American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel

The 2015 American Geriatrics Society (AGS) Beers Criteria are presented. Like the 2012 AGS Beers Criteria, they include lists of potentially inappropriate medications to be avoided in older adults. New to the criteria are lists of select drugs that should be avoided or have their dose adjusted based on the individual's kidney function and select drug–drug interactions documented to be associated with harms in older adults. The specific aim was to have a 13-member interdisciplinary panel of experts in geriatric care and pharmacotherapy update the 2012 AGS Beers Criteria using a modified Delphi method to systematically review and grade the evidence and reach a consensus on each existing and new criterion. The process followed an evidence-based approach using Institute of Medicine standards. The 2015 AGS Beers Criteria are applicable to all older adults with the exclusion of those in palliative and hospice care. Careful application of the criteria by health professionals, consumers, payors, and health systems should lead to closer monitoring of drug use in older adults. **J Am Geriatr Soc 63:2227–2246, 2015.**

Key words: Beers List; medications; Beers Criteria; drugs; older adults; polypharmacy

The American Geriatrics Society (AGS) Beers Criteria for Potentially Inappropriate Medication (PIM) Use in Older Adults is an explicit list of PIMs best avoided in older adults in general and in those with certain diseases or syndromes, prescribed at reduced dosage or with caution or carefully monitored. Beers Criteria PIMs have been found to be associated with poor health outcomes, including confusion, falls, and mortality.[1,2] Avoiding PIMs in older adults is one strategy to decrease the risk of adverse events. Interventions using explicit criteria have been found to be an important component of strategies for reducing inappropriate medication usage.[3–5]

The AGS Beers Criteria for PIM Use in Older Adults are one of the most frequently consulted sources about the safety of prescribing medications for older adults. The AGS Beers Criteria are used widely in geriatric clinical care, education, and research and in development of quality indicators. In 2011, the AGS assumed the responsibility of updating and maintaining the Beers Criteria and, in 2012, released the first update of the criteria since 2003. The AGS has made a commitment to update the criteria regularly. The changes in the 2015 update are not as extensive as those of the previous update, but in addition to updating existing criteria, two major components have been added: 1) drugs for which dose adjustment is required based on kidney function and 2) drug–drug interactions. Neither of these new additions is intended to be comprehensive, because such lists would be too extensive. An interdisciplinary expert panel focused on those drugs and drug–drug interactions for which there is evidence in older adults that they are at risk of serious harm if the dose is not adjusted or the drug interaction is overlooked.

OBJECTIVES

The specific aim was to update the 2012 AGS Beers Criteria using a comprehensive, systematic review and grading of the evidence on drug-related problems and adverse drug events in older adults. The strategies to achieve this aim were to:

- Incorporate new evidence on currently listed PIMs and evidence from new medications or conditions not addressed in the 2012 update.
- Incorporate two new areas of evidence on drug–drug interactions and dose adjustments based on kidney function for select medications.
- Grade the strength and quality of each PIM statement based on the level of evidence and strength of recommendation.
- Convene an interdisciplinary panel of 13 experts in geriatric care and pharmacotherapy who would apply a modified Delphi method to the systematic review and

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grading to reach consensus on the updated 2015 AGS Beers Criteria.
- Incorporate needed exceptions in the criteria as the panel deemed clinically appropriate. These exceptions would be designed to make the criteria more individualized to clinical practice and be more relevant across settings of care.

INTENT OF CRITERIA

The primary target audience for the AGS Beers Criteria is practicing clinicians. The criteria are intended for use in all ambulatory, acute, and institutionalized settings of care for populations aged 65 and older in the United States, with the exception of hospice and palliative care. Consumers, researchers, pharmacy benefits managers, regulators, and policymakers also widely use the AGS Beers Criteria. The intentions of the criteria are to: improve medication selection; educate clinicians and patients; reduce adverse drug events; and serve as a tool for evaluating quality of care, cost, and patterns of drug use of older adults.

The goal of the 2015 AGS Beers Criteria continues to be improving the care of older adults by reducing their exposure to PIMs. This is accomplished by using the criteria as an educational tool and quality measure—two uses that are not always in agreement. These criteria are not meant to be applied in a punitive manner. Prescribing decisions are not always clear-cut, and clinicians must consider multiple factors, including discontinuation of medications no longer indicated. Quality measures must be clearly defined, easily applied, and measured with limited information and thus, although useful, cannot perfectly distinguish appropriate from inappropriate care. The panel considered and vigorously discussed both roles during deliberations. The panel's review of evidence at times identified subgroups of individuals who should be exempt from a given criterion or to whom a specific criterion should apply. Such a criterion may not be easily applied as a quality measure, particularly when such subgroups cannot be easily identified through structured and readily accessible electronic health data. In these cases, the panel felt that a criterion should not be expanded to include all adults aged 65 and older when only certain subgroups have an adverse balance of benefits versus harms for the medication or conversely may be appropriate candidates for a medication that is otherwise problematic.

Despite past and current efforts to translate the criteria into practice, some controversy and myths about their use in practice and policy continue to prevail. The panel addressed these concerns and myths by writing a companion piece to the updated criteria to address the best way for patients, providers, and health systems to use (and not use) the 2015 AGS Beers Criteria. Alternative suggestions to medications included in the current Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly quality measures are presented in another companion paper. Both papers will be published online in this journal.

METHODS

For this new update, the AGS employed a well-tested framework that has long been used for development of clinical practice guidelines.[6,7] Specifically, the framework involved the appointment of a 13-member interdisciplinary expert panel with relevant clinical expertise and experience and an understanding of how the criteria have been previously used. This framework also involved a development process that included a systematic literature review and evaluation of the evidence base by the expert panel. Finally, the Institute of Medicine's 2011 report on developing practice guidelines, which included a period for public comments, guided the framework. These three framework principles are described in greater detail below.

PANEL SELECTION

A panel with expertise in geriatric medicine, nursing, pharmacy practice, research, and quality measures was convened comprising members of the previous panel and new members. Other factors that influenced selection of panel members were the desire to have interdisciplinary representation, a range of medical expertise, and representation from different practice settings (e.g., long-term care, ambulatory care, geriatric mental health, palliative care and hospice). In addition to the 13-member panel, representatives from the Centers for Medicare and Medicaid Services, National Committee for Quality Assurance, and Pharmacy Quality Alliance were invited to serve as ex-officio members.

Each expert panel member completed a disclosure form at the beginning of the guideline process that was shared with the entire panel at the start of each panel meeting and call. Panel members who disclosed affiliations or financial interests with commercial entities are listed in the disclosures section of this article. Panel members were asked to recuse themselves from discussions if they had a potential conflict of interest.

LITERATURE SEARCH

The literature from August 1, 2011 (the end of the previous panel's search) to July 1, 2014, was searched to identify published systematic reviews, meta-analyses, randomized controlled trials, and observational studies that were relevant to the project. The initial literature search was conducted on PubMed and the Cochrane Library. The drugs, drug classes, and conditions included in the 2012 criteria were used as initial search terms and were generally focused on "adverse drug events" and "adverse drug reactions." Individual drugs, drug classes, and conditions were searched individually and in combination. Search filters included human subjects, English language, and aged 65 and older. Case reports, case series, editorials, and letters were excluded. Clinical reviews were included for initial screening as potential background information and for reference list review. The initial searches identified 20,748 citations, of which 6,719 were selected for preliminary abstract review. The panel co-chairs reviewed 3,387 citations and abstracts, of which 2,199 were excluded for not meeting the study purpose or not containing primary data. At the time of the panel's face-to-face meeting, the co-chairs had selected 1,188 unduplicated citations for the full panel review. Subsequent searches (defined by panel workgroups) were conducted until December 15, 2014;

some of these searches included studies published in the prior 10 years. The AGS also gave its members and members of the public a chance to submit evidence they felt the panel should consider. Any evidence submitted had to be evidence based and published in a peer-reviewed journal. Panel members reviewed abstracts, and evidence tables were developed for 342 studies, including 60 systematic reviews and meta-analyses, 49 randomized controlled trials, and 233 observational and other types of publications.

DEVELOPMENT PROCESS

Since the previous update, the AGS had created a group to monitor the literature and to advise the 2015 expert panel of any articles relevant to the 2012 criteria and respond accordingly. Two members of the expert panel (MS, SL) led this group, which was composed of members of the AGS Clinical Practice Committee and other expert members of AGS. The 2015 expert panel convened for a 2-day in-person meeting on July 28–29, 2014, to review the groups' findings and the results of the literature search. Panel discussions were used to define terms and to address questions of consistency, inclusion of infrequently used drugs, strategies for evaluating the evidence, consolidation or expansion of individual criterion, and development of renal dosage and drug–drug interaction tables. The panel then split into four groups, with each assigned a specific set of criteria for evaluation. Groups were assigned as closely as possible according to specific area of clinical expertise (e.g., cardiovascular, central nervous system). Groups reviewed the literature search, selected citations relevant to their assigned criteria, and determined which citations they wanted to see the full-text article for and which should be abstracted into an evidence table. The groups then presented their findings to the full panel for comment and consensus. After the meeting, each group participated in a series of conference calls to continue the literature selection process and resolve any questions.

An independent researcher led the effort to prepare evidence tables and relied on the assistance of one other researcher for the initial drafts of evidence tables. The evidence tables included a summary of the study, as well as a quality rating and rating of the risk of bias for selected articles. The quality rating system was based on the Cochrane Risk of Bias[8] and Jadad scoring system.[9] The ratings were based on six critical elements: evidence of balanced allocation, allocation concealment, blinded outcome assessment, completeness of outcome data, selective outcome reporting, and other sources of bias. Following the Cochrane approach, each article was assigned a quality score (1–6 points) and a risk-of-bias rating. Low risk of bias was indicated by a low risk of bias in all six domains, unclear risk of bias was indicated by an unclear rating on one or more domains (others low) or a high risk of bias on one domain (others low or unclear), and high risk of bias was indicated by a high risk of bias on two or more domains. The independent researcher reviewed all evidence tables and proposed quality and risk-of-bias ratings before they were distributed to the expert panel to use for the Grades of Recommendation Assessment, Development, and Evaluation[10] (GRADE) rating process.

Each panelist independently rated the quality of evidence and strength of recommendation for each criterion using the American College of Physicians' Guideline Grading System[11] (Table 1), which is based on the GRADE scheme developed previously. AGS staff compiled the panelist ratings for each group and returned them to that group, which then reached consensus in a conference call. Additional literature was obtained and included as needed. When group consensus could not be reached, the full panel reviewed the ratings and worked through any differences until consensus was reached. The panel judged each criterion as being a strong or weak recommendation on the basis of the quality of supporting evidence, the frequency and severity of harms, and the availability of better treatment alternatives. For some criteria, the panel provided a "strong" recommendation, even though the quality of evidence was low or moderate, when the potential for harm was substantial and safer or more-effective alternatives were available.

After consensus was reached within the expert panel, the updated guidelines were circulated for peer review to relevant organizations and societies and posted to the AGS website for public comment. Organizations that participated in peer review are listed in the Acknowledgments section of this article. The panel reviewed and addressed all comments.

Table 1. Designations of Quality of Evidence and Strength of Recommendations

Quality of Evidence	
High	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (≥2 consistent, higher-quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing large effects)
Moderate	Evidence is sufficient to determine risks of adverse outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (≥1 higher-quality trial with >100 participants; ≥2 higher-quality trials with some inconsistency; ≥2 consistent, lower-quality trials; or multiple, consistent observational studies with no significant methodological flaws showing at least moderate effects) limits the strength of the evidence
Low	Evidence is insufficient to assess harms or risks in health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes
Strength of Recommendation	
Strong	Benefits clearly outweigh harms, adverse events, and risks, or harms, adverse events, and risks clearly outweigh benefits
Weak	Benefits may not outweigh harms, adverse events, and risks
Insufficient	Evidence inadequate to determine net harms, adverse events, and risks

Adapted from[11].

RESULTS

The panel's recommendations are presented in Tables 2–7. References, as evidence tables, supporting the recommendations appear in the online appendix posted on the AGS website (www.americangeriatrics.org). Consistent with the 2012 AGS Beers Criteria, Tables 2–4 list PIMS for older adults outside the palliative care and hospice setting, including medications to avoid for many or most older adults (Table 2); medications for older adults with specific diseases or syndromes to avoid (Table 3); and medications to be used with caution (Table 4). New to the AGS Beers Criteria are potentially clinically important non-anti-infective drug–drug interactions (Table 5) and non-anti-infective medications to avoid or the dosage of which should be adjusted based on the individual's kidney function (Table 6). Tables 8-10 document the differences between the 2012 and 2015 AGS Beers Criteria.

Noteworthy Changes to PIMs and Older Adults

Based on two retrospective studies, the recommendation to avoid the anti-infective nitrofurantoin in individuals with a creatinine clearance of less than 60 mL/min has been revised, given evidence that it can be used with relative safety and efficacy in individuals with a creatinine clearance of 30 mL/min or greater. The long-term use of nitrofurantoin for suppression should still be avoided because of concerns of irreversible pulmonary fibrosis, liver toxicity, and peripheral neuropathy (Table 2).

The recommendation to avoid antiarrhythmic drugs (Classes 1a, 1c, III) as first-line treatment for atrial fibrillation has been removed in light of new evidence and guidelines that suggest that rhythm control can have outcomes as good as or better than those with rate control. Nevertheless, certain antiarrhythmics remain in the criteria. Amiodarone is still to be avoided as first-line therapy for atrial fibrillation unless the individual has heart failure or substantial left ventricular hypertrophy. Dronedarone is to be avoided in individuals with permanent atrial fibrillation or with severe or recently decompensated heart failure. Disopyramide, a Class 1a antiarrhythmic drug, should also be avoided because it is highly anticholinergic. Digoxin should be avoided as first-line therapy for atrial fibrillation or heart failure and should not be prescribed in daily doses greater than 0.125 mg for any indication.

The nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (eszopiclone, zaleplon, zolpidem) are to be avoided without consideration of duration of use because of their association with harms balanced with their minimal efficacy in treating insomnia. The recommendation to avoid sliding-scale insulin is retained, and further clarification of what constitutes a sliding-scale regimen is provided. An addition to Table 2 is the avoidance of the use of proton-pump inhibitors beyond 8 weeks without justification. Multiple studies and five systematic reviews and meta-analyses support an association between proton-pump inhibitor exposure and *Clostridium difficile* infection, bone loss, and fractures. Desmopressin for the treatment of nocturia or nocturnal polyuria is another addition because of the high risk of hyponatremia.

Noteworthy Changes to Drug–Disease and Drug–Syndrome PIMS

The nonbenzodiazepine, benzodiazepine receptor agonist hypnotics have been added to the list of drugs to avoid in individuals with dementia or cognitive impairment. Opioids have been added to the list of central nervous system (CNS) medications that should be avoided in individuals with a history of falls or fractures. Antipsychotics are to be avoided as first-line treatment of delirium because of conflicting evidence on their effectiveness and the potential for adverse drug effects (Table 3).

Drugs to Be Used with Caution

Table 4, medications to be used with caution in older adults, has not been changed. The panel determined that the medications listed in this table did not rise to the level of meriting inclusion in Tables 2 and 3 and should not be considered key elements of the criteria. Nevertheless, the panel believed that there was sufficient uncertainty or concern about the balance of benefits and harms for the listed medications that clinicians should be aware of potential problems and exercise caution when considering their use.

Drug–Drug Interactions

New to the AGS Beers Criteria are drug–drug interactions (excluding anti-infectives) that are highly associated with harmful outcomes in older adults.[12] The list is selective, and not comprehensive, and is not intended to diminish the clinical importance of known drug–drug interactions not listed. Examples of drug–drug interactions included in this new section include peripheral alpha-1 blockers used in combination with loop diuretics, which increases the risk of urinary incontinence in women, and taking three or more CNS-active drugs concomitantly, which increases the risk of falls. Other interactions manifest as extensions of both drugs' known pharmacological effects (e.g., angiotensin-converting enzyme inhibitors (ACEIs) and potassium-sparing diuretics without indications for use in systolic heart failure (amiloride and triamterene), which together increase risk of hyperkalemia). Other interactions increase the risk of a drug's toxicity (e.g., lithium in combination with an ACEI or loop diuretics) (Table 5).

PIMs Based on Kidney Function

Also new for 2015 are drugs that should be avoided or for which the dose should be adjusted in individuals with a specific degree of kidney impairment to avoid harm. This list was adapted from published consensus guidelines that an expert group including two AGS Beers Criteria panelists developed.[13] The AGS Beers panel reviewed the evidence and selected medications from these earlier consensus guidelines for inclusion; added additional medications, including several anticoagulants; and included spironolactone and triamterene, which in the 2012 criteria had been listed in Tables 2 and 3, respectively. The creatinine clearance thresholds below which use of apixaban, edoxaban, and rivaroxaban are to be avoided are based on clinical trial exclusion criteria and may not be the same as

Table 2. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Anticholinergics				
First-generation antihistamines Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Dimenhydrinate Diphenhydramine (oral) Doxylamine Hydroxyzine Meclizine Promethazine Triprolidine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate	Avoid	Moderate	Strong
Antiparkinsonian agents Benztropine (oral) Trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease	Avoid	Moderate	Strong
Antispasmodics Atropine (excludes ophthalmic) Belladonna alkaloids Clidinium-Chlordiazepoxide Dicyclomine Hyoscyamine Propantheline Scopolamine	Highly anticholinergic, uncertain effectiveness	Avoid	Moderate	Strong
Antithrombotics				
Dipyridamole, oral short-acting (does not apply to the extended-release combination with aspirin)	May cause orthostatic hypotension; more effective alternatives available; intravenous form acceptable for use in cardiac stress testing	Avoid	Moderate	Strong
Ticlopidine	Safer, effective alternatives available	Avoid	Moderate	Strong
Anti-infective				
Nitrofurantoin	Potential for pulmonary toxicity, hepatoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression of bacteria	Low	Strong
Cardiovascular				
Peripheral alpha-1 blockers Doxazosin Prazosin Terazosin	High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk–benefit profile	Avoid use as an antihypertensive	Moderate	Strong

(Continued)

Table 2 (Contd.)

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Central alpha blockers Clonidine Guanabenz Guanfacine Methyldopa Reserpine (>0.1 mg/d)	High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension	Avoid clonidine as first-line antihypertensive Avoid others as listed	Low	Strong
Disopyramide	Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred	Avoid	Low	Strong
Dronedarone	Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or severe or recently decompensated heart failure	Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure	High	Strong
Digoxin	Use in atrial fibrillation: should not be used as a first-line agent in atrial fibrillation, because more-effective alternatives exist and it may be associated with increased mortality	Avoid as first-line therapy for atrial fibrillation	Atrial fibrillation: moderate	Atrial fibrillation: strong
	Use in heart failure: questionable effects on risk of hospitalization and may be associated with increased mortality in older adults with heart failure; in heart failure, higher dosages not associated with additional benefit and may increase risk of toxicity	Avoid as first-line therapy for heart failure	Heart failure: low	Heart failure: strong
	Decreased renal clearance of digoxin may lead to increased risk of toxic effects; further dose reduction may be necessary in patients with Stage 4 or 5 chronic kidney disease	If used for atrial fibrillation or heart failure, avoid dosages >0.125 mg/d	Dosage >0.125 mg/d: moderate	Dosage >0.125 mg/d: strong
Nifedipine, immediate release	Potential for hypotension; risk of precipitating myocardial ischemia	Avoid	High	Strong
Amiodarone	Amiodarone is effective for maintaining sinus rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation; it may be reasonable first-line therapy in patients with concomitant heart failure or substantial left ventricular hypertrophy if rhythm control is preferred over rate control	Avoid amiodarone as first-line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy	High	Strong
Central nervous system				

(Continued)

Table 2 (Contd.)

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Antidepressants, alone or in combination Amitriptyline Amoxapine Clomipramine Desipramine Doxepin >6 mg/d Imipramine Nortriptyline Paroxetine Protriptyline Trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/d) comparable with that of placebo	Avoid	High	Strong
Antipsychotics, first- (conventional) and second- (atypical) generation	Increased risk of cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the older adult is threatening substantial harm to self or others	Avoid, except for schizophrenia, bipolar disorder, or short-term use as antiemetic during chemotherapy	Moderate	Strong
Barbiturates Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital	High rate of physical dependence, tolerance to sleep benefits, greater risk of overdose at low dosages	Avoid	High	Strong
Benzodiazepines *Short- and intermediate- acting* Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults	Avoid	Moderate	Strong

(Continued)

Table 2 (Contd.)

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Long-acting Clorazepate Chlordiazepoxide (alone or in combination with amitriptyline or clidinium) Clonazepam Diazepam Flurazepam Quazepam	May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia			
Meprobamate	High rate of physical dependence; very sedating	Avoid	Moderate	Strong
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zolpidem Zaleplon	Benzodiazepine-receptor agonists have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency department visits and hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration	Avoid	Moderate	Strong
Ergoloid mesylates (dehydrogenated ergot alkaloids) Isoxsuprine	Lack of efficacy	Avoid	High	Strong
Endocrine				
Androgens Methyltestosterone Testosterone	Potential for cardiac problems; contraindicated in men with prostate cancer	Avoid unless indicated for confirmed hypogonadism with clinical symptoms	Moderate	Weak
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women Evidence indicates that vaginal estrogens for the treatment of vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to nonhormonal therapies are advised to discuss the risk and benefits of low-dose vaginal estrogen (dosages of estradiol <25 μg twice weekly) with their healthcare provider	Avoid oral and topical patch Vaginal cream or tablets: acceptable to use low-dose intravaginal estrogen for management of dyspareunia, lower urinary tract infections, and other vaginal symptoms	Oral and patch: high Vaginal cream or tablets: moderate	Oral and patch: strong Topical vaginal cream or tablets: weak
Growth hormone	Impact on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	Avoid, except as hormone replacement after pituitary gland removal	High	Strong

(Continued)

Table 2 (Contd.)

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Insulin, sliding scale	Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting; refers to sole use of short- or rapid-acting insulins to manage or avoid hyperglycemia in absence of basal or long-acting insulin; does not apply to titration of basal insulin or use of additional short- or rapid-acting insulin in conjunction with scheduled insulin (i.e., correction insulin)	Avoid	Moderate	Strong
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong
Sulfonylureas, long-duration				
Chlorpropamide	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes syndrome of inappropriate antidiuretic hormone secretion	Avoid	High	Strong
Glyburide	Glyburide: higher risk of severe prolonged hypoglycemia in older adults			
Gastrointestinal				
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults	Avoid, unless for gastroparesis	Moderate	Strong
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong
Proton-pump inhibitors	Risk of *Clostridium difficile* infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (e.g., due to failure of drug discontinuation trial or H_2 blockers)	High	Strong
Pain medications				
Meperidine	Not effective oral analgesic in dosages commonly used; may have higher risk of neurotoxicity, including delirium, than other opioids; safer alternatives available	Avoid, especially in individuals with chronic kidney disease	Moderate	Strong

(Continued)

Table 2 (Contd.)

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Non-cyclooxygenase-selective NSAIDs, oral: Aspirin >325 mg/d Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam Sulindac Tolmetin	Increased risk of gastrointestinal bleeding or peptic ulcer disease in high-risk groups, including those aged >75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents; use of proton-pump inhibitor or misoprostol reduces but does not eliminate risk. Upper gastrointestinal ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in ~2–4% of patients treated for 1 year; these trends continue with longer duration of use	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol)	Moderate	Strong
Indomethacin	Indomethacin is more likely than other NSAIDs to have adverse CNS effects. Of all the NSAIDs, indomethacin has the most adverse effects.	Avoid	Moderate	Strong
Ketorolac, includes parenteral	Increased risk of gastrointestinal bleeding, peptic ulcer disease, and acute kidney injury in older adults			
Pentazocine	Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other opioid analgesic drugs; is also a mixed agonist and antagonist; safer alternatives available	Avoid	Low	Strong
Skeletal muscle relaxants Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine	Most muscle relaxants poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults questionable	Avoid	Moderate	Strong
Genitourinary				
Desmopressin	High risk of hyponatremia; safer alternative treatments	Avoid for treatment of nocturia or nocturnal polyuria	Moderate	Strong

The primary target audience is practicing clinicians. The intentions of the criteria are to improve the selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality-of-care, cost, and utilization data.
CNS = central nervous system; NSAIDs = nonsteroidal anti-inflammatory drugs.

Table 3. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug–Disease or Drug–Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Cardiovascular					
Heart failure	NSAIDs and COX-2 inhibitors Nondihydropyridine CCBs (diltiazem, verapamil)—avoid only for heart failure with reduced ejection fraction Thiazolidinediones (pioglitazone, rosiglitazone) Cilostazol Dronedarone (severe or recently decompensated heart failure)	Potential to promote fluid retention and exacerbate heart failure	Avoid	NSAIDs: moderate CCBs: moderate Thiazolidinediones: high Cilostazol: low Dronedarone: high	Strong
Syncope	AChEIs Peripheral alpha-1 blockers Doxazosin Prazosin Terazosin Tertiary TCAs Chlorpromazine Thioridazine Olanzapine	Increases risk of orthostatic hypotension or bradycardia	Avoid	Peripheral alpha-1 blockers: high TCAs, AChEIs, antipsychotics: moderate	AChEIs, TCAs: strong Peripheral alpha-1 blockers, antipsychotics: weak
Central nervous system					
Chronic seizures or epilepsy	Bupropion Chlorpromazine Clozapine Maprotiline Olanzapine Thioridazine Thiothixene Tramadol	Lowers seizure threshold; may be acceptable in individuals with well-controlled seizures in whom alternative agents have not been effective	Avoid	Low	Strong
Delirium	Anticholinergics (see Table 7 for full list) Antipsychotics Benzodiazepines Chlorpromazine Corticosteroids[a] H_2-receptor antagonists Cimetidine Famotidine Nizatidine Ranitidine Meperidine Sedative hypnotics	Avoid in older adults with or at high risk of delirium because of the potential of inducing or worsening delirium Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the older adult is threatening substantial harm to self or others Antipsychotics are associated with greater risk of cerebrovascular accident (stroke) and mortality in persons with dementia	Avoid	Moderate	Strong

(Continued)

Table 3 (Contd.)

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Dementia or cognitive impairment	Anticholinergics (see Table 7 for full list) Benzodiazepines H_2-receptor antagonists Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zolpidem Zaleplon Antipsychotics, chronic and as-needed use	Avoid because of adverse CNS effects Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the older adult is threatening substantial harm to self or others. Antipsychotics are associated with greater risk of cerebrovascular accident (stroke) and mortality in persons with dementia	Avoid	Moderate	Strong
History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zaleplon Zolpidem TCAs SSRIs Opioids	May cause ataxia, impaired psychomotor function, syncope, additional falls; shorter-acting benzodiazepines are not safer than long-acting ones If one of the drugs must be used, consider reducing use of other CNS-active medications that increase risk of falls and fractures (i.e., anticonvulsants, opioid-receptor agonists, antipsychotics, antidepressants, benzodiazepine-receptor agonists, other sedatives and hypnotics) and implement other strategies to reduce fall risk	Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure and mood disorders Opioids: avoid, excludes pain management due to recent fractures or joint replacement	High Opioids: moderate	Strong Opioids: strong
Insomnia	Oral decongestants Pseudoephedrine Phenylephrine Stimulants Amphetamine Armodafinil Methylphenidate Modafinil Theobromines Theophylline Caffeine	CNS stimulant effects	Avoid	Moderate	Strong

(Continued)

Table 3 (Contd.)

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Parkinson disease	All antipsychotics (except aripiprazole, quetiapine, clozapine) Antiemetics Metoclopramide Prochlorperazine Promethazine	Dopamine-receptor antagonists with potential to worsen parkinsonian symptoms Quetiapine, aripiprazole, clozapine appear to be less likely to precipitate worsening of Parkinson disease	Avoid	Moderate	Strong
Gastrointestinal					
History of gastric or duodenal ulcers	Aspirin (>325 mg/d) Non-COX-2 selective NSAIDs	May exacerbate existing ulcers or cause new or additional ulcers	Avoid unless other alternatives are not effective and patient can take gastroprotective agent (i.e., proton-pump inhibitor or misoprostol)	Moderate	Strong
Kidney and urinary tract					
Chronic kidney disease Stages IV or less (creatinine clearance <30 mL/min)	NSAIDs (non-COX and COX-selective, oral and parenteral)	May increase risk of acute kidney injury and further decline of renal function	Avoid	Moderate	Strong
Urinary incontinence (all types) in women	Estrogen oral and transdermal (excludes intravaginal estrogen) Peripheral alpha-1 blockers Doxazosin Prazosin Terazosin	Aggravation of incontinence	Avoid in women	Estrogen: high Peripheral alpha-1 blockers: moderate	Estrogen: strong Peripheral alpha-1 blockers: strong
Lower urinary tract symptoms, benign prostatic hyperplasia	Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 7 for complete list)	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Strong

The primary target audience is the practicing clinician. The intentions of the criteria are to improve selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality-of-care, cost, and utilization data.

[a] Excludes inhaled and topical forms. Oral and parenteral corticosteroids may be required for conditions such as exacerbations of chronic obstructive pulmonary disease but should be prescribed in the lowest effective dose and for the shortest possible duration.

CCB = calcium channel blocker; AChEI = acetylcholinesterase inhibitor; CNS = central nervous system; COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug; SSRIs = selective serotonin reuptake inhibitors; TCA = tricyclic antidepressant.

Table 4. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults

Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Aspirin for primary prevention of cardiac events	Lack of evidence of benefit versus risk in adults aged ≥80	Use with caution in adults aged ≥80	Low	Strong
Dabigatran	Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other target-specific oral anticoagulants in adults aged ≥75; lack of evidence of efficacy and safety in individuals with CrCl <30 mL/min	Use with caution in in adults aged ≥75 and in patients with CrCl <30 mL/min	Moderate	Strong
Prasugrel	Increased risk of bleeding in older adults; benefit in highest-risk older adults (e.g., those with prior myocardial infarction or diabetes mellitus) may offset risk	Use with caution in adults aged ≥75	Moderate	Weak
Antipsychotics Diuretics Carbamazepine Carboplatin Cyclophosphamide Cisplatin Mirtazapine Oxcarbazepine SNRIs SSRIs TCAs Vincristine	May exacerbate or cause syndrome of inappropriate antidiuretic hormone secretion or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults	Use with caution	Moderate	Strong
Vasodilators	May exacerbate episodes of syncope in individuals with history of syncope	Use with caution	Moderate	Weak

The primary target audience is the practicing clinician. The intentions of the criteria are to improve selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality-of-care, cost, and utilization data.

CrCl = creatinine clearance; SNRIs = serotonin-norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.

those in their labeling. As with the drug–drug interaction table, this list is not meant to be comprehensive but to highlight potentially important but sometimes overlooked dose adjustments that are of particular concern for older adults. Anti-infective drugs were not included because the focus of the AGS Beers Criteria is on medications often employed for chronic use and because such information is available from multiple other sources (Table 6).

Drugs with Strong Anticholinergic Properties

Numerous scales are available to rank anticholinergic activity. The panel used a composite of several scales to draft Table 7, which provides an updated list of drugs with strong anticholinergic properties.[14–17] Investigators who developed the scales that the panel used in 2012 were asked whether any changes had been made, and the panel considered those. The most notable drug to be removed from the list was the second-generation antihistamine loratadine.

DISCUSSION

The 2015 AGS Beers Criteria for PIMs is the second such update by the American Geriatrics Society of medications to avoid in older adults and the fourth update of the criteria since their original release.[18–21] The criteria were first published in 1991, making them the longest-running criteria for PIMs in older adults. The process improves with each update. The literature search has become more targeted and refined, identifying new and important supporting evidence. The evidence review and grading methodology has been adjusted according to best practices and evolving approaches recommended by expert organizations. As in 2012, this resulted in some changes to the criteria in 2015, including drugs that were modified or dropped and a few new additions. The 2015 update introduced two new areas to improve drug safety in older adults: 1) drugs for which dose adjustment is required based on kidney impairment and 2) drug–drug interactions. Rather than create numerous individual caveats for each criterion excluding individuals in palliative care or hospice settings, the panel chose to exclude individuals in these settings from the criteria. The panel felt justified making this decision because of the shift in benefit-to-harm ratio in end-of-life decisions and paucity of evidence available for avoiding drugs in these populations.

Compared with the 2012 update, the 2015 update has fewer changes and new medications, likely because of the

Table 5. 2015 American Geriatrics Society Beers Criteria for Potentially Clinically Important Non-Anti-infective Drug–Drug Interactions That Should Be Avoided in Older Adults

Object Drug and Class	Interacting Drug and Class	Risk Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
ACEIs	Amiloride or triamterene	Increased risk of Hyperkalemia	Avoid routine use; reserve for patients with demonstrated hypokalemia while taking an ACEI	Moderate	Strong
Anticholinergic	Anticholinergic	Increased risk of Cognitive decline	Avoid, minimize number of anticholinergic drugs (Table 7)	Moderate	Strong
Antidepressants (i.e., TCAs and SSRIs)	≥2 other CNS-active drugs[a]	Increased risk of Falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS-active drugs	Moderate	Strong
Antipsychotics	≥2 other CNS-active drugs[a]	Increased risk of Falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS-active drugs	Moderate	Strong
Benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics	≥2 other CNS-active drugs[a]	Increased risk of Falls and fractures	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS-active drugs	High	Strong
Corticosteroids, oral or parenteral	NSAIDs	Increased risk of Peptic ulcer disease or gastrointestinal bleeding	Avoid; if not possible, provide gastrointestinal protection	Moderate	Strong
Lithium	ACEIs	Increased risk of Lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong
Lithium	Loop diuretics	Increased risk of Lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong
Opioid receptor agonist analgesics	≥2 other CNS-active drugs[a]	Increased risk of Falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS drugs	High	Strong
Peripheral Alpha-1 blockers	Loop diuretics	Increased risk of Urinary incontinence in older women	Avoid in older women, unless conditions warrant both drugs	Moderate	Strong
Theophylline	Cimetidine	Increased risk of Theophylline toxicity	Avoid	Moderate	Strong
Warfarin	Amiodarone	Increased risk of Bleeding	Avoid when possible; monitor international normalized ratio closely	Moderate	Strong
Warfarin	NSAIDs	Increased risk of Bleeding	Avoid when possible; if used together, monitor for bleeding closely	High	Strong

[a]Central nervous system (CNS)-active drugs: antipsychotics; benzodiazepines; nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); and opioids.
ACEI = angiotensin-converting enzyme inhibitor; NSAID = nonsteroidal anti-inflammatory drug.

shorter time span since the criteria were last revised. Only three new medications and two new drug classes were added to Tables 2 or 3, although several were modified or had some changes to the rationale and recommendation statements. In a few instances, the level of evidence was revised based on new literature and the improved modified grading methodology. Some notable changes were the 90-day-use caveat being removed from nonbenzodiazepine, benzodiazepine receptor agonist hypnotics, resulting in an unambiguous "avoid" statement (without caveats) because of the increase in the evidence of harm in this area since the 2012 update.[22,23] In some cases, the rationale or wording of an avoid statement was modified or clarified because the panel and AGS had received comments regarding some confusion about a medication in the criteria. For example, the term "sliding scale" insulin was defined more clearly when referred to in the criteria. Other changes included lowering the creatinine clearance at which nitrofurantoin should be avoided to less than 30 mL/min from less than 60 mL/min. Also, removing Classes 1a, 1c, and III (with the exception of amiodarone) antiarrhythmic drugs as first-line treatment for atrial fibrillation. Constipation was removed as a drug–disease, drug–syndrome category, because this condition is common across the age spectrum and relevant drug–disease, drug–syndrome combinations to avoid are not predominantly specific to older adults.

Some other important additions in the 2015 update were the addition of long-term proton-pump inhibitor use in the absence of a strong indication because of risk of *C. difficile* infection, bone loss, and fractures and the addition of opioids in the diagnosis and condition table for older adults with a history of falls and fractures. If opioids must be used, it is recommended that reducing the use of other CNS-active medications be considered.[24,25] This statement is in recognition of the need to have adequate pain control while balancing the potential harms from opioids and untreated pain. The panel balanced the difficulty and challenges of poorly treated pain with the harms of opioids and available alternatives in older adults. Another critical change was to the language for use of antipsy-

Table 6. 2015 American Geriatrics Society Beers Criteria for Non-Anti-Infective Medications That Should Be Avoided or Have Their Dosage Reduced with Varying Levels of Kidney Function in Older Adults

Medication Class and Medication	Creatinine Clearance, mL/min, at Which Action Required	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Cardiovascular or hemostasis					
Amiloride	<30	Increased potassium, and decreased sodium	Avoid	Moderate	Strong
Apixaban	<25	Increased risk of bleeding	Avoid	Moderate	Strong
Dabigatran	<30	Increased risk of bleeding	Avoid	Moderate	Strong
Edoxaban	30–50	Increased risk of bleeding	Reduce dose	Moderate	Strong
	<30 or >95		Avoid		
Enoxaparin	<30	Increased risk of bleeding	Reduce dose	Moderate	Strong
Fondaparinux	<30	Increased risk of bleeding	Avoid	Moderate	Strong
Rivaroxaban	30–50	Increased risk of bleeding	Reduce dose	Moderate	Strong
	<30		Avoid		
Spironolactone	<30	Increased potassium	Avoid	Moderate	Strong
Triamterene	<30	Increased potassium, and decreased sodium	Avoid	Moderate	Strong
Central nervous system and analgesics					
Duloxetine	<30	Increased Gastrointestinal adverse effects (nausea, diarrhea)	Avoid	Moderate	Weak
Gabapentin	<60	CNS adverse effects	Reduce dose	Moderate	Strong
Levetiracetam	≤80	CNS adverse effects	Reduce dose	Moderate	Strong
Pregabalin	<60	CNS adverse effects	Reduce dose	Moderate	Strong
Tramadol	<30	CNS adverse effects	Immediate release: reduce dose Extended release: avoid	Low	Weak
Gastrointestinal					
Cimetidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Famotidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Nizatidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Ranitidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Hyperuricemia					
Colchicine	<30	Gastrointestinal, neuromuscular, bone marrow toxicity	Reduce dose; monitor for adverse effects	Moderate	Strong
Probenecid	<30	Loss of effectiveness	Avoid	Moderate	Strong

CNS = central nervous system.

chotics[26] in the dementia and delirium drug–disease, drug–syndrome category and the addition of avoiding antipsychotics in persons with delirium as first-line treatment. With increasing evidence of harm associated with antipsychotics[27,28] and conflicting evidence on their effectiveness in delirium and dementia, the rationale to avoid was modified to "avoid antipsychotics for behavioral problems unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible, ***and*** the older adult is threatening substantial harm to self or others."[7] The table of medications with strong anticholinergic properties has been updated. Anticholinergic burden and measurement is an area of literature that is continually evolving. Use of anticholinergic medications remains a concern because it is associated with impaired cognitive and physical function and risk of dementia.[29,30]

These criteria continue to be useful and necessary as a clinical and public health tool to improve medication safety in older adults and to increase awareness of polypharmacy and aid decision-making for choosing drugs to avoid in older adults. The AGS is publishing a companion piece to this update Beers Criteria; *How to Use the Beers Criteria—A Guide for Patients, Clinicians, Health Systems, and Payors*, published online in this journal. Recent work illustrates that prescription drug use has increased in older adults over the past 20 years, with poorer health in older adults associated with being on multiple medications.[31] Using data from the Medical Expenditure Panel Survey (MEPS), it was found that at least 41% of older adults still filled a prescription for a PIM in 2009–10 according to the 2012 AGS Beers Criteria. Even though the rate of PIM use declined from 45.5% in 2006–07 to 40.8% in 2009–10, almost half of older adults still filled a PIM presecription.[32] Despite their potential to increase the risk of falls, fractures, and cognitive impairment, the use of benzodiazepines remains high (~9%).[32,33]

The 2015 AGS Beers Criteria are an essential evidence-based tool to use in decision-making for drugs to avoid in older adults, but they are not meant to override clinical judgment or an individual's preferences, values, and needs. There may be cases in which the healthcare provider determines that a drug on the list is the only reasonable alternative or the individual is at the end of life or receiving palliative care. The criteria were developed in a

Table 7. Drugs with Strong Anticholinergic Properties

Antihistamines	Antiparkinsonian agents	Skeletal muscle relaxants
Brompheniramine	Benztropine	Cyclobenzaprine
Carbinoxamine	Trihexyphenidyl	Orphenadrine
Chlorpheniramine		
Clemastine		
Cyproheptadine		
Dexbrompheniramine		
Dexchlorpheniramine		
Dimenhydrinate		
Diphenhydramine (oral)		
Doxylamine		
Hydroxyzine		
Meclizine		
Triprolidine		
Antidepressants	Antipsychotics	Antiarrhythmic
Amitriptyline	Chlorpromazine	Disopyramide
Amoxapine	Clozapine	
Clomipramine	Loxapine	
Desipramine	Olanzapine	
Doxepin (>6 mg)	Perphenazine	
Imipramine	Thioridazine	
Nortriptyline	Trifluoperazine	
Paroxetine		
Protriptyline		
Trimipramine		
Antimuscarinics (urinary incontinence)	Antispasmodics	Antiemetic
Darifenacin	Atropine (excludes ophthalmic)	Prochlorperazine
Fesoterodine	Belladonna alkaloids	Promethazine
Flavoxate	Clidinium-chlordiazepoxide	
Oxybutynin	Dicyclomine	
Solifenacin	Homatropine (excludes ophthalmic)	
Tolterodine	Hyoscyamine	
Trospium	Propantheline	
	Scopolamine (excludes ophthalmic)	

Table 8. Medications Moved to Another Category or Modified Since 2012 Beers Criteria

Independent of Diagnoses or Condition (Table 2)	Considering Disease or Syndrome Interactions (Table 3)
Nitrofurantoin—recommendation and rationale modified	Heart failure—rationale and quality of evidence modified
Dronedarone—recommendation and rationale modified	Chronic seizures or epilepsy—quality of evidence modified
Digoxin—recommendation and rationale modified	Delirium—recommendation and rationale modified
Benzodiazepines—recommendation modified	Dementia or cognitive impairment—recommendation and rationale modified; new drugs added
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics—recommendation modified	History of falls or fractures—recommendation and rationale modified; new drugs added
Meperidine—recommendation modified	Parkinson disease—recommendation and rationale modified
Indomethacin and ketorolac, includes parenteral—rationale modified	Chronic kidney disease Stage IV or less (creatinine clearance <30 mL/min)—triamterene moved to Tables 5 and 6
Antipsychotics—recommendation and rationale modified	Insomnia—new drugs added
Estrogen—recommendation modified	
Insulin, sliding scale—rationale modified	

Table 9. Medications Removed Since 2012 Beers Criteria

Independent of Diagnoses or Condition (Table 2)	Considering Disease and Syndrome Interactions (Table 3)
Antiarrhythmic drugs (Class 1a, 1c, III except amiodarone) as first-line treatment for atrial fibrillation	Chronic constipation—entire criterion
Trimethobenzamide	Lower urinary tract—inhaled anticholinergic drugs
Mesoridazine—no longer marketed in United States	
Chloral hydrate—no longer marketed in United States	

way that facilitates a team approach (physicians, nurses, pharmacists, therapists, and others) to prescribing and monitoring adverse effects.

The 2015 AGS Beers Criteria encourage the use of nonpharmacological approaches when needed to avoid drugs that have a high risk of causing an adverse event. The evidence base for specific nonpharmacological approaches using a person-centered approach to care is growing, especially in older adults and in persons with dementia and delirium.[34-36] A nonpharmacological toolkit for reducing antipsychotic use in older adults by promoting positive behavioral health, developed by investigators at The Pennsylvania State University and the Polisher Research Institute, was recently released. This toolkit can be accessed online (www.nursinghometoolkit.com). Nonpharmacological strategies for hospitalized older adults and their caregivers can also be accessed online (www.hospitalelderlifeprogram.org). A 2015 systematic review and meta-analysis of nonpharmacological strategies in older adults with delirium found that 11 of 14 studies demonstrated significant reductions in delirium incidence and a reduction in the rate of falls.[37] Several studies have also illustrated effective interventions to improve sleep.[38,39]

The AGS Beers Criteria are one component of a comprehensive approach to medication use in older adults, and they should be used in conjunction with other tools. The Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) criteria, first developed in 2008, are an explicit tool for assessing prescribing in older adults in Europe. They were updated in 2015 to include

Table 10. Medications Added Since 2012 Beers Criteria

Independent of Diagnoses or Condition (Table 2)	Considering Disease and Syndrome Interactions (Table 3)
Proton-pump inhibitors	Falls and fractures—opioids
Desmopressin	Insomnia—armodafinil and modafinil
Anticholinergics, first-generation antihistamines—meclizine	Dementia or cognitive impairment—eszopiclone and zaleplon
	Delirium—antipsychotics

drugs affecting or being affected by renal function, similar to this update of the AGS Beers Criteria.[40] Similar tools have been developed in Europe.[41] The current update of the AGS Beers Criteria confirms and extends this work with a rigorous independent evidence grading process, an open peer-review comment period consistent with Institute of Medicine standards, and the addition of drug–drug interactions and renal dose adjustment.

The 2015 AGS Beers Criteria have several important limitations. Older adults are often underrepresented in drug trials.[11,42] Thus, using an evidence-based approach may underestimate some drug-related problems or lead to weaker evidence grading. The GRADE process was used for evidence grading, which allowed for rigor and greater transparency in the evidence grading process.[10] The criteria cannot account for all individuals and special populations; for instance, they do not comprehensively address the needs of individuals receiving palliative and hospice care, in whom the balance of benefits and harms for many drugs on the list may differ from those of the general population of older adults. Finally, the search strategies used might have missed some studies published in languages other than English and studies available in unpublished technical reports, white papers, or other "gray literature" sources.

The process had many noteworthy strengths, including the use of a 13-member, geographically diverse interdisciplinary panel with ex-officio members from the Centers for Medicare and Medicaid Services, National Committee for Quality Assurance, and Pharmacy Quality Alliance; the use of an evidence-based approach using Institute of Medicine standards and independent grading of the evidence by panel members followed by a consensus approach; and the continued development of a partnership with AGS to update the criteria regularly.

In conclusion, the 2015 AGS Beers Criteria have several important updates, including the addition of new medications, clarification of some of the 2012 criteria language, the addition of selected drugs for which dose adjustment is required based on kidney impairment, and the addition of selected drug–drug interactions. Careful application of the criteria by healthcare professionals, consumers, payors, and health systems should lead to closer monitoring of drug use. Dissemination of the criteria should lead to increased education and awareness of drug-related problems, increased reporting of drug-related problems, active patient and caregiver engagement and communication regarding medication use, targeted interventions to decrease adverse drug events in older adults, and improved outcomes. Continued support from the AGS will allow for the criteria methodology and evidence for PIMs to be evaluated regularly and to remain up to date, relevant and valuable.

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The following individuals were members of the AGS Panel to update the 2015 AGS Beers Criteria: Donna M. Fick, PhD, RN, FGSA, FAAN, College of Nursing and Medicine, The Pennsylvania State University, University Park, PA (co-chair); Todd P. Semla, PharmD, MS, BCPS, FCCP, AGSF, U.S. Department of Veterans Affairs National Pharmacy Benefits Management Services and Northwestern University Feinberg School of Medicine, Chicago, IL (co-chair); Judith Beizer, PharmD, CGP, FASCP, AGSF, St. Johns University, New York, NY; Nicole Brandt, PharmD, BCPP, CGP, University of Maryland, Baltimore, MD; Robert Dombrowski, PharmD, Centers for Medicare and Medicaid Services, Baltimore, MD (nonvoting member); Catherine E. DuBeau, MD, University of Massachusetts Medical School, Worcester, MA; Woody Eisenberg, MD, Pharmacy Quality Alliance, Inc., Baltimore, MD (nonvoting member); Jerome J. Epplin, MD, AGSF, Litchfield Family Practice Center, Litchfield, IL; Nina Flanagan, PhD, GNP-BC, APHM-BC, Decker School of Nursing, Binghamton University, Dunmore, PA; Erin Giovannetti, National Committee for Quality Assurance, Washington, DC (nonvoting member); Joseph Hanlon, PharmD, MS, BCPS, FASHP, FASCP, FGSA, AGSF, Department of Medicine (Geriatric Medicine) School of Medicine, University of Pittsburgh and Geriatric Research, Education and Clinical Center, Veterans Affairs Healthcare (GRECC) System, Pittsburgh, PA; Peter Hollmann, MD, AGSF, Alpert Medical School, Brown University, Providence, RI; Rosemary Laird, MD, MHSA, AGSF, Geriatric Medical Leader for Florida Hospital, Winter Park, FL; Sunny Linnebur, PharmD, FCCP, BCPS, CGP, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, CO; Satinderpal Sandhu, MD, Summa Health Care System and Northeast Ohio Medical University, Akron, OH; Michael Steinman, MD, University of California at San Francisco and San Francisco Veterans Affairs Medical Center, San Francisco, CA.

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