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Title	Dose response of sodium glucose co-transporter-2 inhibitors on urinary tract infections: a systematic review and network meta-analysis of randomized controlled trials
Authors	Jennifer R. Donnan BScPharm MSc, Catherine A. Grandy XX XX, Eugene Chibrikov PhD, Carlo Marra BScPharm PharmD PhD, Kris Aubrey-Bassler MD, Karissa Johnston PhD, Michelle Swab MLIS, Jenna Hache XX XX, Daniel Curnew XX XX, Hai Nguyen PhD, John-Michael Gamble BScPharm PhD
Reviewer 1	Kerry Mansell
Institution	Division of Pharmacy, University of Saskatchewan, Saskatoon, Sask.
General comments (author response in bold)	<p>Thank you for allowing me the opportunity to review this manuscript. Overall, I think the study was well performed and described. The results you displayed with dapagliflozin are similar to what has been described previously (a study published June 2018 found similar findings with respect to UTIs), and this review, although newer and larger than Liu et al in 2017 which included studies >12 weeks, did not significantly add novel information. Overall, It does appear as if your study was well conducted.</p> <p>Thank you for the positive feedback. This paper was originally submitted to CMAJ in March 2018, prior to the June 2018 publication. We have updated the manuscript to include reference to this newest meta-analysis (page 7). Despite being a very recent publication the study published in June 2018 (Puckrin et al), it only included 86 studies while ours included 106, therefore we still feel this update provides some important update as well as discuss in more detail the specific relationship between dose and UTI.</p> <p>There are some grammatical mistakes and odd sentencing in the introduction which do not appear elsewhere, almost giving the appearance that this section was written by one author while another author wrote the rest of the manuscript. This section should be proof-read again. I would also make mention in the intro that the manufacturer-provided product monographs of these products state that these products confer increased risk and have had post-marketing reports to help frame your intro. In addition, as you consider space issues, I am unsure if table 1 is necessary - if you have room to use it, then fine, but if space is an issue you may look at if you think this is necessary.</p> <p>Several grammatical errors were corrected, and reference to the product monographs was added. – Page 3</p> <p>You describe your risk of bias, but make no mention of how you used this or planned to use this in your analysis. As an example, I see no mention in the discussion about potential publication bias or any further mention other than what you describe in the methods.</p> <p>An additional sensitivity analysis has been added to include only studies that were considered to have an overall low risk of bias (page 5, page 7, online appendix), additionally funnel plots were also generated to assess for publication bias (page 3, page 7, online appendix)</p> <p>From what I could see, there was 1 study that was included that had sotagliflozin. As this is an SGLT1/2 inhibitor, you should remove this study and re-do your analysis, or change the title and description of your study so as to acknowledge the combined mechanism of action of this drug that makes it different than the others.</p> <p>Thank-you for picking up on this oversight. The study with sotagliflozin was excluded, and the inclusion criteria was clarified by indicating that combined SGLT1/SGLT1 inhibitors were excluded. – Page 4</p> <p>In the results section, when describing Cana low dose, you refer to Table 1 - I wonder if you mean the reader should be directed to Figure 1A (or elsewhere?) as table 1 describes UGE from what I can tell.</p> <p>The table reference was incorrect, it should have been Table 2. – Page 6</p> <p>Also, you make mention of drawing attention to low-dose canagliflozin in your results. You state that most comparisons found insignificant change except "...low dose canagliflozin compared to active comparators". Yet explanation around its confidence intervals or even any mention at all is not made around this result you reported on in the discussion section. If reporting it as a significant change in the results, you should make mention of this in your discussion.</p> <p>A sentence in the interpretation has been added to highlight the fact that there is no current data to support any speculation of increased risk of UTIs with low dose canagliflozin. (page 7).</p> <p>Nice description of some certain limitations. Thank you.</p>