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Title: Trends in glucose testing among individuals without diabetes in Ontario between 2010 and 2017: a population-based cohort study
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Reviewer 1: Anna Kucharska-Newton PhD MPH
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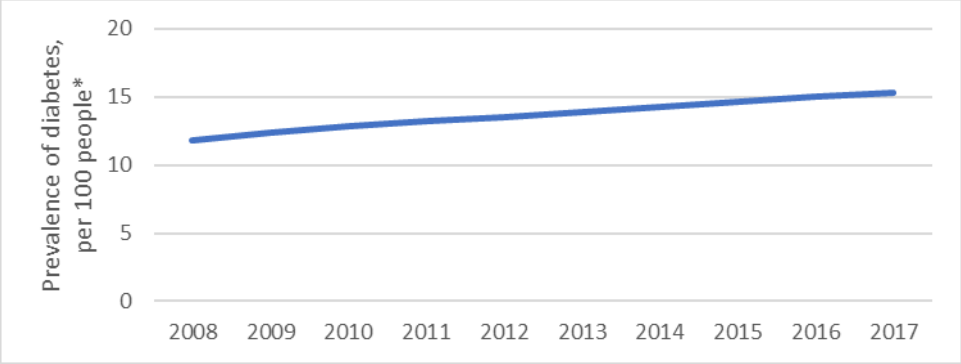
Comment R1-1. In this manuscript the authors take advantage of an impressive resource, consisting of medical records of beneficiaries of the Ontario Health Insurance Plan (OHIP), to examine patterns of diabetes screening in the province during the years 2010-2017. Presented results pertain to screening among individual considered to be free of diabetes. The data suggest that, overall, screening practices remained stable during the 7 years of observation. I would be interested to know how did the prevalence of diabetes and attendant risk factors, such as obesity, change during that time.
Using population size estimates from the Statistics Canada Census and the Ontario Diabetes Database, estimates of the prevalence of diabetes among Ontarians 40 years and older between 2008 and 2017 are shown below. The steady increase is consistent with Diabetes Canada's predictions of a rise in prevalence in Canada between 2015 and 2025. Since this paper focuses on glucose testing, we have decided not to include these results in the paper, but mention the importance of glucose testing for early identification since undiagnosed diabetes has been reported to contribute ~20% to overall prevalence rates (page 10, line 248). Unfortunately, our data sources do not enable us to determine trends in obesity rates.

> **"Combined with reports of undiagnosed diabetes contributing ~20% to overall type 2 diabetes prevalence rates, continued vigilance in diabetes screening is needed."**



*** Among individuals 40 years and older.**

Comment R1-2. The few comments below are meant as an aid in the clarification of study methods and inferences. How representative are the study data of the Ontario population 40 years and older?

The data comprise all persons in Ontario aged 40 years or older irrespective of geography. The only requirement is that they are residents of Ontario with a valid health card number without known diabetes at the beginning of the observation period of interest. We have made this clearer in the methods (page 4, line 85) as:

> **"We conducted a retrospective, population-based cohort study of the entire population of Ontario eligible for the province's universal health insurance plan (Ontario Health Insurance Plan, OHIP) using multiple population-based health administrative databases. Residents without known diabetes…"**

Comment R1-3. It would appear that no sampling of the records was performed prior to the analyses. Please specify that clearly.
Yes, this is correct. As per Response R1-2, the methods have been reworded to make it clearer that the study comprised the entire population of Ontario.

Comment R1-4. Is there are a reason why there is no representation of individuals of Black race and ethnicities other than Chinese or South Asian?
Ethnicity was determined using a surname algorithm linked to our data sources, which has been validated only for Chinese and South Asians. Unfortunately, there is no method for determining Black race in Canadian administrative datasets at this time. We have added this as a Limitation (page 11, line 270) which reads as follows:

> **"Our analyses by ethnicity was also limited in that we could only identify likely Chinese and South Asians, and while they are the two most populous ethnic groups (> 50% of all visible minorities) in Ontario, an investigation of other ethnic or racial groups was not possible."**

Comment R1-5. Further, persons of the latter ethnic groups were identified on the basis of their surnames. How accurate is that method?
The surname algorithms have been validated and reported to have high specificity (99.7%) for both South Asian and Chinese surnames, and 89% and 92% positive predictive value for South Asian and Chinese surnames, respectively.[2] We have cited the validation study in the Methods (page 5, line 113), as follows:

> **"For ethnicity, we used a validated surname algorithm to classify individuals based on likely ethnicity into three groups: Chinese, South Asian and all others in the general population.[27]**

Comment R1-6. How is the frequency of visits to primary care physicians associated with the likelihood of diabetes screening?
We have performed additional analyses examining the above association in 2017 while also adjusting for other factors (age, sex, rural residence, neighbourhood income quintile, ethnicity hypertension, hyperlipidemia, cardiovascular disease). Not surprisingly, greater frequency of visits to a primary care physician is associated with greater likelihood of receiving testing. Among individuals with 0 to 4 visits to a family physician in the prior 3 years, 39.8% were up-to-date with testing compared with 86.9% with 4 or more visits (ORs [95% CI] (ref = 0 visits): 4.48 [4.45, 4.51] for 1-3 visits, 9.16 (9.11, 9.22) for 4-9 visits, 17.51 (17.39, 17.64) for ≥10 visits). Similar to crude results, women, older individuals, and living in a high income neighbourhood were also associated with a greater likelihood of being up-

to-date with testing. These results have been added to the paper as Appendix 4, which is reproduced below:

Appendix 4. Adjusted odds ratios for being up to date with glucose testing among adults aged 40+ years in Ontario, 2017

Variable	Value	Odds ratio (95% CI)	P-value
Sex (ref=male)	Female	1.25 (1.24, 1.25)	<.001
Age, years (ref=40-49)	50-59	1.44 (1.43, 1.45)	<.001
	60-69	1.97 (1.96, 1.98)	<.001
	70-79	2.01 (2.00, 2.03)	<.001
	80+	1.31 (1.30, 1.33)	<.001
Rural residence		1.09 (1.08, 1.09)	<.001
Neighbourhood income quintile (ref=highest, 5)	1 (lowest)	0.84 (0.84, 0.85)	<.001
	2	0.92 (0.92, 0.93)	<.001
	3	0.98 (0.97, 0.98)	<.001
	4	1.02 (1.01, 1.02)	<.001
	Unknown	1.18 (1.05, 1.33)	0.007
Ethnicity (ref=General)	Chinese	0.99 (0.98, 1.00)	0.05
	South Asian	1.21 (1.19, 1.23)	<.001
Number of visits to a primary care physician (2014-16) (ref=0)	1-3	4.48 (4.45, 4.51)	<.001
	4-9	17.51 (17.39, 17.64)	<.001
	10+	9.16 (9.11, 9.22)	<.001
Hypertension		1.59 (1.58, 1.60)	<.001
Hyperlipidemia		2.76 (2.71, 2.81)	<.001
Any history of cardiovascular disease*		1.29 (1.27, 1.31)	<.001

*** Defined as any previous hospitalization for myocardial infarction, stroke, heart failure, percutaneous coronary intervention or coronary artery bypass graft surgery**

Comment R1-7. Do the data contain information on educational attainment? If so, this would be an interesting predictor. As would obesity and level of physical activity, if those data are available.
Unfortunately, our data sources do not have information on education, obesity (or height and weight) or physical activity levels. We have added this to our limitations as (page 11, line 273):

> **"…in our multivariable analyses to identify characteristics associated with up-to-date testing, we were unable to account for some factors which may be associated with testing such as education, obesity and physical activity."**

Comment R1-8. In general, although this was designed as a descriptive study, modeling of the predictors of diabetes screening in Ontario would have been an important inference to obtain from the study data.
See Response R1-6.

Comment R1-9. How did the annual prevalence of diabetes change during the study period?
See Response R1-1.

Comment R1-10. Please specify which guidelines may be eligible for updates (p3., line 49)
References to Diabetes Canada and the C-CHANGE guidelines have been added to the text as suggested, and the sentence (page 3, line 76) reads as follows:

> **"With Canadian guideline updates in the interim and to identify potential gaps in testing by age, sex or ethnicity, our objective was to examine temporal trends in the proportion of adults in Ontario, Canada, 40 years and older without a diabetes diagnosis who received blood glucose testing (including glycosylated hemoglobin (HbA1c)) in the prior three years, making them up-to-date with screening recommendations.[15,16]"**

Comment R1-11. Please provide a reference for screening recommendations (p4 line 3)
References to Diabetes Canada and the C-CHANGE guidelines have been added, and the sentence (page 4, line 96) reads as follows:

> **"Based on the Diabetes Canada and C-CHANGE guidelines, we defined up-to-date testing as having received blood glucose or HbA1c testing at least once during those three years.[15,16] "**

Comment R1-12. I was not sure why study members had to be 40 years of age prior to the year of ascertainment. If that is the case, the earliest age of ascertainment would have been 43 years and not 40 years.
Individuals had to be 40 years of age at the beginning of the 3-year observation period for testing since guidelines recommend testing beginning at 40 years. This would give 40 year olds three years to become up-to-date with testing. It is correct

then, that at the end of each 3-year period (our reporting year), individuals would be at least 43 years. We have clarified this in the manuscript (page 4, line 94) which reads:

"Thus, individuals entered the cohort at a minimum age of 40 years, but evaluation of up-to-date glucose testing began at age 43 years."

Reviewer 2: Osama Elkhateeb MD
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Comment R2-1. This is a large study of glucose testing among Ontario residents for whom guidelines recommend diabetes screening. The study used multisource data linkage to collect the required information. Many of the sources have been validated previously, e.g. ODD and Hypertension database. Interestingly, the only group that showed an increase in glucose testing is the 80+ group. Could the results reflect more universal issues such as access to primary care? For example, table 1 showed differences between the two groups based on the number of visits to primary care physicians.
We were also surprised by the increase in testing among only 80+ year olds, and hypothesized that this was due to the 2013 Diabetes Canada Clinical Practice guidelines introducing HbA1c testing to diagnose diabetes (making testing more convenient for elderly since they do not need to fast). However, on further analysis of our data by test type, the results (added as Appendix 2) suggest increased HbA1c testing only partly contributes to this finding, as a smaller increase in blood glucose testing was also observed between 2013 and 2014 before declining thereafter.

With the reviewer's feedback regarding primary care access, we performed further analyses stratifying on rostering to a primary care physician as a proxy for access (added to Methods page 6, line 142 and results as Appendix 3). In addition to finding individuals with a regular primary care physician being more likely to be up to date with testing, we also found the increase in glucose testing among 80+ year olds was primarily among individuals without a regular primary care physician (i.e., not rostered). In this elderly population, it is possible that much care is focused on the management of other chronic conditions and comorbidities, resulting in primary preventive care including diabetes screening being overlooked. The release of the updated guidelines may have elicited greater attention to the need for glucose testing of individuals in this age range, particularly among those without a regular primary care physician. We discuss this further and state the importance of targeting non-rostered individuals in our discussion (page 9, line 216 and page 10, line 251):

> **"In addition, in this elderly population, much focus may be on the management of existing chronic conditions and comorbidities. As such, primary preventive care such as diabetes screening may have been overlooked until the guidelines' release brought greater attention to the importance of glycemic testing, particularly among those without a regular primary care physician."**

"…those without a regular primary care physician or with hypertension or cardiovascular disease were identified as potential targets in order to improve earlier diagnosis of diabetes."

REFERENCES

1. **Ke, C., Sohal, P., Qian, H., Quan, H. & Khan, N.A. Diabetes in the young: a population-based study of South Asian, Chinese and White people. *Diabet Med* 32, 487-496 (2015).**
2. **Shah, B.R.*, et al.* Surname lists to identify South Asian and Chinese ethnicity from secondary data in Ontario, Canada: a validation study. *BMC Med Res Methodol* 10, 42 (2010).**