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Title	Improved outcomes associated with a pediatric clinical diabetes network: a population-based time-trend analysis in Ontario, Canada
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Reviewer 1	Prof. Elizabeth Cummings MD
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General comments (author response in bold)	<p>1. General comment. This study shows time trends related to the establishment of a diabetes network. A number of other changes have occurred over the time period that is studied. One major change is the increased use of the insulin pump in general and the implementation of provincial funding for insulin pumps. It also seems that there has been a significant increase in the number of pediatric endocrinologists working in Ontario during that time period. These are changes that may also have influenced the outcomes studied. In particular the insulin pump program may have attracted more low SES individuals to specialized diabetes centres to start and manage their pump therapy or possibly affected outcomes. Can the authors comment on this? Can/did they control for this in the analysis? If controlling for this in the analysis is not possible it should at least be acknowledged as a parallel trend and possible confounder.  <b>Please see the response above to the editor's comment #1.</b></p> <p>2) Abstract Conclusion – States – "through improved access to specialized diabetes care", the network was associated with better outcomes. However, the authors have not shown that more individuals accessed specialized care (stated they could not assess this). Therefore, I would remove the first clause in this sentence and say that the establishment of the network was associated with the outcomes as this is what has been shown.  <b>We agree and have modified as follows: "The establishment of a diabetes network is associated with better health outcomes, particularly for those of lower SES."</b></p> <p>3) The introduction is succinct and appropriate. No issues.</p> <p>4) Methods: Analysis: Page 10 Lines 11-18 I am having trouble understanding the "predicted" element of the analysis. The "projected" and "adjusted" elements are clear. This may be some lack of statistical understanding on my part, but a large part of the analysis depends on this and it would help if it was clearer to the readers. Can this be clarified? I have pasted the sentence below.  "From these models, yearly predicted adjusted rates (i.e., rates with the network) and the projected adjusted rates (i.e., rates had the network not been implemented) were calculated using the means method which involved setting each confounder to its mean value."  <b>We apologize for any confusion. The predicted adjusted rates are the post-network ED-visit and hospitalization rates that are calculated from the regression models (i.e., the modeled rates). We have clarified this point and modified the sentence:  "From these models, yearly predicted adjusted rates (modeled rates post-network implementation) and the projected adjusted rates (rates had the network not been implemented) were calculated using the means method which involved setting each confounder to its mean value."</b></p> <p>5) Results: First line of results – implies 14425 cases used for overall analysis and 13806 for SES and geographic analysis, but this is not clearly stated and should be.  <b>Those with missing postal codes were excluded from the final analysis. We have clarified this in the first line of the results: "There were 14,425 cases of established diabetes identified and of these, 13,806 had valid postal codes and were included in the final analysis."</b>  Did those without reliable postal codes differ in rates of visits to ED or Hospitalization?  <b>Please see our response above to the Editor's comment #3.</b></p> <p>6) Results: One of the main outcomes of this paper is that the establishment of the network appeared to be associated with reduced disparity in rates of ED visits and hospitalization by SES. The authors have displayed this graphically for ED visits and hospitalizations and stated that the absolute risk was smaller but did not show the data. This is a key finding and the absolute risk reduction should be shown. (page 10 line 40 and Page 11 line 44)  <b>Thank you for your suggestion and have added the values for the absolute difference in rates between the highest and lowest SES quintiles between 2001 and 2011 to clarify the decreasing trend in SES disparity.  We have modified the text as follows for ED-visits and hospitalizations:  "Further, the absolute difference in the predicted adjusted rates between Q1 and Q5 in 2011(5.2%; 95% CI: 3.29%, 7.14%) was significantly less than in 2001 (9.31%; 95% CI: 6.12%, 12.50%) (Difference: - 4.0 %; 95% CI -0.2%, - 8.0%, p&lt;0.05)."  "As with ED-visits, the relative yearly decrease in hospitalizations in the lowest compared to the highest SES, shifted towards a decreasing disparity (Figure 2B); where the absolute difference in the predicted adjusted rates between Q1 and Q5 decreased from 7.8% (95% CI 5.4%, 10.1%) in 2001 to 3.1% (95% CI 1.7%, 4.5%) in 2011 (Difference: -4.7%; 95% CI -1.8%, -7.6%, p&lt;0.05)."</b></p> <p>7) Results: Page 9 line 51-53 and Page 11 line 25-32 – Changes in ED visits and hospitalization rates are reported. 95% confidence intervals would be helpful to add to assist the reader in interpreting the significance of the data.  <b>The p-value we report for the changes in ED-visits and for hospitalization rates is for the trend (i.e, pre-network trend and post-network trend) and is not a comparison of the first and last year rates of the time intervals; therefore in this situation it is not appropriate to illustrate 95% CI. We have clarified this in the results:  For ED-visits:  "Pre-network, ED-visits remained unchanged, with a rate of 18 to 17 per 100 from 1996 to 2001(p = 0.15 for trend).  Post-network, visits decreased to 10 per 100 by 2011(p&lt;0.001 for trend)."  For hospitalizations:  "Post-network, rates decreased to 5.0 per 100 in 2011 (p&lt;0.001 for trend)."</b></p> <p>8) Interpretation: States that results are consistent with increased access to care especially in those of lower SES. Has this truly been shown that those patients are accessing care more or is it just assumed? Care in this interpretation is warranted. Particularly in saying more equitable access to dietitians and nurses – this is fine to state if it has been shown but there is no reference listed for this statement. (Page 13 first paragraph)  <b>Thank you for your point on the need to clarify this interpretation. We could not capture ambulatory care use and as such could not measure what services children were using within the network. In stating that "Children of</b></p>

	<p>lower SES had the greatest improvements in outcomes, suggesting the network was most successful in increasing access to <b>effective care for these patients</b>, we are providing possible mechanism to explain our findings. We have modified the sentence to reflect that this is a postulated mechanism: <b>"Children of lower SES had the greatest improvement in outcomes, suggesting that the network was most successful in possibly increasing access to effective care for these patients."</b></p> <p>Regarding more equitable access to dietitians and nurses, we are suggesting that by making these resources more available across the province that the network is promoting access and use of these services. We have modified the sentence to reflect this: <b>"In addition, the network promoted more equitable availability of other diabetes professionals such as dietitians and nurses which may have had additional benefits for those of lower SES."</b></p> <p>9) Interpretation: Limitations – see general comments above – would be important to discuss impact of pump therapy and other changes.  <b>Please see our response above to editor's comment # 1.</b></p> <p>Minor comments</p> <p>1) Abstract: The structure of some of the sentences in the results section could be improved to improve clarity and ease of reading.  - First sentence in Results section of abstract is awkward and hard to follow. Suggest stating the decrease before the numbers i.e. After network implementation in 2001, there was significant decrease in rates of ....  - Same for sentence 3 – suggest Compared with highest SES, the lowest SES remained at higher risk of ...  <b>Thank you for your suggestions. We have changed the sentence structures in the abstract as suggested.</b></p> <p>2) I have looked at this using STROBE criteria which states that along with the objectives, a hypothesis should be stated. I do not see an explicit hypothesis although it is implied and may not be necessary.  <b>We agree that in the wording of our objectives it is not necessary to explicitly state our hypothesis in addition since it is implied in our objectives. If the editors feel it is necessary then we would be happy to do so.</b></p> <p>3) Centres should be consistently spelled centres, not centers (e.g. last line page 4)  <b>Thank you for pointing this out, we have edited for consistency.</b></p>
Reviewer 2	Dr. Daniel L. Metzger MD
Institution	BC Children's Hospital, Endocrinology & Diabetes Unit, Vancouver, BC
General comments (author response in bold)	<p>1. ED visits: can you say with any certainty whether these were for diabetes-related reasons or "broken arm in kid with diabetes"? I believe that the hospitalizations tagged were only for DKA or hypoglycemia, not for "kid with diabetes getting a celiac biopsy"?</p> <p><b>We limited our analysis to only ED-visits with a "diabetes" code and did not include all ED-visits in the analysis to ensure we were capturing visits for diabetes related-reasons. With respect to hospitalizations, we limited our analysis where the most responsible diagnosis was for either DKA, hyperglycemia or hypoglycemia and did not include hospitalizations for other causes.</b></p> <p>2. I also can't tell from your M&amp;M what percent of ED visits and hospitalizations were at diabetes diagnosis? Any way to see if having a network decreased DKA/hospitalization at diagnosis?</p> <p><b>Our study population only included children and youth with a diabetes duration of at least one year. We have emphasized this in the methods and have changed the sentence as follows: "We used the Ontario Diabetes Database (ODD), a validated population-based database, to identify all children (ages &lt;18 years) with a diabetes duration of at least 1 year, living in Ontario from April 1st, 1996 - March 31st, 2011."</b></p> <p>We did not examine whether the network reduced DKA at diabetes diagnosis, as it was not the objectives of the study which was mainly focusing on whether a diabetes network was associated with improved outcomes in children with established diabetes. However, we thank the reviewer for raising an important issue on whether the network reduced DKA at diabetes diagnosis through possible mechanisms such as increased public and/or physician awareness and we feel that this would be an important issue to examine for future research.</p> <p>3. Is an ER visit leading to hospitalization one or two separate events?</p> <p><b>The ED data presented are ED-visits not resulting in hospitalizations. This has been clarified in the methods section: "ED-visits not resulting in hospitalizations were identified using OHIP physicians' service claims bearing a diagnostic code for diabetes (ICD-9 250) and indicating that the encounter occurred in the ED."</b></p> <p>4. Page 10, line 51, Fig 1A: Can you explain why there is a negative slope from 1996 to 2001 in ED visits, if in the text you say the rates "remain unchanged" during the pre-network period?</p> <p><b>We had stated that the rates remained unchanged as the trend in the rates of ED-visits pre-network was not statistically significant. We have included the p-value for trend in ED-visit rates pre-network to emphasize this point.</b></p> <p>5. Do you have enough numbers to say whether the decreases you're seeing with the network is for low or high BG-related events?</p> <p><b>We re-examined our data to see if we could look at admissions due to hypoglycemia and hyperglycemia separately. However, most hospital admissions in our study were due to hyperglycemia and those for hypoglycemia were too small and variable to calculate a trend. As such, we did not include a separate analysis for each.</b></p> <p>6. Any way to relate this to increased pump use? I know Ontario has a pump program, but I'm not sure that it's even applied across SESs? Are kids on shots vs. pumps more likely to have an ER visit or a hospitalization?</p> <p><b>Please see the response above to reviewer comment 1.</b></p> <p>7. Page 11, Line 49, Fig 1B: same issue for hospitalizations</p> <p><b>We apologize if there is an error in the image of figure 1B; however the slope in figure 1B is supposed to appear relatively unchanged. We have included the p-value for trend in hospitalization rates pre-network to emphasize this point as well.</b></p> <p>8. Page 11, line 13: you say that lower SES is associated with higher ED visit rates pre- and post-network, but I see no statistical analysis for that.</p>

The statistical analysis is described on page 9, lines 44-51. In addition, we have further clarified that SES was included in the multivariate model in the footnotes for Table 1.

9. Page 11, line 32: SES Q4 also appears to be significant?

That is correct, in addition to the lowest SES, Q3 (middle SES) also demonstrated a significant decrease in the trend in hospitalizations post-network. We did not describe all the significant results from the exhibits in the text due to space constraints.

10. Page 12, line 18: Does the lower rate of ER visits in boys persist after multivariate analysis?

The decreased risk of ED-visits (i.e., aRR) shown in the results is the adjusted rate ratio from the multivariate analysis. We have modified the sentence to clarify this: **"Male gender was also associated with a decreased risk in the multivariate analysis (aRR 0.78; 95% CI 0.72,0.84)."**

11. Any explanation for why boys have fewer ER visits, and girls fewer hospitalizations?

We apologize for the confusion but males had a decreased risk of both ED-visits and hospitalizations compared to girls. We have clarified this in the results: **"Other associations with hospitalizations included males (aRRmale 0.71; 95% CI 0.64, 0.78) and older age (10-14 y.o., aRR 1.67; 95% CI:1.23, 2.27 and 15-18 y.o., aRR 1.91; 95%CI:1.41, 2.59, compared to 1-4 y.o. age respectively)."**

The findings of female gender being associated with an increased risk of diabetes-related ED-visits and hospitalizations have been previously described in children and adolescents with type 1 diabetes, where mechanisms such as an increased risk of disordered eating and insulin misuse among females are at least in part potential drivers (Rewers et al., JAMA 2002; 287 (19): 2511-2518) and Nakhla et al., 2009 Pediatrics (124)). As we were limited by our word count, we did not comment on this association in the discussion as this association has already been described and was outside the objectives of our study.