The impact of multisite pain on functional outcomes in older adults: biopsychosocial considerations

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Abstract: Multisite pain, or pain that occurs simultaneously at >1 anatomical site, is more prevalent than single-site pain. While multisite pain affects over half of older adults, it remains an understudied pain entity that may have important functional implications in an aging population. Greater understanding of this complex pain entity from a biopsychosocial perspective is critical for optimizing clinical and functional outcomes in older adults with pain. Therefore, the primary purpose of this review is to summarize the relationship between multisite pain and functional outcomes in older adults to further elucidate the impact of multisite pain as a distinct entity within this population. A comprehensive literature search revealed 17 peer-reviewed articles. Multisite pain in older individuals is associated with reductions in several physical function domains: 1) lower-extremity mobility; 2) upper-extremity impairments; 3) balance and increased fall risk; and 4) general disability and poor physical function. Further, multisite pain in older individuals is associated with psychological dysfunction (eg, anxiety and depressive symptoms) and social factors (eg, income and education). Overall, this review highlights the scant literature investigating the functional implications of multisite pain in an aging population. Further, while multisite pain appears to have functional consequences, the neurobiological mechanisms contributing to this relationship are unknown. Thus, how this pain characteristic may contribute to the variability in pain-related functional outcomes among older adults is not clear. Future investigations are strongly warranted to advance the understanding of multisite pain and its broad impact on physical and psychosocial function in older adults.

Keywords: multiple pain locations, multiple pain sites, social function, dysfunction, disability, physical function, social factors

Introduction
Multisite pain, or pain that occurs simultaneously at >1 anatomical site, is a prevalent pain condition.1–3 In the general population, those reporting single-site pain often report pain at other sites;1,4–8 additionally, single-site pain increases the risk for pain at other sites.9 The common occurrence of multisite pain is highlighted in findings from a large epidemiological sample where 16.8% of responders reported localized musculoskeletal pain compared to 53% of responders who reported pain at >1 site.4 Notably, evidence suggests that over half of older adults experience multisite pain.10–12 One study indicated that ~74.9% of their older adult sample reported multiple pain sites.12

While multisite pain is highly prevalent in older adults, it remains an under-appreciated and understudied pain characteristic that may represent a distinct pain condition with potential functional implications in this population. Experiencing pain at multiple sites may have greater impact on physical fitness, emotions, or daily and social activities...
compared to single-site pain. Furthermore, consideration of multisite pain in an aging population is critical for these individuals as they often demonstrate greater declines in physical and psychological functions as well as significant levels of chronic pain. Overall, a stronger understanding of the complex biopsychosocial relationships contributing to multisite pain in older adults may provide key insight needed to optimize clinical and functional outcomes within this population (Figure 1). Therefore, the primary purpose of this literature review is to summarize the relationship between multisite pain and functional outcomes (physical function and psychosocial function) in older adults to further elucidate the relevance of identifying and studying multisite pain as a distinct disease entity using a biopsychosocial framework of pain and aging.

Figure 1 Conceptual model of the biopsychosocial considerations of multisite pain in older adults.

Note: This model represents multisite pain using a biopsychosocial framework and depicts the integration of multiple, complex relationships that comprise this distinct disease entity.
Methods
A comprehensive search across several databases was performed to extract peer-reviewed articles published in 2018 or earlier (Figure 2). Databases included PubMed, Google Scholar, and Web of Science. Articles examining multisite pain in older adult populations were targeted through the use of key terms and their combinations; these included but were not limited to: “multisite pain”, “multiple pain locations”, “number of pain sites”, “psychosocial”, “psychological function”, “psychological distress”, “physical function”, “physical dysfunction”, “disability”, “participation”, “networks”, and “social function”. All titles returned from PubMed and Web of Science searches were examined; however, for pragmatic reasons, only the first 200 results from the Google Scholar searches were examined as searches of this database consistently returned >1,000 results. Potential articles for inclusion were identified based on title relevance and then based on a review of the full abstract; finally, a full-text review of remaining articles was conducted. Additionally, the reference section of a relevant extracted article was searched to identify additional potential articles for inclusion. Articles were included if they met all of the following criteria: 1) the study included a clearly defined measure of multisite pain; 2) the study population included only individuals of age 65 or older; 3) the study included physical, psychological, and/or social measures; and 4) the study data analyses were structured to examine the relationship between multisite pain and physical, psychological, and/or social measures. Articles were excluded if they met one or more of the following criteria: 1) the study population included <65 years old; 2) the study did not adequately define multisite pain and/or only examined widespread pain; 3) the study did not use appropriate analyses for the primary purpose of this review; and 4) the study did not include appropriate measures for the primary purpose of this review. Additionally, articles were excluded if they were review articles, intervention studies, or measurement studies. Figure 2 illustrates the results from the search strategy.

Results
The search yielded 17 peer-reviewed articles investigating multisite pain and its associated physical and psychosocial functional implications among older adults. Tables 1 and 2 provide a comprehensive list of included articles. Overall, multisite pain in older individuals is associated with reductions in several aspects of physical function including: 1) reduced lower-extremity mobility; 2) upper-extremity impairments; 3) decreased balance and increased fall risk; and 4) higher general disability and
## Table 1 Summary of articles indicating associations between multisite pain and physical function in older adults

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of subjects</th>
<th>Age (years)</th>
<th>Pain measure</th>
<th>Physical function measure</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asai et al (2015)²⁶</td>
<td>112</td>
<td>≥65</td>
<td>Self-reported pain lasting 1 month or more in the past year across five sites (back, hip, knee, foot, or toe); number of pain sites categorized as: no pain, single site pain, or multisite pain (two or more pain sites)</td>
<td>Gait speed during three conditions (normal, fast, dual-task); self-reported falls in the past year; self-reported fear of falls</td>
<td>Individuals with a higher number of pain sites demonstrate greater fall history in the previous year</td>
</tr>
<tr>
<td>Buchman et al (2010)²⁸</td>
<td>898</td>
<td>≥65</td>
<td>Self-reported pain or aching on most days for at least 1 month during the past year across several joints (back or neck, hands, hips, knees, or feet); sum of reported areas determined the number of painful sites</td>
<td>Duke Older Americans Resources and Services project (instrumental ADL disability); Katz Basic ADL Scale (ADL disability); Rosow-Breslau Scale (mobility disability); Performance Disability (gait speed &lt;0.55 m/s when walking 8 feet)</td>
<td>Each additional painful area is associated with a 20% increase in basic ADL disability, a 10% increase in instrumental ADL disability, and a 13% increase in performance disability (ie, slower gait speed)</td>
</tr>
<tr>
<td>Eggermont et al (2010)²⁶</td>
<td>585</td>
<td>≥70</td>
<td>Self-reported pain for &gt;1–2 weeks identified on a human figure diagram; number pain sites categorized as: no pain, single site pain, multisite pain or widespread pain (according to ACR criteria)</td>
<td>SPPB; self-reported mobility difficulty (walking 2–3 blocks or climbing 10 stairs)</td>
<td>Multisite pain is associated with self-reported mobility difficulty</td>
</tr>
<tr>
<td>Fowler-Brown et al (2013)¹³</td>
<td>736</td>
<td>&gt;70</td>
<td>Self-reported pain on most days for at least 3 months in the preceding year across several sites (hip, knees, feet); sum of reported areas determined the number of painful sites</td>
<td>SPPB; self-reported difficulty with or inability to perform ADLs; SF-12 Physical Component Score</td>
<td>Compared to individuals with no pain, individuals with two pain sites and three or more pain sites demonstrate higher risk for ADL disability, higher risk for reduced SPPB scores, and higher risk for reduced physical component scores</td>
</tr>
<tr>
<td>Landi et al (2009)²⁷</td>
<td>204</td>
<td>≥80</td>
<td>Self-report pain in any area of the body occurring within the last 7 days; number of painful sites categorized as: single pain site or multiple pain sites</td>
<td>Disability defined as self-reported need for assistance with one or more ADLs</td>
<td>Compared to individuals with no pain, individuals with multiple pain sites are at 2.1 times higher risk for disability</td>
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<tr>
<td>Leveille et al (2003)³¹</td>
<td>325</td>
<td>75–85</td>
<td>Self-reported pain rated as 4/10 or greater in four regions (back, hip, knees, feet); number of painful sites categorized as: no sites, one site, two sites, or three/ four sites</td>
<td>Physical Activity Scale for the Elderly; self-reported number of blocks walked per week; Physical Function subscale of the SF-36</td>
<td>Individuals with a higher number of pain sites demonstrate lower physical function and an increased likelihood of walking &lt;1 mile/week</td>
</tr>
<tr>
<td>Leveille et al (2005)³⁰</td>
<td>1,062</td>
<td>72–99</td>
<td>Self-reported pain on most days marked on a diagram (included upper and lower extremity joints, four areas on the back and neck, hand joints, and joints in the feet); number of painful sites categorized as: no pain, pain in 1 region, pain in 2–3 regions, or widespread pain (ACR criteria)</td>
<td>Disability defined as self-reported needing assistance with/ability to perform ADLs or inability to perform lower-extremity activities such as walking or climbing stairs</td>
<td>In men, individuals with a higher number of pain sites demonstrate greater disability</td>
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<tr>
<td>Leveille et al (2009)³⁵</td>
<td>749</td>
<td>≥70</td>
<td>Self-reported pain in the previous month and present for at least 3 months in the previous year across multiple joint regions (hands/wrists, shoulders, back, chest, hips, knees, and feet); number of pain sites categorized as: no pain, pain in a single location, or pain in two or more locations</td>
<td>Self-reported number of falls in the past 18 months; standing balance assessments (side by side stance, semi-tandem stance, tandem stance, single limb stance); gait speed walking 4 m; time to complete sit to stand 5 times; Physical Activity Scale for Elderly</td>
<td>Individuals with multisite pain are more likely to have fallen in the past year and more likely to demonstrate poorer performance on tests of balance and mobility (eg, impaired standing balance, slower gait speed, and slower sit to stand)</td>
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<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Age</td>
<td>Measurements</td>
<td>Findings</td>
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<td>Mänty et al (2014)⁹</td>
<td>1,177 (baseline) and 709 (2-year follow-up)</td>
<td>92-93</td>
<td>Self-reported pain with movement or at rest across several sites (hips, knees, and/or back); number of pain sites categorized as: no pain, single site pain, or multisite pain</td>
<td>Grip strength; gait speed; disability determined by self-reported use of an assistive device, need for assistance, or inability to perform tasks from the Katz Basic ADL Scale. Baseline: individuals with a higher number of pain sites demonstrate lower grip strength, slower gait speed, and increased disability for basic ADLs. Individuals with multisite pain at baseline demonstrate greater risk for developing moderate and severe disability at follow-up.</td>
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<td>Murata et al (2018)⁷³</td>
<td>267 ≥65</td>
<td></td>
<td>Self-reported pain lasting 3 months or more across several areas (neck, low back, shoulder, elbow, hand or wrist, hip, knee, ankle, or foot); sum of reported areas determined the number of painful sites</td>
<td>Physical activity assessed using an accelerometer. Individuals with a higher number of pain sites demonstrate decreased steps and lower moderate to vigorous physical activity.</td>
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<tr>
<td>Patel et al (2013)⁵⁷</td>
<td>7,601 ≥65</td>
<td></td>
<td>Self-reported pain in the last month across several sites (back, hips, knees, legs, feet, hands, wrists, arms, shoulders, stomach, head, and neck); sum of reported areas determined the number of painful sites</td>
<td>SPPB; self-reported ability to perform several functional tasks; gait speed; grip strength. There is a relationship between more pain sites and higher self-reported inability to perform several functional tasks (walk 3 blocks, climb 10 stairs, carry 10 pounds, bend over, and reach overhead); additionally, there is a relationship between more pain sites and weaker grip strength, slower gait speed, and decreased SPPB lower-extremity function scores.</td>
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<tr>
<td>Patel et al (2014)⁵³</td>
<td>7,601 ≥65</td>
<td></td>
<td>Self-report pain in the last month across several sites (back, hips, knees, legs, feet, hands, wrists, arms, shoulders, stomach, head, and neck); sum of reported areas determined the number of painful sites</td>
<td>SPPB; grip strength; gait speed. More pain sites are associated with self-reported balance/coordination problems, decreased balance performance, increased falls, and increased fear of falls.</td>
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<tr>
<td>Sawa et al (2017)²⁰</td>
<td>224 ≥65</td>
<td></td>
<td>Self-reported pain for 1 month or longer across several sites (shoulders, elbows, wrists, hands, hips, knees, feet, low back); number of pain sites categorized as: no pain, pain at one site, or pain at two or more sites</td>
<td>SPPB. Self-reported falls in the past 12 months; gait speed; gait variability. An increase in number of pain sites is associated with a decreased trend in gait speed and gait variability, indicating worsening gait function.</td>
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<tr>
<td>Scudds and Robertson (2000)³⁸</td>
<td>644 ≥65</td>
<td></td>
<td>Self-reported pain shaded on a human figure diagram divided into 45 areas; number pain sites corresponds to number of shaded areas across these 45 predetermined areas</td>
<td>Physical disability defined as self-reported difficulty with &gt;3 tasks included on the 20-item Stanford Health Assessment Questionnaire. More pain sites are associated with greater physical disability; each pain site demonstrates a 1.14 times increased risk of physical disability.</td>
<td></td>
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<tr>
<td>Thapa et al (2018)⁴¹</td>
<td>749 ≥70</td>
<td></td>
<td>Self-reported pain in the prior month and present for at least 3 months in the prior year across several joint areas (hands/wrists, shoulders, back, chest, hips, knees, feet); number of pain sites categorized as: no pain, pain in a single site, or multisite pain (two sites or more)</td>
<td>SPPB. Compared to individuals with no pain, individuals with multisite pain demonstrate lower SPPB scores.</td>
<td></td>
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Abbreviations: ACR, American College of Rheumatology; ADL, activities of daily living; SPPB, Short Physical Performance Battery.
poor physical function. Further, multisite pain in older individuals is associated with psychological dysfunction (specifically, anxiety and depressive symptoms) and social factors (income and education). Detailed descriptions of the functional implications of multisite pain in older adults are outlined below.
Multisite pain and physical function in older adults

Evidence demonstrates that multiple aspects of physical function are impacted by multisite pain in older adults (Table 1).

Reduced lower extremity mobility

Evidence indicates that multisite pain is associated with decreased lower extremity mobility. In older adults, there is a negative association between increased multisite pain and reduced lower extremity mobility test scores.12-14 Older adults with more pain sites demonstrate greater difficulty when performing specific lower extremity tasks, such as standing up, walking, and climbing stairs.12,15,16 Another study indicates that a higher number of pain sites is associated with decreased daily steps and lower moderate to vigorous physical activity as measured by lower-extremity accelerometers.17 Further, community-dwelling older adults with multisite pain also demonstrate slower gait speeds,12,15,18,19 impaired gait function,20 and reduced walking distance.21 Multisite pain-related gait impairments are of particular concern in older populations as slower gait speed is an established risk factor for multiple, negative functional, and clinical outcomes22 (eg, risk for self-care dependence,23,24 falls,25,26 hospitalization, and institutionalization).25,27,28

Upper extremity impairments

There is evidence suggesting a potential relationship between multisite pain and reduced upper extremity performance. Older adults with a higher number of pain sites are more likely to report an inability to reach overhead and carry 10 pounds compared to those with only one pain site.12 Further, individuals with a higher number of pain sites demonstrate decreased grip strength.12,19 The limited evidence investigating the relationship between multisite pain and upper extremity function highlights the large gap in understanding the extent of multisite pain’s impact across functional domains.

Decreased balance and increased fall risk

Falls are commonly experienced by approximately one-third of older adults,29,30 injuries from falls are associated with adverse outcomes, such as death, disability, and hospitalization.31,32 Older individuals are at increased risk for falls due to multiple factors, including decreased balance.33,34 Thus, an examination of multisite pain’s contribution to balance deficits and heightened fall risk is warranted. Indeed, community-dwelling older adults with increased pain sites are more likely to have poor balance performance.15 Older adults with multisite pain are also more likely to report balance and coordination problems and limited activity due to balance and coordination impairments.35 Additionally, a higher number of pain sites and multisite pain are both associated with an increased history of falls.15,35,36 Further, older adults reporting an increased number of pain sites are more likely to report increased fear of falling.35

Higher general disability and poor physical function

Associations between multisite pain and general measures of perceived disability among older adults strongly indicate that multisite pain is positively related to higher levels of self-reported disability in this population. In older adults, a higher number of pain sites increases the risk for disability,37,38 decreased physical function,13,21 and impaired basic and instrumental activities of daily living (ADL).13,18,19 Persistence of multisite pain is associated with a greater likelihood of self-reported difficulty with basic and instrumental ADL, suggesting that this relationship is maintained over time.13 Further, older individuals with multisite pain are more likely to develop moderate to severe self-reported disability.19 Of note, one additional study shows that men with more pain sites demonstrate greater disability, but this relationship was not significant for women.39

Multisite pain and psychosocial function in older adults

Evidence indicates that psychosocial function is impacted by multisite pain in older adults (Table 2). An increased number of pain sites is associated with increased depressive symptoms in older adults.19,40 Of note, in two additional studies, this relationship was only seen in women and not in men, indicating a potential gender interaction.39,41 Older adults with multisite pain also report higher rates of depression and anxiety.14 Furthermore, social factors may also play a role in multisite pain among older adults. Studies suggest that multisite pain is associated with fewer years of education15,18 and lower income.21 While multisite pain appears to be associated with several psychosocial factors, there are limited studies investigating this relationship specifically in older adults. Therefore, a comprehensive investigation of both negative and positive psychological factors, as well as multiple social factors is necessary to address this clear gap in evidence.

Discussion

The current review indicates multisite pain may be associated with both decreased physical and psychosocial function in older adults. However, there continues to be limited understanding of these relationships. This review highlights...
the scant number of studies investigating functional implications of multisite pain in an aging population. This may be due to the current focus of clinical research studies on individual pain sites and/or specific conditions (eg, hand, hip, knee osteoarthritis, low back pain) among older adults. In addition, while multisite pain appears to have functional consequences, the neurobiological mechanisms contributing to this relationship are unclear. Unfortunately, investigation of multisite pain beyond musculoskeletal conditions in older adults is also limited; while some studies include investigation of general widespread pain, examination of specific neuropathic and/or widespread pain conditions as well as other comorbid diseases is currently lacking. Furthermore, what specific conditions may be more strongly associated with multisite pain symptoms and/or development of a multisite pain disease is unclear. Associations between multisite pain and other comorbidities may provide additional insight into the pathophysiological processes leading to certain functional impairments.

This review also highlights the insufficient literature on multisite pain and psychosocial function. Our search only yielded depression and anxiety assessments in relation to multisite pain. Alone, these constructs do not adequately represent overall psychological health. Thus, future studies including more comprehensive psychological batteries validated in older individuals are needed with respect to multisite pain. Finally, 2 of the 17 studies indicate a potential gender interaction in relation to multisite pain.49–41 Given that chronic pain is more common in women compared to men, it is possible that a gender interaction does play a role in the relationship between multisite pain and functional outcomes in older adults. However, future studies designed to address this question specifically are needed to draw any solid conclusions. Overall, this review strongly reiterates that the pathways by which multisite pain contributes to the variability in pain-related clinical and functional outcomes among older adults are still not fully realized.

Furthermore, this review suggests that there is an inadequate understanding of the biological mechanisms underlying multisite pain in older individuals. In aging populations, individuals with increased pain sensitization reflective of central nervous system changes also report multiple pain sites simultaneously.42–44 Similarly, other studies report that impaired conditioned pain modulation in musculoskeletal conditions is often accompanied by multisite pain (eg, chronic low back pain, knee osteoarthritis).45–48 Thus, it is possible that multisite pain is not just simply a consequence of “turning on pain pathways” in the periphery via a particular pathology but, may reflect, the state of excitability of pain circuits within the central nervous system. Multiple pain sites may translate into multiple pain inputs resulting in activity-dependent shifts in the sensitivity of the pain system such that perceptual responses to noxious inputs are exaggerated, prolonged, and widespread.49 In aggregate, current studies do not imply that peripheral factors are unimportant in multisite pain; rather that peripheral factors alone are likely insufficient to account for symptoms in some, or many, older individuals with multisite pain. Whether or not central nervous system augmentation plays a prominent role in multisite pain is likely to be tied to genetic predisposition, environmental stressors, and the degree of morbidity burden a given person experiences consistent with the biopsychosocial model. Overall, investigation of the biological mechanisms associated with, and underlying, multisite pain is warranted in older persons as these changes may be important pathophysiological links explaining how multisite pain leads to subsequent negative disability and mortality.

Future directions

Studies aimed at characterizing these complex relationships using a biopsychosocial framework are necessary to fully understand multisite pain as a distinct clinical pain entity and its impact on function in older adults (Figure 1). This research approach directly aligns with recent calls to consider pain-related nervous system processes and their impact on function in chronic pain diseases.50,51 To advance the understanding of multisite pain specifically in older adults, future studies should include several key components. First, multisite pain must be appropriately defined and measured, distinguishing it from other conditions such as widespread pain conditions like fibromyalgia. Second, further investigations into potential neural peripheral and centrally-mediated mechanisms of multisite pain are of high importance. Future studies must clearly describe: 1) sensory changes including severity and frequency of multisite pain and central sensitization status; 2) pain-related negative and positive psychological processes, such as pain catastrophizing, psychological distress, pain self-efficacy, and optimism; and 3) motor-related factors, such as muscle strength, force output, muscle activation, and speed of motor unit recruitment. Third, future research is needed in older adult population to easily and effectively integrate multisite pain assessment in clinical settings. This will aid in diagnosis, treatment, and monitoring of longitudinal outcomes, including response to interventions specifically in an aging population. Finally, research needs to take into consideration the important interactions among biological, psychological, and social contributors to the multisite
pain experience. For example, gender differences, as well as the role of age-related comorbidities (i.e., pain-related, non-pain-related, and psychological) should be considered. Studies aligned with these research directions are critical to establish how multisite pain impacts function and increases the risk for disability and mortality in an aging population.

Clinical implications

Clinicians should be aware of the functional implications of multisite pain in older adults and should also recognize that multisite site pain may have its own unique underlying mechanisms with a broad impact on physical and psychosocial health. Older individuals with multisite pain may experience a disproportionately greater decline in daily physical activities and may have greater psychological and social barriers to overcome due to this pain condition and multiple, simultaneous pain inputs. Thus, utilization of multisite pain measures, psychosocial screening tools, and performance-based outcomes is essential when evaluating older adults with potential multisite pain. This type of multidimensional approach is critical for guiding selection of effective, personalized medicine strategies to enhance pain relief and optimize clinical and functional outcomes in an aging population. Finally, it is plausible that interventions aimed at controlling pain, reducing psychological distress, improving pain coping, and/or optimizing movement, all have the potential to modify the physical and psychosocial functional outcomes highlighted in this review. Indeed, biopsychosocial treatment approaches and interventions with multiple treatment targets (i.e., cognitive–behavioral therapy and multidisciplinary pain programs) have shown promise across pain populations.32–35 Thus, it is conceivable that these interventions may also be appropriate for treating multisite pain in older adults, especially considering the biopsychosocial aspects of this condition.

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