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Commentary on the New American Geriatric Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Zachary A. Marcum, PharmD, MS[a,b,c,d,e] and **Joseph T. Hanlon, PharmD, MS**[a,b,c,d,e,f,g]

[a]School of Medicine (Geriatrics), University of Pittsburgh, Pittsburgh, PA

[b]School of Pharmacy (Pharmacy & Therapeutics), University of Pittsburgh, Pittsburgh, PA

[c]Center for Health Equity Research and Promotion (CHERP), Veterans Affairs Pittsburgh Healthcare System (VAPHS), Pittsburgh, PA

[d]Geriatric Research Education and Clinical Center (GRECC), VAPHS, Pittsburgh, PA

[e]Geriatric Pharmaceutical Outcomes and Gero-Informatics Research and Training Program, University of Pittsburgh, Pittsburgh, PA

[f]Graduate Schoolof Public Health (Epidemiology), University of Pittsburgh, Pittsburgh, PA

[g]Clinical and Translational Science Institute, University of Pittsburgh, Pittsburgh, PA

Recently, the American Geriatrics Society (AGS) Beers criteria were unveiled as a measure of potentially inappropriate medication use in older adults.[1] We thought it would be timely and relevant to comment on this updated quality measure for medication use. Of note, a recent systematic review summarized the current literature on the more than a dozen measures of potentially inappropriate prescribing in older adults and reported that the Beers criteria and the Screening Tool of Older Persons' Prescriptions (STOPP) criteria were some of the most common measures used.[2] With that in mind, in this commentary we discuss some of the history of the Beers criteria as well as briefly describe the process of updating the criteria, highlighting some of the key changes made. Then, we compare and contrast the new criteria with the STOPP criteria from Europe.[3] Finally, we briefly comment on some future directions for the Beers criteria as an explicit measure of potentially inappropriate medication use in older adults.

History of the Beers Criteria

One of the first set of explicit criteria for inappropriate drug use was developed by Mark H. Beers, MD, while a junior faculty at the University of California, Los Angeles and was published in 1991.[4] He defined inappropriate prescribing as the use of medication where the potential risks outweigh the potential benefits.[4] For the first set of Beers criteria, a 13 member expert panel was part of a two-stage Delphi survey in which consensus was reached regarding 30 therapeutic classes/medications whose use should be avoided in the elderly residing in nursing homes. These criteria were used as a process measure in Dr. Beers' John A. Hartford Foundation-funded cluster randomized trial of a computer feedback intervention aimed at improving prescribing for older nursing home patients. The results of this successful trial were presented by Dr. Beers at the 1993 American Geriatric Society (AGS) Annual Meeting, but to the best of our knowledge were never published as a peer-reviewed

Corresponding author: Zachary A. Marcum, 3471 Fifth Avenue, Suite 500, Pittsburgh, PA, 15213; Phone: 412-864-2894; Fax: 412-692-2370; zam12@pitt.edu.

manuscript. Moving ahead to 1997, Dr. Beers was then employed by Merck & Co., Inc. and published an updated set of criteria.[5] This time, a 6 member expert panel was utilized. Overall, they agreed upon 28 therapeutic classes/medications to avoid in the elderly residing in nursing homes or in the community. In addition, these updated criteria included severity ratings for the "do-not-use" list of medications. Moreover, new explicit criteria were agreed upon for 35 drug-disease interactions to be avoided in older adults. In 1999, a partial list (i.e., 22 "drugs-to-avoid" and 12 drug-disease interaction criteria) was adopted by the Center for Medicare and Medicaid Services (CMS) as quality indicator measures for long-term care facilities (LTCF).[6]

In 2003, Dr. Beers participated in a panel led by Dr. Donna Fick with other health professionals from Georgia to update the 1997 criteria.[7] An expert panel of 12 members was used to establish consensus on 48 medications/classes of "drugs-to-avoid" and 20 drug-disease interactions. In 2006, CMS updated its quality indicator criteria for LTCFs using some of the new criteria.[8] In addition in 2006, the National Committee for Quality Assurance (NCQA) chose some of these "do-not-use" and drug-disease interaction criteria for new ambulatory care quality indicators as one of their HEDIS measures.[9] In 2009, sadly, Dr. Beers passed away.

Updating the Beers Criteria and Highlighting Some Key Changes

In 2011, NCQA asked AGS to revise the 2003 Beers criteria. The co-chair persons (Drs. Fick and Semla) for the 2012 update were also involved in the development of the 2003 criteria. These two individuals and nine others, including one of the authors of this commentary (JTH), served as the members of a multidisciplinary expert panel (two nurses, four physicians, five pharmacists) who completed a two-stage Delphi survey and participated in live and teleconferenced meetings in order to reach consensus. Importantly, a period of time was made available for the public and any key stakeholders to provide comments and feedback on these updated criteria prior to publication. Of note, various professional and public education materials are currently available on the AGS website, including all of the criteria and supportive evidence tables.[10]

In looking at the updated "drugs-to-avoid" list, it is important to note some of the key therapeutic class/medication additions and deletions compare to the 2003 criteria (Table 1). Of those therapeutic classes/medications removed from the previous criteria, seven were due to drugs being withdrawn from the market since the last time the criteria were published in 2003 (e.g., propoxyphene) and one removal was due to the lack of evidence that long-term stimulant laxatives lose effectiveness or result in unacceptable adverse effects (the original reason this drug/class was included in the list of "drugs-to-avoid").[11] Fluoxetine and cimetidine were also dropped from the "drugs-to-avoid" list since the potential drug interaction problems with these medications are not unique to the elderly.[12] Specifically, these are not drugs of choice within their therapeutic classes due to the greater potential for drug-drug interactions as a result of inhibition of CYP-450 hepatic isoenzymes. Similarly, the recommendation NOT to use > 325 mg per day of ferrous sulfate to treat iron deficiency anemia applies to adults of all ages and thus was dropped.[13] Finally, ethacrynic acid was dropped due to its extremely low use and lack of information on ototoxicity risk derived from rigorously designed studies in humans.[14] Among the new therapeutic classes/ medications added to the 2003 criteria, some noteworthy additions of "drugs-to-avoid" include all short-acting benzodiazepines (**regardless of dose**), glyburide, megesterol, metoclopramide, and sliding scale insulin.[1]

Several drug-disease interactions were added to the previous criteria whereas some were removed (Table 2).[1] For the drug-disease interactions dropped from the 2003 criteria, the

main reason was due to the medications no longer being on the market (e.g., phenylpropanolamine and hypertension), or the publication of data that shows insufficient evidence that a therapeutic class/medication can exacerbate a specific disease/syndrome in a clinically important way (e.g., pseudoephedrine and hypertension).[15] Among the new drug-disease interactions added to the 2003 criteria, some noteworthy additions are acetylcholinesterase inhibitors/syncope, selective serotonin reuptake inhibitors/falls or fractures, and pioglitazone/rosiglitazone/heart failure.[1]

One noted difference in the updated criteria compared to previous versions is the creation of a new category of potentially inappropriate medications to be used *with caution* in older adults, with three out of the five warnings being related to an increased risk of bleeding (i.e., aspirin for primary prevention of cardiac events, dabigatran, and prasugrel).[1] Additional updates to the new Beers criteria are detailed in the main publication.[1]

Comparison of 2012 AGS Beers Criteria with 2006 STOPP Criteria

To establish in part the face validity of the new AGS Beers criteria it is important to compare them with the STOPP criteria since it is one of the most common explicit measures of potentially inappropriate prescribing in older adults.[3] Briefly, the STOPP criteria include a list of risky medication situations, involving specific “drugs-to-avoid”, drug-disease interactions, drug-drug interactions, and duration of therapy concerns. For the purposes of this commentary in comparing the Beers and STOPP criteria, we will only be comparing the “drugs-to-avoid” and drug-disease interactions included in these two measures (Tables 1 and 2). There is quite a bit of concordance the between the Beers 2012 and STOPP 2006 criteria. One of the most consistent findings is that the use of NSAIDs in older adults is high-risk, showing up on both “drugs-to-avoid” lists as well as drug-disease interactions with heart failure, chronic renal failure, and peptic ulcer disease.[16] In addition, both the Beers and STOPP criteria include tricyclic antidepressants as a class of drugs that can exacerbate a number of conditions including falls/fractures, and dementia/cognitive impairment.

It is also interesting to note the discordances between the Beers 2012 and STOPP 2006 criteria. This may be due to the different patterns of prescribing quality in the United States compared to Europe where certain medication classes may be more problematic than others. One notable difference with NSAID use is that the STOPP 2006 criteria list a drug-disease interaction with hypertension while the Beers 2012 criteria do not. Although this drug-disease interaction does not appear on the Beers criteria, it is a clinically significant interaction in older adults that deserves attention.[17] Another difference between the Beers 2012 and STOPP 2006 criteria involves benzodiazepine use. While the two instruments both include long-acting benzodiazepines as “drugs-to-avoid”, only the Beers criteria include short- and intermediate-acting benzodiazepines as well. This comprehensive inclusion of all benzodiazepines is supported by literature showing that all benzodiazepines can lead to adverse events (e.g., falls, fractures, cognitive impairment) in older adults and not only the long-acting agents.[18, 19] Furthermore, the STOPP criteria list the use of first generation antihistamines and falls as a drug-disease interaction while the Beers criteria do not. The rationale for the Beers criteria not including this drug-disease interaction is due to the fact that the evidence for these agents being associated with falls is limited to two studies and the findings are mixed.[20,21]

Looking Ahead

Because of the partnership developed with the AGS, the Beers criteria will be regularly updated every three years (AGS press release, March 1, 2012). Similarly, with the support of the European Union Geriatric Medicine Society (EUGMS) an updated version of the STOPP criteria in addition to the START [Screening Tool to Alert doctors to Right Treatment]

criteria will be validated and published later this year (personal communication with Dr. Denis O'Mahony, February 20112). Future research will be needed to assess the psychometric/clinimetric properties of both the new AGS Beers criteria and the EUGMS STOPP criteria. This should include studies of inter- and intra-rater reliability of these measures along with their predictive validity with adverse drug events. Also, it will be important to demonstrate their responsiveness to change in randomized controlled trials designed to improve prescribing. Finally, it would be useful to conduct studies to better understand their concordance with implicit measures of potential inappropriate prescribing (e.g., Medication Appropriateness Index) that consider a greater number of prescribing factors.[22]

Conclusion

The new AGS Beers criteria were carefully and thoughtfully developed based on the current best evidence. It would seem they are a definite step in the right direction toward improving the care of older adults. At the same time, it is important to recognize the areas for future work.

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Table 1

Comparison of the Most Common Explicit Measures for Drugs to Avoid in Older Adults

Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
Central Nervous System and Psychotropic Drugs			
Amphetamines and anorexic agents	X	--	--
Anticholinergics to treat extrapyramidal side effects of neuroleptic medications (e.g., benztropine, trihexyphenidyl)	--	X	X
Antihistamines, 1st generation (select agents in Beers 2003; all agents in Beers 2012; select agents in STOPP 2006)	X	X	X
Antipsychotics, first (conventional) and second (atypical) generation (for behavioral problems of dementia)	--	X	--
Barbiturates (all agents except phenobarbital for seizure control in Beers 2003; all agents in Beers 2012)	X	X	--
Benzodiazepines, short- and intermediate-acting (dose limits in Beers 2003; all doses in Beers 2012)	X	X	--
Chloral hydrate	--	X	--
Dementia treatments, older (i.e., ergot mesylates and isoxsuprine in Beers 2003 and Beers 2012; cyclandelate in Beers 2003)	X	X	--
Fluoxetine, daily	X	--	--
Long-acting benzodiazepines (e.g., clonazepam, diazepam, flurazepam)	X	X	X
Long-term neuroleptics for insomnia	--	--	X
Meprobamate	X	X	--
Mesoridazine	X	X	--
Nonbenzodiazepine (“Z”) hypnotics (i.e., eszoplicone, zaleplon, zolpidem)	--	X	--
Tertiary TCAs, alone or in combination (amitriptyline and doxepin in Beers 2003; all in Beers 2012)	X	X	--
Thioridazine	X	X	--
Cardiovascular			
α-acting and central-acting agents for treatment of hypertension (clonidine, doxazosin, guanethidine, guanadrel, methyldopa, and reserpine in Beers 2003; clonidine, doxazosin, guanabenz, guanfacine, methyldopa, prazosin, terazosin, and reserpine in Beers 2012)	X	X	--
Antiarrhythmic drugs (amiodarone and disopyramide in Beers 2003; Class Ia, Class Ic, and Class III drugs in Beers 2012) for atrial fibrillation	X	X	--
Aspirin for primary prevention (to be used with caution in adults ≥80 years old for primary prevention of cardiac events in Beers 2012; to be avoided in those with no history of coronary, cerebral or peripheral vascular symptoms or occlusive events in STOPP 2006)	--	X	X
Aspirin to treat dizziness not clearly attributable to cerebrovascular disease	--	--	X
Digoxin > 0.125 mg/day	X	X	X
Dipyridamole IR as monotherapy	X	X	X
Ethacrynic acid	X	--	--
Loop diuretic for ankle edema (i.e., no clinical signs of heart failure) or as 1st line monotherapy for hypertension	--	--	X
Nifedipine IR	X	X	--
Spironolactone > 25 mg/day	--	X	--
Ticlopidine	X	X	--
Endocrine			

Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
Androgens (methyltestosterone in both Beers 2003 and Beers 2012; testosterone in Beers 2012)	X	X	--
Chlorpropamide	X	X	X
Dessicated thyroid	X	X	--
Estrogen (estrogens only in Beers 2003; estrogen with or without progestins in Beers 2012; estrogen without progestin in patients with intact uterus in STOPP 2006)	X	X	X
Glyburide/glibenclamide (*European generic name*)	--	X	X
Growth hormone	--	X	--
Megesterol	--	X	--
Sliding scale insulin	--	X	--
Gastrointestinal			
GI antispasmodics (e.g., dicyclomine, hyoscyamine)	X	X	--
Cimetidine	X	--	--
Diphenoxylate, loperamide or codeine for treatment of diarrhea of unknown cause or severe infective gastroenteritis	--	--	X
Long-term use of stimulant laxatives (i.e., bisacodyl, cascara sagrada, and neoloid except in the presence of opioid use)	X	--	--
Metoclopramide	--	X	--
Mineral oil (given orally)	X	X	--
Trimethobenzamide	X	X	--
Miscellaneous			
Ferrous sulfate > 325 mg/d	X	--	--
Nitrofurantoin	X	X	--
Skeletal muscle relaxants (e.g., carisoprodol, cyclobenzaprine, orphenadrine)	X	X	--
Musculoskeletal			
Chronic non-COX-selective NSAIDs (naproxen, oxaprozin, and piroxicam in Beers 2003; all agents in Beers 2012 and STOPP 2006)	X	X	X
Indomethacin	X	X	--
Ketorolac	X	X	--
Long-term corticosteroids as monotherapy for RA or OA	--	--	X
Long-term colchicine for chronic treatment of gout where there is no contraindication to allopurinol	--	--	X
Powerful opiates (e.g., morphine or fentanyl) as first-line therapy for for mild/moderate pain	--	--	X
Meperidine	X	X	--
Pentazocine (Talwin)	X	X	--
Propoxyphene (Darvon) and combination products	X	--	--
Respiratory			
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-to-severe COPD	--	--	X
Theophylline monotherapy for COPD	--	--	X

Abbreviations: COPD, chronic obstructive pulmonary disease; COX, cyclooxygenase; GI, gastrointestinal; IR, immediate release; NSAID, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; TCA, tricyclic antidepressants; RA, rheumatoid arthritis; SR, sustained release

Table 2

Comparison of the Most Common Explicit Measures for Drug-Disease Interactions in Older Adults

Disease – Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
Anorexia and Malnutrition			
CNS stimulants (e.g., dextroamphetamine, methylphenidate, methamphetamine, pemolin)	X	--	--
Bleeding Disorder *			
Antithrombotics/anticoagulants (aspirin, dipyridamole, and clopidogrel in both Beers 2003 and STOPP 2006; NSAIDs and ticlopidine in Beers 2003)	X	--	X
Cardiac Conduction Abnormalities			
Tricyclic antidepressants	X	--	X
Chronic Constipation			
Anticholinergics, not listed below	--	X	--
Anticholinergic GI antispasmodic drugs (e.g., dicyclomine)	X	X	X
Antihistamines, 1st generation (e.g., diphenhydramine)	X	X	--
Antipsychotics	--	X	--
Calcium channel blockers, nondihydropyridine (i.e., diltiazem, verapamil)	X	X	X
Bladder antimuscarinic drugs (e.g., oxybutynin)	--	X	X
Opioids, regular (>2 weeks) and without concurrent use of laxatives	--	--	X
Tricyclic antidepressants (amitriptyline, doxepin, and imipramine in Beers 2003; all in Beers 2012 and STOPP 2006)	X	X	X
Chronic Kidney Disease (Stages IV and V)			
NSAID, all	--	X	X
Triamterene	--	X	--
COPD			
β blockers, non-cardioselective (propanolol in Beers 2003; all in STOPP 2006)	X	--	X
Long-acting benzodiazepines	X	--	--
Diabetes Mellitus and frequent hypoglycemic episodes (i.e., ≥ 1 episode per month)			
β blockers	--	--	X
Delirium			
Anticholinergics	--	X	--
Benzodiazepines	--	X	--
Chlorpromazine	--	X	--
Corticosteroids	--	X	--
H_2-receptor antagonist	--	X	--
Meperidine	--	X	--
Sedative hypnotics (e.g., zolpidem)	--	X	--
Thioridazine	--	X	--
Tricyclic antidepressants, all	--	X	--
Dementia and Cognitive Impairment			
Anticholinergics, not listed below	X	X	--

Disease – Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
Antipsychotics, chronic and as-needed use	--	X	--
Barbiturates	X	--	--
Benzodiazepines	--	X	--
Bladder antimuscarinic drugs	X	X	X
CNS stimulants (dextroamphetamine, methylphenidate, methamphetamine, pemolin)	X	--	--
GI antispasmodics (e.g., dicyclomine, hyoscyamine)	X	X	--
H_2-receptor antagonists	--	X	--
Muscle relaxants	X	X	--
Opioids, long-term (unless indicated for palliative care or management of moderate-severe chronic pain	--	--	X
Tricyclic antidepressants, all	--	X	X
Zolpidem	--	X	--
Depression			
Long-term benzodiazepine use	X	--	--
Sympatholytic agents (methyldopa, reserpine, guanethidine)	X	--	--
Glaucoma			
Bladder antimuscarinic drugs	--	--	X
Ipratropium, nebulized	--	--	X
Tricyclic antidepressants	--	--	X
Gout			
Diuretic, thiazide	--	--	X
Heart Failure (systolic specified in Beers 2012)			
Calcium channel blockers, nondihydropyridine (i.e., diltiazem, verapamil)	--	X	X
Cilostazol	--	X	--
Disopyramide	X	--	--
Dronaderone	--	X	--
High sodium content drugs (sodium and sodium salts)	X	--	--
NSAID, all	--	X	X
Thiazolidinediones (i.e., pioglitazone, rosiglitazone)	--	X	--
History of Breast Cancer or VTE			
Estrogen	--	--	X
History of Falls/Fractures			
Anticonvulsants	--	X	--
Antihistamines, 1st generation	--	--	X
Antipsychotics	--	X	X
Benzodiazepines (short- to intermediate-acting in Beers 2003; all in Beers 2012 and in STOPP 2006)	X	X	X
Nonbenzodiazepine (“Z”) hypnotics (i.e., eszopiclone, zaleplon, zolpidem)	--	X	--
Opioids, long-term	--	--	X
SSRIs	--	X	--

Disease – Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
Tricyclic antidepressants (amitriptyline, doxepin, and imipramine Beers 2003; all in Beers 2012)	X	X	--
History of Peptic Ulcer Disease			
NSAID, non-COX-2-selective, without gastroprotection (non-COX-2 NSAIDs in Beers 2003 and Beers 2012; all NSAIDs in STOPP 2006)	X	X	X
Hypertension			
Amphetamines	X	--	--
Diet pills	X	--	--
NSAIDs (moderate to severe hypertension)	--	--	X
Phenylpropanolamine hydrochloride	X	--	--
Pseudoephedrine	X	--	--
Insomnia			
Decongestants, oral (i.e., pseudoephedrine, phenylephrine)	X	X	--
MAOIs	X	--	--
Stimulants (e.g., amphetamine, methylphenidate, pemoline)	X	X	--
Theobromines (i.e., theophylline, caffeine)	X	X	--
Lower Urinary Tract Symptoms			
Anticholinergics (oral in Beers 2003; oral and inhaled in Beers 2012; bladder antispasmodic agents only in STOPP 2006)	X	X	X
Decongestants, oral	X	--	--
Obesity			
Olanzapine	X	--	--
Parkinson's Disease			
Antipsychotics (conventional antipsychotics in Beers 2003; all except for quetiapine and clozapine for Beers 2012; all for STOPP 2006)	X	X	X
Metoclopramide	X	X	X
Prochlorperazine	--	X	X
Promethazine	--	X	--
Tacrine	X	--	--
Persistent Postural Hypotension			
Vasodilators	--	--	X
Seizures			
Antipsychotics, atypical (clozapine in Beers 2003; clozapine, olanzapine in Beers 2012)	X	X	--
Antipyschotics, conventional (e.g., chlorpromazine, thioridazine, thiothixene)	X	X	X
Bupropion	X	X	--
Maprotiline	--	X	--
Tramadol	--	X	--
SIADH/Hyponatremia †			
SSRIs	X	--	X
Syncope ‡			
Acetylcholinesterase inhibitors	--	X	--

Disease – Therapeutic Class/Medication	Beers 2003	Beers 2012	STOPP 2006
α blockers, peripheral (i.e., doxazosin, prazosin, terazosin)	--	X	--
Chlorpromazine	--	X	--
Olanzapine	--	X	--
Thioridazine	--	X	--
Tricyclic antidepressants (amitriptyline, doxepin, and imipramine Beers 2003; all in Beers 2012)	X	X	--
Urinary Incontinence			
α blockers (stress incontinence in Beers 2003; stress or mixed urinary incontinence, avoid in women in Beers 2012; avoid in men with frequent incontinence in STOPP 2006)	X	X	X
Long-acting benzodiazepines (stress)	X	--	--
Estrogen oral and transdermal dosage forms only (applies to women)		X	
Tricyclic antidepressants (amitriptyline, doxepin, and imipramine with stress incontinence in Beers 2003; all in both Beers 2012 and STOPP 2006)	X	X	X

Abbreviations: COPD, chronic obstructive pulmonary disease; COX, cyclooxygenase; GI, gastrointestinal; H, histamine; MAOI: monoamine oxidase inhibitor; NSAID, non-steroidal anti- inflammatory drugs; SIADH, syndrome of inappropriate diuretic hormone secretion; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitors; TCA, tricyclic antidepressants VTE, venous thromboembolism

*Beers 2012 includes aspirin for primary prevention, dabigatran, and prasugrel in the category of potentially inappropriate medications to be used with caution in older adults due to the increased risk of bleeding.

†Beers 2012 includes antipyschotics, carbamazepine, carboplatin, cisplatin, mirtazapine, SNRIs, SSRIs, TCAs, and vincristine in the category of potentially inappropriate medications to be used with caution in older adults due to increased risk of SIADH/hyponatremia.

‡Beers 2012 includes vasodilators in the category of potentially inappropriate medications to be used with caution in older adults due to increased risk of syncope in individuals with a history of syncope.