PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Diabetes mellitus monitoring and control among adults in Australian general practice: a national retrospective cohort study
AUTHORS	Zheng, Mingyue; Bernardo, Carla; Stocks, Nigel; Hu, Peng; Gonzalez-Chica, David

VERSION 1 – REVIEW

REVIEWER	Medina-Gomez, Oswaldo Instituto Mexicano del Seguro Social, Unidad de Investigación en Epidemiología Clínica
REVIEW RETURNED	26-Dec-2022

GENERAL COMMENTS	In the main page, tropical medicine and infectious diseases are mentioned in the key words, which do not correspond to the main topic of the study. The design of the study according to the authors is a retrospective cohort, however, this design does not correspond to what was performed and the statistical analysis is not congruent with a cohort study. The introduction addresses the importance of diabetes, its regular monitoring and control to reduce its complications, however, three objectives of the study are presented, which are not sufficiently substantiated in the introduction and the role of sociodemographic conditions that also justify their study. There is a problem of classification regarding the parameters considered in the control of the person with diabetes, for example, the blood pressure figures should be differentiated according to the pre-existing condition or not of arterial hypertension of those with diabetes. The study is based fundamentally on the analysis of registries, so the scope of the study is of national interest and it is recommended that it be sent to a local journal.

REVIEWER	Nantha, Yogarabindranath Monash University Malaysia
REVIEW RETURNED	15-Jan-2023

GENERAL COMMENTS	In this study, the authors attempt to examine the nationwide performance of monitoring individuals with diabetes mellitus in GP clinics and tertiary care hospitals.

	To that effect, the author pursues a cross-sectional research strategy, culminating in a data evaluation process that involves a combination of mostly descriptive (without inferential statistics) analysis and logistic regression. Much of the findings in this study are not novel but it does give a clear picture of trends seen in the country and what can be done to improve healthcare services in the future. Having said that, the authors have focused exclusively on a “therapeutic” approach to diabetes when it is increasingly evident nowadays that behavioural aspects related to self-management are the cornerstone of better disease control/monitoring. This is especially true for the discussion section which could have benefited from a more nuanced narrative. I have provided an annotated commentary file (attached) to describe specific details concerning what can be done to improve the quality of the manuscript. In general, here are several comments the authors need to focus on: 1. Diabetes is a well-known cardiovascular risk equivalent. For an international comparison to be made (and in strong adherence to international standards), LDL-C goal/target is the preferred method to measure, monitor, and stratify cardiovascular risk, especially in clinical settings. Despite providing citations here that could plausibly “relegate” the use of LDL-C, I strongly urge the authors to also document analysis that involves LDL-C as well. 2. What about other comorbidities present in this population which could equally influence all other dependent variables in this study (e.g. peripheral vascular disease, COPD, liver disease, etc.)? The authors should use Charlson Comorbidity Index (or any other comorbidity indices) here as a covariate for more inclusiveness. Without this, most other concurrent comorbidities may be missing out or appear deliberately omitted. 3. Please use standard report format to describe the overall integrity of the regression model here (without which, the statistical reporting here remains incomplete) 4. The discussion section, for the most part, appears somewhat discursive. The author could organize the content here using the following subsections: i) main findings, ii) comparison with literature, iii) strength and limitation, iv) practical implications and avenues for future research. 5. The authors need to explain other behavioural aspects that could have a profound influence on the trends described in the discussion section. For example, it is known that most patients go through a process of denial, strict self-monitoring, and only fall into some form of recidivism after several years of living with the disease. Hope this helps and good luck!

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Oswaldo Medina-Gomez, Instituto Mexicano del Seguro Social

Comments to the Author:

- In the main page, tropical medicine and infectious diseases are mentioned in the key words, which do not correspond to the main topic of the study.

Response: We apologize for the error. The appropriate keywords have been updated (Epidemiological Monitoring, Evidence-Based Practice, Population Health).

- The design of the study according to the authors is a retrospective cohort, however, this design does not correspond to what was performed and the statistical analysis is not congruent with a cohort study.

Response: Thank you for bringing to our attention the lack of clarity in the explanation of our study design and the statistical analysis used.

After carefully reviewing our methods, we still consider this is a retrospective cohort design based on electronic medical records: "A cohort study follows-up two or more groups from exposure to outcome…..the investigator might use existing medical records and go back in time several years to identify …exposed and not exposed…and following them up to the present (retrospective cohort study)" [*Grimes DA, Schulz KF. Cohort studies: marching towards outcomes. Lancet. 2002;359(9303):341-5*]. We used data from 2015-2017 to identify the level of exposure (past diagnosed diabetes vs newly diagnosed diabetes), and then records from 2018 to identify the outcome (diabetes monitoring and diabetes control). Thereby, the design fits the criteria of a retrospective cohort study. Nonetheless, in our intention to assess the comparability of these groups according to sociodemographic and clinical variables (secondary objectives) to provide appropriate adjustment for confounders, we emphasized these relationships instead of the main research question (Do patients with recent diabetes diagnosis are more frequently monitored and achieve better diabetes control than those with past diagnosed diabetes?). Therefore, to improve clarity and facilitate the readability of the manuscript, we have substantially changed the text and presentation of results to emphasise the primary objectives and the study longitudinal design (Lines 111-121, 143-170, 196-206).

- The introduction addresses the importance of diabetes, its regular monitoring and control to reduce its complications, however, three objectives of the study are presented, which are not sufficiently substantiated in the introduction and the role of sociodemographic conditions that also justify their study.

Response: As mentioned above, we have revised the whole manuscript to make it clearer, focusing on our main objective that is the comparison of diabetes monitoring and control between patients with past or newly recorded diabetes. Furthermore, in consideration of other reviewer's comments addressing our Introduction, we have modified the section accordingly (Lines 59-99).

- There is a problem of classification regarding the parameters considered in the control of the person with diabetes, for example, the blood pressure figures should be differentiated according to the pre-existing condition or not of arterial hypertension of those with diabetes.

Response: We appreciate your comment and agree that some pre-existing health conditions, such as arterial hypertension, CKD or even liver disease (as this may also affect diabetes pharmacological

therapy because of the hepatotoxicity of oral hypoglycemic drugs [*Tolman KG, Fonseca V, Dalpiaz A, Tan MH. Spectrum of liver disease in type 2 diabetes and management of patients with diabetes and liver disease. Diabetes Care. 2007;30:734–743*]) should be included as control in our analysis. In this sense, we have updated our results, adjusting the models for history of hypertension, CVD, CKD, dyslipidaemia, liver disease and depressive symptoms. We added this information to the Methods (Line 182) and different paragraphs of the Results section.

- The study is based fundamentally on the analysis of registries, so the scope of the study is of national interest and it is recommended that it be sent to a local journal.
Response: The use of electronic health records (EHR) represents a unique data source for investigating the monitoring and management of chronic conditions. Despite concerns about the completeness and feasibility of using EHR-based primary care databases in research, studies conducted in countries such as the United States, Canada, the United Kingdom, France, Sweden, India and Australia have shown EHRs can provide accurate information on diabetes prevalence, management and control.[1-3] Moreover, EHR databases minimise self-report bias by providing information on doctor-reported diagnoses, objective laboratory results, and prescribed medications.[4,5] Therefore, we believe the benefits of using a national sample of EHR from primary care data, which can improve diabetes management without increasing overall treatment costs,[6,7] and has already been used in the last decade to monitor a range of chronic conditions, go beyond the local level. It could serve, internationally, as an example of a valuable low-cost data source as an alternative to laborious and costly studies (we have included a paragraph on this topic in the Introduction - Lines 85-91).

1 Zheng M, Bernardo CDO, Stocks N, Gonzalez-Chica D. Diabetes Mellitus Diagnosis and Screening in Australian General Practice: A National Study. Journal of Diabetes Research. 2022;2022.

2 Varroud-Vial M. Improving diabetes management with electronic medical records. Diabetes Metab. 2011;37:S48-S52.

3 Marson A, Raffoul N, Osman R, Deed G. Management of patients with type 2 diabetes and cardiovascular disease in primary care. Aust J Gen Pract. 2021;50(4):238-245.

4 Henderson J, Barnett S, Ghosh A, et al. Validation of electronic medical data: Identifying diabetes prevalence in general practice. Health Inf Manag J. 2019;48(1):3-11.

5 Havard A, Manski-Nankervis JA, Thistlethwaite J, et al. Validity of algorithms for identifying five chronic conditions in MedicineInsight, an Australian national general practice database. Bmc Health Serv Res. 2021;21(1).

6 Pulleyblank R, Mellace G, Olsen KR. Evaluation of an Electronic Health Record System With a Disease Management Program and Health Care Treatment Costs for Danish Patients With Type 2 Diabetes. JAMA Netw Open. 2020;3(5):e206603.

7 Shah S, Yeheskel A, Hossain A, et al. The Impact of Guideline Integration into Electronic Medical Records on Outcomes for Patients with Diabetes: A Systematic Review. Am J Med. 2021;134(8):952-962.

Reviewer: 2

Dr. Yogarabindranath Nantha, Monash University Malaysia

Comments to the Author:
In this study, the authors attempt to examine the nationwide performance of monitoring individuals with diabetes mellitus in GP clinics and tertiary care hospitals. To that effect, the author pursues a cross-sectional research strategy, culminating in a data evaluation process that involves a combination of mostly descriptive (without inferential statistics) analysis and logistic regression. Much of the findings in this study are not novel but it does give a clear picture of trends seen in the country and what can be done to improve healthcare services in the future. Having said that, the authors have focused exclusively on a "therapeutic" approach to diabetes when it is increasingly evident nowadays that behavioural aspects related to self-management are the cornerstone of better disease control/monitoring. This is especially true for the discussion section which could have benefited from a more nuanced narrative.

- I have provided an annotated commentary file (attached) to describe specific details concerning what can be done to improve the quality of the manuscript.

Response: We appreciate your detailed comments. We have carefully reviewed the annotated commentary file you provided and have made the necessary changes that are marked in red. To improve the overall quality of the manuscript, and readers' clarity of our objectives, we focused our results and discussion on the comparison of diabetes monitoring and control between patients with past or newly diagnosed diabetes using longitudinal analyses. We updated our tables accordingly, and we also modified the discussion section to include a subtler narrative and discuss some important limitations as the lack of behavioural variables in our analyses. We addressed your comments below.

- In general, here are several comments the authors need to focus on:

1. Diabetes is a well-known cardiovascular risk equivalent. For an international comparison to be made (and in strong adherence to international standards), LDL-C goal/target is the preferred method to measure, monitor, and stratify cardiovascular risk, especially in clinical settings. Despite providing citations here that could plausibly "relegate" the use of LDL-C, I strongly urge the authors to also document analysis that involves LDL-C as well.

Response: We agree and appreciate your suggestion from a clinical perspective. We have included analyses of LDL-C monitoring and control. We added this information to the Methods (Lines 150-161), and the results, including the proportion of patients who had LDL-C monitored and controlled and the odds ratio comparing the groups of interest (past or newly diagnosed diabetes) are presented in Table 2 and 3, as well as additional analyses in supplementary Table S3.

2. What about other comorbidities present in this population which could equally influence all other dependent variables in this study (e.g. peripheral vascular disease, COPD, liver disease, etc.)? The authors should use Charlson Comorbidity Index (or any other comorbidity indices) here as a covariate for more inclusiveness. Without this, most other concurrent comorbidities may be missing out or appear deliberately omitted.

Response: We appreciate your comment and agree that health conditions related to diabetes should have been included in the analyses. Some of these variables, such as heart failure, ischemic heart disease and stroke were already included under cardiovascular diseases (CVD), but based on your suggestion, we decided to include other conditions that could affect monitoring, treatment and consequently control of diabetes, namely chronic kidney disease (CKD), liver disease and depressive

symptoms. We added this information to the Methods (Lines 179-184) and all tables and supplemental material.

3. When p values are not reported, other steps need to be taken to provide conclusive evidence about the robustness of statistics. In this case, authors should provide effect sizes for each analysis, especially for the primary endpoint. Please use standard report format to describe the overall integrity of the regression model here (without which, the statistical reporting here remains incomplete)

Response: Thank you for your suggestions. We have updated all our tables and reporting of results. However, we followed the recommendation of the American Statistical Association (*Wasserstein RL, Lazar NA. The ASA's Statement on p-Values: Context, Process, and Purpose. Am Stat. 2016;70(2):129-131*) to report adjusted odds ratios (ORs) with their corresponding 95% confidence intervals (CIs) rather than P-values. We chose to follow these guidelines as they are becoming increasingly adopted by many leading scientific journals, including the Journal of the American Medical Association (JAMA) and The Lancet. We acknowledge that some readers may prefer to see P-values reported instead of CIs, but CIs have the advantage of providing direction and strength of the effect as well as results at the level of data measurement. We hope the changes and inclusions in the manuscript address your concerns.

4. The discussion section, for the most part, appears somewhat discursive. The author could organize the content here using the following subsections: i) main findings, ii) comparison with literature, iii) strength and limitation, iv) practical implications and avenues for future research.

Response: We appreciate your suggestion and agree that having clear subsections in the discussion can improve the flow of the argument and facilitate the manuscript's readability. We have reorganised the section according to your comment.

5. The authors need to explain other behavioural aspects that could have a profound influence on the trends described in the discussion section. For example, it is known that most patients go through a process of denial, strict self-monitoring, and only fall into some form of recidivism after several years of living with the disease.
Response: Thank you for your suggestion. We rewrote our discussion to include a more profound debate on the behavioural aspects that could substantially impact the findings on diabetes monitoring and control. According to the literature, there is a behavioural paradigm of diabetes self-management that tends to reduce after the initial diagnosis without appropriate support or patient willpower (*Lambrinou E, Hansen TB, Beulens JW. Lifestyle factors, self-management and patient empowerment in diabetes care. Eur J Prev Cardiol. 2019;26:55-63*). Despite some behavioural aspects, such as denial or anxiety, may affect the patient's ability to monitor and manage their condition when diabetes is diagnosed (*Kalra S, Jena BN, Yeravdekar R. Emotional and Psychological Needs of People with Diabetes. Indian J Endocrinol Metab. 2018;22(5):696-704*), the self- management tend to deteriorate years after the diagnosis, in part due to the distress of living with diabetes and the high level of self-care needed, but also the lack of appropriate support (*Shrivastava SR, Shrivastava PS, Ramasamy J. Role of self-care in management of diabetes mellitus. J Diabetes Metab Disord. 2013;12(1):14).* We added the abovementioned aspects to the manuscript (Lines 362-367, 388-391, 416-427).