Reviewer’s report

Title: Interactions of clinical relevance associated to concurrent administration of prescription drug and food or medicinal plants: a systematic review protocol

Version: 0 Date: 05 Mar 2019

Reviewer: Jessica Farebrother

Reviewer's report:

Many thanks for inviting me to review the current manuscript, "Interactions of clinical relevance associated to concurrent administration of prescription drug and food or medicinal plants: a systematic review protocol".

This manuscript describes the protocol for a forthcoming systematic review, which is registered on PROSPERO, no. CRD42018117308, dated 13 December 2018.

The aim of the planned systematic review is to synthesise the current literature on pharmacological interactions associated with drug administration concurrent with food or medicinal plants in all population groups. The focus of the review will be given to clinical characteristics of adverse reactions and the characteristics associated with safety issues.

Given the general health importance of potential adverse drug reactions (ADRs) and adverse drug-food or drug-plant reactions (ARs), potential for loss of therapeutic efficacy during pharmacological treatment, potential for additional health service cost, and most importantly, potential for harm or loss of life due to ADRs and ARs, the proposed systematic review is of much interest to this field of public health, and may inform and raise awareness to relevant healthcare providers (doctors in hospitals or in community service, pharmacists, dieticians, nutritionists) of the possible harm that could be incurred as a result of inappropriate combinations of therapies and foods.

Some thoughts:

There is already quite a lot known about ARs across certain pharmaceutical agents, certain foods, and certain herbs. Medically-trained personnel should have some knowledge of most of these interactions, therefore I disagree with the statement that information on drug-food/herb interactions is not widespread.

However, maybe what is lacking, is a better dissemination of this information across "all healthcare settings"? This could include different country settings, different levels of prescriber training, different levels of prescribing (i.e. drug therapy initiated by a prescriber or lay person), and how the food or herb is being used, e.g. as traditional medicine or simply as foodstuffs, etc.
This presents a large playing field, and my concern is that the proposed review, based on the presented protocol, will not properly capture all these differences.

Specific comments:

Major revisions:

The background of the current manuscript, and justification to this systematic review makes too many claims. The resulting systematic review - as with all reviews - can do no more than inform relevant stakeholders. I would advise to tone down the language.

Suggestions:

The protocol could benefit from being more specific:

- Prescription drugs "of interest" - maybe be specific and explain the choice. As written, the list could include the entire pharmacopoeia.
- Will vulnerable population groups e.g. pregnant or lactating women be included?
- Will heterogeneity between studies be assessed somehow, even though the summary will be narrative?
- Study limitations - will these be assessed using JBI checklists?
- Limitations of selected studies will be deeply discussed (line 297-8) - why only selected studies and not all studies? If just selected studies, how will these studies be selected?
- Unless otherwise clear in the literature, how will you distinguish between the specific disease name when the drug has more than one indication?
- How will the narrative review be structured? Can you define this in advance?

Lines 307-309: "...to date, there is no review on clinical characteristics and safety issues related to concurrent drug administration with food or plants..."

Some reviews (e.g. Deng et al (reference 24), and Ased et al., doi: 10.4140/TCP.n.2018.649) have been published, though are perhaps not exactly what the authors are proposing. The authors may wish to be clearer in describing how their systematic review will be different though complementary to the existing literature.

Finally, the PROPSERO registration states a 5-year turnaround for this review. Do you intend to re-run the searches before final manuscript submission?
With best wishes.

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