AGS Geriatrics Healthcare Professionals
Leading Change. Improving Care for Older Adults.

THE AMERICAN GERIATRICS SOCIETY
40 FULTON STREET, SUITE 809
NEW YORK, NEW YORK 10038
212.308.1414 TEL
www.americangeriatrics.org

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The American Geriatrics Society (AGS) submitted these comments in response to the Evidence-based Practice Center (EPC) Division at the Agency for Healthcare Research and Quality (AHRQ) call to nominate topics for a new evidence review. The EPC reviews these as potential topics to develop a report that may inform and provide the foundation for developing and implementing practice guidelines, performance measures, educational programs, and other strategies to improve the quality of healthcare and decision making related to the effectiveness and appropriateness of specific healthcare technologies and services. The AGS is appreciative of the opportunity to nominate a topic for evidence review and we look forward to collaborating on efforts to develop evidence reports and technology assessments related to older adults.

1. **What is the decision or change (e.g., clinical topic, practice guideline, system design, delivery of care) you are facing or struggling with where a summary of the evidence would be helpful?**

   Please describe the issue. Tell us about who is affected by this issue; the treatments, tests, or strategies that you are interested in; and the specific benefits or harms (outcomes) that are important to you.

   The American Geriatrics Society (AGS) recently reviewed and commented on the draft Centers for Disease Control (CDC) Clinical Practice Guideline for Prescribing Opioids–United States, 2022 (see comment letter). In our comments, we expressed our concern about gaps in data related to non-opioid treatment modalities and their risk/benefits to older adults. In addition to requesting that the CDC take a lifespan approach to the opioid prescribing guideline, we encouraged CDC to develop a guideline that is specific to frail older adults living with persistent pain that is informed by an Agency for Healthcare Research and Quality (AHRQ) review (or reviews) of the available evidence.

   AGS believes that there is a critical need for AHRQ to conduct an evidence review that is: (a) focused on managing persistent pain in older adults; (b) addresses the full scope of concerns when prescribing analgesic options that considers not just opioids but also other analgesics that carry risk burden (e.g., non-steroidal anti-inflammatory drugs (NSAIDS), anticonvulsants); and (c) 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. Considering that the population with cognitive impairment are often excluded from research,[1] 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. A recent analysis found that not even one-fifth of the 436 studies reviewed included study participants with mild cognitive

[1] Taylor JS, DeMers SM, Vig EK, Borson S. The Disappearing Subject: Exclusion of People with Cognitive Impairment and Dementia from Geriatrics Research. *J Am Geriatr Soc*. 2012;60(3):413-419. doi:10.1111/ j.1532-5415.2011.03847.x

impairment and just 14% of the studies included participants with Alzheimer's disease and other dementias while 29% actively excluded individuals with Alzheimer's disease and other dementias.[2]

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.[3] 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.[4] 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, while nearly 40% of these populations had four or more in 2018.[5] According to a report published in 2010, some 68% of Medicare beneficiaries had two or more chronic conditions with 36.4% having four 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 two or more chronic conditions account for 93% of Medicare spending.[6] Over 52% of older adults report experiencing bothersome pain in a preceding month.[7] Multiple chronic diseases and persistent pain together significantly impact older adults in multiple ways, including increasing risk of functional impairment, gait impairment, decreased quality of life, and sleep disturbance.[8]

Given the increasing prevalence of diseases among the rapidly growing older population, representative inclusion of this target population in research studies is critically important.[9] An analysis of clinical trials found that 33% of federally funded trials had an upper age limit, with one-quarter of the studies not allowing people 65 and older to participate.[10] When medical evidence is generated from study populations that do not resemble most of the people who need medical care, we miss opportunities to learn how to optimize health and resilience and avoid suffering. The AGS encourages meaningful inclusion of diverse older adults in the evidence review.

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[2] Godbole N, Kwon SC, Beasley JM, et al. Assessing Equitable Inclusion of Underrepresented Older Adults in Alzheimer's Disease, Related Cognitive Disorders, and Aging-Related Research: A Scoping Review. *The Gerontologist.* Published online April 26, 2022. doi:10.1093/geront/gnac060

[3] Colby SL, Ortman JM. *Projections of the Size and Composition of the U.S. Population: 2014 to 2060, Current Population Reports*, *P25-1143,* Washington, DC: U.S. Census Bureau; 2015.

[4] He W, Goodkind D, Kowal P. *U.S. Census Bureau, International Population Reports, P95/16-1, An Aging World.* Washington, DC: U.S. Government Publishing Office; 2016.

[5] Centers for Medicare and Medicaid Services. Utilization/Spending State Level: All Beneficiaries by Sex and Age, 2007-2018: State Table MCC Prevalence by Sex and Age 2018. Updated on December 1, 2021. Accessed April 11, 2022. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Downloads/MCC_Util_Spend_State_All_Sex.zip.

[6] Lochner KA, Cox CS. Prevalence of multiple chronic conditions among Medicare beneficiaries, United States, 2010. *Prev Chronic Dis.* 2013;10:120137. doi:10.5888/pcd10.120137

[7] Reid MC, Eccleston C, Pillemer K. Management of chronic pain in older adults. *BMJ*. 2015;350:h532. doi:10.1136/bmj.h532

[8] Nakad L, Booker S, Gilbertson-White S, et al. Pain and Multimorbidity in Late Life. *Curr Epidemiol Rep.* 2020;7:1-8. doi:10.1007/s40471-020-00225-6

[9] Vaughan CP, Dale W, Allore HG, et al. AGS Report on Engagement Related to the NIH Inclusion Across the Lifespan Policy. *J Am Geriatr Soc.* 2019;67(2):211-217. doi:10.1111/jgs.15784

[10] Lockett J, Sauma S, Radziszewska B, Bernard MA. Adequacy of Inclusion of Older Adults in NIH-funded Phase III Clinical Trials. *J Am Geriatr Soc.* 2019;67(2):218-222. doi:10.1111/jgs.15786

2. Why are you struggling with this issue? It is unclear how to encourage people to use an effective treatment or service. For example, our data indicate that not enough people are using an effective intervention or too many are overusing an ineffective intervention.

Current evidence-based literature does not serve as an adequate guide in many decision-making situations regarding persistent pain that are routinely encountered in clinical practice. AGS recommends that the AHRQ specifically review the diversity of populations studied so that guideline developers have a full understanding of the evidence that is informing the recommendations that they make. In addition to age, data should be extracted from the persistent pain literature on self-identified race/ethnicity, gender identity/expression, sexual orientation, 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 for a pain medication while more than 66% use three or more in any given month.[11] Yet most 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 highly underrepresented in clinical trials and the number of controlled studies involving 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.

Older adults are at increased risk for adverse drug reactions (ADRs) due to age-related loss of physiological organ reserve, increased comorbidities,[12] polypharmacy,[13] and changes in pharmacokinetics.[14] Some specific ADRs of concern that have been documented as a consequence of chronic use of NSAIDs include gastrointestinal (GI), cardiovascular (CV),[15] renal,[16] cerebrovascular, and central nervous system (CNS) toxicities.[17] NSAIDs are potentially inappropriate for use in older adults with persistent pain due to higher risk of adverse effects with prolonged use. Despite its common use as treatment, the evidence base around the safety and effectiveness of NSAIDs in older adults is disproportionately lacking.[18]

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[11] Centers for Disease Control and Prevention/National Center for Health Statistics. Prescription drug use in the past 30 days, by sex, race and Hispanic origin, and age: United States, selected years 1988–1994 through 2011–2014. Published 2017. Accessed June 2, 2022. https://www.cdc.gov/nchs/data/hus/2017/079.pdf.

[12] Lim CC, Ang ATW, Kadir HBA, et al. Short-Course Systemic and Topical Non-Steroidal Anti-Inflammatory Drugs: Impact on Adverse Renal Events in Older Adults with Co-Morbid Disease. *Drugs Aging.* 2021;38:147-156. doi:10.1007/s40266-020-00824-4

[13] Budnitz DS, Lovegrove MC, Shehab N, et al. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med.* 2011;365(21):2002-2012. doi:10.1056/NEJMsa1103053

[14] Farinde A. Overview of pharmacodynamics. In *Merck Manual for the Professional*; Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.;2022.

[15] Moriarty F, Cahir C, Bennett K, et al. Economic impact of potentially inappropriate prescribing and related adverse events in older people: A cost-utility analysis using Markov models. *BMJ Open.* 2019;9(1):1-9. doi:10.1136/bmjopen-2018-021832

[16] Lim CC, Tan NC, Teo EPS, et al. Non-steroidal anti-inflammatory drugs and risk of acute kidney injury and hyperkalemia in older adults: A retrospective cohort study and external validation of a clinical risk model. *Drugs Aging.* 2022;39:75-82. doi:10.1007/s40266-021-00907-w

[17] Hanlon JT, Guay DRP, Ives TJ. Oral analgesics: efficacy, mechanism of action, pharmacokinetics, adverse effects, and practical recommendations for use in older adults. In: Gibson SJ, Weiner DK, eds. *Pain in Older Persons.* IASP Press; 2005: 205–222.

[18] Reid MC, Bennett DA, Chen WG, et al. Improving the Pharmacologic Management of Pain in Older Adults: Identifying the Research Gaps and Methods to Address Them. *Pain Medicine*. 2011;12(9):1336-1357. doi:10.1111/j.1526-4637.2011.01211.x

3. **What do you want to see changed? How will you know that your issue is improving or has been addressed?**

   There are significant gaps in the evidence base for how best to manage acute and persistent pain in frail older adults due to the lack of inclusion of frail older adults with multiple chronic conditions in studies and clinical trials. 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. AGS believes a comprehensive evidence review that identifies the gaps in research and is specific to frail older adults living with persistent pain that encompasses all pharmacologic and nonpharmacologic treatment modalities available is a critical first step in ensuring that persistent pain is appropriately managed in older adults. Such a review will inform current clinical practice, serve as a "roadmap" for researchers who seek to address the identified knowledge gaps, and support all of us to remain active in our communities as we age.

4. When do you need the evidence report?

The time needed to complete different types of evidence reports can range widely, and can take up to two years to fund and complete. Deciding which kind of report depends on what type of evidence is needed and when it is needed. Quicker reviews may be less thorough but can still provide useful about decisions about a healthcare-related issue. Please let us know about your timeframe/evidence needs.

July 1, 2024

5. What will you do with the evidence report?

Our reports have been used in many ways. These ways include healthcare decisions, practice guidelines, coverage decisions, program planning and others. Tell us about how you think an evidence report will help you with your healthcare-related issue. (Please include information about timing.)

The AGS will use the evidence report to inform its own work educational and clinical tools that support clinicians who care for older adults, including the next update of the AGS Beers Criteria®, and Geriatrics at Your Fingertips, a tool supporting clinicians who care for older adults. We will continue to encourage the CDC to develop a clinical practice guideline that is specific to care of older adults with persistent pain given the heterogeneity and complexity of this patient population.

6. Upload Supporting Documentation

Attachment: AGS Comments on the Draft Centers for Disease Control and Prevention Clinical Practice Guideline for Prescribing Opioids-United States, 2022

Optional Information About You

What is your role or perspective?

(e.g., patient/consumer, physician/clinician/provider, professional society, or administrator)

Professional Society

If you are you making a suggestion on behalf of an organization, please state the name of the organization

American Geriatrics Society

May we contact you if we have questions about your nomination?

Anna Kim

Senior Manager of Public Affairs and Advocacy

akim@americangeriatrics.org