



HHS Public Access

Author manuscript

Prog Neuropsychopharmacol Biol Psychiatry. Author manuscript; available in PMC 2020 July 13.

Published in final edited form as:

Prog Neuropsychopharmacol Biol Psychiatry. 2019 July 13; 93: 284–290. doi:10.1016/j.pnpbp.2019.04.006.

The silent epidemic of chronic pain in older adults

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Abstract

Chronic pain is highly prevalent among older adults where it is associated with significant suffering, disability, social isolation, and greater costs and burden to health care systems. Pharmaceutical treatment of chronic pain in older adults is usually only partially effective and is often limited by side effects including urinary retention, constipation, sedation, cognitive impairment, and increased risk of falls. Since older adults are underrepresented in clinical trials testing treatments for chronic pain, the potential impacts of polypharmacy and frailty on reported outcomes and side effect profiles are largely unknown. Thus, for current treatments providers and patients must balance anticipated benefits of pain reduction with the known and unknown risks of treatment. Chronic pain is also a risk factor for premature death as well as accelerated cognitive decline, suggesting potential shared mechanisms between persistent pain (or its treatment) and dementia. Cognitive decline and dementia may also impact pain perception and the ability to report pain, complicating treatment decisions. Associations between persistent pain and the risks of premature death and accelerated cognitive decline make estimates for chronic pain in these populations particularly challenging. Future research is needed to improve estimates for chronic pain in older adults, to elucidate underlying mechanisms of pain with aging, and to develop and advance safer, more effective treatment options for chronic pain in older adults.

Keywords

chronic pain; aging; age-related disease; dementia; cognitive

1. Introduction

Chronic pain is among the most common, and consequential diseases in the United States and worldwide^{1–6}. Chronic pain is defined as pain that persists past the normal time of healing (usually characterized as pain for at least 3 months), making it distinct from acute pain which is generally regarded as a local sensation^{7,8}. In U.S. adults alone, estimated costs

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attributable to chronic pain—including disability, lost work, and treatments—exceed \$600 billion annually⁸

Chronic pain is particularly common and problematic in older adults (age 65) where it is associated with significant suffering, social isolation, disability, and greater costs and burden to health care systems^{1,2,9–12}. Pharmaceutical treatment of chronic pain in older adults is usually only partially effective and is often limited by side effects. Older adults are underrepresented in clinical trials testing treatments for chronic pain¹³. As a consequence, the effectiveness, side effects, and potential impacts of polypharmacy and frailty on reported outcomes of many pain medications are largely unknown¹⁴. Thus, providers and patients must balance anticipated benefits of pain reduction with the known and unknown risks of treatment.

Chronic pain is also a risk factor for premature death¹⁵ as well as accelerated cognitive decline¹⁶ suggesting potential shared mechanisms between pain (or its treatment) and dementia. Cognitive decline and dementia may also impact pain perception and the ability to report pain, further complicating treatment decisions¹⁷. Associations between persistent pain and the risks of premature death and accelerated cognitive decline make estimates for chronic pain in these populations particularly challenging. Future research is needed to improve estimates and better appreciate the scope and impact of chronic pain in older adults, to elucidate underlying mechanisms of pain with aging and potential shared mechanisms with dementia, and to develop and advance safer, more effective treatment options for chronic pain in older adults.

In this topical review of chronic pain in older adults we summarize evidence from epidemiological studies reporting the prevalence and impact of chronic non-cancer pain, and describe the challenges and limitations of assessing and treating chronic pain in older adults. Specifically, we make the case that, chronic pain may be substantially underestimated in older adults and that the association between chronic pain and higher mortality may partially be responsible for this underestimation. We dedicate a significant portion of the manuscript to the relationship between chronic pain and Alzheimer's Disease, two common and consequential diseases in older adults, and suggest that these diseases may share common underlying mechanisms. We discuss limitations and risk of available pharmacological treatments for chronic pain in older adults and discuss, briefly, the evidence for nonpharmacological treatment strategies in this population. Finally, we make the case that future research is needed to improve estimates for chronic pain in older adults, to elucidate underlying mechanisms of pain with aging and dementia, and to develop and advance safer, more effective treatment options.

2. Epidemiology of Chronic Pain in Older Adults

Epidemiological studies report that increased age is a risk factor for chronic pain² and painful conditions such as chronic low back pain¹⁸, chronic neck pain^{19,20} as well as chronic pain in the hip and knee^{21,22}. Population studies in both the US and globally reveal a higher prevalence of chronic pain in adults over the age of 65 as compared to the general adult population^{1,2,4}; The most frequent chronic pain conditions in older adults are chronic

unspecified joint pain²³, chronic back pain¹⁸ and chronic neck pain²⁴ affecting an estimated 40, 5–45, and 20%, respectively (figure 1). Notably, the literature is not clear as to the role of neuropathic pain in older adults, as epidemiological studies indicate that the prevalence of neuropathic pain in adults older than 65 ranges from 10–52%^{25–29}. Some caution should be exercised when interpreting chronic pain prevalence, as results vary widely, likely due to differences in how chronic pain was assessed (i.e. self-report vs. diagnosis), definitions of chronic pain (i.e. duration, frequency, intensity), and other factors. Despite these limitations, studies reviewed here point to chronic pain being among the most common and consequential diseases in older adults⁶.

3. Chronic pain as a risk factor for early death

The previous section summarized the magnitude of the impact of chronic pain in older adults, indicating that the prevalence of people reporting chronic pain conditions increases almost linearly with increasing age². Paradoxically, however, in cross-sectional studies chronic pain prevalence is often reported to peak at age 60 and possibly to decrease thereafter^{30–35}. It was recently suggested, based on data from a large, longitudinal cohort study, that this apparent plateau of chronic pain prevalence at age 60 may be due to a markedly higher risk of death in chronic pain patients³⁶. The concept that chronic pain is a risk factor for early death was corroborated in a large British longitudinal cohort and accompanying meta-analysis which found that chronic widespread pain was associated with a 57% increased risk of excess all-cause mortality¹⁵. Obesity, lack of physical activity, smoking and diet not containing alcohol were identified as mediators accounting for some (but not all) of the increased risk of early death observed in chronic pain sufferers. It is possible that other factors associated with chronic pain such as increased prescription medication use^{37–39}, illicit substance use⁴⁰, dementia¹⁶, falls^{10,41,42} and/or shared biochemical mechanisms linking pain and death (i.e. inflammation or disease)⁴² could contribute to the early mortality observed in chronic pain sufferers. It should be noted that though the most recent meta-analysis found a link between pain and excess mortality, studies are not unanimous. In summary, the relationship between aging and pain is not fully understood and requires further study. However, available data suggest that chronic pain disproportionately affects older adults, and that the pain itself and possibly pain treatments are associated with increased risk of death.

4. Impact of chronic pain on quality of life and function in older adults

Some of this pain and its impact on daily life will reflect the specific pain location. For example, knee pain can often be eased by treatments directed at that specific pathology (e.g. joint replacement)⁴³. However, chronic pain is also a condition-in-its-own-right, with features common across multiple locations and impacts on physical, psychological and social functioning. These general features may often require mixed approaches that address multiple impacts of living with pain. In patients of all ages, chronic pain is well-known to have adverse impacts on quality of life^{44–46}, physical and mental function¹⁶, mood^{2,11}, ability to work¹¹, and participation in leisure activities¹¹. Age has been reported as a risk factor for high impact chronic pain (HICP - chronic pain accompanied by activity/life participation limitations)^{1,11}. HICP is associated with increased risk of depression¹¹ a

significant morbidity in older adults that is often comorbid with chronic pain. Moreover, older adults report greater levels of pain intensity as compared to younger adults (though, similar to pain prevalence data, not when compared with middle aged adults)⁴⁷. Higher pain intensities and impacts, in older adult populations is of great societal importance as both pain intensity and high impact chronic pain have been linked to greater healthcare costs and resource utilization^{11,12}. Additionally, less physical activity, as is observed in HICP sufferers, is believed to be one of the lifestyle factors that modulates the increased mortality that is seen in people suffering from chronic pain in general¹⁵ which makes HICP particularly troubling.

5. Differences in Pain Perception

Aging is associated with declines in sensations such as hearing and vision^{48,49}. As pain likely includes a peripheral sensory component it is possible that it too declines, or is at least altered, with aging⁵⁰. Could differences in pain perception or tolerance explain the increased complaints of chronic pain in older adults? One of the first investigations into pain perception with aging was conducted in 1944 where the authors demonstrated that pain threshold increases with age⁵¹. Since then a large number of cross-sectional studies have reported pain thresholds in young and old participants (a recent meta-analysis included 31 studies in healthy adults⁵²). While results of studies assessing pain thresholds over the lifespan have been inconsistent^{52,53}, many suggest an increased pain threshold associated with aging. However, studies assessing this are likely dependent on pain modality tested, site of pain, and testing paradigm^{54,55}.

Increased pain threshold with aging is consistent with declines in other peripheral sensory systems with aging, however, it does not explain the increased prevalence, or overall increased pain complaints among older adults⁵⁵. Several plausible explanations could account for these apparently contrasting observations. One likely explanation, is an overall increased tissue injury as evidenced by increased levels of degenerative arthritis in older adults¹. Moreover, it has been postulated that deficits in sensing pain that accompany aging, evidenced by increased pain thresholds in older adults, could lead to higher risk of injury in older adults^{50,52} although evidence for this hypothesis remains anecdotal.

However, chronic pain is more than the sensation of painful stimuli. While acute pain is a sensory experience that alerts the body of possible tissue damage, chronic pain, by definition, is quite different and may therefore be independent of pain thresholds. Indeed, pain threshold does not appear to predict susceptibility for developing chronic pain^{56,57} or chronic pain condition severity⁵⁸, although mixed evidence exists for its ability to predict chronic pain severity⁵⁸⁻⁶⁰. Pain threshold tests are generally considered to be measures of peripheral sensory input, yet the subjective experience of pain is impacted by central nervous system (CNS) mechanisms such as descending inhibition and emotion and motivational circuits⁶¹. Therefore, it is possible that aging differentially affects CNS and PNS pain circuitry⁵⁰. Indeed, neuroimaging studies have shown aging-associated decreases in activation of somatosensory cortex (S1), medial insular cortex and basal ganglia, however, the impact of these deficits on chronic pain are unknown^{62,63}. The emotional and motivational component of pain perception is believed to be represented by pain tolerance

measures⁵⁰, which have been reported to decrease with increasing age^{50,52}. Additionally, CNS mechanisms of pain can be measured by using different testing paradigms such as temporal summation of pain (increased pain response to repeated pain stimuli) and conditioned pain modulation. Similar to pain tolerance data, results from studies assessing the effect of aging on summation and conditioned pain modulation are mixed and may be dependent on testing factors (i.e. type of stimuli, intensity, location etc.)^{55,64–72}. Therefore, the evidence of both PNS and CNS pain processing systems being altered with age indicates pain may be experienced differentially in older adults.

6. Dementia and Chronic Pain

Alzheimer's disease (AD) and related dementias are significant sources of morbidity and mortality in older adults. A detailed review of dementia and chronic pain in older adults was recently published⁷³; here we will briefly discuss the relationship of chronic pain in Alzheimer's disease and dementia. Chronic pain has been linked to increased risk of cognitive decline and dementia¹⁶, suggesting that shared environmental exposures, genetics, or molecular mechanisms could play a role in both conditions. Notably, degenerative changes in brainstem regions that modulate descending pain inhibition—including the periaqueductal gray matter—have been reported in Alzheimer's disease⁷⁴. However, the potential role of neurodegeneration in chronic pain is largely unexplored.

Importantly, chronic pain has been associated with accelerated functional limitations¹⁶ and, in dementia patients, has been reported to be associated with neuropsychiatric symptoms such as aggression, anxiety and depression as well as worse overall quality of life^{44,45}. Changes in pain have also been correlated, longitudinally, with neuropsychiatric symptoms and quality of life, highlighting the importance of treating pain in this population⁴⁵.

Findings from epidemiological studies estimating analgesic usage and prevalence of pain in patients with AD and dementia are inconsistent. For example, it is often reported that pain is undertreated in AD^{17,75,76} which is in line with the results of a recent meta-analysis in patients in aged care facilities⁷⁷. By contrast, several recent reports indicate that AD sufferers use more analgesics than older adults not suffering from AD^{78,79}. Highlighting the complexity of this field, two reports from the MEDALZ cohort published in 2017 found that AD patients were more likely than non-AD patients to use strong opioid medications⁷⁹ and less likely to be long-term opioid users⁸⁰, thus, indicating differences in analgesic usage between these two groups may be dependent on analgesic type, strength, and duration of use. Epidemiological evidence of differences in pain prevalence among AD and dementia patients vs. age-matched controls is mixed and inconsistent^{73,81}. For example, in a large, nationally representative sample of US, community dwelling adults, dementia was reported to be significantly associated with increased likelihood of pain⁹. On the contrary, a recent meta-analysis compiling studies from aged care facilities found patients with dementia were less likely to report or be observed to have pain⁷⁷. Importantly, a recent review by Gagliese et al; assessed reported prevalence of pain in AD and dementia patients and concluded that these rates were at least comparable to rates of older adults without dementia⁷³.

Patients with dementia may have impaired ability to report pain⁸² and there are a variety of new tools that rely on non-verbal pain responses (e.g. facial expressions, vocalizations, body movements) to assess pain in these patients that may not be able to communicate⁸². Neuroimaging studies have reported that AD patients have differences in neuronal connectivity between pain relevant brain regions as well as lower pain sensitivities as compared to age- matched controls^{17,83,84}. Study authors proposed that these differences may have been due to AD patients being less able to accurately assess the experimental pain situation^{17,83}. Importantly, these studies measured pain thresholds by self-report in response to a stimulus. A recent systematic review and meta-analysis found that pain thresholds (self-report) were not different between AD sufferers and healthy controls⁸⁵. However, in AD patients, pain sensitivity increased when facial assessments of pain response was used as a measure⁸⁵. Altogether, these data indicate that AD and dementia patients have an altered experience of pain that may not be captured by standard pain self-report measures.

The previous sections summarized the prevalence and impact of chronic pain in older adults. The final section of this review addresses some challenges associated with treating chronic pain in older adults.

7. Polypharmacy and other treatment complications

Polypharmacy is the phenomenon of a patient taking more than one medication simultaneously (most often defined as consumption 5 or more medications daily⁸⁶). Polypharmacy is associated with many undesirable outcomes including: increased health costs, adverse drug events, drug interactions, functional and cognitive declines and falls⁸⁷. Polypharmacy is prevalent in older adults regardless of their care setting (ambulatory, hospital or nursing home)⁸⁷. For example, in the US general population adults greater than 65 years old take a median of 4 prescription meds and approximately 41% consume 5 or more medications per day. Concerningly, the prevalence rates of polypharmacy among older Americans increased approximately 3-fold since 1988^{88,89}.

Chronic pain is an independent risk factor for daily analgesic consumption in older adults⁹⁰ and pain and analgesic use have previously been reported to be risk factors for polypharmacy⁹¹⁻⁹⁴. An estimated 16% of older adults are taking prescription analgesics⁸⁹, and approximately 70% of older adults consume non-prescription analgesics at least every other day⁹⁵. Among arthritis sufferers, 40% of adults older than 65 experience polypharmacy compared to 29% of adults aged 50-64⁴⁶. Among pain sufferers polypharmacy has been reported to be associated with decreased quality of life⁴⁶.

The widespread polypharmacy among older adults is concerning as pharmacokinetics of many drugs is altered with age, and many trials testing pharmaceuticals exclude older adults limiting assessments of efficacy and side effects in this population^{13,14,96}. An additional concern with older adults consuming pharmaceuticals is the potential impact of frailty (reviewed here¹⁴). Among older adults, analgesic use is most common in frail individuals, however, how frailty impacts analgesic drug toxicity is not fully understood^{14,97}. Analgesics are involved in a significant proportion of drug related adverse events in older adults⁹⁸⁻¹⁰⁰. Additionally a significant proportion of older chronic pain sufferers report they need

stronger pain medication¹⁰¹. In particular, anti-epileptic and anti-depressant drugs are commonly prescribed to treat chronic neuropathic pain, however, side effects associated with anticonvulsants—including cognitive impairment, sedation and increased falls—make prescribing these drugs to older adults risky and, in some instances, contraindicated^{102–104}. While the benefits of properly treating chronic pain are well-established in older adults¹⁶, medical pain management must be balanced with the risks of side effects such as bleeding^{105,106}, urinary and gastrointestinal side effects^{105,106}, increased falls^{105,107} and cognitive symptoms¹⁰⁵ associated with common pain medications.

In summary a complex balance between adequately treating pain while avoiding pitfalls associated with medication overuse in older adults needs to be achieved to enhance quality of life and function. Older adults are often excluded from clinical trials of analgesics making assessments of analgesics efficacy limited in this population¹³. In light of the complications with pharmacological interventions to treating pain and the limited ability to assess efficacy of pharmacological analgesics in older adults, non-pharmacological modalities may be especially suitable to treat pain in this patient population. In fact, many official bodies have recently highlighted the utility of multimodal/multidisciplinary approaches, that include non-pharmacological therapies, for the treatment of chronic pain^{108–110}. Specific to older adults, in 2012 the American College of Rheumatology recommended a number of non-pharmacological approaches for management of osteoarthritis, including exercise, acupuncture and Tai Chi¹¹¹. More recently, a randomized controlled trial found that a mindfulness based stress-reduction intervention significantly improved low back pain related function in older adults¹¹². It should be noted that, though non-pharmacological approaches to treat chronic pain are recommended and low-risk relative to pharmacological interventions, more evidence from larger and more strictly controlled clinical trials are needed to determine efficacy of non-pharmacological treatments to chronic pain. Therefore, safer, more effective treatment options for chronic pain in older adults are needed. Until then, based on the limited evidence available, the best approach to treat pain in older adults is likely a multi-modal approach encompassing pharmacological and non-pharmacological approaches as well as lifestyle modifications, where the provider and patient attempt to balance the adequate pain control while limiting adverse side-effects.

8. Conclusions

In summary, chronic pain is highly prevalent among older adults where it is associated with significant suffering, disability, social isolation, and a burden to health care systems. Pharmaceutical options for treating chronic pain in older adults tend to be only partially effective and associated with important side effects. Future research is needed to improve estimates for chronic pain in older adults, to elucidate underlying mechanisms of pain with aging and dementia, and to develop and advance safer, more effective treatment options.

Acknowledgments

This work was supported by the intramural research program of the National Institute on Aging and National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health.

Abbreviations:

HICP	High Impact Chronic Pain
CNS	Central Nervous System
S1	Primary Somatosensory Cortex

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Highlights

- Chronic pain is prevalent and disabling in older adults
- The experience of chronic pain may change with increased age
- Chronic pain has been linked to increased mortality and dementia
- Efficacy and safety of pharmacological treatments for chronic pain in older adults has not been fully evaluated

Prevalence of Pain in Adults aged 65 years or older by site of pain

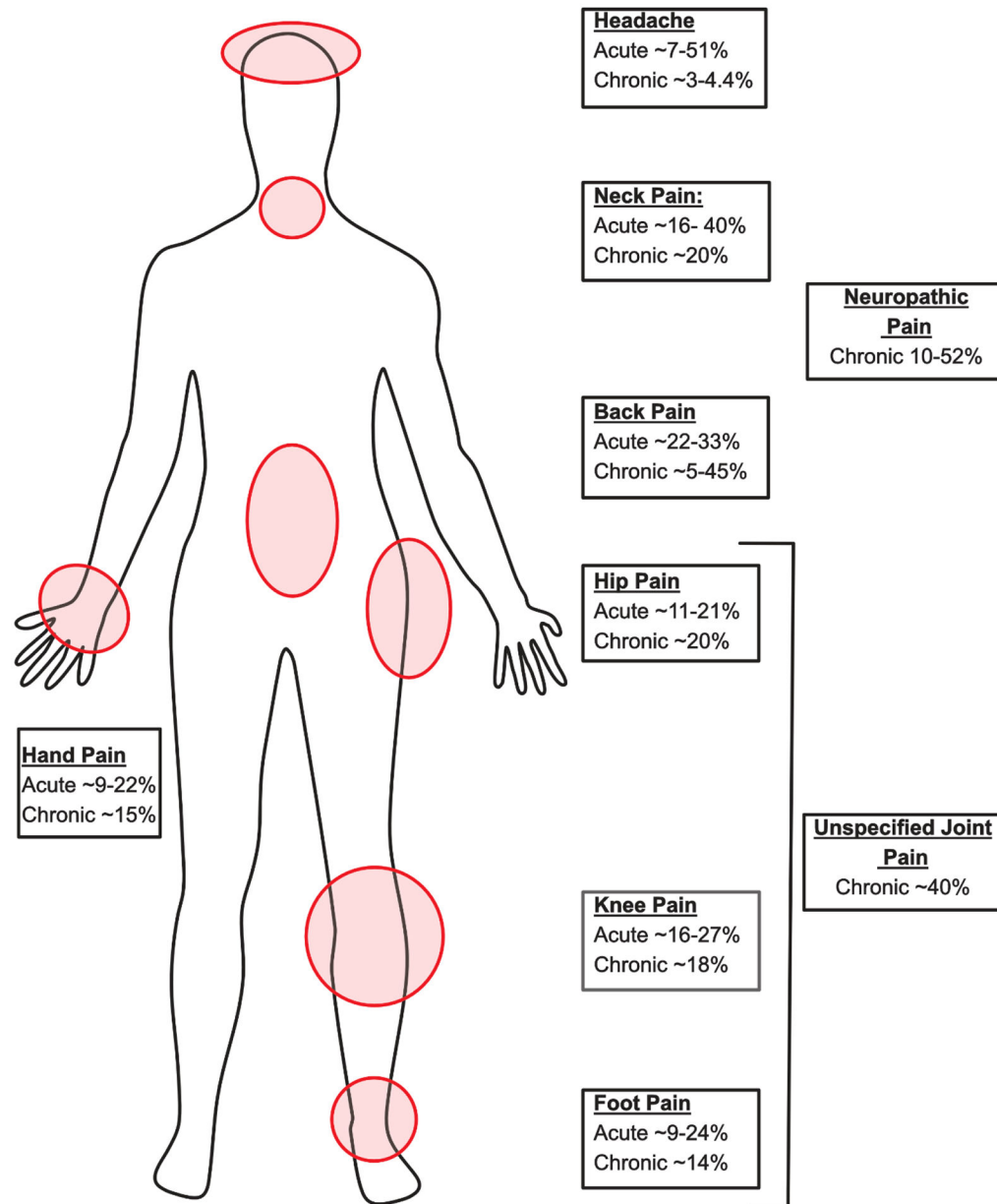


Figure 1: Prevalence of chronic pain in older adults by site.

Older adults suffer from a number of acute and chronic pain conditions including neuropathic pain^{25,26}, unspecified joint pain^{23,33}, back pain^{9,18,23,113,114}, neck pain^{9,23,24,33}, knee pain^{9,33,34,115}, hip pain^{9,33,34,115}, foot pain^{9,33,115,116}, hand pain^{33,115} and headache^{23,117,118}.