

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Associations between adolescent experiences, parent experiences and HbA1c: results following two surveys based on The Norwegian Childhood Diabetes Registry (NCDR)
AUTHORS	Iversen, Hilde; Bjertnaes, Oyvind; Skriverhaug, Torild

VERSION 1 – REVIEW

REVIEWER	Yanglu Zhao UCLA, US Consultant of MUSE Microscopy, Inc.
REVIEW RETURNED	09-Jul-2019

GENERAL COMMENTS	<p>This paper examined a unique and important topic in adolescent type 1 diabetes: how is the adolescent and parent outpatient experience associated with HbA1c among T1DM. The study design and questionnaire is overall reasonable and comprehensive. The conclusion could be better justified by adding the following analysis and clarification.</p> <ol style="list-style-type: none">1. While it is very important to use original HbA1c value as the primary outcome, binary indicators such as controlled vs. uncontrolled based on HbA1c value could also be used as secondary outcome. Correspondingly, Table 1 and 2 could present the comparison of characteristics between high and low HbA1c groups.2. The authors mainly used Pearson correlation test to examine the proposed association. While it is a valid stats method, the author did not stated the distribution of the variables, which may influences the appropriateness of Pearson test. Moreover, Pearson correlation does not handle confounding by other factors such as age, gender, SES, etc. Linear regression adjusted for these factors should be included to draw the conclusion.3. Another interesting analysis could be potentially added: how the disparity between child and parent indicator scores may influence the child HbA1c? My hypothesis is that larger difference between the child and parent indicator scores may be related with poorer HbA1c control however such association could be heterogeneous in different subgroups.
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REVIEWER	Dougal Hargreaves Imperial College London
REVIEW RETURNED	23-Jul-2019

GENERAL COMMENTS	Thank you for the opportunity to review this interesting and well-written paper, which addresses an important topic for the care of adolescents with diabetes and other long term conditions.
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	<p>MAJOR COMMENTS</p> <p>1. The authors appropriately highlight the potential concerns about the generalisability of their findings from the 181 adolescent-parent dyads. It would be useful to present this as the proportion of eligible dyads invited to take part (I think this is 685, making the overall response rate 26.5% but please clarify). Is it possible to compare any sociodemographic or clinical characteristics of these 181 dyads with non-responders or partial responders?</p> <p>2. Further justification would be useful regarding the use of Pearson's r. Could the authors comment on</p> <ul style="list-style-type: none"> - the validity of combining many Likert scores into a continuous variable - whether the resulting score is normally distributed. - whether alternatives such as the Intraclass correlation (ICC) were considered (findings are likely to be very similar but the ICC also takes into account differences between means in the two groups) - whether regression models were considered, which could adjust for patient characteristics. <p>3. As with all studies showing associations, care is needed not to imply causation. In most cases, the wording in this manuscript is entirely appropriate, but the statement in the conclusion of the abstract and paper might be better worded by presenting the impact of improving parent experience on clinical outcomes as a future research question. For example, it is possible that interventions such as deciding not to challenge risk behaviours among young people might improve patient experience but worsen clinical outcomes.</p> <p>MINOR COMMENTS</p> <p>4, In the results section of the abstract, it would be useful to present some numerical findings (eg r values or equivalent statistic). Either here or in the results section, it would also be helpful to present a measure of the statistical significance of these findings (eg 95% confidence interval, or power calculation showing what magnitude of difference in HbA1C could be detected in a study of this size).</p> <p>5. Strengths and limitations section, 2nd bullet point. The questionnaire score didn't seem a good overall measure of adherence.</p> <p>6. The introduction section was very clearly written, with a good overview of previous literature and the reason for doing the current study.</p> <p>7. As comparisons are made in the text between adolescents' and parents' responses, could table 2 be reformatted to present these values side by side? t tests/Mann Whitney tests could then be used to compare differences between the two groups.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

This paper examined a unique and important topic in adolescent type 1 diabetes: how is the adolescent and parent outpatient experience associated with HbA1c among T1DM. The study design and questionnaire is overall reasonable and comprehensive. The conclusion could be better justified by adding the following analysis and clarification.

We want to thank the reviewer for positive and constructive feedback. We have added the suggested analyses and hope that the manuscript has improved.

1. While it is very important to use original HbA1c value as the primary outcome, binary indicators such as controlled vs. uncontrolled based on HbA1c value could also be used as secondary outcome. Correspondingly, Table 1 and 2 could present the comparison of characteristics between high and low HbA1c groups.

This is a good point, and we have changed Table 2 accordingly. In Norway the treatment goal at the diabetes outpatient clinics follows the ISPAD treatment goals, HbA1c aimed < 7.5%, and we now present scores for the total sample, those who achieve the treatment goal and those who did not achieve the treatment goal. The Mann–Whitney U test was used to test difference in scores. We did not change the information on the background characteristics in Table 1, because the sample size was considered too small to categorize further. We have made the following adjustments in the text:

Statistical analysis, page 9:

“The Mann-Whitney U test was used to test the differences in scores between patients that reached the recommended < 7.5% treatment goal, and patients that did not reach the recommended treatment goal. Corresponding analyses were conducted for the parents, based on the HbA1c value of their children.”

Results, page 11:

“Table 2 also shows the indicator scores and item scores for patients who achieved the recommended < 7.5% treatment goal and patients who did not achieve the < 7.5% treatment goal. Corresponding results are shown for parents, based on the HbA1c values of their children. No significant differences in scores were found for patients who achieved the < 7.5% treatment goal and patients who did not achieve the treatment goal. Parents of children who reached the treatment goal had significantly higher scores on one of the single items (nurses knowledgeable).”

Discussion, page 14:

“The results from the current study also showed that parents of children who reached the recommended < 7.5% treatment goal reported better experiences related to the nurses’ knowledge.”

2. The authors mainly used Pearson correlation test to examine the proposed association. While it is a valid stats method, the author did not stated the distribution of the variables, which may influences the appropriateness of Pearson test. Moreover, Pearson correlation does not handle confounding by other factors such as age, gender, SES, etc. Linear regression adjusted for these factors should be included to draw the conclusion.

Thanks for a good suggestion. We have now changed Tables 3-5, and replaced all Pearson’s correlation coefficients with Spearman’s rank correlation coefficients. Tables 3-5 also shows results from linear regression analyses, were we have adjusted for age, gender and HbA1c. The

standardized regression coefficients are included in all tables. Hopefully, these amendments have improved the relevance of the analyses and corresponding results. Corresponding changes have been made in the text:

Methods, page 9 and 10:

“The relationship between the patient and parent experiences at the outpatient clinic was tested by calculating Spearman’s rank correlation coefficients for indicator scores, the overall scores and single items. Multivariate linear regression analyses were used to further assess the associations between the patient and parent experiences, controlling for age, gender and HbA1c level.”

Methods, page 10:

“The indicator scores and overall scores were also correlated with the HbA1c level analysed as a continuous variable. Correlations were assessed using Spearman’s rank correlation. Multivariate linear regression analyses were used to assess the associations, controlling for age and gender.”

Results, page 11 and 12:

“All of the correlations were statistically significant except the adolescent score for nurse contact and the parent score for doctor contact, and the adolescent score for doctor contact and the parent score for equipment. The significant correlation coefficients ranged from 0.16 to 0.42. The strongest correlations were between the adolescent score for the consultation indicator and the parent score for the outcome indicator ($\rho=0.42$, $P<0.001$) and the overall score indicator ($\rho=0.41$, $P<0.001$) respectively. The correlation coefficient between the adolescent score for the overall score indicator and the parent score for the outcome indicator was also 0.41 ($P<0.001$). The coefficient for the correlation between the parent and adolescent overall scores was 0.41 ($P<0.001$).”

“Table 4 indicates that all correlations between individual questions with identical wordings in the two surveys were significant. The strongest correlation was for the questions pertaining to meeting the same doctor ($\rho=0.50$, $P<0.001$) and if the patient and parent were well received ($\rho=0.32$, $P<0.001$).”

“No significant correlations were found between the adolescent indicators and their HbA1c level (Table 5). Three of the seven parent indicators were significantly correlated with the HbA1c level of the child. The strongest correlation was found between HbA1c level and nurse contact and organization, both with a correlation coefficient of 0.21 ($P<0.01$).”

3. Another interesting analysis could be potentially added: how the disparity between child and parent indicator scores may influence the child HbA1c? My hypothesis is that larger difference between the child and parent indicator scores may be related with poorer HbA1c control however such association could be heterogeneous in different subgroups.

This is an interesting and relevant comment. We constructed a new variable based on the difference in overall mean scores for the parent and the adolescent. The difference score was divided into three groups: 5 points or less was considered a small difference, a score of 6 to 12 points as a medium difference and a score of 13 points or more was considered a large difference. One-way analysis of variance was carried out to compare the HbA1c levels in the three groups, but we did not find any significant differences in mean scores. We conducted the analysis with both HbA1c as a continuous variable and as a dichotomous variable (below or above 7.5%), but the results were the same. Statistical outliers were identified in a bivariate regression with HbA1c as dependent variable and overall scores as independent variables, using Cook’s $D > 4/n$ as criteria for detecting outliers. Ten respondents identified as outliers were excluded from the analyses, but the results were the same;

the results did not show significant differences in overall mean scores. Accordingly, we have included the following text in the results section:

Results, page 12:

“We also tested if the difference in overall mean scores for the parent and the adolescent had an influence on the HbA1c level, but the results did not support this association (results not shown here).”

Reviewer 2

Thank you for the opportunity to review this interesting and well-written paper, which addresses an important topic for the care of adolescents with diabetes and other long term conditions.

Major comments

1. The authors appropriately highlight the potential concerns about the generalisability of their findings from the 181 adolescent-parent dyads. It would be useful to present this as the proportion of eligible dyads invited to take part (I think this is 685, making the overall response rate 26.5% but please clarify). Is it possible to compare any sociodemographic or clinical characteristics of these 181 dyads with non-responders or partial responders?

You are right, the response rate related to eligible dyads should be specified. We now include the following sentence regarding the response rate:

Results, page 11:

“We were able to match 181 parents with the adolescent survey, and the overall coverage rate in this study was 26.4%.”

We have also added the following reflections in other sections of the manuscript:

Abstract, page 3:

“Most of the parent experience indicators were significantly related to the HbA1c levels of adolescents, but replication in future research with larger sample sizes is warranted.”

Discussion, page 15 (related to the limitations regarding the generalizability of the findings): “Only 181 paired parental and patient responses were analysed, an overall coverage rate of 26.4%.”

We were not able to compare the sample characteristics with non-respondents, but we refer to a recent article from the parent survey that showed sample characteristics for all the 1399 respondents:

Discussion, page 15:

“Data on non-respondents were not available, and we were not able to compare the characteristics of the current sample with the characteristics of those who did not respond to the survey. However, results from the national parent survey was published in a recent article and showed similar background characteristics for the current sample and the total national sample of 1399 respondents.”

2. Further justification would be useful regarding the use of Pearson's r . Could the authors comment on

- the validity of combining many Likert scores into a continuous variable
- whether the resulting score is normally distributed.

- whether alternatives such as the Intraclass correlation (ICC) were considered (findings are likely to be very similar but the ICC also takes into account differences between means in the two groups)
- whether regression models were considered, which could adjust for patient characteristics.

See responses to point 2 above. We have replaced all Pearson's correlation coefficients in Table 3-5 with Spearman's rank correlation coefficients. Multivariate linear regression analyses were used to further assess the associations between the patient and parent experiences, controlling for age, gender and HbA1c level."

3. As with all studies showing associations, care is needed not to imply causation. In most cases, the wording in this manuscript is entirely appropriate, but the statement in the conclusion of the abstract and paper might be better worded by presenting the impact of improving parent experience on clinical outcomes as a future research question. For example, it is possible that interventions such as deciding not to challenge risk behaviours among young people might improve patient experience but worsen clinical outcomes.

We agree, care has to be taken when addressing the direction of the assumed associations. We have tried to avoid this throughout the manuscript. We have changed one sentence in the conclusion of the abstract and two sentences in the discussion section addressing causation:

Page 3:

"Three of the seven parent experience indicators were significantly related to the HbA1c levels of adolescents, but replication in future research with larger sample sizes is warranted."

Page 14:

"The implication is that interventions to improve parent experiences also might improve clinical outcomes, but more research conducted with larger sample sizes is needed to conclude upon this observed association."

Page 15:

"Three of seven parent experience indicators were significantly related to the adolescent HbA1c level. However, more research is needed to further explore the associations between parent experiences and the HbA1c level."

Minor comments

4. In the results section of the abstract, it would be useful to present some numerical findings (eg r values or equivalent statistic). Either here or in the results section, it would also be helpful to present a measure of the statistical significance of these findings (eg 95% confidence interval, or power calculation showing what magnitude of difference in HbA1C could be detected in a study of this size).

This is a good point. We have rewritten the results section of the abstract to the following:

Page 2 and 3:

"There was a moderate but significant correlation between the responses of the patients and parents. For 40 of the 42 associations the correlations were significant, ranging from 0.16 to 0.42. A weak but significant negative correlation was found between the indicator scores of parents and the HbA1c levels of the adolescents. The strongest correlations were between HbA1c level and nurse contact

and organization, both with a correlation coefficient of 0.21 ($P < 0.01$). There was no significant correlation between HbA1c level and patient indicator scores.”

5. Strengths and limitations section, 2nd bullet point. The questionnaire score didn't seem a good overall measure of adherence.

Thanks. We agree, and have rewritten the sentence to the following:

Article summary, Page 4:

“Both parents and adolescents experiences were explored, and the results can provide guidance concerning the most appropriate care to provide at outpatient clinics.”

6. The introduction section was very clearly written, with a good overview of previous literature and the reason for doing the current study.

Thanks for this positive comment.

7. As comparisons are made in the text between adolescents' and parents' responses, could table 2 be reformatted to present these values side by side? t tests/Mann Whitney tests could then be used to compare differences between the two groups.

This is a relevant comment. We agree that the presentation of these results side by side could be useful, but the PEQ-DC and APEQ-DC had only similar contents, not identical. The results obtained in the development process showed that certain themes or questions were not relevant for both groups, the items included in the APEC-DC were also age-appropriate. The PEQ-DC included six indicators, the APEQ-DC included five indicators. Accordingly, we did not compare the differences by using t-tests or Mann Whitney U tests. However, direct comparisons were possible between the self-reported experiences of the parents and patients for eight questions, and we tested these differences with Mann-Whitney U tests.

However, considering the aim of the article and that the extensive content of Table 2 (it now also includes indicator scores and item scores for patients who achieved the recommended $< 7.5\%$ treatment goal and patients who did not achieve the $< 7.5\%$ treatment goal), we comment on the results from the comparisons of the eight items in the text:

Methods, page 9:

“The Mann-Whitney U test was also used to compare the self-reported experiences of the parents and patients for eight single items.”

Results, page 11:

“Analyses showed that for four of the single items the adolescent scores were significantly higher than the parent scores (results not shown).”

VERSION 2 – REVIEW

REVIEWER	Yanglu Zhao UCLA
REVIEW RETURNED	18-Sep-2019

GENERAL COMMENTS	All my questions have been addressed and responses to other reviewers' comments seem appropriate as well.
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REVIEWER	Dougal Hargreaves Imperial College London, UK
REVIEW RETURNED	30-Sep-2019

GENERAL COMMENTS	<p>I thank the authors for their thoughtful and detailed responses to the initial reviews.</p> <p>My only further comment is that they might consider presenting 95% confidence intervals and exact p values for some findings (for example, the results of the regression analyses in Tables 3, 4 & 5). But this is largely a matter of style or personal preference.</p> <p>I have no other comments to make and would recommend publication of this interesting paper.</p>
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