjustment. In the revised manuscript we now discuss this issue in more detail (p. 17; paragr. 2)

#12 Reviewer: „To me the order of the studies in the tables according to the outcome measure doesn’t make much sense. It is noted, that the studies are grouped by major outcome variables but this is not really the fact. Alden et al. and Bjornstad et al. both assessed DSM-IV Diagnosis but are not grouped. I would therefore rather prefer a sorting according to the order in the text. This would make the search for a particular study easier. “

Revisions made: The reviewer is correct. The order of studies in the tables of our original manuscript may be a bit confusing. We have therefore regrouped the papers in the revised paper according to the suggestions of the reviewer (see Tables 2a and 2b).

#13 Reviewer: „Page 4: When explaining QoL it is said, that the mentioned indices alone are not sufficient but there is no statement concerning what else should be observed instead or additional. “

Revisions made: As mentioned in the manuscript traditional indices related to health outcomes such as cardiopulmonary exercise capacity alone are not sufficient to reflect QoL of cardiac patients in all its facets. Therefore, assessment of QoL must be multidimensional, including physical, psychological and social dimensions. In order to clarify this issue we have reformulated the paragraph (p. 4; paragr. 3).

#14 Reviewer: „Page 5: When mentioning the quality assessment it should be noted, which total score of the quality ranking indicates “high quality”/”low quality” – since those terms are used in the review later. “

Revisions made: The reviewer has pointed out an important issue. We now define high (9-11 points), moderate (6-8 points) and poor (0-5 points) quality with regard to the scores in our quality ranking (p. 6; paragr. 2, last sentence).

#15 Reviewer: „Page 6: When mentioning the data extraction and synthesis it is said, that the heterogeneity of assessment methods did not permit a formal meta-analysis. Was this primarily intended? “

Revisions made: In fact, we initially intended to do a meta-analysis. However, due to the heterogeneity of methods this was not possible. This is stated in our manuscript (p. 7; paragr. 1).

#16 Reviewer: „Page 12, line 7: It is mentioned that some of the studies did not adhere to statistical standards? Which studies? –Unfortunately there is no citation. “

Revisions made: We have clarified this sentence. Since there are too many studies that did not adhere to these strict standards, we did not cite them all. However, the statistical quality of the studies are also reflected in the overall quality rating listed in Table 2a and 2b.

#17 Reviewer: „Page 13. In which way may the parents play a role in the long-term adjustment? “

Revisions made: Referring to the pertinent literature the role of parents in the long-term adjustment is now mentioned in more detail (p. 16; paragr. 2 and 3).

#18 Reviewer: „Page 5: For each study there was a quality ranking made. Unfortunately the range and the total mean score are not reported. “

Revisions made: Range and total mean score of the quality rankings have been added (p. 7; paragr. 1).
Reviewer: „Page 5: When explaining data extraction it is mentioned that the studies differed significantly with regard of heart defect etc. According to the inclusion criteria this is not very surprising; moreover this is rather a result than a data extraction description.“

Response: We do not totally agree with the reviewer. In fact, using our inclusion criteria, individual studies could still have examined more homogeneous patient groups, such as TGA, which in fact has been done. However, most studies have assessed mixed patient groups which makes it difficult to interpret the findings.

Reviewer: „Page 8, line 3-9: Are those findings based on proxy or on self-reports?“

Revisions made: The findings are based on proxy-reports. We have clarified the source of findings in our revision (p. 10; paragr. 2).

Reviewer: „Page 9: The heading „Risk factors for impaired quality of life” is misleadingly bold (in contrast to risk factors of psychological malfunctioning which is not bold).“

Revisions made: This has been corrected (p. 12; paragr. 2).

Reviewer: „Page 10, line 13: It must be „is comparable” instead of „compares”.“

Revisions made: This has been corrected (p. 13.; paragr. 3).

Reviewer: „Page 13: As a limitation of the findings it is criticized that the reviewed studies didn’t include patients with chromosomal anomalies although studies which exclusively assessed samples with genetic disorders were explicit excluded from the review. Therefore this is not very surprising.“

Revisions made: The reviewer is correct. We thus have changed the statement in the discussion as suggested. (p. 17; paragr. 2).

Reviewer: „Page 13, line 23: What does the superscripted „11” mean?“

Revisions made: This mistake has been deleted.

Reviewer: „6th reference: “- -“ The dashes are doubled.“

Revisions made: This mistake has been corrected (p. 19; reference 6).

Reviewer: „14th reference: The square brackets are not necessary.“

Revisions made: This mistake has been corrected (p 20; reference 14).

We hope that these revisions sufficiently respond to the points of critique mentioned by the reviewers and we hope that the paper is now suitable for publication in BMC Pediatrics.

We look forward to hearing from you.

Sincerely

Markus A. Landolt, Ph.D.
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