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What Types of Inappropriate Prescribing Predict Adverse Drug Reactions in Older Adults?

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Abstract

Adverse drug events happen all too often in older adults, but we still do not have a clear understanding of potentially modifiable risk factors, with the exception of polypharmacy. This paper critiques the article in this issue of *The Annals* entitled, “Inappropriate Prescribing Predicts Adverse Drug Events in Older Adults.” A validated measure for self-reported adverse drug events was used, along with a modified measure for inappropriate prescribing that we developed nearly 2 decades ago (ie, Medication Appropriateness Index). Besides discussing the strengths and weaknesses of this article, we also recommend future research directions in this area.

Keywords

adverse drug events; aged; medication errors

In this issue of *The Annals* is an important article that examines the predictive validity of both an explicit and implicit method to relate inappropriate prescribing with adverse drug events (ADEs) in older adults.¹ This study is important for several reasons; one is that there are limited data regarding self-reported ADEs in elderly community-dwelling or outpatient clinic populations, with yearly rates ranging from 10% to 35%.^{2–6} The authors found a self-reported ADE rate of 14% in 240 older outpatient veterans, which is consistent with these previous studies.¹ The accuracy of this finding would be improved if the self-reported ADEs were matched to medical record documentation of ADEs, if 2 clinical pharmacists rated the ADEs and measured their agreement, and if the pharmacists used a standardized causality

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algorithm. Even so, one wonders whether this single question should become a routine part of ambulatory care practice, given that the question is easy to use, reliable, and valid.^{7,8}

The second reason this study is important is that few studies have examined the association between explicit measures of inappropriate prescribing and ADEs.^{6,9} In the Lund et al. study, the point estimate for the risk of exposure to inappropriate drugs as measured by the 2003 Beers criteria for drugs with an ADE was 1.43, but this odds ratio was not statistically significant.¹ We agree with the authors' assessment that this could be due to insufficient power. It is important to note that a recent study by one of the article's authors found a point estimate for the risk of exposure to inappropriate drugs as measured by explicit criteria with an ADE was 1.62, which was statistically significant.⁶ However, only 2 of 6 other studies have found an increased risk of ADEs with exposure to Beers criteria drugs.^{6,9} It is unclear whether the Beers criteria will be updated or whether they will be replaced by modified lists developed by others (eg, Screening Tool of Older Persons' potentially inappropriate Prescriptions criteria, National Committee for Quality Assurance) if they are shown to be consistently associated with ADEs.^{10,11}

A third reason this study is important is that no previous study has examined the association between an implicit measure of 10 types of inappropriate prescribing (ie, Medication Appropriateness Index [MAI]) and ADEs.¹ The authors found, after controlling for age, number of drugs, comorbidities, and study group, that the original MAI scoring did not significantly increase the risk of the occurrence of 1 or more self-reported ADEs. However, they did find that a modified MAI score (reflecting clinicians' assessments of which MAI items are likely to be related with ADEs) did significantly increase the risk of self-reported ADEs. We created the MAI nearly 2 decades ago for the specific purpose of having a reliable, valid measure that would detect change over time in response to a pharmacist intervention as part of a randomized controlled trial.¹²⁻¹⁵ Since then, we and other investigators have confirmed that the MAI has good reliability and face validity and is responsive to change over time in health services intervention trials.⁹ Prior to the Lund et al. study, the only predictive validity testing done with the MAI was a simple bivariate analysis published in *The Annals* over a decade ago showing associations between worse MAI scores and poorer blood pressure control and use of more health services.¹⁶ One might ask why it has taken so long to examine this issue further. As noted by Lund et al., the MAI, while comprehensive, is burdensome, as it can take up to 10 minutes per drug to apply the instrument and it requires a well-trained health professional.

So, what studies are needed to further assess the predictive validity of this implicit measure of inappropriate prescribing? One approach is to test the relationship between the modified MAI as described in the current study and ADEs in larger population samples other than veterans. In addition, studies using larger samples that include older women could determine whether drug-drug and drug-disease interactions that received the largest weights are associated with the greatest risk of ADEs. Finally, the current version of the MAI (last updated in 2010) accounts for over- and underdosing separately. It would be of interest to see whether over- and underdosing, respectively, predict ADEs and therapeutic failure.

The determination of risk for ADEs by measures of inappropriate prescribing is not an easy task. Lund et al. are to be commended for adding to our knowledge of this critically important area of geriatric pharmacotherapy.

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