

Comparing the Tools to Identify Potentially Inappropriate Medications in the Elderly and Future Research Directions

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Commentary

Since they were first introduced over 20 years ago, the Beers Criteria have been a go-to tool for clinicians to identify potentially inappropriate medications (PIMs) [1-3]. The Beers Criteria include drugs to always avoid in those over 65 years of age, drugs to use with caution, and important drug-disease and drug-drug interactions where risk generally outweighs benefit in older adults [3,4]. Having been developed in the United States (US), the Beers Criteria have had limited applicability outside the US [5,6]. In response, several country-specific variations have been developed [1,2]. More recently, the widely regarded Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) was introduced along with its companion tool to address both under- and over-prescribing [7,8].

Our group compared these tools by their prevalence, agreement, overlap, and predictive ability for adverse events in a US-based elderly population published in the Journal of the American Geriatrics Society [9]. The study included evaluation of the 2003 [10] and the updated 2012 [3] versions of the Beers Criteria and the 2008 STOPP [7] Criteria. In the population of 174,275 elderly adults studied, 41.6% were exposed to at least one PIM and 19.7% were exposed to all three [9]. This included a prevalence of 34.1% for the 2012 Beers, 32.2% for the 2003 Beers, and 27.6% for the STOPP Criteria PIM definitions. Predictive validity was evaluated across three separate outcomes: adverse drug events, all cause hospitalizations, and all cause emergency department visits. All three criteria were found to be modestly prognostic of these events with hazard ratios ranging between 2-3 and c-indices of 0.65-0.70 in fully adjusted, time-varying, Cox proportional hazard models [9].

These results are encouraging as they support that these criteria are capable of identifying harmful medications. However, more striking was the lack of agreement and overlap between the criteria and the sensitivity/specificity of the criteria to identify patients with outcome events. The 2012 Beers and the STOPP Criteria agreed on only 64% of PIM exposed individuals. Further, the 2012 Beers criteria had a sensitivity of 60.6% for the composite outcome and specificity of 73.9% while the STOPP had 53.4% and 80.2%, respectively. Based on the lack of substantial agreement between the Beers and STOPP Criteria, each criteria missed opportunities to identify important adverse outcomes. Our primary conclusions were that 1) the Beers and STOPP Criteria can be used complementary to increase sensitivity to detect adverse outcomes and 2) future updates to the individual Criteria should learn from each other to broaden and strengthen the evidence-based PIM criteria [9].

As with any guidelines for patient care, particularly those which identify a list of medications, the document can quickly become outdated as new evidence is developed. In 2014 and 2015, the STOPP and Beers Criteria were updated [4,8]. These updates included the addition, removal, and update of several PIM criteria where new evidence has emerged or where limitations in prior versions were noted. These updates also had considerations for medications that have been introduced to the market after the prior update (e.g. direct oral anticoagulants).

For use of the Beers Criteria by US based clinicians, notable additions as PIMs included proton pump inhibitors and desmopressin. Studies of proton pump inhibitor use beyond 8 weeks has been associated with *Clostridium difficile* infection, bone loss and fractures. Exceptions where long-term use may be appropriate include gastrointestinal esophageal reflux disease and use in high-risk patients using non-steroidal anti-inflammatory drugs or corticosteroids. Desmopressin is now recommended to be avoided in the treatment of nocturia or nocturnal polyuria due to its propensity to cause hyponatremia.

Further Beers Criteria updates were informed by new retrospective evidence regarding efficacy of nitrofurantoin in renal insufficiency for use in treating urinary tract infections in patients with a creatinine clearance of less than 60 mL/min to a cutoff of 30 mL/min. The recommendation to avoid amiodarone and Class Ia, or Ic anti-arrhythmics for first line treatment of atrial fibrillation was removed with the exception of the Class III drug, dronedarone. The digoxin recommendation was changed to a drug to be avoided as first line therapy in atrial fibrillation and heart failure due to recently identified data regarding increased toxicity and mortality. Finally, the 2015 Beers Criteria removed spironolactone as a drug to avoid. Previously it was listed as PIM at doses over 25 mg daily because of issues with drug accumulation in renal insufficiency and concerns in heart failure. However, it is now an important component of heart failure therapy.

Despite multiple changes and many PIM criteria that overlap, the Beers and STOPP Criteria remain quite different from each other [11]. For example, both criteria now call for limited use of anticholinergic medications, benzodiazepines, non-benzodiazepine hypnotics, opioids, and antipsychotics in certain subgroups of the elderly but differ in their precise applications of the criteria. Further, both Beers and STOPP Criteria include PIM definitions that are not applicable in all countries due to medication availability. Therefore, a definitive answer to which criteria may be better is difficult, and many call for the Beers and STOPP Criteria to be used in a complementary manner [11].

The criteria work well as educational tools to inform clinicians on a number of recommendations for medication management in the older population. They also include evidence-based therapeutic alternatives to help address the need for continued patient management with effective medications. While individual criteria are informed by best evidence, what remains lacking are definitive studies to determine if hat implementation these tools as prescribing guidelines provides positive clinical outcomes. Studies like ours have shown that there is an association between exposure to PIMs and adverse health outcomes like emergency department visits, hospitalizations, and increased length of stay and medical costs [9,12-17]. However, the Beers or the STOPP Criteria only exhibit a modest level of discrimination to predict adverse outcomes [9]. Future research will have to determine if revised versions of the criteria will increase the ability to predict harmful outcomes and implementation research of scalable and sustainable interventions at clinical, care management, and population levels is needed [11].

The Beers and STOPP Criteria are powerful and increasingly complex tools to improve medication use in elderly patients that have broad implications for the care of elderly patients [18,19]. Continued updates and refinements will be necessary to include new evidence and account for newly marketed medications. Given the persisting differences between the Criteria despite recent updates, clinicians should be aware of both tools while recognizing such tools are not a replacement for clinical judgment and collaborative care decisions made between clinicians and patients. We eagerly anticipate further studies to answer these questions and provide additional information to inform clinicians, researchers and policy-makers in the most appropriate and safe use of medications in the older adult.

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