

PEER-REVIEW REPORT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 78556

Title: Potential for the use of Sodium Glucose Cotransporter 2 Inhibitors in the Management of Metabolic Syndrome: A Systematic Review and Meta-analysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05391966

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-07-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-03 09:51

Reviewer performed review: 2022-07-06 04:33

Review time: 2 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This manuscript was well prepared, and the content was interesting to readers, the analysis results could also support the conclusion. I recommend the acceptance after minor revision. Some minor concerns are as followed. 1. The Figure a, b, c...could be revised as Figure 1, Figure 2.... 2. The reference style should revise according to the guideline of BPG.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03940498

Position: Editorial Board

Academic degree: PsyD

Professional title: Academic Fellow, Professor

Reviewer's Country/Territory: Poland

Author's Country/Territory: United States

Manuscript submission date: 2022-07-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-02 08:25

Reviewer performed review: 2022-08-05 07:21

Review time: 2 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The study raises an important issue in the clinical practice. Thus the effort to drive the conclusions from various studies in the field are of praiseworthy quality. The major concern is the fact that MetS is regarded by the Authors as one homogenous feature. In my understanding, this is not the case as the metabolic syndrome accompanies various medical conditions, including medications' side-effects. Therefore one should rather consider the MetS as a heterogenous entity. This raises the question why the treatment with flozines was introduced to all patients? It is hard to believe that numerous patients included in the studies cited were diagnosed with the same disease and therefore treated with only two medications. For instance the CV diseases include many different conditions. Thus the suggestion is to describe in details the groups of patients included in studies which underwent the revision.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05459871

Position: Peer Reviewer

Academic degree: PhD

Professional title: Adjunct Associate Professor

Reviewer's Country/Territory: Saudi Arabia

Author's Country/Territory: United States

Manuscript submission date: 2022-07-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-01 07:21

Reviewer performed review: 2022-08-09 23:38

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

Comments to the Author Reviewer Summary and General Comments This manuscript aims to evaluate the impact of SGLT-2 inhibitors on MetS and its components. It is based on placebo-controlled RCTs that evaluated the impact of these drugs on cardiovascular disease and its risk factors, as well as on pre/post treatment values of MetS components. The contribution of these results to the literature is very important given the limited and conflicting data that address this topic. However, there are some points that are unclear and should be clarified prior to the publication of this study. Please see the list by section below:

General Concept Comments Great confusion: The authors selected RCTs reporting baseline and posttreatment values of ≥ 1 MetS component, however, they stated in the discussion that MetS was considered defined by NCEP ATP III criteria. In my opinion, this study addresses all MetS-related biomarkers, not just those defined by NCEP ATP III. Several clarifications are needed. Many abbreviations have been used. The authors should limit themselves to those that are commonly used. The discussion section requires extensive review. Authors should describe, analyze and interpret their main results. They should also explain the significance of their results and bring it back to the research questions and not just replicate what exists in the literature. The citation of references in the text needs to be revised. The language requires extensive review by a native speaker. Note: Continuous line numbers have been added to the manuscript.

Specific Section Comments Abstract Line 33 - cardiovascular disease (CVD) or cardiovascular (CV) disease. Please change. Line 35 - DM. Please add the full name. Please provide information about the retained randomized controlled trials in the methods section. Please include the analyses conducted on the data in the

methods section. Introduction Lines 63-65 – Please add reference (s). Line 67 – Table 1? I can't find it in the manuscript. In my opinion, it is best to summarize the definition of MetS in a few sentences. In addition, there are several different definitions of MetS, leading to considerable confusion as to whether they identify the same individuals or represent a proxy for risk factors. A number of factors other than those traditionally used to define MetS that are related to the syndrome were also identified (Kassi et al., 2011). The authors should give readers a brief explanation of MetS and all the components used to define it. METHODS Data sources and searches: Please briefly describe all steps taken until the final list of studies is obtained. Please insert the flow chart in the manuscript. Please move the names of the authors from the text to the "Author Contributions" section. Line 97- FM: You mean Farouk Mookadam? Lines 102-106 – Each abbreviation must be mentioned the first time the full name appears in the text. Line 105 – “All outcome data were reported as mean with standard deviation and were converted to conventional units” Please move it to the Data Analysis section.

Line 107 – Quality Assessment: To assess the quality of open-label randomized controlled trials, the use of the Jadad standard is not recommended and the Cochrane risk of bias tool was considered more appropriate (Ma et al., 2012). The authors did not indicate whether or not this type of RCT was evaluated; if so, they should at least mention it as a limitation of the study. Line 112- Please add “and” before BP. The primary, and BP. RESULTS Search results and study inclusion: Please move this paragraph to the “Methods” section. Line 129 - Figure 1? I can't find it in the manuscript. Lines 129-130 – Of these, 3 studies reported WC..... Please add the reference numbers of these studies. Line 133 – Please add the number of participants in each study (smallest - largest). Line 137 – Same remark as above (short duration - long duration). Line 138 – Same remark for age. Lines 144, 154, 165, and 170 – Please add the reference numbers of these studies. Line 174 – TGL is commonly used



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as a biomarker for MetS. Do the authors have an explanation for the absence of data regarding this parameter? Line 178 - HbA1C and UA are among the MetS biomarkers, but as far as body weight is concerned, I don't think so. Please justify your choice. DISCUSSION Line 198 - This is the first time the authors have stated that MetS has been considered as defined by NCEP ATP III. This statement is not in line with what is mentioned above (line 93). The authors should either limit themselves to the 5 criteria used by NCEP ATP III or delete this sentence and refer to the components of MetS. Lines 209 - In contrast to other studies [43] [44] [51]..... Please delete "other".

Lines 235-256 - This is a simple citation of what exists in the literature. The authors should limit themselves to discussing their main findings.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05459871

Position: Peer Reviewer

Academic degree: PhD

Professional title: Adjunct Associate Professor

Reviewer's Country/Territory: Saudi Arabia

Author's Country/Territory: United States

Manuscript submission date: 2022-07-03

Reviewer chosen by: Xiao-Fang Liu

Reviewer accepted review: 2022-09-19 20:38

Reviewer performed review: 2022-09-22 11:04

Review time: 2 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Authors are invited to correct some grammatical errors.