Reviewer’s report

Title: Prevalence of potential drug-drug interactions and associated factors among outpatients and inpatients in Ethiopian Hospitals: a systematic review and Meta-analysis of observational studies

Version: 0 Date: 27 Apr 2020

Reviewer: Mary Carpenter

Reviewer's report:

Background

General comments
Would re-write background. It seems to be all over the place. The beginning introduces DDIs with classifications and severity levels, and potential effects, but the rest of the background is jumping all over the place-risk factors for DDIs are mentioned several times (paragraph 5, 9, 15). Would describe DDIs, then discuss the major reasons DDIs occur (patient characteristics (age, common disease states, polypharmacy, etc), prescriber issues (multiple prescribers including primary care provider and specialists managing a patients regimen, "alert fatigue"- see below for comment re: "alert fatigue"), impact of hospitalization. Describe the impact on economy and healthcare. Then tie in data re: DDIs in Ethiopia and the reason for this study. Would mention "alert fatigue". Several issues have been addressed in the background, but a very common reason for patients receiving interacting drugs is physicians and pharmacist alert fatigue was not mentioned. - Could maybe incorporate this into page 3, paragraph 6.

Page 3, paragraph 2 (lines 21-23)
Would re-word to say: "DDIs can be categorized by severity. Major DDIs may be life-threatening or may cause prolonged or permanent damage. Moderate DDIs may require medical intervention or change in therapy, whereas minor DDIs do not usually require a change in therapy. Regardless of the DDI severity, patient's should be monitored for possible manifestations of the interaction." 

Page 3, paragraph 4 (lines 25-31)
Would re-word this paragraph. The way this sentence is currently worded is confusing and is a run-on sentence.

Page 3, paragraph 5 (lines 34-45)
"The possible reasons behind include older age, multiple drug regimens, PK or PD nature of drugs used in cardiology, and the influence of heart disease on drug metabolism."- this sentence is taken directly from the reference article (Diksis et al, 2019). Would re-write in different wording. Last reference in this section (Haftay Berhane Mezgebe et al, 2017) is not in listed references. Would also consider mentioning patients with renal and hepatic insufficiency (CKD, cirrhosis, etc) can have a significant effect on severity of DDIs- you only mention HIV, cardiovascular disease, and psychiatric patients as being most common disease states with reported DDIs. Would look into this more.
Methods

Page 6, line 29
Exclusion criteria- not clear why studies that were conducted in primary health care settings were excluded as one of your inclusion criteria was patients who had any disease and were outpatients?

Page 7, lines 20-28
Would include the details of the 12 quality scores.

Results

Page 20, lines 6-10
Should the CI be reported as % or decimal number?

Discussion
Page 21, line 22
Are you able to make the assumption that 2.67 potential DDIs were found in one patient?"

Page 21, line 55
"almost all HIV infected patients…” Would provide the percentage since the percentages for the others listed were included.

Figures/Tables

Page 13, Table 3
Were the classifications of severity defined the same between studies (i.e., how did each study classify major, moderate, minor?). This is a potential limitation of this study.

Page 19, Table 6
Would add a column for "mechanism of DDI" (i.e., PK, PD, both, unknown)
Would add a column for "effect of interaction" (example: simvastatin+clarithromycin: Increased statin concentration)
Would add a column for "Recommended Monitoring" - this will be helpful for providers reading this article. Example: clarithromycin + simvastatin: monitor for evidence of simvastatin toxicity (e.g., muscle aches or pains, renal dysfunction, etc.)

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess
Are the conclusions drawn adequately supported by the data shown? 
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? 
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English 
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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