Reviewer's report

Title: Association between anthraquinone laxatives and colorectal cancer: protocol for a systematic review and meta-analysis

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Reviewer: Samuel Abariga

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Comments

Abstract

Page 2 Line: 13 reads "As no firm evidence exists to the potential association between the CRD42019125414 of…” please fix error

Background: The proposed mechanism by which AQs may exert a laxative effect and cause damage to epithelial cells is not convincing enough. What specific compound in AQs are responsible for this mechanism? And via what cellular path ways do they affect this? Sodium or potassium channels or cyclic AMP? Etc. The evidence from this review will be of interest to both experts in the field of oncology and lay people alike. Hence the need to have these groups of consumers in mind.

Methods?

Any reason why authors choose to exclude clinical trials and randomized controlled trials? These are the highest form of evidence if you are looking for safety (although real world evidence from observational studies in the long term is important). You can only settle on observational studies if no clinical trials are found or evidence from trials found no adverse events (understandable due to their often-short duration of follow up and lack of latency). But to ignore these designs from the get-go is not advisable. Any evidence adduced in the end, in the absence of contribution from clinical trials, will be weak. Under data items, authors intend to collect information on randomization and blinding yet this type of study design are excluded in their study selection criteria outline about. Any reason why the Newcastle-Ottawa Quality Assessment Scale is used instead of the Cochrane ROB tool for non RCT?

Unit of analysis is unclear. Each intervention deals with participants. Therefore, your unit of analysis is participants as opposed to a body part of participants such as (eyes or teeth of participants) assuming these were the units the interventions were applied.

Authors should consider including RCTs. There appears to be no restriction to the timing of outcomes. This need to be set a priori judging from prior studies, the reasonable time points within which adverse events could have occurred. For instances, if a participant takes AQ and
after two weeks, receives a diagnosis of CRC would you attribute this to the consumption of AQs?

**Level of interest**
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

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

Needs some language corrections before being published

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