Reviewer’s report

Title: Inappropriate Medication Use among the Elderly: a Systematic Review

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Reviewer: Paul F Gallagher

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1. General Comment:

Inappropriate medication use in the elderly is a very important public health issue and efforts to identify and reduce the prevalence of inappropriate medication use have been the focus of much research to date. This study is well written and nicely presented.

The title of this study implies that the authors have conducted a systematic review of inappropriate medications use among the elderly. Indeed the axes of study mentioned in the methods section i.e. “prevalence, interventions and outcomes” lead the reader to believe that a comprehensive systematic review is being presented. However, the authors have really only conducted a review of the reported prevalence of inappropriate medication use in a highly selected cohort of community-dwelling patients using select criteria and specific “secondary” reporting mechanisms (thereby compromising and limiting the prevalence estimates). It is misleading to say that this study is “a systematic review of inappropriate medication use among the elderly” as it does not apply to all elderly people and does not include all methods of identifying inappropriate medications, related interventions and outcomes. The purpose of a systematic review is to (a) frame a precise question for review; (b) systematically identify relevant work; (c) assess the quality of the relevant work; (d) summarize the evidence (data synthesis and meta-analysis or subgroup analysis) and (e) interpret the findings and generate inferences / recommendations according to the strengths and weaknesses of the available evidence. It is the opinion of this reviewer that this study does not achieve these objectives in its current format and therefore cannot be labelled as a systematic review. Because of these serious limitations, it is unclear to this reviewer what this study adds or contributes to the existing literature.

2. Abstract:

(i) Why did the authors exclude rural populations? Did the studies which were selected for the review only include community dwelling older people residing in urban areas? Why is it necessary to distinguish between urban and rural community-dwelling older patients?

(ii) The authors should inform the readers in the abstract that only 19 of 338
studies were selected for review. This will allow the reader to see that the results presented in this study were based on data reported by a relatively small number of studies i.e. it is a limited review.

3. Background:

(i) The sentence “In developing countries, medication use also increases with age, with 85% to 90% prevalence observed” is unclear. Over what age is this prevalence observed?

(ii) The authors should give an example of how pathophysiological changes influence pharmacokinetics and pharmacodynamics in order to inform the reader of the clinical relevance of careful considered medication selection in older people.

(iii) The sentence beginning “Inappropriate medication use by the elderly has quantitative and qualitative aspects relating….” is difficult to understand and should be revised. The statement should be supported by clinical examples. The introduction section should provide the reader with examples of why inappropriate medication use is such an important public health issue e.g. is there an association between inappropriate prescribing and ADRs, hospitalization, institutionalization, functional decline, resource utilization etc. Does the everyday clinical application of criteria for inappropriate medication use impact on clinical outcomes for patients?

(iv) The authors should give examples of implicit criteria and explicit criteria other than Beers criteria. Why did the authors choose to exclude studies based on implicit criteria from their review?

(v) The authors should provide a reference to support the assertion that a “knowledge of inappropriate use can improve pharmacotherapy among the elderly…”. Has this assertion been proven? If so, why is the prevalence of inappropriate prescribing so high despite the availability of criteria for inappropriate medication use for >20 years?

(vi) The authors state that the aims of this review are to identify and describe studies of inappropriate medication use among elderly people resident in the community. However, they exclude rural community dwellers and exclude data sources other than those provided by insurance company and social security administrative databases i.e. secondary data sources. This is a major limitation in drawing conclusions on the prevalence of potentially inappropriate medication use in older populations. Such data are usually retrospective, lack clinical detail (thereby excluding drug-disease interactions) and do not take into account previously tried/failed treatment options or patient choice.

4. Methods

(i) The limitations of the search criteria limit the ability of this paper to provide “a systematic review of inappropriate medication use among the elderly”. Why was “aged not frail elderly” chosen? Why were frail elderly community-dwelling older
people excluded? What are the reasons behind all exclusion criteria? Why were studies without abstracts excluded? The authors state that the axes of the search equation were “population, intervention and outcome” yet none of the search terms pertain to intervention or outcomes. The authors do not present any results that pertain to the use of inappropriate prescribing criteria as an intervention or on the outcomes of using such drugs. It would appear that the authors have only conducted a review of the prevalence of inappropriate medication use in a highly selected group of studies based on secondary data sources. This is a major limitation and emphasizes the somewhat misleading nature of the title of this study.

(ii) How did the authors assess the quality of the studies? Was there a minimum acceptable level of study design? Was heterogeneity explored? How were decisions made regarding suitability for meta-analysis? Were data pooled? Was sub-group analysis performed?

(iii) The authors mention that “data were extracted from selected articles … using a previously tested instrument”. What was this instrument? Is it valid and reliable? How was consensus achieved when discussing contentious issues with a third author – was this systematic according to pre-defined parameters?

5. Results

(i) The authors state in the methods section that they excluded criteria that had been “adapted”. In the results section, the authors state that “12 of the 14 studies using Beers criteria adapted the criteria to restrict them to inappropriate drugs regardless of dosage or specific clinical conditions or even to drugs available in the country of study”. This is inconsistent and in the opinion of this reviewer, these constitute significant adaptations that would clearly impact on the measurement of the prevalence of inappropriate medication use. It is well established that studies which limit their measurement of inappropriate medication use to criteria “independent of diagnosis” underestimate the prevalence of inappropriate medication use by excluding highly prevalent and important drug-disease interactions in older people e.g. benzodiazepines with falls, calcium channel blockers with constipation, vasodilator medications with orthostatic hypotension etc.

(ii) For the benefit of the reader, the authors should briefly allude to the key differences between Beers, Zhan and HEDIS criteria (mentioned in table 1).

(iii) The results section does not allude to “intervention and outcome” axes as mentioned in the methods section.

(iv) The authors describe the analysis of factors associated with inappropriate medication use i.e. female gender, age and number of drugs. This information is already published. The authors have not gone beyond this (i.e. meta-analysis). They have not truly analysed or commented on the strengths or weaknesses of these studies in the context or their research question.

6. Discussion
(i) The subgroup analysis presented in the discussion section should be presented in the results and the methodology should be described in the methods section.

(ii) The authors should discuss the limitations of secondary databases as mentioned above.

(iii) The authors conclude that “Educational measures contribute to improving pharmacotherapy”. This statement cannot be concluded from this review as interventions to improve pharmacotherapy were not evaluated. The authors should support such statements with references.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.