

## Editorial



# One More Beers? It's time to STOPP!

## *The need for better tools to guide medication prescribing*

Howard S. Smith, MD, and Timothy S. Lesar, PharmD

**P**roblematic medication use is highly prevalent among older people, particularly those presenting to a hospital with acute illness (1,2). Beers criteria were developed in the United States and first published in 1991 (3) and subsequently revised in 1997 (4), and most recently in 2003 (5). Beers criteria explicitly caution prescribers to avoid certain drugs (independent of diagnosis) in all older people and to avoid other drugs in some older people with certain medical conditions because of a poor risk-to-benefit-ratio and the consequent increased risk of adverse drug events (ADEs) (6).

Although a few studies have suggested that there may be a significant association between potentially inappropriate medications (PIMs) and ADEs (7-9), large retrospective studies have found no such significant associations. Two large-scale retrospective studies that specifically examined the association between Beers criteria PIMs and the incidence of ADEs (1,10) found no statistically significant association. An Italian study of 1,756 older patients admitted to a geriatric unit found that 4.4% of hospitalizations were related to ADEs that were definitely or possibly avoidable (11). The second study was US-based and utilized the 2003 iteration of Beers criteria to identify PIMs and ADEs from 177,504 emergency department older patient visits. Budnitz et al (12) found that compared with other medications, Beers criteria medications caused lower numbers of and fewer risks for emergency department visits for adverse events. Performance measures and interventions targeting warfarin, insulin, and digoxin use could prevent more emergency department visits for adverse events. Thus, even though there is little evidence supporting the Beers criteria, it is often used to label prescribing of certain medications in the elderly as "inappropriate." However, as a concept, the use of criteria to identify potentially problematic therapies in a patient is highly attractive and could help guide physicians when prescribing. A research group led by Dr. Denis O'Mahoney devised and validated a new set of PIM criteria in older people, called STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) in an effort to make them more clinically meaningful (13,14). STOPP criteria include 65 instances of more common and more important PIMs that may predispose to ADEs in older people (6). The inter-rater reliability of STOPP has been established, as well as its performance in languages other than English, in a recent study involving 6 teaching hospitals in Europe (15). The differences between STOPP criteria and Beers criteria include:

- ◆ STOPP criteria are organized according to physiological systems, whereas Beers criteria are not
- ◆ STOPP criteria deal with drugs that are currently in widespread use; Beers criteria include several drugs that are no longer available in most European countries, e.g., trimethobenzamide, carisoprodol, clidinium, chlordiazepoxide, guanadrel, oxaprozin, and ethacrynic acid
- ◆ STOPP criteria place special emphasis on potential adverse drug-drug interactions and duplicate drug

From: Albany Medical College, Albany, NY

Dr. Smith is Editor-in-Chief of Pain Physician, Associate Professor & Academic Director of Pain Management, Albany Medical College, Albany, New York.

E-mail: smithh@mail.amc.edu

Dr. Lesar is with the Department of Pharmacy, Albany Medical Center, Albany New York  
e-mail: lesart@mail.amc.edu

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: None.

- ◆ class prescription, whereas Beers criteria do not
- ◆ STOPP criteria contain several common instances of potentially inappropriate prescribing that are not mentioned in Beers criteria (13,14).

Commonly prescribed PIMs per STOPP criteria include: proton pump inhibitors for uncomplicated peptic ulcer disease at full therapeutic dosage for > 8 weeks; aspirin with no history of coronary, cerebral, or peripheral vascular symptoms or occlusive arterial events; benzodiazepines in patients who have had  $\geq$  one fall in the past 3 months; duplicate drug class prescriptions; long-term (> one month) long-acting benzodiazepines or benzodiazepines with long-acting metabolites; loop diuretic as first-line monotherapy for hypertension; long-term use of nonsteroidal anti-inflammatory drugs (> 3 months) for relief of mild joint pain in osteoarthritis; long-term opiates in those with recurrent falls ( $\geq$  one fall in the past 3 months); neuroleptic drugs in those with recurrent falls ( $\geq$  one fall in the past 3 months) (6).

Common ADEs that were classified as causal or contributory to admission and possibly or definitely avoidable (per Hallas criteria) include: fall(s) while receiving benzodiazepines, symptomatic orthostasis while receiving antihypertensives, falls while receiving opiates, hyponatremia while receiving diuretics, constipation while receiving opiates, falls while receiving sedative hypnotics, acute kidney injury while receiving diuretics, symptomatic orthostasis while receiving diuretics, falls while receiving neuroleptics, NSAID-related gastritis/peptic ulcer disease, and bradycardia while receiving  $\beta$ -blockers (6).

Hamilton and colleagues (6) reported 4 key findings from their study:

- ◆ Adverse drug events in acutely ill older patients presenting to a hospital involved STOPP criteria PIMs 2.54 times more frequently than Beers criteria PIMs
- ◆ Avoidable or potentially avoidable ADEs identified in these patients involved STOPP criteria PIMs in 67.7% of instances, compared with Beers criteria PIMs in 28.5% of instances
- ◆ Adverse drug events that were definitely or possibly avoidable and simultaneously causal or contributory to urgent hospitalization were listed in STOPP criteria almost 2.8 times more frequently than in Beers criteria—a significant difference
- ◆ After adjusting for age, sex, activities of daily living, functional status, comorbidity, cognitive impairment, and number of medications, the likelihood of patients experiencing an ADE was almost 85% higher if they were prescribed STOPP criteria PIMs than if they were not prescribed STOPP criteria PIMs—a significant difference. In contrast, being medicated with Beers criteria PIMs did not significantly increase patients' odds of experiencing an ADE.

Prediction of PIMS with STOPP represents an improvement over using Beers criteria to help determine appropriateness of drug therapy. But poor use of medications extends well beyond a few medications in this at-risk population and encompasses most, if not all patient types and medication classes. A large proportion of problems with drug prescribing can be traced back to 3 fundamental problems. These fundamental problems are intertwining and compound each other. In many populations, such as pain patients, these problems are even more significant given the toxicity and potential for abuse of the drugs used, and the complexity of the patients being treated. (16)

### **Misdiagnosis and/or Errant Assessment of Drug Benefits and Effects**

Obviously, a wrong diagnosis has a high likelihood of exposing the patient to adverse events and cost without benefit. More common is the failure to objectively and accurately assess and document the resulting benefits of new or ongoing drug therapy. Drug benefits are commonly overestimated and adverse effects underestimated, fueled by pharmaceutical manufacturer promotion and a desire for positive effects by both the prescriber and patient. This failure to objectively assess outcomes results in a continuation of unneeded medications or therapies that may no longer provide clinical benefits that outweigh harm or cost.

### **Misapplication of Drug Therapy**

This problem results from the purposeful use of medications outside specific indications and populations for which substantial evidence of positive outcomes exist (16-19). This is a common situation with medications used outside of FDA-approved indications or strong evidence-based indications. The decision to use drugs in this way is often based on the pharmacologic activity of a drug (as opposed to a documented therapeutic benefit), poor or limited data, and "extrapolation" beyond populations and indications that have been well studied. The marketing and promotion of pharmaceuticals again contribute significantly to this

problem. Misapplication occurs commonly when multiple drugs are used for the same indication (few studies examine combination drug use), an issue seen in clinical situations in which drugs are largely ineffective or only marginally effective (20-26), prompting attempts to improve response. Such combination use needs to be as evidence-based as possible, and appropriate only when combined with objective patient re-assessment demonstrating benefits. A more troubling practice is continued use despite strong evidence of ineffectiveness or actual negative patient outcomes (17,18,27,28).

### Mismanagement of Medication Therapy

Mistake-free and effective management of drug therapy is a difficult, complex, and time consuming activity that is usually underappreciated by prescribers. Medication management obviously involves diagnosis and assessment and drug therapy selection, but also involves designing and implementing a drug therapy plan, executing an error-free prescription, documentation, drug dosing, dose adjustments, determining therapy duration, patient education, and coordination and communication with other caregivers. Prescribers are all too often left managing complex patients taking a large number of unfamiliar medications which they have not prescribed. While pathophysiology and pharmacology are universally taught in medical schools, "therapeutics" and systematic drug therapy management are not.

Given the scope of the problem and complexities involved, what then can be done to help prescribers im-

prove medication use? There is no one solution to the problem of suboptimal use, but the basic fundamentals are clear.

- ◆ Prudent and conservative prescribing practices that are evidence-based as possible (17-19).
- ◆ Ongoing individual patient assessment and review of medications to demonstrate objective benefit and to minimize harm (29).
- ◆ Skill to effectively manage medication therapy (29,30).

Validated tools such as STOPP and its sister tool Screening Tool to Alert doctors to Right Treatment (START) can, and should, be systematically utilized to more safely design, evaluate and execute drug therapies. While integrating STOPP/START into electronic prescribing system decision support is attractive, current systems are based on using simple quantitative information such as drug, drug dose, drug-drug combinations, drug- lab results combinations, and not other criteria such as falls risk. Other tools, concepts, and guides based on "design principles" are available and can provide a consistent safety-based framework for medication management (31-35) (Table 1). Safely managing medications is a daunting task that will only continue to grow. Optimally, more such tools that will foster appropriate and safe medication practices should be developed and validated, as well as strategies on how best to combine multiple tools; however, prescribers need to be willing to use them.

Table 1. *Example of a possible short checklist for use when executing opioid prescriptions. (reprinted from ref 32 with permission).*

<b>"PAINEDx4 -R" Checklist for Safe Opioid Prescribing</b>	
<b>P</b>	<input type="checkbox"/> Patient's full name and second unique identifier such as date-of-birth; include patient address for outpatients.
<b>A</b>	<input type="checkbox"/> <u>A</u> mount of dose units prescribed to be dispensed is minimum necessary.
<b>I</b>	<input type="checkbox"/> <u>I</u> nstructions are complete and specific for use in terms the patient understands including the dose to be taken, frequency of dosing, and reason for use (never only "as directed").
<b>N</b>	<input type="checkbox"/> <u>N</u> o <u>abbreviations</u> used for drug names and <u>No zeroes</u> leading or trailing a decimal point.
<b>E</b>	<input type="checkbox"/> <u>E</u> quations for doses and final calculated dose included.
<b>Dx4</b>	<input type="checkbox"/> <u>D</u> rug, <u>D</u> ose-unit, <u>D</u> ose to be taken, and <u>D</u> osage form clearly specified. <input type="checkbox"/> <u>D</u> rug <u>n</u> ame – Provide both the full generic and brand names and include name suffix if any, with brand name. <input type="checkbox"/> <u>D</u> ose <u>u</u> nit in "mg" units (e.g., 5 mg tablets) - not package unit or volume only, in machine- printed type or hand- printed in block letters for clarity. <input type="checkbox"/> <u>D</u> ose to be taken in total "mg" amounts and if more than one dose units-also number of dose units to be taken per dose (e.g., "10mg (two) tablets"). <input type="checkbox"/> <u>D</u> osage <u>f</u> orm,- tablet/capsule, oral liquid, patch, "sustained release."
<b>- R</b>	<input type="checkbox"/> <u>R</u> efills prescribed only when clearly needed – then specify number of refills to be provided in both Arabic numeral and spelled out (e.g., 2 [two]), if no refills, write "no refills," not "0."

## REFERENCES

- Onder G, Landi F, Liperoti R, Fialova D, Gambassi G, Bernabei R. Impact of inappropriate drug use among hospitalized older adults. *Eur J Clin Pharmacol* 2005; 61:453-459.
- Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): Application to acutely ill elderly patients and comparison with Beers' criteria. *Age Ageing* 2008; 37:673-679.
- Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC; UCLA Division of Geriatric Medicine. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med* 1991; 151:1825-1832.
- Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly: An update. *Arch Intern Med* 1997; 157:1531-1536.
- Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts. *Arch Intern Med* 2003; 163:2716-2724.
- Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med* 2011; 171:1013-1019.
- Chang CM, Liu PY, Yang YH, Yang YC, Wu CF, Lu FH. Use of the Beers criteria to predict adverse drug reactions among first-visit elderly outpatients. *Pharmacotherapy* 2005; 25:831-838.
- Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: Inappropriate prescription is a leading cause. *Drugs Aging* 2005; 22:767-777.
- Chrischilles EA, VanGilder R, Wright K, Kelly M, Wallace RB. Inappropriate medication use as a risk factor for self-reported adverse drug effects in older adults. *J Am Geriatr Soc* 2009; 57:1000-1006.
- Laroche ML, Charmes JP, Nouaille Y, Picard N, Merle L. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? *Br J Clin Pharmacol* 2007; 63:177-186.
- Franceschi M, Scarcelli C, Niro V, Seripa D, Paziienza AM, Pepe G, Colusso AM, Pacilli L, Pilotto A. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: A prospective study of 1756 patients. *Drug Saf* 2008; 31:545-556.
- Budnitz DS, Shehab N, Kegler SR, Richards CL. Medication use leading to emergency department visits for adverse drug events in older adults. *Ann Intern Med* 2007; 147:755-765.
- O'Mahony D, Gallagher PF. Inappropriate prescribing in the older population: Need for new criteria. *Age Ageing* 2008; 37:138-141.
- Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment): Consensus validation. *Int J Clin Pharmacol Ther* 2008; 46:72-83.
- Gallagher P, Baeyens JP, Topinkova E, Madlova P, Cherubini A, Gasperini B, Cruz-Jentoft A, Montero B, Lang PO, Michel JP, O'Mahony D. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. *Age Ageing* 2009; 38:603-606.
- Smith HS, Lesar TS. Analgesic prescribing errors and associated medication characteristics. *J Pain* 2011; 12:29-40.
- Avorn J. A hemorrhage of off-label use. *Ann Intern Med* 2011; 154:566-567.
- Topol EJ. The lost decade of nesiritide. *NEJM* 2011; 365:81-82.
- Schiff GD, Galanter WM. Promoting more judicious prescribing. *JAMA* 2009; 301:865-867.
- Tamminga, CA. When Is polypharmacy an advantage? *Am J Psychiatry* 2011; 168:663.
- Bril V, England J, Franklin, GM, Backonja M, Cohen J, Del Toro D, Feldman E, Iversen DJ, Perkins B, Russell JW, Zochodne D. Evidence-based guideline: Treatment of painful diabetic neuropathy. *Neurology* 2011; 76:1758-1765.
- Krystal JH, Rosenheck RA, Cramer JA, Vessicchio JC, Jones KM, Vertrees JE, Horney RA, Huang GD, Stock C; Veterans Affairs Cooperative Study No. 504 Group. Adjunctive risperidone treatment for antidepressant-resistant symptoms of chronic military service-related PTSD. A randomized trial. *JAMA* 2011; 306:493-502.
- Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. *N Engl J Med* 2008; 358:252-260.
- Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. *Health Aff* 2011; 30:1434-1442.
- Banerjee S. HTA-SADD a definitive multicentre placebo controlled RCT of the clinical effectiveness of sertraline and mirtazapine for the treatment of depression in dementia. AAIC 2011; Abstract O2-05-04.
- Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: Population-based cohort study. *BMJ* 2011; 343.
- McAlister FA, Zhang J, Tonelli M, Klarenbach S, Manns BJ, Hemmelgarn BR; Alberta Kidney Disease Network. The safety of combining angiotensin-converting-enzyme inhibitors with angiotensin-receptor blockers in elderly patients: A population-based longitudinal analysis. *CMAJ* 2011; 183:655-662.
- Weintraub D, Chen P, Ignacio RV, Mamikonyan E, Kales HC. Patterns and trends in antipsychotic prescribing for parkinson disease psychosis. *Arch Neurol* 2011; 68:899-904.
- Steinman MA, Hanlon J. Managing medications in clinically complex elders. *JAMA* 2010; 304:1592-1601.
- Sketris IS, Langille Ingram EM, Lummis HL. Strategic opportunities for effective optimal prescribing and medication management. *Can J Clin Pharmacol* 2009; 16:e103-e125.
- Gawande A. *Checklist Manifesto: How to Get Things Right*. Metropolitan, New York, 2009.
- Lesar TS, Smith HS. Making opioids safer- Time for a checklist? *Pain Management* 2011; 4:279-285.
- Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical Guidelines for the use of chronic opioid therapy in chronic non-cancer pain. *J Pain* 2009; 10:113-130.
- McMaster University. The Opioid manager. Available at: <http://nationalpaincentre.mcmaster.ca/opioidmanager/>
- Schnipper JL. Medication safety- are we there yet? *Arch Intern Med* 2011; 171:1019-1020.