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Title	Association between interpersonal continuity of care and medication adherence in type 2 diabetes: an observational cohort study
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Reviewer 1	Dr. M Bouma
Institution	Nederlands Huisartsen Genootschap, Netherlands
General comments (author response in bold)	<p>Nice article, but difficult to investigate.</p> <p>1. Proposed minor revision: In the UK and The Netherlands, patients with type 2 diabetes are often seen by a (specialised) nurse. In this study, it is not clear of the 'others' on page 7 are doctors or can be (specialized' nurses as well. If nurses provide shared care with a doctor and are in fact the ones providing the most continuous interpersonal care, it is important to know whether they can prescribe medication themselves or not. If the researchers don't know this, please pay some attention to this aspect in the discussion.</p> <p>'Others' are indeed doctors. It has been clarified both in the method section and in Table 1. 'Specialty of prescriber' has been replaced with 'specialty of physician who prescribed the initial oral antidiabetes drug'.</p>
Reviewer 2	Prof. Joan E. Tranmer RN MSc PhD
Institution	Queen's University, School of Nursing, Kingston, Ont.
General comments (author response in bold)	<p>Brief summary: This paper reports on cohort study exploring the relationships between interpersonal continuity of care and medication adherence in newly diagnosed diabetic patients receiving oral anti-diabetic agents (AD) for the first time.</p> <p>Introduction: Authors argue that high levels of interpersonal continuity of care (ICoC) are associated with positive outcomes, yet there is limited (if any evidence) exploring the relationship between ICoC and medication adherence and outcomes. A few studies have reported varying results and have not addressed the issue of temporality. Thus the rational for the study is supported.</p> <p>1. However, the authors need to provide a summary of "usual care practice" for patients with newly diagnosed diabetes. According to the CDA guidelines, interprofessional team care is recommended. Thus, this suggests that ICoC may not be the best measure of quality of care for "new patients diagnosed with diabetes". It is likely an important component. Need to address how ICoC should be interpreted within the context of quality care for newly diagnosed patients.</p> <p>We thank the reviewer for pointing this out. It is now being addressed in the limitations. We have added the following sentence:</p> <p>'Next, since Canadian guidelines recommend an interprofessional team care approach for patients newly diagnosed with diabetes ²⁶, the continuity of care index may not be the best measure as it is not taking into consideration the contribution of other health professionals in the continuity of the patients care.'</p> <p>Addressing both persistence and compliance is a strength.</p> <p>Methods: Comprehensive study design and measures. Addressed the potential bias of exclusion criteria in the limitations.</p> <p>2. Authors could consider exploring other patient descriptors: i.e., total number of ambulatory patient visits by physician type and comorbid conditions. Consider using established comorbidity indices to describe populations.</p> <p>We used the number of distinct drugs as a co-morbidity index. We are aware that other co-morbidity indices could have been used, for example, the Charlson index. We used instead the number of distinct drugs which is also a well-established index (see ref no 17 – Schneeweiss, Am J Epidemiol. 2001;154:854-64). We did so because this variable is also a potential barrier associated to persistence and compliance.</p> <p>Was there an age restriction related to patients eligible for coverage?</p> <p>In regards of age restriction related to drug coverage eligibility, there was none. This has been clarified by adding the following sentence in the Method section (see above our response to Editor's comment no.2):</p> <p>'The Quebec drug plan covers prescribed drugs for all permanent residents of Quebec province aged 65 or more, welfare recipients and those without a private drug insurance group plan.'</p> <p>Could you consider other patient outcomes (do you have access to laboratory data for evidence of glycemic control?)</p> <p>Unfortunately, laboratory data are not captured in the Quebec administrative databases.</p> <p>3. My major concern with the description of ICoC – is the categorization based on tertiles. You have 2/3 of your sample in a range of .24 or lower. Did you consider using the approach as described by Chen et al – this would allow for comparability across studies. Consider another analysis that includes the Chen cutoffs.</p> <p>See above our response to Editor's comment no 5.</p>

	<p>4. As well, your results would suggest that patients in the “intermediate” category receive different care (i.e, more likely to be seen by an endocrinologist). It would be important to explore the patterns of care. In example, if a new patient is initially seen by the internist then followed predominantly by GP – was this classified as high-intermediate or low. Would it be better to determine the ICoC within those “visits” that would be typical for diabetes management and not all ambulatory visits. It seems that you have lost some ability to detect the influence of ICoC using this generalized approach. If a different approach is not feasible, then you need to address the importance of considering interprofessional team contribution and patterns of care and how this was or was not addressed.</p> <p>We agree with the reviewer that our general approach carries limitations. It would have been a better approach to measure ICoC only using consultations relevant to the management of diabetes. This level of analysis was unfortunately not possible given the administrative data we had access to. In Quebec, physicians are asked to provide only one reason for the consultation even if the patient is treated for multiple conditions. As suggested by the reviewer, we have added the following in the limitations:</p> <p>‘ In addition, continuity of care was measured using all ambulatory visits. The results may have been different if we had been able to measure continuity of care using only visits relevant to the management of diabetes.’</p> <p>5. Why is your adherence rate substantially higher than what has been reported in the literature? Discuss.</p> <p>This is in part due to the fact that we measured persistence and compliance separately as opposed to what is generally being done in other studies. We are not specifically discussing this result as it has been discussed elsewhere (see ref no 10 in our manuscript - Guenette et al, 2013) and as we are limited in the number of words. However, we would be happy to discuss it if the Editor believes it should be.</p> <p>6. Interpretation: You over generalize the results. While there may be statistically different associations – these are minor, and likely not clinically relevant. I do not suggest that ICoC is not important. But, your study, as designed was not able to capture a significant influence on medication adherence. This may suggest that other factors are influencing adherence or your measures or design did not capture the “pattern” of adherence. These need to be discussed.</p> <p>We agree with the reviewer. Associations are weak and may not be clinically relevant. We hope that our revision of the Interpretation and conclusion sections is better reflecting that issue. See above our responses to the Editor’s comments no 8 and 9.</p> <p>7. This study does describe an important concept – medication adherence - for this patient population. I would recommend a more robust interpretation within the context CDA guidelines and diabetic care.</p> <p>This is a good point. The concept of medication adherence in the type 2 diabetic population is not comprehensively discussed in our paper. Due to the limited number of words, we chose to focus our discussion on the relationship between continuity of care and medication adherence. For a more comprehensive discussion on medication adherence, readers can refer to one of our studies we refer to in the manuscript (see Guenette et al¹⁰).</p>
Reviewer 3	Dr. Hafsa Suhail Najim Al-anbari PhD (Clin. Pharm., USM), Assistant Professor
Institution	Uruk University, Department of Pharmacy, Al-Esraa University College, Department of Pharmacy, Iraq
General comments (author response in bold)	<p>Minor comments</p> <p>1. The authors well-presented and discussed the results, including the interpretations.</p> <p>2. The article throws upon exclusive new idea (assess the association between ICoC and each of the two main constructs of medication adherence among new users of oral AD: 1) persistence with AD; 2) compliance with AD among those persistent).</p> <p>3. Methodology has its own limitations that the authors fortunately highlighted them.</p> <p>4. Page 6, lines 45-50: this section is better to be clarified more to the reader.</p> <p>The reviewer is probably referring to the fact that we did not mention how covariates were selected. We have therefore added the following sentence:</p> <p>‘Covariates were variables previously shown to be associated with persistence or compliance with antidiabetic drugs in this population ^{10,16}.’</p> <p>5. Page 7, lines 39-41: “ni= number of visits to ith different physician”, what does that mean? This sentence needs to be explained in another word.</p> <p>We understand the complexity to mathematically define the index. This information may not be essential for the CMAJ Open readership. Since readers can refer to the article by Bice to understand the mathematics of the index construction, this sentence has been deleted.</p>
Reviewer 4	Ms. Brittany Gerber MA
Institution	Medlior Health Outcomes Research Ltd., Calgary, Alta.
General comments (author response in bold)	I enjoyed reading your article, which provided an interesting application of administrative data to look at the relationship between interpersonal continuity of care

bold)	<p>and medication adherent among patients who have initiated on an oral anti-diabetes drug. Please find my comments and questions below:</p> <p>1. In the Introduction (pg. 3, paragraph 3) you state “However, to a large extent the use of those drugs is not optimal.”; please expand on what you mean by ‘use’? Do you mean patient adherence to medication? Please provide a supporting reference for this statement.</p> <p>Thank you for pointing this out. We have clarified. This section now reads: ‘Patient adherence to oral antidiabetes drugs is not optimal. For example, in one study conducted in Quebec, 79% of patients were persistent with the oral antidiabetes drug one year after initiation and among them, only 78% were compliant as they obtained drug supplies for at least 80% of days during the year ¹⁰.’</p> <p>2. In the Introduction (pg. 3, paragraph 3), you state that “In one study conducted in Quebec, less than 79% of patients persisted with the oral AD one year after initiation.....”; Did you mean to state that “79% of patients persisted”? Please clarify the text.</p> <p>It has been clarified. It now reads: ‘... in one study conducted in Quebec, 79% of patients were persistent with the oral antidiabetes drug...’</p> <p>3. Could you please provide a rationale for measuring ICoC in year one, and adherence in year two? It seems plausible that ICoC as measured in the same year as adherence may be a stronger approach to examine whether ICoC impacts adherence – perhaps a patient had a high ICoC in the 1st year, but a lower ICoC in the 2nd year (or vice versa); the current analysis does not account for these possible changes and how these may influence adherence. It would be interesting to see if ICoC remained the same in the second year, and how this measure was associated with adherence.</p> <p>As opposed to previous studies, we designed this study so we could establish a temporal relationship between ICoC and medication adherence. Measuring ICoC and adherence concurrently in the same year would have allowed studying only the cross-sectional relationship between those variables.</p> <p>4. In addition, it does not appear that other covariates (such as number of distinct drugs used, loyalty to a pharmacy, or hospitalization for any cause) were measured during year two and utilized in the statistical models. A note that these covariates were only measured in the 1st year should be added to the limitations section.</p> <p>The reviewer is right. Those covariates included in the statistical analyses were measured in year 1. We did so for the same reason as mentioned above (to have a clear temporal relationship).</p> <p>5. In the Variables Section (pg. 5), you state “Since index scores have no validated thresholds, we categorized ICoC in three categories (low, intermediate and high) using tertiles, as did previous researchers” – Please clearly define the categories here (this definition is currently under “Results” on pg 7).</p> <p>The reviewer is right. We report in the Variables section how ICoC was defined and further categorized using tertiles. We did not report tertiles values in this section as those are issued from the analysis. This is why they are reported later in the Results section.</p>
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