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Title	Acute diabetes complications across transition from pediatric to adult care in Ontario and Newfoundland and Labrador: a population-based cohort study
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Reviewer 1	Dr. Kaberi Dasgupta
Institution	Division of Clinical Epidemiology, Center for Outcome Research and Evaluation (CORE), McGill University Health Centre, Montréal, Que.
General comments (author response in bold)	1. I really appreciate the spirit of trying to draw some comparisons between two provinces. However, the sample from Newfoundland is too small for precise estimates and between group comparisons for a rare outcome like DKA. There are also many differences between Newfoundland and Ontario (ethnocultural composition, culture of place, health systems, etc) so it is really challenging to understand the source of any differences that do or do not emerge. I think this needs to be better addressed in the Methods and Discussion. **Thank you for this comment. We agree and have now highlighted these issues in the methods and interpretation.** **In the analysis paragraph in the methods, we added the following sentence: "We had insufficient power, due to the small sample size in NL, to make precise estimates or between group comparisons for rare outcomes such as diabetes-related admissions and DKA."** **We agree that there are many differences between ON and NL. We intentionally selected 2 provinces with different resources in order to test whether models which may need to rely on less specialized care can deliver the same outcome. We clarified this in the introduction by adding:** **"Little is known about the impact of system-level transition processes that reflect these resourcing differences on health outcomes"** **In the methods, we added a description of the differences in resources and transition processes in each province.** **"There are several important differences in the structure and delivery of diabetes transition care in Ontario and NL which led us to select these two provinces."** **We also added the following in the interpretation section in the paragraph about the limitations of our study:** **"We cannot specifically attribute any observed differences in outcomes to the many differences in demographic composition and care delivery between provinces."** **We also agree that it is challenging to understand the source of any differences that do or do not emerge. Therefore, in the interpretation we elaborate on some possible factors (social services and primary care), based on existing evidence, that may be impacting health outcomes. (Methods and interpretation)** 2. I am having some difficulty lining up the methods section with the data presented in Table 2. In this table, there are three age categories presented: 15 to 17 years, 17 to 19 years, and 19 to 21 years. Under each, the next row for the Ontario data indicates an identical number of person-years (5,050 person-years). The cohort entry criterion required the 17th birthday to be between 2006 and 2011 and the follow-up was to 2015. Therefore, many could have had follow-up beyond 21 years (if entry was 2006). I am guessing that follow-up ended at 21 years? The total number in the cohort as per Table 1 is 3,834. If everyone had exactly three

	years of follow-up within each age category, there should be 11,502 person-years per category (3,834*3). If everyone had two years, it would be 7,668 person-years. It would be helpful to have a participant flow to indicate how many participants were involved during each period of follow-up. **The total number in the Ontario cohort as per table 1 is 2,525. Follow-up ended at age 21. We included the person-years that contributed to each new period of follow-up in Table 2. We also included the number of person-years that contributed to each period of follow-up in the new participant flow diagram. (Table 2 and Figure 1)** 3. On what basis were the age categories selected? What is the age of transition in Ontario? In Newfoundland? Is there a 'mandatory' age? For example, would it make more sense to look at 15 to 18 and then 18 to 21 to compare across the transition point? Having two age categories instead of three would increase the number of person-years per category. **We agree and re-did our analysis based on these suggested age categories. (Methods and Results)** 4. I think that the Ontario data could be analyzed in a more comprehensive way. If the aim is to look at differences in DKA rates before and after transition, these should be compared in a multivariate logistic regression model or using survival analysis, with adjustment for co-variates and potential confounders such as sex. This was done in another paper by the authors: Shulman R, Shah BR, Fu L, Chafe R, Guttmann A. Diabetes transition care and adverse events: a population-based cohort study in Ontario, Canada. Diabet Med. 2018 Nov;35(11):1515-1522. doi: 10.1111/dme.13782. Epub 2018 Aug 3. PubMed PMID: 30022524. **In our other paper that you reference, we examined the association between patterns of primary and diabetes care during transition age and adverse events in early adulthood.** **As per the reviewer's suggestion, we now compare the rate and proportion with any diabetes admission before and after age 18 using a Poisson and Logistic regression model respectively in our Ontario cohort only. The sample size in NL is too small to do this comparison. This was added to the methods and results sections. (Methods and Results)**
Reviewer 2	Mr. Marc Simard
Institution	BIESP, Institut national de sante publique du Quebec, Québec, Que.
General comments (author response in bold)	1. small diabetes population in NL In the analysis paragraph in the methods, we added the following sentence: **"We had insufficient power, due to the small sample size in NL, to make precise estimates or between group comparisons for rare outcomes such as diabetes-related admissions and DKA." (Methods)** 2. hypothesis about the expected effect of transition care structure in each province and why one province is supposed to have less poor outcome during transition than the other aren't specify. **We removed the hypothesis and added the following:** **"Little is known about the impact of system-level transition processes that reflect these resourcing differences on health outcomes. In some jurisdictions, shortages of specialists means that not all patients can be cared for by endocrinologists. In Ontario, a large province with a**

	coordinated pediatric diabetes network that primarily transfers patients to adult diabetes specialists (12), and Newfoundland and Labrador (NL), a smaller province with a single pediatric centre that transfers patients primarily to generalist physicians for adult diabetes care. **Because of variations in how different provinces organize transition care, a comparison of outcomes across provinces may indicate whether jurisdictions which rely on a generalist model of care have comparable outcomes to ones with a more organized network of paediatric diabetes care and a transition to predominantly specialist-led adult care. In this study, we examine the occurrence of acute diabetes complications across the transition period in two Canadian provinces, both with some of the highest reported rates of diabetes globally (13, 14) but different structures for transition and post-transition care." (Introduction)** 3. Abstract: In results section, there is an indication of increase in rate of ketoacidosis in ON and no difference in NL. In the conclusion the authors state that they found consistency in poor outcome between ON and NL. Why this contradiction? **Given that we re-did the analysis for this revision, we removed both these sentences from the abstract. (Abstract)** 4. Authors hypothesised that "the rates of adverse events across transition-age in Ontario might be lower compared to NL because pediatric diabetes care is coordinated by a dedicated network of pediatric centres in Ontario that has been associated with better health outcomes" What is the link between "having better health outcome before 17 year old" and having better transition? **Given that we removed this hypothesis in our revision, we also removed this sentence as it no longer is relevant. (Introduction and Interpretation)** 5. Author should hypothesised what is the expected effect of transition care structure in each province and why one province is supposed to have less poor outcome during transition than the other. **Given that we are unable to test our hypothesis due to insufficient power, we removed the hypothesis from the introduction and instead clarified that the rationale for this study is to test whether transition models which rely on less specialized care can deliver the same outcomes.** **We added the following to the introduction to explain this:** **"Because of variations in how different provinces organize transition care, a comparison of outcomes across provinces may indicate whether jurisdictions which rely on a generalist model of care have comparable outcomes to ones with a more organized network of paediatric diabetes care and a transition to predominantly specialist-led adult care." (Introduction)** 6. Is it possible to have an estimate of the proportion of adolescent that are referred to an adult clinic? It's seems to be about 50% in NL, but how much in ON? **This information is now added to the methods section:** **"In 2015, 28/35 (80%) of [Ontario] centres referred at least some individuals to an adult endocrinologist and there was a wide range of clinic-specific transition practices (ref)" (Methods)** 7. Algorithm definition should be indicate.

	We added the following to the methods section: **"…the Pediatric Ontario Diabetes Database, a validated registry of all Ontario residents (aged <19 years) with a diagnosis of diabetes based on a validated algorithm that uses four diabetes-related physician billing claims over 2 years (83% sensitivity, 99% specificity)" (Methods)** 8. What is the population reference in the attribution of the material deprivation quintiles? Is the Canadian population or the population in each province? It looks strange that more than 40% of children in NL are in the most deprived quintiles. **We re-did the material deprivation quintiles based on the Canada Marginalization index 2006. Now we present the material deprivation quintiles based on the Canada Marginalization index 2006. We clarified this in the methods section as follows:** **"…the 2006 Canadian Census to assign neighbourhood material deprivation quintiles based on the Canada Marginalization index 2006." (Methods and Table 1)** 9. Author state that "the vast majority of youth have type 1 diabetes". How many percent does it mean? **We specified as follows:** **"we have previously shown that the vast majority (94.8%) of children in Ontario with diabetes, have type 1 (ref)" (Methods)** 10. Comparison of rate for each age category between provinces is done by inspecting overlapping between confidence intervals. A statistical test should be performed to do such comparison. **Given that we how inadequate power, we have removed this figure and opted not to conduct any statistical tests to compare groups. (Methods)** 11. The small size of youth with diabetes in the Newfoundland cohort is an issue in this study. What is the power of the study to detect "clinically significance difference" between NL and ON? **We lack statistical power to detect a clinically significant difference between provinces. We address this in the analysis section of the methods.** **In the methods, we now state:** **"For both provinces, we describe the rates and the occurrence of at least one event of all admissions, diabetes-related (including DKA) and DKA admissions in two mutually exclusive age categories (15 to <18 and 18 to <21 years) standardized according to material deprivation. We had insufficient power, due to the small sample size in NL, to make precise estimates or between group comparisons for rare outcomes such as diabetes-related admissions and DKA." (Methods)** 12. Comparison between NL and ON are done using crude rate. Why the author didn't standardised according to a standard population (for example, Canada 1991, or the repartition in age, material deprivation and sex in ON in 2001…)? **We revised Table 2 and now present the outcomes standardized according to the Canadian Marginalization Index.** **We did not standardize according to age and sex because these variables were similar between groups. (Table 2)**

	13. Are age categories mutually exclusives? (15-17, 17-19, 19-21 aren't mutually exclusive) **We re-did our age categories. They are now:** **15 to <18 and 18 to <21. They are mutually exclusive. We specify this in the methods section as follows:** **"we describe the crude rates and the occurrence of at least one event of all admissions, diabetes-related (including DKA) and DKA admissions across transition-age in two mutually exclusive age categories (15 to <18 and 18 to <21 years)" (Methods)** 14. DKA rate is lower (but not statistically different) in NL at age 15-17 in comparison to older. What would be impact if 17-19 and 19-21 years old group would be merge? **As indicated above, we did merge our age categories. They are now 15 to <18 and 18 to <21 years. We still lack the statistical power to detect a difference between these new groups. However, we describe the outcomes using these new age categories. (Results)** 15. Title of table 2 should indicate that proportion are include in the table. **We changed the title of Table 2 to:** **"Standardised rates and proportion with any admission, diabetes-related admission, and DKA-related admission across transition-age in Ontario and Newfoundland according to the Canadian Marginalization Index" (Table 2)** 16. In table 2, proportion confidence interval should be shown. **In our revised Table 2, we include 95% confidence intervals.** 17. Rural VS urban status is sometime associated to DKA. What are the impact on comparison between ON and NL? **We are not able to do any statistical modeling to examine the association of rurality and our outcomes. However, we do present rural vs. urban status in our baseline table 1.** **We acknowledge the known association between rural status and DKA and how this may influence our results in the interpretation:** **"There is a known association between both lower socioeconomic status and rural residence and an increased risk of DKA (refs). Factors such as the delivery of health services or other social services, might be mitigating the occurrence of adverse events especially for those of low socioeconomic status and those living in rural areas in NL." (Interpretation)** 18. DKA rate is lower (but not statistically different) in NL at age 15-17 in comparison to older. This observation should be discuss based on both clinical and statistical significance. **We agree and have removed this sentence. We have changed our analytic approach as discussed above. (Interpretation)** 19. The author state in the interpretation that small sample size is challenge of conducting multi-jurisdictional studies. Since this information was available when the study was planned, why selection of NL was necessary for the purpose of comparing two different models of transition care? **In order to test whether transition models which may need to rely less specialized care can deliver the same outcomes, we selected NL, despite its**

	small sample size because it is a province that relies on less specialized diabetes care. We now explain this justification in our introduction: **"Little is known about the impact of system-level transition processes that reflect these resourcing differences on health outcomes. In some jurisdictions, shortages of specialists means that not all patients can be cared for by endocrinologists. In Ontario, a large province with a coordinated pediatric diabetes network that primarily transfers patients to adult diabetes specialists (12), and Newfoundland and Labrador (NL), a smaller province with a single pediatric centre that transfers patients primarily to generalist physicians for adult diabetes care.** **Because of variations in how different provinces organize transition care, a comparison of outcomes across provinces may indicate whether jurisdictions which rely on a generalist model of care have comparable outcomes to ones with a more organized network of paediatric diabetes care and a transition to predominantly specialist-led adult care."** **And in the methods:** **"There are several important differences in the structure and delivery of diabetes transition care in Ontario and NL which led us to select these two provinces." (Introduction and Methods)** 20. Expected effect of transition care structure in each province and why one province is supposed to have better transition than the other should be discuss. **We removed the hypothesis regarding the effect of transition care structure in each province and its effect on outcomes. Instead we re-framed our research question as follows:** **"Little is known about the impact of system-level transition processes that reflect these resourcing differences on health outcomes. In some jurisdictions, shortages of specialists means that not all patients can be cared for by endocrinologists. In Ontario, a large province with a coordinated pediatric diabetes network that primarily transfers patients to adult diabetes specialists (12), and Newfoundland and Labrador (NL), a smaller province with a single pediatric centre that transfers patients primarily to generalist physicians for adult diabetes care.** **Because of variations in how different provinces organize transition care, a comparison of outcomes across provinces may indicate whether jurisdictions which rely on a generalist model of care have comparable outcomes to ones with a more organized network of paediatric diabetes care and a transition to predominantly specialist-led adult care. In this study, we examine the occurrence of acute diabetes complications across the transition period in two Canadian provinces, both with some of the highest reported rates of diabetes globally (13, 14) but different structures for transition and post-transition care." (Introduction)** 21. Conclusion of the author is not clearly state. **We clarified our conclusions as they relate to our revised articulation of our study aim as follows:** **"Acknowledging the limitations of our data, it is reassuring that we did not find large differences in the occurrence of acute diabetes complications across transition-age within provinces or within age categories between provinces despite important differences in access to specialized adult diabetes care between provinces. Although the standardized rates of adverse outcomes appear to be similar between provinces it is possible that**

	there are different mitigating factors influencing outcomes in each province; this should be further explored. Finally, this cross-provincial comparison study highlights two system-level transition processes that reflect resourcing differences between provinces and provides insight into the impact of these on health outcomes." (Interpretation)
Reviewer 3	Dr. Marie-Eve Robinson
Institution	Division of Endocrinology, Department of Pediatrics, McGill University Health Centre, Montréal, Que.
General comments (author response in bold)	1. The term "transition-age" can be confusing. Because the authors do not use this term to refer to the age at the time of transition to adult diabetes care, the term "age" could be used instead. **We removed all use of the term transition-age in the manuscript. We replaced it with the specific age in years to which it referred. (Through the manuscript)** 2. In the Limitation section, please consider discussing that although most individuals should be transitioning at 18 years old, some individuals could in fact transition before or even after 18 years old. The exact transition age is specific to each individual. **We added the following to the paragraph about limitations in the interpretation section:** **"We assume that most individuals transfer to adult care at age 18 years, however that may not be true for all individuals." (Interpretation)** 3. In the discussion, could the authors provide possible explanations/hypothesis on why younger individuals (15-17 years) had a lower rate of DKA compared to the 19-21 years? **Given our re-analysis of the data, this is no longer applicable. (Interpretation)** 4. In table 2, could the authors hypothesize on why the crude rates and proportion of individuals with non-DKA diabetes-related admissions are higher in the 15-17 age groups than in the 17-10 and 19-21 age group? **Due to the low rate of events we did not re-analyze this outcome using our new age categories and therefore we do not report this outcome in our revised Table 2. (Results)** 5. The authors have excluded individuals with no diabetes-physician visits from age 15-<17 years. Those could potentially be individuals who were lost to follow-up around the transition period and potentially have a risk to resurface later with diabetes-related complications. Could the authors briefly discuss how excluding individuals with no diabetes-physician visits from age 15-<17 years could impact their results? **We added the following explanation to the methods section to justify our decision to exclude individuals age 15 to <17 with no diabetes physician visits:** **"We also excluded individuals in Ontario with no diabetes physician visits from age 15-<17 because they may have moved out of the province or were receiving care from providers who do not bill the provincial health plan. Further, it would be highly unlikely for an individual living with type 1 diabetes to have no diabetes physician visits over this period of time."** **We also added the following to the limitations paragraph in the interpretation**

	to discuss how this exclusion could impact our results: **“Related, we may be underestimating the rate of adverse events in those aged 18 to <21 years because we excluded individuals with no diabetes physician visits from age 15 to <17 because either they previously had moved out of the province, were receiving diabetes care from providers who do not bill the provincial health plan, or less likely, were not accessing care during that time.” (Methods and Interpretation)**