Peer Review Report

Review Report on Polypharmacy in older adults: the hazard with hospitalization and mortality is mediated by inappropriate prescriptions, findings from the Moli-sani study

Original Article, Int J Public Health

Reviewer: Vittorio Simeon Submitted on: 05 Aug 2024

Article DOI: 10.3389/ijph.2024.1607682

EVALUATION

Q 1 Please summarize the main findings of the study.

In this manuscript entitled 'Polypharmacy in older adults: the hazard with hospitalization and mortality is mediated by inappropriate prescriptions, findings from the Moli-sani study' the authors examined the impact of polypharmacy on health in community-dwelling older adults. The study is based on the cohort of the Molisani Study, which was randomly recruited among the residents in the Molise region. Polypharmacy has been categorized as chronic polypharmacy therapy (≥5 therapeutic groups and >2 daily defined doses) or non-chronic polypharmacy therapy (polypharmacy but ≤2 daily defined doses), while the mediating role of the potentially inappropriate prescriptions -PIP- (by Beers' criteria) was examined. The authors concluded that polypharmacy is associated with a higher hazard of mortality and hospitalization, with PIPs playing an important role. This is an interesting work on an interesting topic and, in my opinion, there are some minor suggestions to consider.

Q 2 Please highlight the limitations and strengths.

The work is really well done, based on a very large cohort and with measurements carried out methodically and rigorously. Like all cohort studies, it suffers from the classic limitations of observational studies, especially in the difficulty of identifying the causal path between the expection of interest and outcome. The authors have carried out a series of analyses to try to minimise these problems.

Please provide your detailed review report to the authors. The editors prefer to receive your review structured in major and minor comments. Please consider in your review the methods (statistical methods valid and correctly applied (e.g. sample size, choice of test), is the study replicable based on the method description?), results, data interpretation and references. If there are any objective errors, or if the conclusions are not supported, you should detail your concerns.

Minor points

- Please report specifically on the reasons for the potentially inappropriate prescriptions. In the results, there is the overall frequency following Beers' Criteria but it would be useful and interesting to understand how this total breaks down into the various criteria proposed (e.g. drug interactions, renal impairment).
- Demographic and lifestyle characteristics by polypharmacy are shown in Table S2. It emerges that there are also differences concerning education, social class, and SES in childhood. In the various models, these variables are not taken into account for possible adjustment.

Discuss this motivation, whether it could be an error, and possibly carry out additional analyses with a factor encompassing the educational and socio-economic status of the subjects. The hypothesis is that these factors may be determinants of adherence to therapy, another aspect that could influence success and clinical outcome.

_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_
T	•	2)	۲1	ti	n	C	1/	/t	У	/ľ) i	r	10	7	ŗ) ľ	(ol	o	le	21	r	15	5

- It is not always well reported whether the chronic group is greater than 5 or greater/equal to 5. See for example between abstracts and methods.
- Review the legend of table S5, there is an error in the sequence model 2 model 3.

PLEASE CO	DMMENT
Q 4	Is the title appropriate, concise, attractive?
Yes	
Q 5	Are the keywords appropriate?
Yes	
Q 6	Is the English language of sufficient quality?
Yes	
Q 7	Is the quality of the figures and tables satisfactory?
Yes.	
Q 8	Does the reference list cover the relevant literature adequately and in an unbiased manner?)
Yes	
QUALITY A	ASSESSMENT
Q 9	Originality
Q 10	Rigor
Q 11	Significance to the field
Q 12	Interest to a general audience
Q 13	Quality of the writing
Q 14	Overall scientific quality of the study
REVISION	LEVEL
Q 15	Please make a recommendation based on your comments:

Minor revisions.