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, MD[l,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 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.[1] 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.[2] 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).[3] 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,

From the [a]Division of Geriatrics, Department of Medicine; [b]Department of Biomedical Informatics, School of Medicine; [c]Department of Pharmacy and Therapeutics, School of Pharmacy; [d]Department of Epidemiology, School of Public Health; [e]Geriatric Pharmaceutical Outcomes and Gero-Informatics Research and Training Program; [f]Clinical and Translational Science Institute, University of Pittsburgh; [g]Geriatric Research, Education, and Clinical Center; [h]Center for Health Equity Research and Promotion, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; [i]Department of Veterans Affairs, Pharmacy Benefits Management Services, Hines; [j]Departments of Medicine; [k]Psychiatry and Behavioral Science, Feinberg School of Medicine, Northwestern University, Chicago, Illinois; [l]Division of Geriatrics, Department of Medicine, School of Medicine, Duke University Medical Center; and [m]Geriatric Research, Education, and Clinical Center, Durham Veterans Affairs Medical Center, Durham, North Carolina.

Address correspondence to Mary Jordan Samuel, Manager, Special Projects & Governance, American Geriatrics Society, 40 Fulton Street, 18th Floor, New York, NY 10038. E-mail: msamuel@americangeriatrics.org

DOI: 10.1111/jgs.13807

0002-8614/15/$15.00

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 publically 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 1. Alternatives for Medications Included in the High-Risk Medications in the Elderly Measure

Therapeutic Class	High-Risk Medications	Alternatives	References (Appendix 1)
Anticholinergic			
First-generation antihistamine	Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Diphenhydramine (oral) Doxylamine Hydroxyzine Promethazine Triprolidine	Intranasal normal saline Second-generation antihistamine (e.g., cetirizine, fexofenadine, loratadine) Intranasal steroid (e.g., beclomethasone, fluticasone, over the counter)	41–46
Parkinson disease	Benztropine (oral) Trihexyphenidyl	Carbidopa/levodopa	14–17
Antiplatelets	Dipyridamole (oral immediate release) Ticlopidine	Antithrombotic therapy for the secondary prevention of noncardioembolic stroke Clopidogrel, aspirin 25 mg with extended-release dipyridamole 200 mg	47
Cardiovascular			
Alpha agonists, central	Guanabenz Guanfacine Methyldopa	Thiazide-type diuretic, ACEI, ARB, long-acting dihydropyridine CCB In black individuals—thiazide-type diuretic, CCB For heart failure, diabetes mellitus, chronic kidney disease—ACEI or ARB preferred	48–50
Other	Disopyramide	Atrial fibrillation: For rate control—nondihydropyridine CCB (e.g., diltiazem), beta-blocker For rhythm control—dofetilide flecainide, propafenone	51,52
	Nifedipine (immediate release)	Long-acting dihydropyridine CCB (e.g., amlodipine)	48–50
Central nervous system			
Tertiary tricyclic antidepressant	Amitriptyline Clomipramine Imipramine Trimipramine	For depression—SSRI (except paroxetine), SNRI, bupropion (also see Appendix 3) For neuropathic pain—SNRI, gabapentin, capsaicin topical, pregabalin, lidocaine patch	53–54 22,55
Barbiturate	Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital	For epilepsy—other anticonvulsants (e.g., lamotrigine, levetiracetam)	26,56–58
Vasodilator	Ergot mesylates Isoxsuprine	Acetylcholinesterase inhibitors, memantine, Vitamin E	59–66
Central nervous system, nonbenzodiazepine hypnotics	Eszopiclone Zaleplon Zolpidem	None (see Appendix 3)	67–73
Other	Thioridazine	For schizophrenia—other nonanticholinergic antipsychotic (not chlorpromazine, loxapine, olanzapine, perphenazine, thioridazine, trifluoperazine)	74
	Meprobamate Chloral hydrate (no longer marketed in United States)	For anxiety—buspirone, SSRI, SNRI	75, 76
Endocrine system			
Estrogens with or without progestins (oral or patch)	Conjugated estrogen Esterified estrogen Estradiol Estropipate	Use of vaginal estrogen formulations acceptable for treatment of dyspareunia and vulvovaginitis Vasomotor symptoms—SSRI, SNRI, gabapentin	32 36, 38, 77–82
Sulfonylureas, long-duration	Chlorpropamide Glyburide	Short-acting sulfonylureas (glipizide, gliclazide), metformin	83

(Continued)

Table 1 (Contd.)

Therapeutic Class	High-Risk Medications	Alternatives	References (Appendix 1)
Other	Desiccated thyroid	Levothyroxine	84,85
	Megestrol	None (see Appendix 3)	
Pain medication			
Skeletal muscle relaxants	Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine	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>30 mL/min and given with PPI for gastroprotection if used for >7 days	18, 86–88
Specific nonsteroidal antiinflammatory drugs	Indomethacin, Ketorolac (oral and parenteral)	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 >30 mL/min and given with PPI for gastroprotection	18, 86–88
Opioids	Meperidine Pentazocine	For acute moderate to severe pain—tramadol, morphine, oxycodone immediate release with acetaminophen	18, 22, 60, 88
		For chronic moderate to severe pain—all the above; avoid long-duration, sustained-release dosage forms in opioid-naïve individuals; see neuropathic pain alternatives above under tertiary tricyclic antidepressant alternatives	89

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).

Chronic oral NSAID use increases the risk of gastrointestinal bleeding and acute kidney injury in older adults, particularly in those with common underlying comorbidities of peptic ulcer disease, chronic kidney disease, or congestive heart failure.[18] One potential alternative to chronic oral NSAID therapy for chronic pain is topical therapy. Topical NSAIDs, capsaicin, and lidocaine have the advantage of low risk of adverse events and ease of use, but it is unclear whether all are 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.[19] 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.[20] 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.[21] 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.[22] 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.[23] 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.[24] 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.[25] 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.[26] Moreover, there is growing evidence that the use of multiple CNS medications or higher combined doses further increases the risk of falls.[27–29] 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 2. Alternatives to Medications Included in the Potentially Harmful Drug-Disease Interactions in the Elderly*

Diseases and Potentially Harmful Drugs		Alternatives	References (Appendix 2)
Disease	**Drugs**		
Falls[a]	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	26, 56–58
	Benzodiazepines Nonbenzodiazepine hypnotics ("Z" drugs: eszopiclone, zaleplon, zolpidem)	For anxiety—buspirone, SNRI For sleep—see Appendix 3	75, 76 67–73
	Tricyclic antidepressants (tertiary and secondary) SSRIs	For depression—e.g., SNRI, bupropion For neuropathic pain—SNRI, gabapentin, pregabalin, capsaicin topical, lidocaine patch	53, 54 22, 55
	Antipsychotics	For delirium—short-term use of antipsychotics (e.g., haloperidol, quetiapine) should be restricted to individuals who are distressed or considered a risk to themselves or others and in whom verbal and nonverbal de-escalation techniques are ineffective or inappropriate For schizophrenia—nonanticholinergic agents may be acceptable (not chlorpromazine, loxapine, olanzapine, perphenazine, trifluoperazine, thioridazine) 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	24, 74, 90, 91 74 74, 92
Dementia	Tricyclic antidepressants (tertiary and secondary)	For depression—SSRI, SNRI, bupropion For neuropathic pain—SNRI, capsaicin topical, gabapentin, pregabalin, lidocaine patch	53, 54 22, 55
	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	74, 92
	H2 blockers	Proton pump inhibitor	93
	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	41–46 14–17
	Benzodiazepines	For anxiety—buspirone, SSRI, SNRI For sleep—see Appendix 3	75, 76 67–73
	Nonbenzodiazepine hypnotics ("Z" drugs)	See Appendix 3	
Chronic kidney disease or chronic renal failure (eGFR <30 mL/min)	All nonaspirin nonsteroidal antiinflammatories (including cyclooxygenase-2 selectives)	For pain—acetaminophen, SNRI, topical capsaicin lidocaine patch	18, 22, 55, 88

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).
[a]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).

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]

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 Lundebjerg, 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

1. Huisman-Baron M, van der Veen L, Jansen PAF et al. Criteria for drug selection in frail elderly persons. Drugs Aging 2011;28:391–402.
2. NCQA. HEDIS 2015 final NDC lists [on-line]. Available at http://www.ncqa.org/HEDISQualityMeasurement/HEDISMeasures/HEDIS2015/HEDIS2015NDCLicense/HEDIS2015FinalNDCLists.aspx Accessed April 23, 2015.
3. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. AGS Updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616–631.
4. O'Mahony D, O'Sullivan D, Byrne S et al. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. Age Ageing 2015;44:213–218.
5. Shrank WH, Polinski JM, Avorn J. Quality indicators for medication use in vulnerable elders. J Am Geriatr Soc 2007;55:S373–S382.
6. Basger BJ, Chen TF, Moles RJ. Inappropriate medication use and prescribing indicators in elderly Australians: Development of a prescribing indicators tool. Drugs Aging 2008;25:777–793.
7. Renom-Guiteras A, Meyer G, Thurman PA. The EU(7)-PIM list: A list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol 2015;71:861–875.
8. Hauser RA, Isaacson S, Clinch T. Randomized, placebo-controlled trial of trimethobenzamide to control nausea and vomiting during initiation and continued treatment with subcutaneous apomorphine. Parkinsonism Relat Disord 2014;20:1171–1176.
9. Fox C, Smith T, Maidment I et al. Effect of medication with anti-cholinergic properties on cognitive function, delirium, physical function and mortality: A systematic review. Age Ageing 2014;43:868–872.
10. Gray SL, Anderson ML, Dublin S et al. Cumulative use of strong anticholinergics and incident dementia: A prospective study. JAMA Intern Med 2015;175:401–407.

11. Hilmer SN, Mager DE, Simonsick EM et al. Drug burden index to define the functional burden of medications in older people. Arch Intern Med 2007;167:781–787.
12. Salahudeen MS, Duffull SB, Nishtala PS. Anticholinergic burden quantified by anticholinergic risk scales and adverse outcomes in older people: A systematic review. BMC Geriatr 2015;15:31. Available at http://www.biomedcentral.com/1471–2318/15/31 Accessed April 23, 2015.
13. Connally BS, Lang AE. Pharmacologic treatment of Parkinson's disease: A review. JAMA 2014;311:1670–1683.
14. Miyasaki JM. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. Neurology 2002;58:11–17.
15. Scottish Intercollegiate Guideline Network. Diagnosis and pharmacologic management of Parkinson's disease: A national clinical guideline, No. 113, January 2010 [on-line]. Available at http://www.sign.ac.uk/pdf/sign113.pdf Accessed April 1, 2015.
16. Ferreria JJ, Katzenschlager R, Bloem BR et al. Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management. Eur J Neurol 2013;20:5–15.
17. Katzenschlager R, Sampaio C, Costa J et al. Anticholinergics for symptomatic management of Parkinson's disease. Cochrane Database Syst Rev 2003;(2):CD003735.
18. AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological Management of Persistent Pain in Older Persons. J Am Geriatr Soc 2009;57:1331–1346.
19. Derry S, Moore RA, Rabbie R. Topical NSAIDS for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev 2012;(9):CD007400.
20. Derry S, Moore RA. Topical capsaicin (low concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev 2012;(9):CD010111.
21. Derry S, Sven-Rice A, Cole P et al. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev 2013;(2):CD007393.
22. Dworkin RH, O'Conner AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence based recommendations. Pain 2007;132:237–251.
23. Glass J, Lanctôt KL, Herrmann N et al. Sedative hypnotics in older people with insomnia: Meta-analysis of risks and benefits. BMJ 2005;331:1169.
24. Inouye SK, Marcantonio ER, Metzger ED. Doing damage in delirium: The hazards of antipsychotic treatment in elderly people. Lancet Psychiatry 2014;1:312–315.
25. Maust DT, Kim HM, Seyfried LS et al. Antipsychotics, other psychotropics, and the risk of death in patients with dementia: Number needed to harm. JAMA Psychiatry 2015;72:438–445.
26. Pugh MJ, Berlowitz DR, Rao JK et al. The quality of care for adults with epilepsy: An initial glimpse using the QUIET measure. BMC Health Serv Res 2011;11:1.
27. Weiner D, Hanlon JT, Studenski S. CNS drug-related falls liability in community dwelling elderly. Gerontology 1998;44:217–221.
28. Hanlon JT, Boudreau RM, Roumani YF et al. Number and dosage of central nervous system medications on recurrent falls in community elders: The Health, Aging and Body Composition study. J Gerontol A Biol Sci Med Sci 2009;64A:492–498.
29. Pratt NL, Ramsay EN, Ellett LMK et al. Association between use of multiple psychoactive medicines and hospitalization for falls: Retrospective analysis of a large healthcare claim database. Drug Saf 2014;37:529–535.
30. Gilad R. Management of seizures following a stroke. Drugs Aging 2012;29:533–538.
31. Beghi E, Giussani G, Grosso S et al. Withdrawal of antiepileptic drugs: Guidelines of the Italian League Against Epilepsy. Epilepsia 2013;54:2–13.
32. The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of the North American Menopause Society. Menopause 2013;20:888–902.
33. Tan O, Bradshaw K, Carr BR. Management of vulvovaginal atrophy-related sexual dysfunction in postmenopausal women: An up-to-date review. Menopause 2012;19:109–117.
34. McLendon AN, Clinard VB, Woodis CB. Ospemifene for the treatment of vulvovaginal atrophy and dyspareunia in postmenopausal women. Pharmacotherapy 2014;34:1050–1060.
35. Cui Y, Zong H, Yan H et al. The efficacy and safety of ospemifene in treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy: A systematic review and meta-analysis. J Sex Med 2014;11:487–497.
36. Hayes LP, Carroll DG, Kelley KW. Use of gabapentin for the management of natural or surgical menopausal hot flashes. Ann Pharmacother 2011;45:388–394.
37. Avis NE, Crawford SL, Greendale G et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med 2015;175:531–539.
38. Freeman EW, Guthrie KA, Cann B et al. Efficacy of escitalopram for hot flashes in healthy menopausal women: A randomized controlled trial. JAMA 2011;305:267–274.
39. LaCroix AZ, Freeman EW, Larson J et al. Effects of escitalopram on menopause-specific quality of life and pain in healthy menopausal women with hot flashes: A randomized controlled trial. Maturitas 2012;73:361–368.
40. Pinkerton JV, Archer DF, Guico-Pabia CJ et al. Maintenance of the efficacy of desvenlafaxine in menopausal vasomotor symptoms: A 1-year randomized controlled trial. Menopause 2012;20:38–46.

APPENDIX I REFERENCES FOR ALTERNATIVE MEDICATIONS INCLUDED IN TABLE 1

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

41. Hansen J, Klimek L, Hörmann K. Pharmacological management of allergic rhinitis in the elderly: Safety issues with oral antihistamines. Drugs Aging 2005;22:289–296.
42. Cardona V, Guilarte M, Luengo O et al. Allergic diseases in the elderly. Clin Transl Allergy 2011;1:1.
43. Bousquet J, Khaltaev N, Cruz AA et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update. Allergy 2008;63(Suppl 86):8–160.
44. Scadding GK, Durham SR, Mirakian R et al. BSACI guidelines for the management of allergic and non-allergic rhinitis. Clin Exp Allergy 2008;38:19–42.
45. Wallace DV, Dykewicz MS, Bernstein DI et al. The diagnosis and management of rhinitis: An updated practice parameter. J Allergy Clin Immunol 2008;122(Suppl 2):S1–S84.
46. Bousquet J, Khaltaev N, Cruz AA et al. Consensus statements, evidence-based medicine and guidelines in allergic diseases. Allergy 2008;63:1–4.

Anticholinergics, for Parkinson's: levodopa/carbidopa

14. Miyasaki JM, Martin W, Suchowesky O et al. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. Neurology 2002;58:11–15.
15. Scottish Intercollegiate Guideline Network. Diagnosis and pharmacologic management of Parkinson's disease: A national clinical guideline, No. 113, January 2010 [on-line]. Available at http://www.sign.ac.uk/pdf/sign113.pdf Accessed April 1, 2015.
16. Ferreria JJ, Katzenschlager R, Bloem BR et al. Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management. Eur J Neurol 2013;20:5–15.
17. Katzenschlager R, Sampaio C, Costa J et al. Anticholinergics for symptomatic management of Parkinson's disease. Cochrane Database Syst Rev 2002;(3):CD003735.

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

47. Guyatt G, Akl E, Crowther M et al. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Executive summary: Antithrombotic therapy and prevention of thrombosis, 9th ed. Chest 2012;141(Suppl):34S.

Cardiovascular, alpha agonists, central: alternative hypertensives

48. Aronow W, Fleg J, Pepine C et al. ACCF/AHA 2011 Expert Consensus Documentation on Hypertension in the Elderly. Executive Summary. J Am Coll Cardiol 2011;57:240.
50. Weber M, Schiffrin E, White W et al. Clinical Practice Guidelines for the management of hypertension in the community: A statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens 2014;1:14–26.
59. James P, Oparil S, Carter B et al. 2014 Evidence-Based Guideline for the management of high blood pressure in adults (JNC 8). JAMA 2014;311:507–520.

Cardiovascular, Disopyramide for atrial fibrillation non - dihydropyridine calcium channel blockers or beta blockers

48. Aronow W, Fleg J, Pepine C et al. ACCF/AHA 2011 Expert Consensus Documentation on Hypertension in the Elderly. Executive Summary. J Am Coll Cardiol 2011;57:240.
51. January C, Wann L, Alpert J et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: Executive summary. Circulation 2014;130:2054.
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

48. Aronow W, Fleg J, Pepine C et al. ACCF/AHA 2011 Expert Consensus Documentation on Hypertension in the Elderly. Executive Summary. J Am Coll Cardiol 2011;57:240.
49. James P, Oparil S, Carter B et al. 2014 Evidence-Based Guideline for the management of high blood pressure in adults (JNC 8). JAMA 2014;311:507–520.
50. Weber M, Schiffrin E, White W et al. Clinical Practice Guidelines for the management of hypertension in the community: A statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens 2014;1:14–26.

Central nervous system, tertiary tricyclic antidepressants: alternatives for depression and neuropathic pain

22. Dworkin RH, O'Connor AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237–251.
53. The Management of MDD Working Group. VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. Washington, DC: U.S. Department of Veterans Affairs and Department of Defense, 2009.
54. Gartlehner G, Hansen RA, Kahwati L. Drug class review on second generation antidepressants [on-line]. 2006. Available at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm Accessed April 1, 2015.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.

Central nervous system, barbiturates: epilepsy—other anticonvulsants

26. Pugh MJ, Berlowitz DR, Rao JK et al. The quality of care for adults with epilepsy: An initial glimpse using the QUIET measure. BMC Health Serv Res 2011;11:1.
56. Rowan AJ, Ramsay E, Collins JF et al. New onset geriatric epilepsy: A randomized study of gabapentin, lamotrigine, and carbamazepine. Neurology 2005;64:1868–1873.
57. Correll CM, Bazil CW. Management of seizures in the elderly. Curr Geriatr Rep 2014;3:73–82.
58. Werhahn KJ, Trinka E, Dobesberger J et al. A randomized, double-blind comparison of antiepileptic drug treatment in the elderly with new-onset focal epilepsy. Epilepsia 2015;56:450–459.

Central nervous system, vasodilators: acetylcholinesterase inhibitors and memantine, Vitamin E

59. Practice Guideline for the treatment of patients with Alzheimer's disease and other dementias, 2nd Ed. From the American Psychiatric Association's Workgroup on Alzheimer's Disease and Other Dementias and Steering Committee on Practice Guidelines. Available at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/alzheimers.pdf Accessed April 1, 2015.
60. Fillit HM, Doody RS, Binaso K et al. Recommendations for best practices in the treatment of Alzheimer's disease in managed care. Am J Geriatr Pharmacother 2006;4(Supp A):S9–S24.
61. Qaseem A, Snow V, Cross TJ Jr. Current pharmacologic treatment of dementia: A clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med 2008;143:370–378.
62. Parminer R, Santaguida P, Ismaila A et al. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: Evidence review for a clinical practice guideline. Ann Intern Med 2008;148:379–397.
63. National Institute for Health and Clinical Excellence (NICE). Alzheimer's disease—donepezil, galantamine, rivastigmine (Review) and memantine (amended) [on-line]. Available at www.nice.org.uk/TA111 Accessed January 20, 2014.
64. Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006;(1):CD005593.
65. Sano M, Ernesto C, Thomas RG et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer disease. N Engl J Med 1997;336:1216–1222.
66. Dysken MW, Sano M, Athana S et al. Effect of vitamin E and memantine on functional decline in Alzheimer's disease: The TEAM-AD VA Cooperative Randomized trial. JAMA 2014;311:33–44.

Central nervous system, nonbenzodiazepine hypnotics: none

67. Leshner A, Baghdoyan H, Bennett S et al. NIH statement regarding the treatment of insomnia. Manifestations and Management of Chronic Insomnia in Adults June 13–15, 2005. Sleep 2005;28:1049–1057.
68. Morin C. Efficacy of behavioral and psychological treatments of chronic insomnia. J Clin Sleep Med 2005;1:e482–e483.
69. Cluydts R, Peeters K, DeBouyalisky I et al. Comparison of continuous vs. intermittent administration of zolpidem in chronic insomniacs: A double-blind, randomized, pilot study. J Int Med Res 1998;26:13–24.
70. Hajak G, Cluydts R, Declerck A et al. Continuous versus non-nightly use of zolpidem in chronic insomnia: Results of a large-scale, double-blind, randomized, outpatient study. Int Clin Psychopharmacol 2002;17:9–17. Erratum in: Int Clin Psychopharmacol 2002;17:206.
71. Perlis ML, McCall WV, Krystal AD et al. Long-term, non-nightly administration of zolpidem in the treatment of patients with primary insomnia. J Clin Psychiatry 2004;65:1128–1137.
72. Solvertsen B, Omvik S, Pallesen S et al. Cognitive behavioral therapy or zopiclone for treatment of chronic primary insomnia. JAMA 2006;295:2851–2858.
73. Walsh JK, Roth T, Randazzo A et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. Sleep 2000;23:1087–1096.

Central nervous system, other: alternatives for schizophrenia and anxiety

74. Maher AR, Maglione M, Bagley S et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: A systematic review and meta-analysis. JAMA 2011;306:1359–1369.
75. Baldwin D, Woods R, Lawson R et al. Efficacy of drug treatments for generalised anxiety disorder: Systematic review and meta-analysis. BMJ 2011;342:d1199.
76. Stewart RE, Chambless DL. Cognitive-behavioral therapy for adult anxiety disorders in clinical practice: A meta-analysis of effectiveness studies. J Consult Clin Psychol 2009;77:595–606.

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

32. The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. Menopause 2013;20:888–902.
36. Hayes L, Carroll DG, Kelley KW. Use of gabapentin for the management of natural or surgical menopausal hot flashes. Ann Pharmacother 2011;45:388–394.
38. Freeman EW, Guthrie KA, Caan B et al. Efficacy of escitalopram for hot flashes in healthy menopausal women. JAMA 2011;305:267–274.
77. Carpenter JS, Guthrie KA, Larson JC et al. Effect of escitalopram on hot flash interference: A randomized, controlled trial. Fertil Steril 2012;97:1399–1404.
78. Pinkerton JV, Archer DG, Guico-Pabia CJ et al. Desvenlafaxine compared with placebo for treatment of menopausal vasomotor symptoms: A 12-week, multicenter, parallel-group randomized, double-blind, placebo-controlled efficacy trial. Menopause 2013;20:28–37.
79. Guttuso T Jr, Kurlan R, McDermott MP et al. Gabapentin's effects on hot flashes in postmenopausal women: A randomized, controlled trial. Obstet Gynecol 2003;101:337–345.
80. Reddy SY, Warner H, Guttuso T et al. Gabapentin, estrogen, and placebo for treating hot flashes. A randomized controlled trial. Obstet Gynecol 2006;108:41–48.

81. Butt DA, Lock M, Lewis JE et al. Gabapentin for the treatment of menopausal hot clashes: Randomized, controlled clinical trial. Menopause 2008;15:310–318.
82. Aguirre W, Chedraui P, Mendoza J et al. Gabapentin vs. low dose transdermal estradiol for treating postmenopausal women with moderate to severe hot flushes. Gynecol Endocrinol 2010;26:333–337.

Endocrine system, sulfonylureas, long-duration: short-acting sulfonylureas or metformin

83. American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus. Guidelines Abstracted from the American Geriatrics Society Guidelines for Improving the Care of Older Adults with Diabetes Mellitus: 2013 Update. J Am Geriatr Soc 2013;61:2020–2026.

Endocrine system, other: levothyroxine

84. Dong B, Gambertoglio JG, Greenspan FS et al. Bioequivalence of generic and brand-name levothyroxine products in the treatment of hypothyroidism. JAMA 1997;277:1205–1213.
85. Bensenor IM, Olmos RD, Lotufo PA. Hypothyroidism in the elderly: Diagnosis and management. Clin Interv Aging 2012;7:97–111.

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

18. AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009;57:1331–1346.
86. Graham DY, Agrawal NM, Campbell DR et al. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: Results of a double-blind, randomized, multicenter, active- and placebo-controlled study of misoprostol vs lansoprazole. Arch Intern Med 2002;162:169.
87. Lin KJ, Hernández-Díaz S, García Rodríguez LA. Acid suppressants reduce risk of gastrointestinal bleeding in patients on antithrombotic or anti-inflammatory therapy. Gastroenterology 2011;141:71–79.
88. Abdulla A, Adams N, Bone M et al. Guidance on the management of pain in older people. Age Ageing 2013;42(Suppl 1):i1–i57.

Pain medications, specific nonsteroidal antiinflammatory 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

18. AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009;57:1331–1346.
86. Graham DY, Agrawal NM, Campbell DR et al. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: Results of a double-blind, randomized, multicenter, active- and placebo-controlled study of misoprostol vs lansoprazole. Arch Intern Med 2002;162:169.
87. Lin KJ, Hernández-Díaz S, García Rodríguez LA. Acid suppressants reduce risk of gastrointestinal bleeding in patients on antithrombotic or anti-inflammatory therapy. Gastroenterology 2011;141:71–79.

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

18. AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009;57:1331–1346.
22. Dworkin RH, O'Connor AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237–251.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.
88. Abdulla A, Adams N, Bone M et al. Guidance on the management of pain in older people. Age Ageing 2013;42(Suppl 1):i1–i57.
89. American academy of pain medicine. use of opioids for the treatment of chronic pain. http://www.painmed.org/library clinicol_6delines.aspx.

APPENDIX II REFERENCES FOR ALTERNATIVE MEDICATIONS INCLUDED IN TABLE 2

Falls, anticonvulsants

22. Dworkin RH, O'Connor AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237–251.
26. Pugh MJ, Berlowitz DR, Rao JK et al. The quality of care for adults with epilepsy: An initial glimpse using the QUIET measure. BMC Health Serv Res 2011;11:1.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.
56. Rowan AJ, Ramsay E, Collins JF et al. New onset geriatric epilepsy: A randomized study of gabapentin, lamotrigine, and carbamazepine. Neurology 2005;64:1868–1873.
57. Correll CM, Bazil CW. Management of seizures in the elderly. Curr Geriatr Rep 2014;3:73–82.
58. Werhahn KJ, Trinka E, Dobesberger J et al. A randomized, double-blind comparison of antiepileptic drug treatment in the elderly with new-onset focal epilepsy. Epilepsia 2015;56:450–459.

Falls, benzodiazepines and nonbenzodiazepine hypnotics

67. Leshner A, Baghdoyan H, Bennett S et al. NIH statement regarding the treatment of insomnia. Manifestations and Management of Chronic Insomnia in Adults June 13–15, 2005. Sleep 2005;28:1049–1057.
68. Morin C. Efficacy of behavioral and psychological treatments of chronic insomnia. J Clin Sleep Med 2005;1:e482–e483.
69. Cluydts R, Peeters K, DeBouyalisky I et al. Comparison of continuous vs. intermittent administration of zolpidem in chronic insomniacs: A double-blind, randomized, pilot study. J Int Med Res 1998;26:13–24.
70. Hajak G, Cluydts R, Declerck A et al. Continuous versus non-nightly use of zolpidem in chronic insomnia: Results of a large-scale, double-blind, randomized, outpatient study. Int Clin Psychopharmacol 2002;17:9–17. Erratum in: Int Clin Psychopharmacol 2002;17:206.
71. Perlis ML, McCall WV, Krystal AD et al. Long-term, non-nightly administration of zolpidem in the treatment of patients with primary insomnia. J Clin Psychiatry 2004;65:1128–1137.
72. Solvertsen B, Omvik S, Pallesen S et al. Cognitive behavioral therapy or zopiclone for treatment of chronic primary insomnia. JAMA 2006;295:2851–2858.
73. Walsh JK, Roth T, Randazzo A et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. Sleep 2000;23:1087–1096.
75. Baldwin D, Woods R, Lawson R et al. Efficacy of drug treatments for generalized anxiety disorder: Systematic review and meta-analysis. BMJ 2011;342:d1199.
76. Stewart RE, Chambless DL. Cognitive-behavioral therapy for adult anxiety disorders in clinical practice: A meta-analysis of effectiveness studies. J Consult Clin Psychol 2009;77:595–606.

Falls, tricyclic antidepressants and selective serotonin reuptake inhibitors

22. Dworkin RH, O'Conner AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence based recommendations. Pain 2007;132:237–251.
53. US Department of Veterans Affairs and Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. Washington, DC: US Department of Veterans Affairs and Department of Defense, 2009.
54. Gartlehner G, Hansen RA, Kahwati L. Drug class review on second generation antidepressants 2006 [on-line]. Available at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm Accessed April 1, 2015.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.

Falls, antipsychotics, delirium and dementia

24. Inouye SK, Marcantonio ER, Metzger ED. Doing damage in delirium: The hazards of antipsychotic treatment in elderly people. Lancet Psychiatry 2014;1:312–315.

74. Maher AR, Maglione M, Bagley S et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: A systematic review and meta-analysis. JAMA 2011;306:1359–1369.
90. Leentjens AF, Molag ML, Van Munster BC et al. Changing perspectives on delirium care: The new Dutch guideline on delirium. J Psychosom Res 2014;77:240–241.
91. The American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Postoperative delirium in older adults: Best practice statement from the American Geriatrics Society. J Am Coll Surg 2015;220:136–148.
92. Pietro G, DeFazio P, Manfredi VGL et al. Use and safety of antipsychotics in behavioral disorders in elderly people with dementia. J Clin Psychopharmacol 2014;34:109–123.

Dementia Tricyclic antidepressants (tertiary and secondary)

22. Dworkin RH, O'Connor AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237–251.
53. The Management of MDD Working Group. VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. Washington, DC: U.S. Department of Veterans Affairs and Department of Defense, 2009.
54. Gartlehner G, Hansen RA, Kahwati L. Drug class review on second generation antidepressants [on-line]. 2006. Available at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm Accessed April 1, 2015.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.

Dementia, antipsychotics

74. Maher AR, Maglione M, Bagley S et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: A systematic review and meta-analysis. JAMA 2011;306:1359–1369.
92. Pietro G, DeFazio P, Manfredi VGL et al. Use and safety of antipsychotics in behavioral disorders in elderly people with dementia. J Clin Psychopharmacol 2014;34:109–123.

Dementia, histamine blockers

93. Achem SR, DeVault KR. Gastroesophageal reflux disease and the elderly. Gastroenterol Clin North Am 2014;43:147–160.

Dementia, anticholinergics

14. Miyasaki JM. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. Neurology 2002;58:11–17.
15. Scottish Intercollegiate Guideline Network. Diagnosis and pharmacologic management of Parkinson's disease: A national clinical guideline, No. 113, January 2010 [on-line]. Available at http://www.sign.ac.uk/pdf/sign113.pdf Accessed April 1, 2015
16. Ferreria JJ, Katzenschlager R, Bloem BR et al. Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management. Eur J Neurol 2013;20:5–15.
17. Katzenschlager R, Sampaio C, Costa J et al. Anticholinergics for symptomatic management of Parkinson's diesase. Cochrane Database Syst Rev 2002;(3):CD003735.

Dementia, benzodiazepines

67. Leshner A, Baghdoyan H, Bennett S et al. NIH statement regarding the treatment of insomnia. Manifestations and Management of Chronic Insomnia in Adults June 13–15, 2005. Sleep 2005;28:1049–1057.
68. Morin C. Efficacy of behavioral and psychological treatments of chronic insomnia. J Clin Sleep Med 2005;1:e482–e483.
69. Cluydts R, Peeters K, DeBouyalisky I et al. Comparison of continuous vs. intermittent administration of zolpidem in chronic insomniacs: A double-blind, randomized, pilot study. J Int Med Res 1998;26:13–24.
70. Hajak G, Cluydts R, Declerck A et al. Continuous versus non-nightly use of zolpidem in chronic insomnia: Results of a large-scale, double-blind, randomized, outpatient study. Int Clin Psychopharmacol 2002;17:9–17. Erratum in: Int Clin Psychopharmacol 2002;17:206.
71. Perlis ML, McCall WV, Krystal AD et al. Long-term, non-nightly administration of zolpidem in the treatment of patients with primary insomnia. J Clin Psychiatry 2004;65:1128–1137.
72. Solvertsen B, Omvik S, Pallesen S et al. Cognitive behavioral therapy or zopiclone for treatment of chronic primary insomnia. JAMA 2006;295:2851–2858.
73. Walsh JK, Roth T, Randazzo A et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. Sleep 2000;23:1087–1096.
75. Baldwin D, Woods R, Lawson R et al. Efficacy of drug treatments for generalised anxiety disorder: Systematic review and meta-analysis. BMJ 2011;342:d1199.
76. Stewart RE, Chambless DL. Cognitive-behavioral therapy for adult anxiety disorders in clinical practice: A meta-analysis of effectiveness studies. J Consult Clin Psychol 2009;77:595–606.

Dementia, nonbenzodiazepine hypnotics

67. Leshner A, Baghdoyan H, Bennett S et al. NIH statement regarding the treatment of insomnia. Manifestations and Management of Chronic Insomnia in Adults June 13–15, 2005. Sleep 2005;28:1049–1057.
68. Morin C. Efficacy of behavioral and psychological treatments of chronic insomnia. J Clin Sleep Med 2005;1:e482–e483.
69. Cluydts R, Peeters K, DeBouyalisky I et al. Comparison of continuous vs. intermittent administration of zolpidem in chronic insomniacs: A double-blind, randomized, pilot study. J Int Med Res 1998;26:13–24.
70. Hajak G, Cluydts R, Declerck A et al. Continuous versus non-nightly use of zolpidem in chronic insomnia: Results of a large-scale, double-blind, randomized, outpatient study. Int Clin Psychopharmacol 2002;17:9–17. Erratum in: Int Clin Psychopharmacol 2002;17:206.
71. Perlis ML, McCall WV, Krystal AD et al. Long-term, non-nightly administration of zolpidem in the treatment of patients with primary insomnia. J Clin Psychiatry 2004;65:1128–1137.
72. Solvertsen B, Omvik S, Pallesen S et al. Cognitive behavioral therapy or zopiclone for treatment of chronic primary insomnia. JAMA 2006;295:2851–2858.
73. Walsh JK, Roth T, Randazzo A et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. Sleep 2000;23:1087–1096.

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

18. AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological Management of Persistent Pain in Older Persons. J Am Geriatr Soc 2009;57:1331–1346.
22. Dworkin RH, O'Connor AB, Backonja M et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237–251.
55. Moulin DE, Clark AJ, Gilron I et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12:13–21.
88. Abdulla A, Adams N, Bone M et al. Guidance on the management of pain in older people. Age Ageing 2013;42(Suppl 1):i1–i57.

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

94. Holroyd-Leduc J, Reddy M, eds. Evidence-Based Geriatric Medicine. London: BMJ Books, 2012.
95. Reuben DB, Herr KA, Pacala JT et al. Geriatrics at Your Fingertips: 2015, 17th Ed. New York: American Geriatrics Society, 2015.
96. Abraha I, Cruz-Jentoft A, Soiza RL et al. Evidence of and recommendations for non-pharmacological interventions for common geriatric conditions: The SENATOR-ONTOP systematic review protocol. BMJ Open 2015;5:e007488.
97. Durso SC, Sullivan GM, eds. Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine, 8th Ed. New York: American Geriatrics Society, 2013.

Appetite

98. Hanson LC, Ersek M, Gilliam R et al. Oral feeding options for people with dementia: A systematic review. J Am Geriatr Soc 2011;59:463–472.

Delirium

91. The American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Postoperative delirium in older adults: Best practice statement from the American Geriatrics Society. J Am Coll Surg 2015;220:136–148.
99. Rossom R, Anderson P, Greer N. Delirium: Screening, Prevention, and Diagnosis: A Systematic Review of the Evidence. Washington, DC: Department of Veterans Affairs; September 2011 [on-line]. Available at http://www.hsrd.research.va.gov/publications/esp/delirium.cfm Accessed April 24, 2015.

Dementia Behavioral Complications

100. Caring for a Person with Alzheimer's Disease: Your Easy-to-Use Guide from the National Institute on Aging [on-line]. Available at https://www.nia.nih.gov/alzheimers/publication/caring-person-alzheimers-disease/about-guide Accessed April 1, 2015.
101. O'Neil MA, Freeman M, Chistensen V et al. A Systematic Evidence Review of Non-pharmacological Interventions for Behavioral Symptoms of Dementia [on-line]. Washington, DC: Department of Veterans Affairs, 2011. Available at http://www.hsrd.research.va.gov/publications/esp/dementia_nonpharm.cfm Accessed April 24, 2015.
102. Gitlin LN, Kales HC, Lyketsos C. Managing behavioral symptoms in dementia using nonpharmacologic approaches: An overview. JAMA 2012;308:2020–2029.
103. Kolanowski A, Van Haitsma K. Promoting positive behavioral health: A nonpharmacologic toolkit for senior living communities (2013) [on-line]. Available at www.nursinghometoolkit.com Accessed May 7, 2015.

Pain

104. Park J, Hughes AK. Nonpharmacological approaches to the management of chronic pain in community-dwelling older adults: A review of empirical evidence. J Am Geriatr Soc 2012;60:555–568.
105. Makris UE, Abrams RC, Gurland B et al. Management of persistent pain in the older patient: A clinical review. JAMA 2014;312:825–836.
106. Age Page. Pain: you can get help. National Institute on Aging [on-line]. Available at https://www.nia.nih.gov/sites/default/files/pain_you_can_get_help.pdf Accessed April 1, 2015.

Transcutaneous electrical nerve stimulation

107. Dubinsky RM, Miyasaki J. Assessment: Efficacy of transcutaneous electrical nerve stimulation in the treatment of pain in neurological disorders (an evidence based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2010;74:173–176.
108. Khadilkar A, Odebiyi DO, Brosseau L et al. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. Cochrane Database Syst Rev 2008;(4):CD003008.

Percutaneous Electrical Nerve Stimulation

109. Weiner DK, Perera S, Rudy TE et al. Efficacy of percutaneous electrical nerve stimulation and therapeutic exercise for older adults with chronic low back pain: A randomized controlled trial. Pain 2008;140:344–357.
110. Weiner DK, Schmader KE. Postherpetic pain: More than sensory neuralgia? Pain Med 2006;7:243–249.

Acupuncture

111. Vickers AJ, Cronin AM, Maschino AC et al. Arch Intern Med 2012;172:1444–1453.
112. Furlan AD, van Tulder MW, Cherkin DC et al. Acupuncture and dry-needling for low back pain. Cochrane Database Syst Rev 2005;(1):CD001351.
113. Manheimer E, Cheng K, Linde K et al. Acupuncture for peripheral joint osteoarthritis. Cochrane Database Syst Rev 2010;(1):CD001977.

Cognitive Behavioral Therapy

114. Keefe FJ, Porter L, Somers T et al. Psychosocial interventions for managing pain in older adults: Outcomes and clinical implications. Br J Anaesth 2013;111:89–94.
115. Dixon KE, Keefe FJ, Scipio CD et al. Psychosocial interventions for arthritis pain management in adults: A meta-analysis. Health Psychol 2007;26:241–250.
116. Williams AC, Eccleston C, Morley S. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev 2012;(11):CD007407.
117. Cook AJ. Cognitive-behavioral pain management for elderly nursing home residents. J Gerontol B Psychol Sci Soc Sci 1998;53B:51–59.

Urinary Incontinence

118. Qaseem A, Dallas P, Forciea MA et al. Nonsurgical management of urinary incontinence in women: A clinical practice guideline from the American College of Physicians. Ann Intern Med 2014;161:429–440.
119. Age Page. Urinary incontinence guide. National Institute on Aging [on-line]. Available at https://www.nia.nih.gov/sites/default/files/Urinary PartsAPfinalproof_0.pdf Accessed April 1, 2015.

Sleep

68. Morin C. Efficacy of behavioral and psychological treatments of chronic insomnia. J Clin Sleep Med 2005;1:e482–e483.
120. Teodorescu MC, Husain NF. Nonpharmacologic approaches to insomnia in older adults. Ann Long Term Care 2010;10:20.
121. Sleep and aging [on-line]. Available at http://nihseniorhealth.gov/sleepandaging/aboutsleep/01.html Accessed April 1, 2015.
122. McCurry SM, Logsdon RG, Teri L et al. Evidence-based review of psychological treatments for insomnia in older adults. Psychol Aging 2007;22:18–27.
123. Sivertsen B, Omvik S, Pallesen S et al. Cognitive behavioral therapy vs. zopiclone for treatment of chronic primary insomnia in older adults: A randomized clinic trail. JAMA 2006;295:2851–2858.