Continuing Education

Guidelines Updates: Venous Thromboembolism, American Diabetes Association, Opioids, and Beers Criteria

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EDUCATIONAL OBJECTIVES

After the completion of this activity, pharmacists will be able to:

- Explain the latest updates for the 2016 CHEST Guidelines: Antithrombotic Therapy for Venous Thromboembolism Disease
- Describe the 2016 American Diabetes Association Standards of Medical Care in Diabetes changes
- Determine if opioid therapy is appropriately prescribed and monitored based on the 2016 CDC Opioid Prescribing Guidelines
- Identify major changes in the 2015 American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

INTRODUCTION

Health care providers rely on national guidelines to provide evidence-based recommendations for treating different medical conditions. Multiple guidelines have recently been updated including the CHEST Guideline for Antithrombotic Therapy for Venous Thromboembolism (VTE) Disease and the American Diabetes Association (ADA) Standards of Medical Care in Diabetes. Also the Centers for Disease Control (CDC) recently published a guideline for the prescribing of opioids in chronic pain.[1,2,3] Lastly, the Beers Criteria for Potentially Inappropriate Medication (PIM) Use in Older Adults was updated in 2015 which included major additions to the existing recommendations.[4] The objective of this program is to discuss changes from previous major guidelines and summarize the CDC's recent publication on prescribing opioids.

2016 CHEST GUIDELINE: ANTITHROMBOTIC THERAPY FOR VENOUS THROMBOEMBOLISM DISEASE[1]

The American College of Chest Physicians (ACCP) published the 10th edition of the CHEST Guideline and Expert Panel Report on Antithrombotic Therapy for VTE Disease in February 2016 updating the 9th edition published in 2012. The latest guideline provides updates on 12 existing VTE topics, and created three new topic areas. The new topics address the use of aspirin in VTE patients, subsegmental pulmonary embolisms (PEs), and recurrent VTEs when a patient is appropriately anticoagulated. Table 1 provides the quality of evidence for the following summary of graded recommendations:

Table 1: Grading Evidence

Grading Evidence	
Grade	**Evidence**
Grade 1	Strong evidence
Grade 2	Weak evidence
Grade A	High quality evidence
Grade B	Moderate quality evidence
Grade C	Low quality evidence

RECOMMENDATIONS:

- ***Previous*:** In the 2012 CHEST guidelines, warfarin was the first line agent for the long-term (first 3 months) treatment of patients with a deep vein thrombosis (DVT) of the leg or PE, second line was low molecular weight heparin (LMWH) followed by rivaroxaban or dabigatran.
  Updated: The panel changed the recommendations in the 10th edition and suggested dabigatran, rivaroxaban, apixaban, or edoxaban for first line agents, warfarin for second line followed by LMWH for the long-term (first 3 months) treatment of a DVT or PE (Grade 2B). The novel oral anticoagulant agents are effective at preventing VTEs compared to warfarin but are not associated with a high risk of bleeding.
- ***Previous:*** The 9th edition suggested low molecular weight heparin (LMWH) first line for long-term anticoagulation therapy in patients with a DVT or PE and cancer (ie "cancer-associated thrombosis"), warfarin second line, and rivaroxaban or dabigatran as last line.
  Updated: LMWH remains first line, but the 10th edition guidelines suggest using warfarin,

dabigatran, rivaroxaban, apixaban, or edoxaban as potential second line therapies (Grade 2C).

- ***Previous:*** If physicians choose to extend anticoagulation therapy (over 3 months) for a DVT, continuing the same anticoagulant is suggested.
  Updated: The newest guidelines suggest continuing the same anticoagulant if physicians extend therapy in patients with a DVT or PE (Grade 2C).
- ***New:*** If anticoagulation therapy is stopped in a patient with an unprovoked proximal VTE it is suggested that the patient take aspirin rather than nothing for recurrent VTE prevention (Grade 2C). Though aspirin is not a replaceable alternative to anticoagulation, sometimes patients decline extended anticoagulation therapy or decide they want to stop anticoagulants regardless of healthcare professionals' recommendations. Aspirin is a reasonable therapy compared to no therapy. It is always important to weigh the benefits versus the risks of bleeding.
- ***Previous:*** The 2012 CHEST guidelines suggested compression stockings to decrease the risk of post-thrombotic syndrome (PTS) after a DVT. Patients are at increased risk for this syndrome after a DVT occurs. PTS is when damaged veins and valves from the DVT impair blood flow leading to symptoms like painful, red, swollen legs or swollen ankles.[5]
  Updated: Compression stockings should not be routinely used to prevent PTS considering the latest evidence indicates compression stockings do not decrease PTS (Grade 2B).
- ***New:*** The second new topic addressed in the 10th edition CHEST guidelines is regarding subsegmental PEs which are PEs that occur in the subsegmental pulmonary arteries. As the capabilities of computerized tomography (CT) pulmonary angiography have increased, so has the ability to diagnose subsegmental PEs. For patients diagnosed with a PE (and no proximal DVT in the legs) at low risk for a recurrent VTE, the guidelines suggest clinical surveillance rather than initiation of anticoagulation; however, in high risk patients, anticoagulation is suggested (Grade 2C).
- ***Previous:*** For patients diagnosed with an acute PE at low-risk for a subsequent PE, the 9th edition guidelines suggested early discharge rather than standard discharge.
  Updated: The latest guidelines suggest treating patients with an acute PE at low risk for a subsequent PE at home or discharging them early from the hospital (rather than keeping them there for 5 days) as long as the home environment is adequate (Grade 2B). This is the first guideline update that states some patients may be treated entirely at home.
- ***Previous:*** It was suggested to give thrombolytics to patients presenting with an acute PE without hypotension, at low bleed risk, but whose clinical presentation suggested a high risk for developing hypotension.
  Updated: The 10th edition guidelines state for most patients presenting with an acute PE without hypotension, do not give systemic thrombolytic agents (Grade 1B). However, if a patient starts deteriorating after initiation of anticoagulants and they have a low bleed risk, the guidelines suggest using systemic thrombolytic therapies (Grade 2C). If thrombolytics are used, it is suggested to infuse in a peripheral vein rather than a catheter-directed thrombolysis. Patients are classified as having a low bleed risk if they have none of the following risk factors: age >65 years, cancer, renal or liver failure, thrombocytopenia, previous stroke, diabetes, anemia, previous bleeding, antiplatelet therapy, nonsteroidal anti-inflammatory drugs (NSAIDS), poor anticoagulant control, recent surgery, frequent falls, alcohol abuse, comorbidities and reduced functional capacity.
- ***New:*** The last new topic addressed in the 2016 CHEST guidelines is the treatment of recurrent VTEs when a patient's anticoagulant is already in therapeutic range, a very unusual situation. If the patient is compliant and diagnosed with a recurrent VTE while on therapeutic doses of warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban, it is suggested to switch temporarily to LMWH (Grade 2C). LMWH is usually continued for around a month. The practitioner should consider assessing compliance, look for underlying malignancies, and decide if the patient truly has a recurrent VTE, especially considering how unusual this situation would be with a fully anticoagulated patient. If the patient is compliant and on long-term LMWH when diagnosed with a recurrent VTE, the authors suggest increasing the dose of LMWH by 25-33% (Grade 2C).

AMERICAN DIABETES ASSOCIATION: STANDARDS OF MEDICAL CARE IN DIABETES 2016 UPDATE[2]

The ADA: Standards of Medical Care in Diabetes are annually updated guidelines that provide health care professionals with a holistic approach to diabetes management. They provide treatment goals for diabetes and associated diagnosis. The guidelines are divided into 14 sections ranging from Strategies for Improving Care to Diabetes Advocacy. New updates have occurred in most sections and will be discussed along with the strength of evidence (refer to Table 2) for each recommendation.

Table 2: Strength of Evidence

Grading Evidence	
Level of Evidence	**Evidence Description**
A	Clear evidence
B	Supportive evidence from well conducted cohort studies
C	Supportive evidence from poorly controlled or uncontrolled studies
E	Expert consensus or clinical experience

General Changes: The word "diabetic" will no longer be used to define individuals with diabetes.

Section 1. Strategies for Improving Care:
This section discusses incongruences related to ethnicity, culture, sex, and socioeconomic differences. Also, recommendations on tailoring treatment to vulnerable populations with diabetes like:

Food insecurity:

Food insecurity should be considered when evaluating hyper and hypoglycemia and make appropriate resources available (Evidence: A).

Cognitive dysfunction and/or mental illness:

- Hyperglycemic individuals with poor cognitive function should not use intensive glucose control for improvement of cognitive function (Evidence: B).
- In individuals with poor cognitive function or severe hypoglycemia, glycemic therapy should be tailored to avoid significant hypoglycemia (Evidence: C).
- The cardiovascular benefit of statins outweighs the risk of cognitive dysfunction for individuals at high cardiovascular risk (Evidence: A).
- Weight, glycemic control, and cholesterol levels should be monitored for patients taking a second-generation antipsychotic medication. Treatment regimens should be reassessed (Evidence: C).

HIV:

Patients with HIV should be screened for diabetes and pre-diabetes with a fasting glucose level before starting antiretroviral therapy and 3 months after starting or changing it. Continue checking fasting glucose each year. If pre-diabetes is detected, continue monitoring every 3–6 months for progression to diabetes (Evidence: E).

Section 2. Classification and Diagnosis of Diabetes:

- Diagnostic tests (fasting plasma glucose, 2-hr plasma glucose after a 75-g oral glucose tolerance test, and A1C criteria) were revised to make it clear that they are all equally appropriate (Evidence: B).
- To clarify the relationship between age, BMI, and risk for type 2 diabetes and pre-diabetes the ADA changed their recommendation to now test all adults beginning at age 45, regardless of weight (Evidence: B).
- Testing is recommended for asymptomatic adults of any age who are overweight or obese and who have one or more additional risk factors for diabetes (Evidence: B).

- For monogenic diabetes syndromes, such as neonatal diabetes mellitus and maturity-onset diabetes of the young, there is specific guidance and text on testing, diagnosing, and evaluating individuals and their family members.
    - Genetic testing should be done for all children diagnosed with diabetes in the first 6 months of life (Evidence: B).
    - Individuals with mild stable fasting hyperglycemia and a family history of diabetes not characteristic of type 1 or 2 diabetes should be considered for maturity-onset diabetes of the young (Evidence: E).
    - Consider referring individuals with diabetes not typical of type 1 or type 2 diabetes and occurring in successive generations (suggestive of an autosomal dominant pattern of inheritance) to a specialist, because this can affect therapy and help identify other affected family members (Evidence: E).

Section 3. Foundations of Care and Comprehensive Medical Evaluation:

A major change from the 2015 Standards of Care was the combining of Section 3 "Initial Evaluation and Diabetes Management Planning" and Section 4 "Foundations of Care: Education, Nutrition, Physical Activity, Smoking Cessation, Psychosocial Care, and Immunization." This was done as a tool to highlight the importance of integrating medical evaluation, patient engagement, and ongoing care of lifestyle and behavioral modification. Nutrition and vaccination recommendations were streamlined from last year to focus on what is relevant to people with diabetes.

Section 4. Prevention or Delay of Type 2 Diabetes

A recommendation was added this year to encourage technology use like: Internet-based social networks, distance learning, DVD-based content, and mobile applications for weight loss (e.g. My Fitness Pal, Lose It) and diabetes prevention strategies (Evidence: B).

Section 5. Glycemic Targets

Due to the increasing number of older adults with insulin-dependent diabetes, the ADA added the recommendation that people who successfully use continuous glucose monitoring should have continued access after age 65 through insurance (Evidence: E).

Section 6. Obesity Management for the Treatment of Type 2 Diabetes

This is a new section; it has some previous recommendations and new recommendations about assessment of weight in diabetes and treatment options.

- BMI should be calculated and documented at each patient encounter (Evidence: B).
- Medications approved by the FDA for long-term treatment of obesity:
    - Orlistat (Alli or Xenical)
    - Lorcaserin (Belviq)
    - Phentermine/Topiramate ER (Qsymia)
    - Naltrexone/Bupropion(Contrave)
    - Liraglutide (Saxenda)

Section 7. Approaches to Glycemic Treatment

Bariatric surgery is no longer in this section and is now in Section 6.

Section 8. Cardiovascular Disease and Risk Management

- "Atherosclerotic cardiovascular disease" (ASCVD) has replaced the former term "cardiovascular disease" (CVD), due to ASCVD being a more specific term.

A new recommendation for pharmacological treatment in older adults:

- For patients > 75 years old moderate intensity statins and lifestyle changes are appropriate but when additional atherosclerotic cardiovascular disease risk factors are present moderate or high intensity statins along with lifestyle changes should be considered (Evidence: B).
- The recommendation to consider aspirin therapy in women with an increased cardiovascular risk (10 year risk >10%) aged >60 years has been

changed to include women aged ≥50 years (Evidence: C).
- Antiplatelet use in patients aged <50 years with multiple risk factors (e.g., 10-year risk 5–10%) requires clinical judgment (Evidence: E).
- Patients with a recent acute coronary syndrome with LDL ≥50 mg/dL or those who cannot tolerate a high intensity statin can consider adding ezetimibe to moderate intensity statin therapy (Evidence: A).

Section 9. Microvascular Complications and Foot Care

- "Nephropathy" was changed to "diabetic kidney disease" to emphasize that it is kidney disease that is directly related to diabetes.

Major recommendations in this section include:

- Referral for renal replacement (dialysis or transplant) treatment evaluation is necessary if they have an estimated glomerular filtration rate < 30 ml/min/1.73m$^{2.}$ (Evidence: A).
- Promptly refer to a physician experienced in kidney disease if uncertain about etiology, difficult management issues, and rapidly progressing kidney disease (Evidence: B).
- Intravitreal injections of anti-VEGF agents are indicated for center-involved diabetic macular edema, which may threaten reading vision (Evidence: A).

Section 10. Older Adults

This section did not have any major changes. The section discusses neurocognitive function, hypoglycemia, treatment goals, care in skilled nursing facilities/nursing homes, and end-of-life considerations.

Section 11. Children and Adolescents

New recommendations were given for psychosocial issues, family involvement, and appropriate age for lipid screenings.

- Patients with diabetes aged <18 years should receive culturally sensitive and age appropriate individualized diabetes self-management education and support at diagnosis and routinely thereafter (Evidence: B).
- Psychosocial issues and family stresses that can impact adherence should be addressed at diagnosis and follow-up visits. Also, provide appropriate referrals to trained mental health professionals, preferably experienced in childhood diabetes when appropriate (Evidence: E).
- Encourage age appropriate family involvement in diabetes management to prevent nonadherence and poor glycemic control (Evidence: B).
- Consider mental health professionals as integral members of the pediatric diabetes team (Evidence: E).
- A fasting lipid profile should be performed in children ≥ 10 years of age soon after diagnosis and glucose control is established (Evidence: E).

Section 12. Management of Diabetes in Pregnancy

Pregestational Diabetes

- Counseling should be provided before conception that addresses the importance of glycemic control, ideally A1C <6.5% to reduce the risk of congenital anomalies (Evidence: B).
- Effective contraception should be prescribed and used until a woman is ready to become pregnant (Evidence: A).
- Risk of developing/progressing diabetic retinopathy during pregnancy increases for patients previously diagnosed with diabetes and not tightly controlled during pregnancy. Eye exams should be conducted before pregnancy, every trimester, and for 1 year postpartum as indicated by degree of retinopathy (Evidence: B).

Gestational Diabetes Mellitus

- Lifestyle change can be used to manage gestational diabetes but medications should be added if needed to achieve glycemic goals (Evidence: A).
- Preferred medications in gestational diabetes mellitus are insulin and metformin. Glyburide may be used but may have a higher rate of neonatal hypoglycemia and macrosomia (Evidence: A).

General Principles for Management of Diabetes in Pregnancy

The A1C target in pregnancy is 6–6.5%. Other goals may be appropriate depending on hypoglycemia risk (Evidence: B).

Section 13. Diabetes Care in the Hospital

This section now focuses only on diabetes care in the hospital setting. No new recommendations are made but this section now has more detail on previous recommendations.

Section 14. Diabetes Advocacy

No new recommendations were made in this section since the 2015 Standards of Medical Care in Diabetes.

2016 CENTER FOR DISEASE CONTROL GUIDELINES FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN[3]

On March 18th, 2016, the CDC released new guidelines targeting the use of opioids for chronic pain. This report was created in response to the alarming increase of opioid prescriptions, overdoses, and deaths. Physicians have reported numerous concerns regarding pain medication abuse and often report insufficient training in prescribing opioids. The CDC published these guidelines to offer recommendations based on the most recent evidence.

Overall, these guidelines strive to reduce the overprescribing of opioids. In addition to these guidelines, the CDC has also published a checklist for prescribing opioids available at (http://stacks.cdc.gov/view/cdc/38025) and will be launching a mobile application to aid physicians in implementation.[6] While the quality of evidence supporting these recommendations is low, it demonstrates the need for studies regarding opioid efficacy and safety. The CDC has stated that these guidelines will be revisited as new studies showing more compelling evidence become available. Table 3 describes how each evidence type and category is determined.

Table 3:

Recommendation Categories and Evidence Type	
Category A	Applies to all persons; most patients should receive the recommended course of action
Category B	Individual decision making needed; choices should be appropriate for individual patients
Type 1 Evidence	Randomized clinical trials or overwhelming evidence from observational studies
Type 2 Evidence	Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies
Type 3 Evidence	Observational studies or randomized clinical trials with notable limitations
Type 4 Evidence	Clinical experience and observations, observational studies with important limitation, or randomized clinical trials with several major limitations

The CDC categorized its recommendations into three areas for consideration. These recommendations are classified based on the following assessments:

- No evidence has shown long-term benefit associated with opioids in pain and function compared to no opioids for chronic pain. These outcomes were examined at least 1 year later.
- There has been extensive evidence showing possible harms of opioids including opioid use disorder, overdose, and motor vehicle injury.
- There has also been extensive evidence showing some benefits of nonpharmacological therapy and non-opioid therapy which are associated with less harm than long-term opioid therapy.

Recommendations

Determining when to initiate or continue opioids for chronic pain

- For the purpose of these guidelines, chronic pain is defined as pain continuing or expected to continue for more than 3 months or past the time of normal tissue healing. The CDC recommends nonpharmacologic therapy and nonopioid pharmacologic therapy for chronic pain. Several nonpharmacologic therapies including physical therapy and weight loss have evidence supporting pain improvement. Nonopioid pharmacologic therapy such as acetaminophen and NSAIDs have proven effective for arthritis and lower back pain. Anticonvulsants and antidepressants are useful agents in the treatment of chronic pain associated with neuropathy and post-herpetic neuralgia. Opioids are only recommended in situations where benefits outweigh the substantial risk incurred with opioid therapy. If opioid therapy is deemed appropriate, it should be used in conjunction with nonpharmacologic and nonopioid pharmacologic therapy to increase the likelihood of effectiveness (Category A, Type 3).
- When deciding to initiate or continue opioid therapy, it is important to establish realistic treatment goals for pain and function. Patients should be informed that while opioids can reduce pain in short-term use, no evidence clearly shows improvements in pain or function with long-term therapy. It is also important to provide information about serious adverse effects such as potentially fatal respiratory depression and lifelong opioid use disorder. If benefits do not outweigh risks, it is important to consider how to discontinue opioids. Therapy is only recommended to be continued if there is a clear clinically meaningful improvement in pain and function which outweighs the patient's risk (Category A, Type 3).

Opioid selection, dosage, duration, follow-up, and discontinuation

- When initiating opioid therapy for chronic pain, the CDC recommends prescribing immediate-release opioids rather than extended release(ER) or long-acting(LA) formulations. This recommendation is based primarily on a study showing a higher risk for overdose among patients initiating treatment with ER or LA opioids rather than immediate release. It is also noted that experts concluded that there is not enough evidence to determine the safety of using immediate release opioids for breakthrough pain for patients treated with ER or LA formulations. ER/LA formulations should be reserved for patients with severe, continuous pain who have received immediate release therapy daily for at least 1 week (Category A, Type 4).
- The lowest effective dosage should always be used when prescribing opioid therapy. Caution is strongly advised when considering increasing opioid dosage to ≥50 morphine milligram equivalents (MME) per day. If a patient's dose is increased to ≥50 MME/day, follow-up frequency should also be increased and naloxone should be considered as well as overdose prevention education to the patient and family members. Dose increases to ≥90 MME/day should be avoided or very carefully justified with

appropriate documentation. Pain specialists should generally be consulted for dosages exceeding 90 MME/day (Category A, Type 3).

- When prescribing opioid therapy for acute pain, prescriptions should be for the lowest effective dose and for no greater quantity than required for the expected duration of pain. Clinical evidence showed that opioid use for acute pain was closely linked to long-term opioid use. It is also noted that higher doses increased the risk for long-term use. Three days or less is often sufficient for the treatment of acute pain and greater than 7 days should rarely be needed. Experts agreed that limiting the days supplied is necessary due to each day of unnecessary opioid use significantly increases the risk to the patient and the likelihood of physical dependence (Category A, Type 4).
- Patients should be reassessed within 1 to 4 weeks of starting opioid therapy or after dose escalation to evaluate the benefits and harms of continued therapy. If benefits are not seen, other therapies should be optimized while tapering opioids to lower dosages or to discontinuation. When tapering, a method slow enough to minimize signs and symptoms of opioid withdrawal is appropriate. Generally, a 10% opioid decrease per week is recommended as an initial taper regimen which can be individualized based on goal and patient tolerance (Category A, Type 4).

Assessing risk and addressing harms of opioid use

- It is recommended that a patient's risk for opioid-related harms be assessed periodically during therapy, at least every 3 months. Naloxone should be considered for patients with factors which increase their risk for opioid overdose. These factors include: a history of overdose, substance use disorder, opioid dosages ≥50 MME/day, and concurrent benzodiazepine use (Category A, Type 4).
- Each patient's history of controlled substance prescriptions should be reviewed using the state's prescription drug monitoring program (PDMP) to determine if the patient is receiving duplicate therapy or dangerous combinations that put them at risk of overdose. PDMP should be reviewed prior to initiation of opioid therapy and periodically during therapy. Monitoring should range from each prescription to a minimum of every 3 months (Category A, Type 4).
- The guidelines recommend urine drug tests for patients receiving opioids prior to initiation and at least annually to screen for other controlled substances and illicit drugs. This recommendation is primarily for patients with an elevated risk of overdose or abuse (Category B, Type 4).
- It is recommended to avoid prescribing opioid therapy in patients taking benzodiazepines whenever possible. Both of these drug classes have the potential to cause respiratory depression and concurrent use places patients at significantly greater risk for overdosing. The CDC found evidence that concurrent use of benzodiazepines and opioids is associated with a near-quadruple risk of overdose death when compared to opioid use alone (Category A, Type 3).
- Finally, any patients with evidence of opioid use disorder should be offered evidence-based treatment. If a physician is not comfortable offering this support, arrangements should be made with an appropriately qualified physician (Category A, Type 2).

BEERS CRITERIA UPDATE[4]

The American Geriatrics Society (AGS) Beers Criteria for Potentially Inappropriate Medication (PIM) Use in Older Adults was updated in 2015. The Beers Criteria is a widely-used resource regarding the safety of medications in the geriatric population and aims at reducing patients' exposure to PIMs. Since the 2012 revision, the review committee added drugs needing dose adjustments based on kidney function, drug-drug interactions, and updated the evidence and strength of recommendation on existing recommendations in the 2015 release. Table 4 defines the quality of evidence and strength of recommendations for the following graded recommendations.

Table 4

Grading: Quality of Evidence	
High	Evidence from strong well-designed studies which assess effects on health outcomes
Moderate	Evidence sufficient to determine risks, but is limited by number, quality, size, or consistency of included studies
Low	Evidence insufficient to assess harms or risks in health outcomes
Strength of Recommendation	
Strong	Benefits clearly outweigh harms, ADRs, and risks or risks clearly outweigh benefits
Weak	Benefits may not outweigh harms, ADRs, and risks
Insufficient	Evidence inadequate to determine net harms, ADRs, and risks

Potentially Inappropriate Medications in Geriatrics: Updated Drugs

- **Nitrofurantoin:** Avoid in patients with a CrCl <30mL/min or long-term use especially considering there are other safer drugs. Patients that use nitrofurantoin for long periods of time may experience pulmonary toxicity, hepatotoxicity, and peripheral neuropathy (Evidence-moderate, Recommendation-strong).
- **Dronedarone:** Avoid in patients with permanent atrial fibrillation (AFib), severe or recent decompensated heart failure since outcomes may be worse (Evidence-high, Recommendation-strong).
- **Digoxin:** Avoid as first-line agent for AFib or heart failure patients. For AFib, there are more efficacious agents and it may cause increased mortality. Digoxin may have worse outcomes in heart failure patients (AFib: Evidence-moderate, Recommendation-strong; Heart failure: Evidence-low, Recommendation-strong).
- **Benzodiazepines:** Avoid these agents due to increased risk of side effects including falls, fractures, and cognitive impairment (Evidence-moderate, Recommendation-strong).
- **Non-benzodiazepines, benzodiazepine receptor agonist hypnotics (eszopiclone, zolpidem, zaleplon):** Avoid these agents considering the side effects are similar to benzodiazepines including risk of falls, fractures, and delirium (Evidence-moderate, Recommendation-strong).
- **Meperidine:** Avoid meperidine considering there are safer analgesics available. Elderly patients are at an increased risk of side effects including neurotoxicity and delirium compared to other opioids (Evidence-moderate, Recommendation-strong).
- **Indomethacin and ketorolac (includes parenteral):** Avoid considering indomethacin. It has the worst side effect profile in the NSAIDs class and has increased likelihood of CNS effects. Risk of side effects with ketorolac include: peptic ulcer disease, gastrointestinal bleeding, and

acute kidney injury (Evidence-moderate, Recommendation-strong).

- **Antipsychotics:** Generally avoid in elderly patients unless they have a diagnosis of schizophrenia, bipolar disorder, or use short-term as an antiemetic during chemotherapy. Patients with dementia who are prescribed antipsychotics are at an increased stroke risk and faster rate of cognitive decline. These agents should not be given for dementia or delirium related behavior problems unless the following criteria are met: nonpharmacologic options have been tried and failed or are not possible AND the patient threatens harm to self or others (Evidence-moderate, Recommendation-strong).
- **Estrogen (with or without progestins):** Avoid oral and topical patch in elderly patients but vaginal cream or tablets are acceptable for the treatment of certain conditions like dyspareunia. Vaginal estrogens are safe and effective based on the currently available evidence (Oral and patch: Evidence-high, Recommendation-strong; vaginal cream or tablets: Evidence-moderate, Recommendation-weak).
- **Insulin, sliding scale:** Avoid in elderly patients considering sliding scale has not been shown to improve hyperglycemia management and patients are at an increased risk of hypoglycemia. This only refers to the singular use of short acting insulins without basal therapy (Evidence-moderate, Recommendation-strong).

New drugs added since 2012 BEERS:

- **Proton-pump inhibitors (PPIs):** Avoid using for > 8 weeks except for certain patients including those with erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, high risk patients (oral corticosteroids, chronic NSAID use), or need for maintenance therapy (failure of drug discontinuation trial or H2 blockers). Patients that chronically use PPIs may experience bone loss, fractures, or *Clostridium difficile* infections (Evidence-high, Recommendation-strong).
- **Desmopressin:** Should not be used to treat nocturia or nocturnal polyuria considering the risk of hyponatremia and safer drugs are available for treatment (Evidence-moderate, Recommendation-strong).
- **Anticholinergics, first-generation antihistamines-meclizine:** Avoid use. First-generation antihistamines are highly anticholinergic and patients are at risk of dry mouth, constipation and confusion (Evidence-moderate, Recommendation-strong).

The following drugs were removed from this section since the 2012 guidelines:

- Antiarrhythmic drugs (Class Ia, Ic, III except amiodarone) for first line AFib treatment
- Trimethobenzamide
- Mesoridazine
- Chloral hydrate

Potentially Inappropriate Medications in Geriatrics: Drug-Disease or Drug-Syndrome Interaction

- **Heart failure**: In the treatment of heart failure avoid using NSAIDs and COX-2 inhibitors, nondihydropyridine CCBs (only in reduced ejection fraction), thiazolidinediones, cilostazol, and dronedarone (severe or recently decompensated heart failure) due to the potential to promote fluid retention and exacerbate heart failure (Evidence-low to high depending on drug, Recommendation-strong).
- **Chronic seizures or epilepsy**: In the treatment of chronic seizures or epilepsy, avoid the use of bupropion, chlorpromazine, clozapine, maprotiline, olanzapine, thioridazine, thiothixene, and tramadol due to a lowering of the seizure threshold. These may be acceptable in patients with well-controlled seizures in whom alternative agents have failed (Evidence-low, Recommendation-strong).
- **Delirium**: Avoid anticholinergics, antipsychotics, benzodiazepines, chlorpromazine, corticosteroids, H_2-receptor blockers, meperidine, and sedative hypnotics

in older adults with or at risk for delirium due to the potential of inducing or worsening delirium. Antipsychotics were added to the list with this revision (Evidence-moderate, Recommendation-strong).

- **Dementia or cognitive impairment:** In patients with dementia or cognitive impairment, avoid anticholinergics, benzodiazepines, H_2-receptor antagonists, eszopiclone, zolpidem, zaleplon, and antipsychotics due to adverse CNS effects. Eszopiclone and zaleplon were added to the list in this update (Evidence-moderate, Recommendation-strong).
- **History of falls or fracture:** Avoid anticonvulsants, antipsychotics, benzodiazepines, eszopiclone, zaleplon, zolpidem, TCAs, SSRIs, and opioids unless safer alternatives are unavailable or if an anticonvulsant is being used for seizures or mood disorders. Opioids was added to this list with this guideline revision (Evidence-high, opioids-moderate; Recommendation-strong).
- **Parkinson's disease:** When treating Parkinson's disease, avoid all antipsychotics (except aripiprazole, quetiapine, clozapine), metoclopramide, prochlorperazine, and promethazine considering dopamine-receptor antagonist may make symptoms worse. The three antipsychotic exceptions have a decreased likelihood to worsen Parkinson's compared to other antipsychotics (Evidence-moderate, Recommendation-strong).
- **Insomnia:** In the treatment of insomnia, avoid using pseudoephedrine, phenylephrine, amphetamine, armodafinil, methylphenidate, modafinil, theophylline, and caffeine due to the CNS stimulating effects. Armodafinil and modafinil were added to the list in this revision. (Evidence-moderate, Recommendation-strong).

Disease/syndrome interactions removed from this section since the 2012 guidelines:

- Chronic constipation (entire criterion)
- Lower urinary tract (inhaled anticholinergic drugs)

Drug Interactions (Non-Anti-Infective) to Avoid in Older Adults

- **ACEIs and amiloride or triamterene**: Avoid this combination due to an increased risk of hyperkalemia (Evidence-moderate, Recommendation-strong).
- Avoid the use of **multiple anticholinergic agents** due to increased risk of cognitive decline (Evidence-moderate, Recommendation-strong).
- **Avoid using 3 or more CNS-active drugs** such as **antidepressants, antipsychotics, opioids, and benzodiazepines** due to increased risk of falls and fractures (Evidence-moderate to high, Recommendation-strong).
- **Corticosteroids and NSAIDs**: Avoid this combination due to increased risk of peptic ulcer disease or gastrointestinal bleeding (Evidence-moderate, Recommendation-strong).
- **Lithium and ACEIs or loop diuretics**: Avoid this combination due to increased risk of lithium toxicity (Evidence-moderate, Recommendation-strong).
- **Peripheral alpha-1 blockers and loop diuretics**: Avoid in older women due to increased risk of urinary incontinence (Evidence-moderate, Recommendation-strong).
- **Theophylline and cimetidine**: Avoid this combination due to increased risk of theophylline toxicity (Evidence-moderate, Recommendation-strong).
- **Warfarin and amiodarone or NSAIDs**: Avoid when possible due to increased risk of bleeding (Evidence-moderate to high, Recommendation-strong).

Renal Dose Adjustments for Non-Anti-Infective Medications in Geriatrics

Cardiovascular or hemostasis:

- **Amiloride**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to the increase in potassium and decrease in sodium concentrations (Evidence-moderate, Recommendation-strong).

Cardiovascular or hemostasis (cont):

- **Apixaban**: At a CrCl <25 mL/min, avoid use in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Dabigatran**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Edoxaban**: At a CrCl of 30-50 mL/min, reduce the dose of edoxaban in older adults. When the CrCl is <30 mL/min or >95 mL/min, avoid use in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Enoxaparin**: At a CrCl of <30 mL/min, reduce the dose of enoxaparin in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Fondaparinux**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Rivaroxaban**: At a CrCl of 30-50 mL/min, reduce the dose of rivaroxaban in older adults. When the CrCl is <30 mL/min, avoid use in older adults. This is due to an increased risk of bleeding (Evidence-moderate, Recommendation-strong).
- **Spironolactone**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to the increase in potassium concentrations (Evidence-moderate, Recommendation-strong).
- **Triamterene**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to the increase in potassium and decrease in sodium concentrations (Evidence-moderate, Recommendation-strong).

Central nervous system and analgesics:

- **Duloxetine**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to the increased gastrointestinal adverse effects (Evidence-moderate, Recommendation-weak).
- **Gabapentin**: At a CrCl of <60 mL/min, reduce the dose of gabapentin in older adults. This is due to CNS adverse effects (Evidence-moderate, Recommendation-strong).
- **Levetiracetam**: At a CrCl of ≤80 mL/min, reduce the dose of levetiracetam in older adults. This is due to CNS adverse effects (Evidence-moderate, Recommendation-strong).
- **Pregabalin**: At a CrCl of <60 mL/min, reduce the dose of pregabalin in older adults. This is due to CNS adverse effects (Evidence-moderate, Recommendation-strong).
- **Tramadol**: When using the immediate release product at a CrCl of <30 mL/min, the dose should be reduced but the extended release product should be avoided in older adults. This is due to CNS adverse effects (Evidence-low, Recommendation-weak).

Gastrointestinal:

- **Cimetidine**: At a CrCl of <50 mL/min, reduce the dose of cimetidine in older adults. This is due to mental status change (Evidence-moderate, Recommendation-strong).
- **Famotidine**: At a CrCl of <50 mL/min, reduce the dose of famotidine in older adults. This is due to mental status change (Evidence-moderate, Recommendation-strong).
- **Nizatidine**: At a CrCl of <50 mL/min, reduce the dose of nizatidine in older adults. This is due to mental status changes (Evidence-moderate, Recommendation-strong).
- **Ranitidine**: At a CrCl of <50 mL/min, reduce the dose of ranitidine in older adults. This is due to mental status changes (Evidence-moderate, Recommendation-strong).

Hyperuricemia:

- **Colchicine**: At a CrCl of <30 mL/min, reduce the dose of colchicine and monitor for adverse effects in older adults. This is due to gastrointestinal, neuromuscular, or bone marrow toxicity (Evidence-moderate, Recommendation-strong).

Hyperuricemia (cont):

- **Probenecid**: At a CrCl of <30 mL/min, avoid use in older adults. This is due to a loss of effectiveness. (Evidence-moderate, Recommendation-strong)

Conclusion:

Recent guideline changes will likely impact prescribing practices for the treatment of VTE, diabetes, pain, and elderly patients. The 2016 CHEST VTE guidelines updated several topic areas and provided three new recommendations. New recommendations addressed the use of aspirin for recurrent VTE prevention in patients with an unprovoked proximal VTE, treatment of subsegmental PEs, and treatment of recurrent VTEs when a patient's anticoagulant is within therapeutic range. The ADA guidelines provided updates to treatment goals for several groups of diabetes patients. . The CDC recently released opioid prescribing recommendations targeting the dramatic increase in opioid prescription rates. These recommendations primarily focused on reducing the number of patients who should be prescribed opioids and also encouraged reduced duration of therapy for acute pain episodes. The Beers Criteria were revised in 2015 which updated prior recommendations and added new tables regarding dosing in renal impairment and important drug-drug interactions in the elderly. Recent guideline changes have provided the latest evidence-based recommendations for healthcare providers to utilize in practice.

References

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