JAMDA xxx (2022) 1

JAMDA

journal homepage: www.jamda.com

Letter to the Editor

An International Consensus List of Potentially Clinically Significant Drug-Drug Interactions in Older People: Clinical Utility?

We thank Dr Lisi for her interest in our article[1] and we are pleased to provide some additional information and clarifications in relation to their comments.[2]

First, as described in the methods, the literature review focused on identifying existing explicit lists (also referred to as explicit tools) of DDIs in the older people. These lists could be drawn from literature reviews and/or from original research using consensus-based approaches (eg, Delphi, RAND/UCLA method). Eleven explicit lists were identified and are presented in Table 1 of the article, among which 9 were developed using consensus-based methods. All individual DDIs from these lists were extracted and included in the next evaluation steps. Although potentially relevant, it was beyond the scope of our work to review and grade the evidence base behind each DDI.

Second, we appreciate that it might be complex to track the data, given that some DDIs were merged or split in order to maximize relevance for clinicians. We did not report each individual merge or split in a specific table because we doubted the value and relevance of doing so. However, we provided all results for each of the 3 rounds in the supplementary tables, and in contrast to Dr Lisi's statement, there are no additional revised scores to report on. It is then still possible to track what DDIs were merged or split by comparing subsequent Supplementary Tables S1 to S3. The 50th percentile or median is provided for each DDI evaluated during rounds 1 and 2 (see Supplementary Tables S1 and S2).

Third, it is correct that adding up all DDI pairs from the 11 explicit lists total 241 DDIs. However, as mentioned in the method, there were some overlap between lists—which is reassuring—and we merged DDIs that overlapped in order to avoid reporting duplicates. For example: "Digoxin + macrolides," "Digoxin + Erythromycin," "Digoxin + Clarithromycin." In this case, 3 DDIs were restated in "Digoxin + Macrolides."

Fourth, it is true that many DDIs involve drugs that are rarely used in clinical practice in many countries. This issue was discussed among research team members when preparing the protocol, and it was decided to keep all potential DDIs involving medications that are still available on the international market. This point was addressed in the instructions for the panelists: "the frequency of use of the drug in your practice should not be taken into account in your assessment." As explained in the discussion, we believe it was relevant to have included them because clinicians may be less aware of these DDIs because of infrequent use. Furthermore, there can be significant differences in prescribing patterns across countries. Our approach, therefore, enhances external validity for countries who may have limited access to more recent medications.

As for any DDI, the route of administration can impact clinical significance. DDI-58 refers to the use of ciclosporin for prevention or organ rejection, so this DDI does not apply to the use of ophthalmic ciclosporin and this was also not included in the ATC codes used to detect DDIs.

Lastly, there might be many factors that will influence the clinical relevance of DDIs in older adults, including among others genotype/phenotype. There are still many barriers to the routine use of genetic tests in clinical practice, and yet having access to such data will not prevent clinicians from identifying DDIs in their patient.

For all these reasons, we disagree with Dr Lisi that the utility of our DDI consensus list is limited in clinical practice.

References

1. Anrys P, Petit AE, Thevelin S, et al. An international consensus list of potentially clinically significant drug-drug interactions in older people. J Am Med Dir Assoc 2021;22:2121–2133.e24.
2. Response to "An International Consensus List of Potentially Clinically Significant Drug-Drug Interactions in Older People." J Am Med Dir Assoc 2021.

Pauline Anrys
Anne Spinewine
Clinical Pharmacy Research Group (CLIP)
Louvain Drug Research Institute
Université catholique de Louvain
Brussels, Belgium

https://doi.org/10.1016/j.jamda.2021.11.038