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Title	Cost-effectiveness analysis of diabetic retinopathy screening with pharmacy-based tele-ophthalmology versus in-person eye examination
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Reviewer 1	John D. Whited, MD, MHS
Institution	Durham Veterans Affairs Medical Center and Division of General Internal Medicine, Duke University School of Medicine, Durham, North Carolina, USA
General comments (author response in bold)	1. Overall a well written, well designed, and comprehensive cost-effectiveness analysis. **RESPONSE:** Thank you for your comment! 2. Page 6, Line 14. The epidemiology of diabetic retinopathy in Type 1 and Type 2 diabetes mellitus differs. The sentence that begins "The model was tailored for a mixed..." seems to address this but better clarification that, when applicable, weighted averages or other summary values were used for the combined Type 1 and Type 2 populations should be added. **RESPONSE:** yes, more details were added under that section. 3. If space is a consideration, Figure 2 could be deleted as the sentence on page 10, line 22 could adequately address the result of non-dominance. If space is not an issue, Figure 2 does provide a helpful graphical representation of the non-dominance. **RESPONSE:** OK, left as is. 4. Page 10, Line 21. The second effectiveness measure (cases correctly diagnosed) and associated ICER ($102 per case) is referenced here as though the respective incremental cost-effectiveness data appears in Table 5 but it does not. A second tier to Table 5 should be added or simply a new Table 6. Also the current title does not make it clear that the data refer only to the first effectiveness measure (cases detected). **RESPONSE:** A second tier has been added to Table 5. There were mistakes with some of the numbers ($102 vs $73.2) at this section, and they have been corrected accordingly in Table 5, abstract and manuscript. 5. A cost-effectiveness analysis that terminates in diagnosis of diabetic retinopathy is reasonable. However, text in the Discussion is warranted to address the following: The goal of screening diabetic retinopathy is not simply to diagnosis it. Rather the goal of screening is to diagnosis and then intervene, when appropriate, to prevent severe vision loss. The model does not account for severe vision loss prevented versus occurring with either screening modality. Assuming the associated costs of treatment of diabetic retinopathy and severe vision loss occurring (versus prevented) with each modality are attributed to the public healthcare system (or whichever economic perspective is taken) the conclusion about cost-effectiveness may or may not differ compared to the more "upstream" diagnosis. I am not suggesting that the model be presented differently, but rather that these features of diabetic retinopathy screening be acknowledged in the Discussion as a potential feature or limitation of the current model. **RESPONSE:** Thank you for your comment! The lack of “downstream” analysis was added to the Discussion section (under Limitations).
Reviewer 2	Rory A. Tekanoff
Institution	Urban Care Health Group, Community Medical Programs, London, Ontario
General comments (author response in bold)	My analysis of this paper is based on the conclusion that the intrinsic objectives of the study are two fold; epidemiological reporting and cost sensitivity related to methodology involved in assessing DR (Diabetic retinopathy). Its a complex study, incorporating a number of segments and informational pathways (i.e "model probablities" and "Deterministic Sensitivity Analysis") contributing to the overall completion of the objective. This in itself can be arduous for the reader in interpretation, and I do applaud the authors' attempt to explain their processes to allow "non-experts" to gain some perspective and understanding of the objectives, however for the average reader, it is a very complicated and byzantine effort, which in my opinion may

	be a better suited article for specialized periodicals such as the Journal of Clinical Ophthalmology or Ophthalmic Epidemiology. However, my review included using STROBE guidelines which directed a fair analysis of the article provided for submission for the CMAJ. My comments are directed primarily at more clarity in some areas: The authors utilized a DR screening method which does not reflect the current standard in assessment (live consultation) which will be an introduction to a novel method of assessing DR. Consequently, readers may not have a specific understanding of tele-medicine. The authors should include a more detailed description of the tele-ophthalmology approach in order for the readers to properly assess the comparison to the current methodology in screening for DR. The objectivity of the study would be enhanced. More details on tele-opthalmology should be provided, for those readers who may be naive in this field. -Exactly what it is, what is involved -How its marketed -How its staffed (personnel, level of knowledge, etc.) -What equipment is involved -What role the pharmacy plays -Recruitment methods for tele-screening(how was this marketed to patients in under-serviced areas?) -Number of sites used in the tele-screening arm, and why specifically selected. -Patient population, demographics, etc. should be described. (For example, Aboriginal peoples living in Canada are among the highest risk populations for diabetes and related complications. Community-based and culturally appropriate prevention strategies and surveillance of diabetes indicators among this high risk population are essential to reducing health disparities- CDA Guidelines) **RESPONSE:** All of these questions were addressed in the colored text in the method section. Also, Appendix C was added to provide more clarity about the exact locations and the mobile route. Had this study included a large number of aboriginals with DR in the TOA (Tele-Ophthalmology Arm), the cost effectiveness numbers may have been affected, based on a greater number of DR patients seen, and the resulting in a greater positive diagnosis. It is unclear from this paper as to what types of patients were included. I would like to see a more specific example either in descriptor or graph form of patient demographics for clarity. **RESPONSE:** These questions were addressed in methods section (under the Decision-Tree Model and Study Interventions). This study focused on general population only. Although 3.7% of the area population has an aboriginal identity, we assumed they were not reached by this program. Such population would have the most benefit with a TO program culturally tailored to their communities and specifically directed to reserves, as opposed to a municipal pharmacy-based program. -Role of pharmacy and/or pharmacist (since pharmacy is the assigned vehicle for the mobile intervention?) **RESPONSE:** Addressed in methods section (under Characteristics of a tele-ophthalmology program and TO Model). Additionally: - It is difficult to ascertain from the publication the time frame of the study and EXACT numbers of patients involved. **RESPONSE:** Table 4 provides the information on the exact number of patients involved in the base case analysis, in both the in-person arm and the TO arm. The time frame is specified in the methods section, as a 12-month time frame (the last line of Method, Decision-tree model and study interventions). Perhaps the table headline is a little confusing, but based on the 2011 census estimates of number of people over age 15 and the DR incidence rates in Ontario, we estimate our target population at the start of the program would be 10,354 patients who are over age 15 and diabetic. - Descriptions of graphs and figures should be clarified. Figure 1 for example, has little value in the article, as the tele-ophthalmology arm does not show the progression of assessment beyond the "Introduction". This would bring great value to the reader if it were included to provide a clear comparator to current assessment methods. Without revision, I would recommend figure 1 be removed as

	it brings no contributive importance to the article. **RESPONSE:** Agree. The full decision model (Figure 1) has been moved to the appendix A. In summary: I would recommend a thorough review of the article to include more specifics as outlined above to bring a level of clarity and understanding which healthcare providers who are not experts in ophthalmology, epidemiology and cost-analyses. Contrarily, this study may be better suited for more specific disease journals.
Reviewer 3	R. Liisa Jaakkimainen
Institution	Institute for Clinical Evaluative Sciences and Sunnybrook Health Sciences Centre, Primary Care Research Unit, Toronto, Ont.
General comments (author response in bold)	Overall a well conducted cost-effectiveness study comparing screening programs for the detection of diabetic retinopathy amongst people with diabetes living in semi-urban centres. I think this has relevance for policy and decision makers. My comments mostly relate to minor revisions which I believe would make the paper easier to read. Minor Revisions 1. There are terms that make the abstract difficult read. For example, "Modified Airlie House Classification" may be obvious to ophthalmologists, but for a general medical audience it took a few pages into the study to realize this was a classification system for diabetic retinopathy. **RESPONSE:** Thank you. 2. Similarly, it is sometimes referred to as pharmacy-based tele-ophthalmology or tele-ophthalmology or mobile tele-ophthalmology and I think some consistency would read better. In fact a brief description of the personal needed for the mobile pharmacy-based tele-ophthalmology would help in understanding its costs. **RESPONSE:** they have all been changed to one term consistently (using Tele-ophthalmology with the abbreviation of TO). A brief description of the personal has been added under the "Characteristics of a TO program". 3. Page 5, third paragraph health is missing an "L". **RESPONSE:** Thanks, changed. 4. References need to be updated. For example reference to a meta-analysis is made (number 22) yet it says submitted in 2013. **RESPONSE:** References were updated and more references were added. 5. Not sure the equation is necessary? More important is the sources used to estimate screening rates etc. It good they are Canadian sources. **RESPONSE:** The equation was moved to the Appendix B. 6. Table 2 may be easier to understand is the costs associated with in-person vs mobile pharmacy based tele-ophthalmology are presented separately. Also, I can't see a cost for pharmacists? There was a mention that they may administer eye drop, but not sure a cost was associated with this? **RESPONSE:** "The pharmacist fee" was not listed in Table 2, but the estimated fee of the pharmacist involving in this study has been incorporated in the fee of "coordinator and ophthalmic photographer". Thus the final outcome of our study shall remain the same. 7. There is also a mention of Appendix K which I can't see in the paper. **RESPONSE:** "Appendix K" was mentioned in Table 2. The wording of Appendix K was removed from the Table 2. 8. Are there costs associated with letting patients or primary care physicians know about the service? Or is it assumed this would be an equal cost? **RESPONSE:** Recruitment method was revised in the Method section (under Our TO Model). Similarly cost was revised in the Method section (under Identification and Calculation of Model Costs). It was assumed recruitment would not incur additional costs compared to in-person examination. 9. I am not sure what cost difference there is with an "introduction" versus existing tele-ophthalmology DR screening? Is it just the capital costs of purchasing equipment? How long would they last or need upkeep? In other words, I can't see what the

	difference in cost between introducing the program versus maintaining the program are. Declaration of competing interests: I have no financial competing interest. I have not collaborated on research projects with any of the authors. **RESPONSE:** The "introduction" would require capital cost purchasing which is not necessary during maintenance. We have considered "maintenance" fee of $460 annually showed in Table 2.