Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug–Disease Interactions in the Elderly Quality Measures

Joseph T. Hanlon, PharmD, MS,a,b,c,d,e,f,g,h Todd P. Semla, MS, PharmD,i,j,k and Kenneth E. Schmader, MDl,m

The National Committee for Quality Assurance (NCQA) and the Pharmacy Quality Alliance (PQA) use the American Geriatrics Society (AGS) Beers Criteria to designate the quality measure Use of High-Risk Medications in the Elderly (HRM). The Centers for Medicare and Medicaid Services (CMS) use the HRM measure to monitor and evaluate the quality of care provided to Medicare beneficiaries. NCQA additionally uses the AGS Beers Criteria to designate the quality measure Potentially Harmful Drug–Disease Interactions in the Elderly. Medications included in these measures may be harmful to elderly adults and negatively affect a healthcare plan’s quality ratings. Prescribers, pharmacists, patients, and healthcare plans may benefit from evidence-based alternative medication treatments to avoid these problems. Therefore the goal of this work was to develop a list of alternative medications to those included in the two measures. The authors conducted a comprehensive literature review from 2000 to 2015 and a search of their personal files. From the evidence, they prepared a list of drug-therapy alternatives with supporting references. A reference list of nonpharmacological approaches was also provided when appropriate. NCQA, PQA, the 2015 AGS Beers Criteria panel, and the Executive Committee of the AGS reviewed the drug-therapy alternatives and nonpharmacological approaches. Recommendations by these groups were incorporated into the final list of alternatives. The final product of drug-therapy alternatives to medications included in the two quality measures and some nonpharmacological resources will be useful to health professionals, consumers, payers, and health systems that care for older adults. J Am Geriatr Soc 63:e8–e18, 2015.

Key words: inappropriate medications; Beers Criteria; medication management

The pharmacopeia of treatment options available to clinicians is vast, and its navigation complicated. A number of factors must be considered when selecting medications for elderly adults, including each individual’s parameters that may affect drug pharmacokinetics/pharmacodynamics, formulary choices and related costs, ease of use, and the likelihood the treatment will be safe and effective. The Centers for Medicare and Medicaid Services (CMS) uses the National Committee for Quality Assurance (NCQA) and Pharmacy Quality Alliance (PQA) quality measure Use of High-Risk Medications in the Elderly (HRM) to monitor and evaluate the quality of care provided to Medicare beneficiaries. In addition, NCQA publishes a second quality measure, Potentially Harmful Drug-Disease Interactions in the Elderly. Both measures, published in 2015, were based on the 2012 American Geriatrics Society (AGS) Beers Criteria and include some medications that elderly adults should avoid, along with drugs that could potentially exacerbate three diseases or conditions (falls, dementia, chronic kidney disease). Sometimes these potentially suboptimal medications are appropriate for an individual elderly adult, but these measures can influence a prescriber’s choice and result in denial of medication, resulting in treatment delays. In addition,
prescribing these suboptimal medications may negatively affect a healthcare plan’s quality ratings.

Prescribers, pharmacists, patients, and healthcare plans might benefit from having a list of evidence-based alternative medication treatments to avoid these problems, along with some nonpharmacological approaches when appropriate. For this reason, the authors’ goals were to develop a list of alternative medications that may be used instead of the potentially high-risk medications included in the two quality measures. This is not meant to diminish the importance of nonpharmacological alternatives for the potentially high-risk medications.

This list of medication alternatives coincides with the publication of the 2015 AGS Beers Criteria. At this time, it is unknown how the quality measures will be revised based on the 2015 AGS Beers Criteria. We anticipate updating the list of medication alternatives based upon the 2015 AGS Beers Criteria and the CMS, NCQA, and PQA quality measures in the future and making it publicly available.

METHODS

The list of medications identified as potentially harmful and included in each measure was divided among the three authors based on their areas of expertise and interest. Each author then identified and searched for evidence from the scientific literature supporting alternative medication treatments using common search tools, including PubMed, the Cochrane Library, and Google Scholar for 2000 to 2015. Additional articles identified from the authors’ personal files were also considered. Because comparative clinical trials in elderly adults are uncommon, explicit expert panel consensus criteria were also consulted and referenced.4–7

The three authors individually chose drug therapy alternatives along with some nonpharmacological approaches when appropriate and provided supporting articles. All three authors reviewed and critiqued these during a series of conference calls. Preliminary findings were presented at the 2014 AGS annual meeting, and feedback was sought and received from NCQA, PQA, the 2015 AGS Beers Criteria panel, and the Executive Committee of the AGS.

RESULTS

Table 1 shows alternatives for high-risk medications organized into 15 therapeutic classes according to the measure specifications for HRM published in 2015. There are multiple alternatives given for some high-risk medications that can be used for multiple indications (e.g., tricyclic antidepressants). In addition, trimethobenzamide is not included because of recent data showing it to be effective in reducing nausea and vomiting in individuals with Parkinson’s disease taking subcutaneous apomorphine, prompting its absence from the 2015 AGS Beers Criteria.8 References supporting drug therapy alternatives listed in Table 1 are provided in Appendix 1.

Table 2 shows 10 therapeutic drug classes that are included in the Potentially Harmful Drug–Disease Interactions in the Elderly measure (a prior history of falls, dementia, chronic kidney disease). Several high-risk medications (e.g., benzodiazepine receptor agonists, tricyclic antidepressants) can exacerbate more than one disease or condition (e.g., falls, dementia). Similar to Table 1, drugs that can be used for more than one indication may have more than one alternative. References supporting alternatives listed in Table 2 are provided in Appendix 2.

Nonpharmacological alternatives may be appropriate first-line alternatives. Appendix 3 provides resources in which clinicians can find information about nonpharmacological treatment of selected problems and conditions in older adults.

DISCUSSION

This article outlines a list of alternative medications to those included in two quality measures, HRM and Potentially Harmful Drug–Disease Interactions in the Elderly. It is hoped that this list, along with the nonpharmacological approaches identified in Appendix 3, will be helpful to healthcare professionals caring for older adults. By no means is this list of alternatives and resources comprehensive or exhaustive; rather it is a starting point. The strength of these outlined alternatives and resources is that they are based upon information contained in guidelines, metaanalyses, randomized controlled trials, and rigorous observational studies. In addition, in some older adults, the use of a potentially suboptimal medication may be appropriate. Alternatives to some anticholinergic medications, nonsteroidal antiinflammatory drugs (NSAIDs), central nervous system (CNS) medications, and estrogen are elaborated upon below.

Drugs with strong anticholinergic activity are to be avoided because of their potential to be constipating, worsen some forms of lower urinary tract symptoms, dry mucous membranes, and induce delirium or dementia.9–12 Older persons who take multiple drugs with anticholinergic activity, be they strong, moderate, or weak in potency, are at greater risk of physical, functional, and cognitive decline.11 Two types of highly anticholinergic drugs (first-generation antihistamines, drugs used for Parkinson’s disease) are discussed below.

First-generation antihistamines are notoriously anticholinergic and sedating, often requiring prolonged dosage titration to achieve a therapeutic dose. Their sedating properties, particularly those of diphenhydramine, have been used as the therapeutic effect in many over-the-counter (OTC) sleep aids. Several alternative treatments are available for allergic rhinitis, including first-line options of intranasal saline flushes, a less- or nonsedating oral (second generation) antihistamine, and intranasal corticosteroids. All of these include OTC options. For best results, the latter two options are best started before allergen exposure.

Tremor is an early symptom of Parkinson disease that can be treated with an anticholinergic drug, yet tremor in older adults is often less pronounced, thus shifting the benefit to harm ratio away from the anticholinergic drugs. Evidence-based reviews and guidelines recommend the carbidopa-levodopa combination as first-line treatment for older adults.13–17 Dopamine agonists are reserved for later in the disease, given their greater likelihood to cause CNS disturbances.13
<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>High-Risk Medications</th>
<th>Alternatives</th>
<th>References (Appendix 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticholinergic</strong></td>
<td>First-generation antihistamine</td>
<td>Brompheniramine</td>
<td>Intranasal normal saline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carboxinamidine</td>
<td>Second-generation antihistamine (e.g., cetirizine, fexofenadine, loratadine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chlorpheniramine</td>
<td>Intranasal steroid (e.g., beclomethasone, fluticasone, over the counter)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clemastine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cyproheptadine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dextromethorphan</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diphenhydramine (oral)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doxylamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydroxyzine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Promethazine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Triprolidine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intranasal normal saline</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Second-generation antihistamine (e.g., cetirizine, fexofenadine, loratadine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intranasal steroid (e.g., beclomethasone, fluticasone, over the counter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>Benztropine (oral)</td>
<td>Carbidopa/levodopa</td>
<td>14–17</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>Dipyridamole (oral immediate release)</td>
<td>Antithrombotic therapy for the secondary prevention of noncardioembolic stroke</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>Ticlopidine</td>
<td>Clopidogrel, aspirin 25 mg with extended-release dipyridamole 200 mg</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Alpha agonists, central</td>
<td>Guanabenz</td>
<td>Thiazide-type diuretic, ACEI, ARB, long-acting dihydropyridine CCB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Guanfacine</td>
<td>In black individuals—thiazide-type diuretic, CCB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylidopa</td>
<td>For heart failure, diabetes mellitus, chronic kidney disease—ACEI or ARB preferred</td>
</tr>
<tr>
<td>Other</td>
<td>Disopyramide</td>
<td>Atrial fibrillation:</td>
<td>51,52</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For rate control—nondihydropyridine CCB (e.g., diltiazem), beta-blocker</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For rhythm control—dofetilide flecainide, propafenone</td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Nifedipine (immediate release)</td>
<td>Long-acting dihydropyridine CCB (e.g., amlodipine)</td>
<td>48–50</td>
</tr>
<tr>
<td>Tertiary tricyclic antidepressant</td>
<td>Amitriptyline</td>
<td>For depression—SSRI (except paroxetine), SNRI, bupropion (also see Appendix 3)</td>
<td>53–54</td>
</tr>
<tr>
<td></td>
<td>Clomipramine</td>
<td>For neuropathic pain—SNRI, gabapentin, capsaicin topical, pregabalin, lidocaine patch</td>
<td>22,25</td>
</tr>
<tr>
<td></td>
<td>Imipramine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trimipramine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbiturate</td>
<td>Amylobarbital</td>
<td>For epilepsy—other anticonvulsants (e.g., lamotrigine, levetiracetam)</td>
<td>26,56–58</td>
</tr>
<tr>
<td></td>
<td>Butobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Butalbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mephobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pentobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phenobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Secobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasodilator</td>
<td>Ergot mesylate</td>
<td>Acetylcholinesterase inhibitors, memantine, Vitamin E</td>
<td>59–66</td>
</tr>
<tr>
<td></td>
<td>Isosuxprpine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central nervous system, nonbenzodiazepine hypnotics</td>
<td>Zolpidem</td>
<td>None (see Appendix 3)</td>
<td>67–73</td>
</tr>
<tr>
<td>Other</td>
<td>Zaleplon</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eszopiclone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine system</td>
<td>Conjugated estrogen</td>
<td>Use of vaginal estrogen formulations acceptable for treatment of dyspareunia and vulvovaginitis</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Esterified estrogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estradiol</td>
<td>Vasomotor symptoms—SSRI, SNRI, gabapentin</td>
<td>36, 38, 77–82</td>
</tr>
<tr>
<td></td>
<td>Estriol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas, long-duration</td>
<td>Glyburide</td>
<td>Short-acting sulfonylureas (glipizide, gliclazide), metformin</td>
<td>83</td>
</tr>
</tbody>
</table>
Pain medication in high concentrations (8% patch) has been shown to be effective for chronic musculoskeletal pain, such as chronic back or osteoarthritis pain, and neuropathic pain, such as postherpetic neuralgia. Topical NSAID preparations are effective for knee and hand osteoarthritis pain, with the strongest data coming from randomized controlled trials of topical diclofenac. The Food and Drug Administration (FDA) has approved topical diclofenac for this use, although these topical NSAIDs lack evidence of effectiveness for chronic back pain or postherpetic neuralgia, and there can be some systemic absorption. Topical capsaicin in low concentrations (<1%) is effective for osteoarthritis pain, but the data are inconclusive regarding effectiveness in neuropathic pain. Topical capsaicin in high concentrations (8% patch) has been shown to be effective for postherpetic neuralgia in randomized controlled trials and is FDA approved for this use but is expensive and best considered when first- and second-line treatments have failed. Capsaicin products are not effective for chronic low back pain, must be applied carefully, and can cause an unbearable burning sensation. The topical lidocaine patch is effective for postherpetic neuralgia, based on high-quality randomized controlled trials, is FDA approved for this use, and is a first-line therapy for postherpetic neuralgia. The effectiveness of topical lidocaine for chronic musculoskeletal pain is unclear because there are no definitive randomized controlled trials, and therefore it is not FDA approved, but case reports and small trials suggest it may be useful in this situation.

CNS medications (antipsychotics, TCAs, SSRIs, antiepileptics, benzodiazepine receptor agonists) increase the risk of falls, especially in individuals with a prior history of falls. Given the literature showing the considerable risk and minimal effectiveness of benzodiazepine receptor agonists for sleep in older adults, new prescriptions for these agents should be avoided. Nonpharmacological options are recommended to treat insomnia initially, including sleep hygiene combined with behavioral interventions (Appendix 3). It is also important to limit the dose and duration of use of antipsychotics to only a few days, especially when used for delirium, for which there is little data suggesting they are helpful. Limited duration of antipsychotic use at the lowest dose possible is also important when used to treat behavioral complications of dementia, given the well-known greater risk of mortality. There will be times in those older adults with a previous history of falls when it will be necessary to prescribe a new CNS medication (e.g., new-onset epilepsy). In these cases, it is important to choose the most-effective, least-risky antiepileptic. In addition, the use of older hepatic metabolism enzyme–inducing agents (phenobarbital, phenytoin, carbamazepine) that can interact with numerous other medications should be avoided. Moreover, there is growing evidence that the use of multiple CNS medications or higher combined doses further increases the risk of falls. When at all possible, decreasing the dosage of currently prescribed CNS medications before initiating a new CNS agent in older adults with a previous history of falls is clinically sensible. It is also clinically sensible, when possible, to discontinue CNS medications such

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>High-Risk Medications</th>
<th>Alternatives</th>
<th>References (Appendix 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other</td>
<td>Desiccated thyroid</td>
<td>Levothyroxine</td>
<td>None (see Appendix 3)</td>
</tr>
<tr>
<td>Pain medication</td>
<td>Diclofenac</td>
<td>For acute mild or moderate pain—acetaminophen, nonacetylated salicylate (e.g., salsalate), propionic acid derivatives (e.g., ibuprofen, naproxen) if no heart failure or eGFR &lt; 30 mL/min and given with PPI for gastroprotection if used for &gt; 7 days</td>
<td></td>
</tr>
<tr>
<td>Skeletal muscle relaxants</td>
<td>Carisoprodol</td>
<td>For mild or moderate chronic pain—acetaminophen, nonacetylated salicylate (e.g., salsalate), propionic acid derivatives (e.g., ibuprofen, naproxen) if no heart failure or eGFR &gt; 30 mL/min and given with PPI for gastroprotection</td>
<td></td>
</tr>
<tr>
<td>Specific nonsteroidal antiinflammatory drugs</td>
<td>Indomethacin, Ketorolac (oral and parenteral)</td>
<td>For acute moderate to severe pain—tramadol, morphine, oxycodone immediate release with acetaminophen For chronic moderate to severe pain—all the above; avoid long-duration, sustained-release dosage forms in opioid-naive individuals; see neuropathic pain alternatives above under tertiary tricyclic antidepressant alternatives</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Meperidine Pentazocine</td>
<td>18, 22, 60, 88</td>
<td></td>
</tr>
</tbody>
</table>

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; CCB = calcium channel blocker; PPI = proton pump inhibitor; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor. In all instances including those specified, nonpharmacological approaches should be sought first when appropriate (Appendix 3).
as antiepileptics (e.g., in individuals who experienced a single seizure around the time of a stroke with no further seizures in these subsequent 2 years and have normal electroencephalograms). It is important, though, that this class of CNS medications be tapered over a 6- to 12-month period to avoid a withdrawal seizure and only after considering individual and family preferences and current driving status.30,31

**Table 2. Alternatives to Medications Included in the Potentially Harmful Drug-Disease Interactions in the Elderly**

<table>
<thead>
<tr>
<th>Diseases and Potentially Harmful Drugs</th>
<th>Alternatives</th>
<th>References (Appendix 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Falls</strong></td>
<td>Anticonvulsants For new-onset epilepsy—newer agents preferred (e.g., lamotrigine, levetiracetam and calcium/vitamin D ± bisphosphonate) For neuropathic pain—SNRI, gabapentin, pregabalin, topical capsaicin, lidocaine patch</td>
<td>26, 56–58</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines Nonbenzodiazepine hypnotics (&quot;Z&quot; drugs: eszopiclone, zaleplon, zolpidem) For anxiety—buspirone, SNRI For sleep—see Appendix 3</td>
<td>75, 76 67–73</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants (tertiary and secondary) SSRI For depression—e.g., SNRI, bupropion For neuropathic pain—SNRI, gabapentin, pregabalin, capsaicin topical, lidocaine patch</td>
<td>53, 54 22, 55</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics For depression—e.g., SNRI, bupropion For neuropathic pain—SNRI, gabapentin, pregabalin, capsaicin topical, lidocaine patch</td>
<td>24, 74, 90, 91</td>
</tr>
<tr>
<td></td>
<td>For behavioral complications of dementia—if nonpharmacological approaches have failed and psychosis and danger to self or others, low-dose nonanticholinergic agent (e.g., risperidone, quetiapine) for shortest duration possible may be acceptable</td>
<td>74, 92</td>
</tr>
<tr>
<td><strong>Dementia</strong></td>
<td>Tricyclic antidepressants (tertiary and secondary) SSRI For depression—SSRI, SNRI, bupropion For neuropathic pain—SNRI, capsaicin topical, gabapentin, pregabalin, lidocaine patch</td>
<td>53, 54 22, 55</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics For behavioral complications of dementia—if nonpharmacological approaches have failed, and psychosis and danger to self or others, low-dose nonanticholinergic agent (e.g., risperidone, quetiapine) for shortest duration possible may be acceptable</td>
<td>74, 92</td>
</tr>
<tr>
<td><strong>H2 blockers</strong></td>
<td>Proton pump inhibitor</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>Anticholinergics (see table 7 in 2015 AGS Beers criteria for complete list of classes) (e.g., first-generation antihistamines, and anti-Parkinson agents) For allergy—second-generation antihistamine, nasal steroid For Parkinson disease—levodopa with carbidopa</td>
<td>41–46 14–17</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines For anxiety—buspirone, SSRI, SNRI</td>
<td>75, 76</td>
</tr>
<tr>
<td></td>
<td>Nonbenzodiazepine hypnotics (&quot;Z&quot; drugs) See Appendix 3</td>
<td>67–73</td>
</tr>
<tr>
<td><strong>Chronic kidney disease or chronic renal failure (eGFR &lt;30 mL/min)</strong></td>
<td>All nonaspirin nonsteroidal antiinflammatories (including cyclooxygenase-2 selectives) For pain—acetaminophen, SNRI, topical capsaicin lidocaine patch</td>
<td>18, 22, 55, 88</td>
</tr>
</tbody>
</table>

eGFR = estimated glomerular filtration rate; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor.

In all instances including those specified, nonpharmacological approaches should be sought first when appropriate (See references 68, 94–123 in Appendix 3). *Also includes noncancer, nontrauma hip fracture. If agent must be used, consider reducing the use of other central nervous system-active medications that increase the risk of falls and fractures (anticonvulsants, antipsychotics, antidepressants, benzodiazepine receptor agonists).
Oral and transdermal estrogens are effective treatments for vulvovaginitis, dyspareunia, and vasomotor symptoms, but they increase the risk of ovarian, endometrial, and breast cancers; thromboembolic events; gallbladder disease; and kidney stones. Thus their use should be avoided in women aged 65 and older. Topical alternatives such as water-based vaginal lubricants and silicone-based vaginal moisturizers offer relief from dyspareunia for many women.\(^{32,33}\) Vaginal estrogen is another alternative that replenishes the affected tissue with a lower or negligible risk of the serious adverse events of their systemic counterparts.\(^{32,33}\) Ospemifene, a specific estrogen receptor modifier, is approved for the treatment of dyspareunia and is another potential alternative,\(^ {34,35}\) although it shares many of the same warnings as estrogens, and long-term evidence in women aged 65 and older is lacking. The SSRI escitalopram, the SNRI venlafaxine, and gabapentin have all demonstrated efficacy for treating the symptoms of vasomotor instability, most notably hot flashes.\(^ {36-40}\) Much of this evidence is from trials in women in midlife or with a history of breast cancer. Women with a history of falls should avoid SSRIs and gabapentin. 

There are potential limitations to the process that created this list of alternatives. Space limitations prevented alternatives for the other seven drug classes with strong anticholinergic properties from the 2015 AGS Beers Criteria (see table 7) that can exacerbate dementia from being discussed. Suboptimal dose (digoxin, doxepin, reserpine) and duration of use (nitrofurantoin, nonbenzodiazepine hypnotics) criteria were also not addressed. These will be addressed in a future published alternative list based on the response of NCQA, PQA, and CMS to the numerous new suboptimal drugs with these two types of problems included in the 2015 AGS Beers Criteria. The size of the panel that created this list of alternatives was small, although the NCQA, PQA, the 13-member expert panel for the 2015 AGS Beers Criteria panel, and Executive Committee of the AGS also reviewed the list of alternatives that the three-person panel created. A formal evaluation of the quality of evidence or strength of recommendation for each alternative was not provided, but this information is available in some metaanalyses and consensus publications referenced. In addition, the alternatives provided are clinically sensible and are consistent with other expert lists.\(^ 7\) Finally, some insurers or individual healthcare systems may provide allowances for coverage of nonpharmacological approaches, such as cognitive behavioral therapy, whereas others may not.

CONCLUSION

A list of drug therapy alternatives to medications included in the Use of High Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly quality measures was created from a comprehensive review of the literature and evidence. This list of drug therapy alternatives is intended to be a useful tool for health professionals, consumers, payers, and health systems that care for older adults.

ACKNOWLEDGMENTS

The authors thank the AGS for its encouragement to undertake this endeavor, particularly Nancy Lundeberg, Elvy Ickowicz, and Mary Jordan Samuel. They also express their gratitude to members of the 2015 AGS Beers Criteria panel; Woody Eisenberg, MD, of the Pharmacy Quality Alliance; Erin Giovannetti, PhD, of the National Committee for Quality Assurance; and the AGS Executive Committee for their thoughtful review and comments.

The opinions expressed are those of the authors and not necessarily those of the U.S. government or the U.S. Department of Veterans Affairs.

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper. Todd P. Semla receives honoraria from the AGS and LexiComp, Inc. He is a member of Omnicare, Inc. Pharmacy and Therapeutics Committee (consultant). His spouse is an employee of AbbVie and owns stock in AbbVie, Abbott Labs, and Hospira.

Financial Disclosure: Dr. Hanlon is supported by National Institute of Aging grants P30AG024827 and R01AG037451, a Donoghue Foundation grant, and Department of Veterans Affairs Health Services Research and Development Service Merit Awards IIR12–379 and IIR14–297. Dr. Schmader is supported by National Institute on Aging Grant P30AG028716.

Author Contributions: All authors: Concept and design, literature search, analysis and interpretation, preparation of manuscript.

Sponsor’s Role: Not applicable.

REFERENCES


APPENDIX I REFERENCES FOR ALTERNATIVE MEDICATIONS INCLUDED IN TABLE 1

Anticholinergics, first-generation antihistamines: intranasal normal saline, second-generation antihistamines, intranasal steroid


Anticholinergics, for Parkinson’s: levodopa/carbidopa


Dipyridamide (oral immediate release) and Ticlopidine, Antithrombotic Therapy for the Secondary Prevention of Noncardioembolic Stroke: Clopidogrel or aspirin 25 mg/extended released Dipyridamole 200 mg combination


Cardiovascular, alpha agonists, central: alternative hypertensives


Cardiovascular, Disopyramide for atrial fibrillation non-dihydropyridine calcium channel blockers or beta blockers
52. Stewart S, Ball J, Horowitz D et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: Pragmatic, multicentre, randomised controlled. Lancet 2015;385:775–784.

Cardiovascular, Nifedipine immediate-release for hypertension: long-acting dihydropyridine calcium channel blockers
52. Stewart S, Ball J, Horowitz D et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: Pragmatic, multicentre, randomised controlled. Lancet 2015;385:775–784.

Central nervous system, vasodilators: acetylcholinesterase
centraveal system, barbiturates: epilepsy

Central nervous system, nonbenzodiazepine hypnotics:
alternatives for depression and neuropathic pain

Central nervous system, vascular dilitators: acetylcholinesterase inhibitors and memantine, Vitamin E

Central nervous system, other: alternatives for schizophrenia and anxiety

Endocrine system, estrogens with or without progestins: short-term use of vaginal dosage form acceptable for treatment of dyspareunia; vasomotor symptoms—selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, gabapentin
Endocrine system, sulfonylureas, long-duration: short-acting sulfonylureas or metformin


Endocrine system, other: levothyroxine


Pain medications, skeletal muscle relaxants: acute mild to moderate pain


Pain medications, specific nonsteroidal anti-inflammatory drugs: mild to moderate chronic pain—acetaminophen, nonacetylated salicylate or propionic acid derivatives if no heart failure or estimate glomerular filtration rate >30 mL/min and given with proton pump inhibitor for gastroprotection


Pain medications, opioids: alternatives for acute and chronic moderate to severe pain


APPENDIX II REFERENCES FOR ALTERNATIVE MEDICATIONS INCLUDED IN TABLE 2

Falls, anticonvulsants


Falls, benzodiazepines and nonbenzodiazepine hypnotics


Falls, tricyclic antidepressants and selective serotonin reuptake inhibitors


Falls, antipsychotics, delirium and dementia


Dementia, anticholinergics

Dementia, antipsychotics

Dementia Tricyclic antidepressants (tertiary and secondary)

JAGS NOVEMBER 2015–VOL. 63, NO. 11


Dementia Tricyclic antidepressants (tertiary and secondary)


Dementia, antipsychotics


Dementia, histamine blockers


Dementia, anticholinergics


Dementia, benzodiazepines


Dementia, nonbenzodiazepine hypnotics


Chronic kidney disease or chronic renal failure (estimate glomerular filtration rate <30 mL/min), nonsteroidal anti-inflammatory drugs


APPENDIX III RESOURCES FOR NONPHARMACOLOGICAL ALTERNATIVES TO MEDICATIONS INCLUDED IN THE USE OF HIGH-RISK MEDICATIONS IN THE ELDERLY AND POTENTIALLY HARMFUL DRUG–DISEASE INTERACTIONS IN THE ELDERLY QUALITY MEASURES

General


Appendite

Delirium

Dementia Behavioral Complications

Pain

Transcutaneous electrical nerve stimulation

Percutaneous Electrical Nerve Stimulation

Acupuncture

Cognitive Behavioral Therapy

Urinary Incontinence

Sleep