April 11, 2022

Angela K. Oliver  
Executive Secretary  
Centers for Disease Control and Prevention  
1600 Clifton Rd.  
Atlanta, GA 30329-4027

Subject: AGS Comments on the draft Centers for Disease Control and Prevention Clinical Practice Guideline for Prescribing Opioids—United States, 2022, Docket No. CDC-2022-0024

Dear Ms. Oliver:

The American Geriatrics Society (AGS) appreciates the opportunity to review and comment on the draft CDC Clinical Practice Guideline for Prescribing Opioids–United States, 2022. Founded in 1942, the American Geriatrics Society (AGS) is a nationwide, not-for-profit society of geriatrics healthcare professionals dedicated to improving the health, independence, and quality of life of older people. Our nearly 6,000 members include geriatricians, geriatric nurses, social workers, family practitioners, physician assistants, pharmacists, and internists who are pioneers in advanced-illness care for older individuals, with a focus on championing interprofessional teams, eliciting personal care goals, and treating older people as whole persons. The AGS believes in a just society, one where we all are supported by and able to contribute to communities where ageism, ableism, classism, homophobia, racism, sexism, xenophobia, and other forms of bias and discrimination no longer impact healthcare access, quality, and outcomes for older adults and their caregivers. The AGS advocates for policies and programs that support the health, independence, and quality of life of all of us as we age.

GENERAL COMMENTS

The U.S. Census Bureau projects that the number of people aged 65 and older will more than double between 2014 and 2060 to 98.2 million or 23.5 percent of the population; and those 85 and older will increase threefold to 19.7 million.1 Even as we live longer, diseases and conditions that threaten the health of older people remain a serious concern. This is particularly true for the “oldest old” (age 80 and older) who are at the highest risk of having multiple health problems and constitute the fastest growing age group in the U.S.2 According to the Centers for Medicare and Medicaid Services (CMS), 71.5% of women and 68.8% of men over the age of 65 had two or more chronic conditions with nearly 40% of these populations had four

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or more in 2018. According to a report published in 2010, some 68% of Medicare beneficiaries had 2 or more chronic conditions with 36.4% having 4 or more. The report noted that multiple chronic conditions are more prevalent in women across all age groups and prevalence increases with age. In Medicare, older adults with 2 or more chronic conditions account for 93% of Medicare spending. Over 52% of older adults report experiencing bothersome pain in a preceding month. Multiple chronic diseases and persistent pain can significantly impact older adults including functional impairment, decreased quality of life, and sleep disturbance.

AGS strongly recommends that the guidelines be modified to take a lifespan approach to management of persistent pain in older adults that recognizes the physiologic/functional heterogeneity of this population. By this we mean that managing persistent pain in healthy, active older adults differs from managing persistent pain in frail older adults. Furthermore, frailty and multiple chronic comorbidities (MCC) are chronological, age independent and often influence thresholds of tolerability for opioids and opioid-related adverse effects. The CDC guideline should reflect that there are different categories of frailty and MCC and/or separate age-appropriate recommendations by functional/physiological age and comorbidities. There is ample evidence that the physiology and associated evidence base is very different for each adult age group and this guideline should reflect that evidence.

AGS appreciates that the proposed update acknowledges older adults as a group in which pain may be underrecognized and undertreated. So too, the Society appreciates the increased focus on clinical judgement, shared decision-making between clinicians and their patients, and the reduction in hard caps on prescribing. However, the Society believes that there is still a clear need for additional guidance on management of persistent, chronic pain in older adults that goes beyond opioid prescribing to encompass all the pharmacologic and nonpharmacologic treatment modalities that are available. To address these weaknesses, AGS strongly recommends the following two actions:

1. Add specific reference to older adults with multiple chronic conditions and/or frailty to the patient populations described on pages 14 (starting at line 304), page 15 (starting at line 337), page 18 (starting at line 396). Like people living with sickle cell anemia or cancer, older adults are a population for which this guideline may not be appropriate due to multiple chronic conditions, frailty, or functional/physiologic age. CDC should revise this section to provide a more nuanced discussion of patients who may fall outside of this guideline, one that captures the heterogeneity of the U.S. population aged 18+ and that

5 Reid MC, Eccleston C, Pillemer K. Management of chronic pain in older adults. *BMJ.* 2015;350:h532. [https://doi.org/10.1136/bmj.h532](https://doi.org/10.1136/bmj.h532)
maintains the focus on the person, individualized decision-making, and on providing goal concordant care. As currently written, there is an inconsistency in this section in that for two patient populations (people living with cancer or sickle cell anemia), there is a focus on the person and for other populations there is a focus on the type of clinical care/services a person is receiving (e.g., palliative care and long-term services and supports) instead of on meeting a person’s therapeutic needs. Because of this, the guideline excludes older people and other adults who are living with persistent pain due to chronic illness and/or physiologic age as people for whom this guideline might be inappropriate. Specific to older adults living with persistent pain, they are likely to meet the definitions provided on page 18-19 (Lines 409-412) of serious illness and/or be near the end of life. An example of a subset of the older adult population that this definitional approach currently excludes is older people suffering from Osteoarthritis (OA), which is a progressive incurable chronic medical condition that often causes pain of sufficient intensity to limit full participation in activities of daily living. Currently more than 4 out of 10 older adults experience OA.7

Having exhausted all other non-opioid pain management avenues, older people with severe OA may rely on opioid medications to remain independent and active in their communities. Further, opioids continue to be a reasonable option for frail older adults with multiple chronic conditions and opioids should be available to this patient population as clinicians develop treatment plans for managing their persistent pain because they are the patient population that is most often living with progressive chronic conditions, like OA, that, absent appropriate pain management, can impact their quality of life. AGS also recommends that CDC retain the specific references to patients who are receiving palliative care or are near the end of life in this section to be sure that access to opioids is not diminished for people who are receiving palliative care or near the end of their lives.

2. Consider developing a guideline that is specific to frail older adults living with persistent pain that is informed by an AHRQ review (or reviews) of the available evidence that is specific to this population. AGS recommends that this guideline consider all treatment options as these relate to older adults, including frail older adults. Specifically, the guideline should address the full scope of concerns when prescribing analgesic options that considers not just opioids but also other analgesics that carry risk burden (e.g., NSAIDS) and that also addresses non-pharmacologic treatments. Organ impairments common in older adults impact the safety of analgesic options, particularly NSAIDs and anxiolytics, and often limit analgesic therapy options. It would be important to include attention to the millions of older Americans who are living with Alzheimer’s Disease and other dementias, or other mental illnesses.

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DIVERSITY IN RESEARCH AND ACCESS

Diversity in Research
In the introduction, AGS recommends that the CDC include a discussion of the diversity of the population studied in the evidence that forms the foundation for these guidelines. Factors that should be included in this discussion include, but are not limited to, self-identified race/ethnicity, gender identity/expression, sexual orientation, age, functional impairment, English-language ability, and immigration status. Acknowledging the historic lack of inclusion in study populations is particularly critical for older adults who currently make up 13% of the U.S. population with more than 90% of this population using at least one prescription while more than 66% use three or more in any given month. Yet much existing clinical research evidence is focused on disease-specific conditions or on younger populations. Older adults, particularly those who are frail with multiple chronic conditions, are under-represented in clinical trials and the number of controlled studies involving only patients aged 75 and older remains low. Furthermore, high-quality studies involving older patients from different ethnic groups are rare. As a result, current evidence-based literature does not serve as an adequate guide in many decision-making situations that are routinely encountered in clinical practice.

Access
Older adults are among the most vulnerable populations with significant barriers in accessing health care which are exacerbated in those with multiple chronic conditions. Concomitantly, there are social determinants of health that further impede access for this population, including education and socioeconomic status. While the older people with multimorbidity need coordinated services and supports, many experience short appointment times with providers, lack access to specialists, and in lieu some caregivers engage in medication management for the patient. Further, accessing the services and supports is also a challenge, where older adults with multiple chronic conditions are treated disparately in the healthcare system—such as lacking access to rehabilitation to help restore function—suggesting ageism. Transportation challenges may also lead to missed appointments and/or delayed prescription use, contributing to worse health outcomes and exacerbating chronic illnesses. The lack of access to services and supports and their coordination negatively impacts the daily lives of older adults with multimorbidity as well as their caregivers and providers. Health care professionals, particularly geriatrics health professionals, who focus on treating the whole person take the time to listen, focusing on what matters to the patient, but may have many more patients who are waiting for their own appointments in addition to the provider’s tasks beyond appointments.

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Repeat prescriptions make up 75 percent of general practice prescriptions and these often require collaboration between the patient, clinician, family or other caregiver, and pharmacist to ensure safety.\textsuperscript{11} Moreover, there are several challenges that may arise from managing repeat prescriptions due to the lack of standardized protocol, automated refills, absence of synchronicity in between the refill visits and follow-up visits. Primary care providers typically have a heavy workload outside of clinic, including processing refill requests and facilitating prior authorizations, spending approximately an average of six hours a workday on such indirect care.\textsuperscript{12} Given the substantial number prescriptions used by the older population, particularly for those with multiple chronic conditions, we encourage consideration of the significant healthcare burden with repeat medication prescriptions—typically filled for stable chronic illnesses—on primary care practices.\textsuperscript{13}

The AGS believes telemedicine, including audio-only services, would be critically important in improving access for older adults with multimorbidity as well as reducing the burden on primary care practices. While telemedicine is not recommended for all medical care, it may eliminate some of the barriers, such as transportation and dearth of providers or specialists locally, increasing the potential for greater access to the health care system. The COVID-19 public health emergency highlighted the high value of audio-video and audio-only services. We have learned that coverage of audio-only services is essential due to challenges the beneficiary population often faces in using technology, the sporadic failure of technology, and limitations in access to the technology due to infrastructure or economic reasons. Telemedicine would be an additional resource for health care professionals to provide timely and efficient care in certain circumstances, such as remote patient management to help patients with multimorbidity and may support increasing their reach of patients—reducing prolonged wait times—as well as facilitating communication for coordinated care and services.\textsuperscript{14}

**ORGANIZATION AND LANGUAGE**

**Five Guiding Principles (page 63, Lines 1434 – 1451)**

AGS recommends that the five principles that are provided on page 63 be included in the summary and in the introduction. These guiding principles provide an important framework for the document and its recommendations and are currently buried in their current location.


Re-organize this guideline so that more detailed and nuanced guidance for treating persistent pain in older adults is summarized in a single section of the guideline. Doing so would support clinicians, particularly primary care clinicians, who are caring for older people with persistent pain in providing care is focused on maintaining function, is person-centered, goal-directed, and that takes into account a person’s disease burden, frailty, and physiologic age. Our line-by-line comment on page 68, Lines 1569-1580 is a specific example of why this is critically important to optimizing treatment of older adults with persistent pain who fall within the scope of this guideline. While AGS appreciates the discussion of the adverse risks associated with chronic use of NSAIDS to manage persistent pain, the recommendations regarding older adults should be separated out and there be an explicit discussion of the risks of NSAIDS in this population included in an expanded section of the guideline that is specific to treating persistent pain in older people. Specifically, older adults are at increased risk for adverse drug reactions (ADRs) due to age-related loss of physiological organ reserve, increased comorbidities, polypharmacy, and changes in pharmacokinetics. Some specific ADRs of concern with chronic use of NSAIDs include gastrointestinal (GI), cardiovascular (CV), renal, cerebrovascular, and central nervous system (CNS) adverse effects.

Language Recommendations
AGS recommends that the guideline be reviewed for consistency around the choice of “persistent” or “chronic” to describe pain. CDC should consider inclusion of caregivers in addition to patients (as appropriate) given the important role that they have in caring for people living with serious, chronic illness or disability. For older adults, caregivers are critical members of the team who are often involved in managing prescription regimens and complex medical tasks as a part of the support they provide to their loved ones to remain independent for as long as possible. Finally, CDC should adhere to AMA style guidance when referring to older adults.

Summary of Clinical Recommendations
This guideline would benefit from the addition of a plain language summary of clinical recommendations.

MEDICATION RECONCILIATION
As noted in our line-by-line comments (page 91, Lines 2131-2133), there is an increased risk of drug-drug interactions in older adults given their limited ability to process and clear medications via renal or hepatic mechanisms with changing pharmacokinetics and pharmacodynamics of aging. Further, older adults with multiple chronic conditions are more likely to be taking multiple medications with increased potential for adverse events due to drug-drug interactions. For this population, we believe it is particularly important that CDC include a recommendation that a clinician complete a full review of current medications (inclusive of over-the-counter drugs and natural remedies) before prescribing any new drugs.5,21

LINE-BY-LINE COMMENTS AND RECOMMENDATIONS
We have divided our line-by-line recommendations into two sections:
(1) General Line-by-Line Comments; and
(2) Potentially Inappropriate Drugs for Use in Older Adults

General Line-by-Line Comments

Page 7, Lines 127-129
• Uncontrolled pain itself can lead to delirium in older adults, particularly in those with underlying cognitive impairment who are more susceptible to delirium because of inadequately treated pain.22,23,24

Page 8, Lines 151-164
• CDC should add a discussion of the available evidence that is stratified by age.

Pages 8-9, Lines 165-189
• AGS recommends that CDC include explicit reference to people with disabilities and older adults who often have more difficulty accessing treatments, particularly nonpharmacologic interventions. This section would also benefit from a specific discussion of how socio-economic factors, race, and ethnicity can impact access to appropriate care and treatment (see our general comments above for a discussion of the access and the impact on primary care for the recommendations pertaining to monitoring patients over time).

Page 16
• Line 341: Add geriatricians, nurse practitioners, and physician assistants.

• Lines 344-347: Add a discussion of home and community-based services given that elsewhere in the document (page 18, starting at line 396), there is an explicit recommendation that the people living in skilled nursing facilities or people receiving home and community-based support may fall outside of this guideline.

Pages 18-20, Lines 396 to 439
• AGS encourages the inclusion of resources specific to management of persistent pain in older adults and palliative care.\textsuperscript{25,26,27,28,29,30,31,32,33}

Page 64, Lines 1480-1482
• Older patients especially those with moderate to advanced cognitive impairment may not be able to articulate pain needs (as has also been mentioned earlier in the draft CDC 2022 Guideline). AGS recommends inclusion of specific guidance on how to approach older adults with dementia and overt pain behaviors such as the Pain Assessment in Advanced Dementia (PAINAD) scale.\textsuperscript{34,35,36,37}

Page 71, Line 1653
• AGS recommends advising clinicians to exercise extreme caution when considering deprescribing or tapering opioids or other pain medications in all older adults who have been on opioids for a long-time. In persons living with Alzheimer’s Disease, dementia, or mild cognitive impairment, clinicians should focus more on behavioral manifestations

\textsuperscript{26} National Consensus Project for Quality Palliative Care. Clinical Practice Guidelines for Quality Palliative Care, 4th ed. National Coalition for Hospice and Palliative Care; 2018. https://www.nationalcoalitionhpc.org/ncp
\textsuperscript{34} Husebo BS, Ballard C, Sandvik R, et al. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. BMJ. 2011;343. https://doi.org/10.1136/bmj.d4065
such as acute confusion/delirium, increased agitation, and “sundowning” as these are often signs that pain is being undertreated. Further, this section of the guideline would benefit from recognizing caregivers’ knowledge of an older adult loved one’s health and the important role that they have in managing drug regimens and other complicated tasks.

Page 78, Lines 1835-1841
- AGS recommends a separate discussion of risks and benefits related to prescribing in older adults. Of particular importance when discussing specific drugs is including any cautions about use of those drugs in specific populations. Please see the AGS’ line-by-line comments on potentially inappropriate drugs for use in older adults.

Page 86, Lines 2011 – 2034
- AGS recommends that CDC include a description of Patient Priorities Care (PPC) as a potential tool for guiding shared decision-making around opioid prescriptions. This tool has been proven to optimize patient and clinician experience and decrease utilization of burdensome care. PPC could prove a practically useful tool in achieving the specific guideline recommendation that clinicians and people with persistent pain identify functional goals and what would constitute success of the treatment plan for the patient.

Page 89, Lines 2089-2092
- See comment on page 71 (Line 1653). It would be important to include guidance for the clinician on assessment of persistent pain in older adults with cognitive impairment given that this patient population can have difficulty articulating that they are in pain. Attention should be paid to educating caregivers as to the symptoms/signs that an older adult with cognitive impairment maybe in pain due to undertreatment or the absence of

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treatment for pain. These signs acute confusion/delirium, increased agitation, and “sundowning”.

Page 107, Lines 2552-2554
• Nowhere in this draft guideline does CDC define “advanced age” or outline the serious risks that are associated with advanced age that would support inclusion of “advanced age” alone as a reason for tapering opioid treatment. Further, advanced age is not a medical condition and should not be labeled as such. AGS strongly recommends that the CDC delete the reference to advanced age from this sentence. Please see our General Comments about the definitions that CDC is using to define patient populations that are outside of these guidelines (under General Comments). As noted in those comments, many older adults would meet the definition serious illness, be receiving care that is palliative in nature (e.g., management of geriatric syndromes), or receiving long-term services and reports. For this patient population, access to an opioid treatment may be quite aligned with patient goals of care and care preferences.

Page 109, Lines 2610-2615
• AGS suggests advising primary care clinicians to seek input from a health professional who is trained in geriatrics given their understanding of aging brain physiology as well as of their knowledge regarding drugs that are considered inappropriate for use in older adults (see section on Potentially Inappropriate Drugs for Use in Older Adults).

Page 121
• Lines 2914-2917: – In-person follow up visits are challenging for frail, older patients regardless of where they live. AGS recommends including reference to this population as one for which a virtual visit would also be recommended. Further, although this may be outside of the purview of this guideline, CDC should partner with other agencies to ensure that telehealth visits for these populations meet federal/state requirements for continued opioid prescription as opposed to requiring in person visits which will lessen the burden on patients and caregivers.
• Lines 2924-2932: Please see our comments above on Page 86 (Lines 2011 – 2034). This section seems to start from the premise that there is no patient population that would benefit from opioid treatment. AGS suggests the addition of a recommendation that is explicit to continuation of opioid treatment when goal directed discussion with a patient leads to the conclusion that benefits of continuing opioids DO outweigh risks AND/OR when a patient has had partial benefit from opioids and has requested an increased dose or change in frequency of administration. This is consistent with the geriatrics approach to prescribing which is to start a new drug at the lowest possible dose and go slow when increasing the dose.

Page 122, Lines 2951-2956
• Please see comment on page 121 (lines 2914-2917). The scenarios described in this section do not apply to older adults who have functional limitations that are a barrier to frequent, in-person office visits. AGS recommends expanding this section to include reference to frail older adults whose follow up would be similarly difficult and for whom telehealth should be available.

Page 130-131, Lines 3168-3192
• AGS appreciates the attention to the impact of pain on function and the need for careful evaluation of risks and benefits of opioids in adults age 65+. As noted in our general comments, the “oldest old” (age 80 and older) are at the highest risk of having multiple health problems and constitute the fastest growing age group in the U.S.² In Medicare, older adults with 2 or more chronic conditions account for 93% of Medicare spending.⁴,⁶ Further, over 52% of older adults report experiencing bothersome pain in a preceding month.⁵ For these reasons, we are deeply concerned that this section:
  1. Does not recognize the heterogeneity of adults age 65+;
  2. Focuses solely on the risks of opioids in older adults and does not include a discussion of the risks of other treatment modalities;
  3. Does not provide a more nuanced and detailed discussion of how clinicians caring for older adults can assess whether an older person falls outside of this guideline due to disease burden, frailty, or physiologic age.

As noted in our comments on page 86 (lines 2011-2034), we recommend inclusion of reference to Patient Priorities Care as a specific tool that guides shared decision-making and supports goal concordant treatment. We also recommend that this section be expanded to include:
  o A discussion of the risks of under treating pain in this population with a focus on tools that support a clinician in accessing behavioral manifestations of pain (e.g., acute confusion/delirium,³⁷ increased agitation,⁴⁰ and “sundowning”.⁴¹,⁴⁶ Other risks associated with untreated pain include falls, anxiety, impaired sleep, nutrition, depression, and decreased function due to lack of mobility.
  o The important role of caregivers, especially for older persons with cognitive impairment, in management of opioid treatment and stewardship.

Page 137, Lines 3373-3374
• Additionally, older patients with cognitive impairment may also be unable to convey their medications accurately. For these patients, it is important to include caregivers.

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AGS recommends including older adults on this list given ageism in health care. An understudied but important consideration is the intersection of ageism with structural racism and other types of discrimination. This is an important consideration for all guideline developers given the underrepresentation of older adults, particularly older adults of color, in study populations.

Potentially Inappropriate Drugs for Use in Older Adults

Decisions about prescribing Benzodiazepines (a high risk class of medications for older adults per the AGS Beers Criteria®) in combination with opioids should be made judiciously and on a case-by-case basis.

Older patients are particularly susceptible to the adverse effects as listed – Would suggest specifying how many older adults were included in the relevant studies.

AGS appreciates the discussion of the adverse risks associated with chronic use of NSAIDS to manage persistent pain. However, we ask that recommendations regarding older adults be separated out and that there be an explicit discussion of the risks of NSAIDs in this population. Specifically, older adults are at increased risk for adverse drug reactions (ADRs) due to age-related loss of physiological organ reserve, increased comorbidities, polypharmacy, and changes in pharmacokinetics. Some specific ADRs of concern with chronic use of NSAIDs include gastrointestinal (GI), cardiovascular (CV), renal, cerebrovascular, and central nervous system (CNS) adverse effects.

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The American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults52 identifies the following medications as potentially inappropriate for use in older adults:

- **Lines 1757-1761, 1762-1764, 1765-1767**: NSAIDs are potentially inappropriate for use in older adults with chronic pain due to higher risk of adverse effects with prolonged use (see comments above on Page 68, Lines 1569-1580).
- **Line 1762**: Tricyclic antidepressants are potentially inappropriate for use in older adults due to anticholinergic side effect.
- **Lines 1768**: “Tricyclic” and **Line 1774**: “In patients with fibromyalgia, tricyclic (amitriptyline)”. Most Tricyclics can cause confusion and falls in older people. Some older adults may be able to tolerate these drugs and decisions to use should be made judiciously and on a case-by-case basis.

**Page 76, Lines 1784-1789**: Recommend inclusion of a specific reference to frail older adults and/or older adults with multiple chronic conditions6 as a patient population for which opioids may be the most appropriate pharmacologic therapy in the management of persistent pain.

**Page 76, Lines 1784-1789**: Recommend inclusion of a specific reference to frail older adults and/or older adults with multiple chronic conditions6 as a patient population for which opioids may be the most appropriate pharmacologic therapy in the management of persistent pain.

**Page 82, Lines 1917-1934**
- For older adults, given the toxicity of NSAIDS, acetaminophen remains the safest option and should be considered in first analgesic trial and early treatment for older adults with osteoarthritis or other conditions. Clinicians always should consider physiologic age, presence of other diseases, and frailty when prescribing in this population.53,54
- See comments on page 76 (Lines 1757-1765, 1767-1761, 1762-1764). AGS recommends that CDC consider dropping oral NSAIDs for older adults from the recommendations for non-opioid pharmacological options and instead just including topical NSAIDs or specifying very sparing use of oral NSAIDS as needed only and never scheduled.

**Page 83, Line 1954-1960**
- Given anticholinergic adverse effects in older adults associated with Tricyclics in general and Amitriptyline in particular (see page 76, line 1768 and 1774), we recommend including a clear caution against use in older adults in this discussion.

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Page 87, Lines 2062-2066

- The AGS does not consider its 2009 guideline to be current. Given that this recommendation should be made to all adults age 18+, we recommend that CDC identify a different reference that supports the guidance for discussion of acetaminophen.\textsuperscript{55,56}

Page 91, Lines 2131-2133

- This section should include a discussion of the increased risk of drug-drug interactions in older adults given their limited ability to process and clear medications via renal or hepatic mechanisms with changing pharmacokinetics and pharmacodynamics of aging. We recommend including a recommendation that a clinician complete a full review of current medications (inclusive of over-the-counter drugs and natural remedies) before prescribing any new drugs.\textsuperscript{5,21}

Pages 111-112, Lines 2660-2674

- This should include a specific discussion of tapering in frail older adults with serious illness and/or multiple chronic conditions. A number of the drugs on this list (e.g., NSAIDs, Tizanidine, Prochlorperazine, promethazine and Ondansetron) are considered potentially inappropriate for use in older adults (see prior comments on page 76).

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Thank you for taking the time to review our feedback and recommendations. For additional information or if you have any questions, please do not hesitate to contact, Mary Jordan Samuel at mjsamuel@americangeriatrics.org.

Sincerely,

Peter Hollmann, MD
President

Nancy E. Lundebjerg, MPA
Chief Executive Officer

\textsuperscript{55} Alchin J, Dhar A, Siddiqui K, et al. Why paracetamol (acetaminophen) is a suitable first choice for treating mild to moderate acute pain in adults with liver, kidney or cardiovascular disease, gastrointestinal disorders, asthma, or who are older. [published online ahead of print March 29, 2022]. \textit{Curr Med Res Opin.} 2022:1-36. \url{https://doi.org/10.1080/03007995.2022.2049551}

\textsuperscript{56} Gerriets V, Anderson J, Nappe TM. \textit{Acetaminophen}. StatPearls Publishing; 2021.
\url{https://www.ncbi.nlm.nih.gov/books/NBK482369/#_NBK482369_pubdet}