

**Journal of Pharmaceutical Advanced Research****(An International Multidisciplinary Peer Review Open Access monthly Journal)**Available online at: [www.jpardonline.com](http://www.jpardonline.com)R  
E  
V  
I  
E  
W  
  
A  
R  
T  
I  
C  
L  
E  
  
J  
P  
A  
R  
2  
0  
2  
4**Knee Osteoarthritis, Falls, and Opioids: Interactions and Recommendations**

Akash S Ingale\*, Parag R Patil

KYDSCTS College of Pharmacy, Sakegaon, Bhusawal, Maharashtra-425201, India.

Received: 01.02.2023

Revised: 10.02.2024

Accepted: 16.02.2024

Published 29.02.2024

**ABSTRACT:** An elevated risk of falls and injuries is increasingly demonstrated to effect and/or be affected by knee osteoarthritis, a very painful and crippling joint disease that is ubiquitous. This synopsis summarizes the most recent studies that have been released about the usage of opioids to relieve pain in this regard and the potential negative effects on falls. In order to achieve this, the following keywords were used to find information explicitly related to the topic: falls, fall injuries, knee osteoarthritis, opioids, and pain. PUBMED and other data base indexes were also chosen. The results indicate that older persons with knee osteoarthritis who have fallen or are at risk of falling should be advised to use opioids carefully, according to a reasonable body of current science-based data. On the other hand, failing to recognize this risk and it is reasonable to anticipate that the role of alternative pain management and relief techniques will, at most, result in subpar clinical outcomes.

**Corresponding author:**

Mr. Akash Sudhakar Ingale  
Assistant Professor  
KYDSCTS College of Pharmacy, Sakegaon,  
Bhusawal, Maharashtra-425201, India.  
Tel: +91-8551958446  
E. Mail ID: [ingaleakash111@gmail.com](mailto:ingaleakash111@gmail.com)

**INTRODUCTION:**

As of January 6, 2024, more than 117,040 reports pertaining to more than a century of discussions on the causes, consequences, and remedies to counter the widespread joint disease known as osteoarthritis generally prevail. Pertaining to knee osteoarthritis alone there were 50,979 related citations, yet in either case most citations failed to address falls related injuries (409 citations) despite their widespread occurrence, deleterious impacts and consequences in the context of the older individual, worldwide. Moreover, in the context of osteoarthritis in general, most failed to offer any universal solution for reducing this disabling health condition, regardless of site or numbers of affected joints, other than various medications and surgery. Additionally, even when these latter interventions are

**Keywords:** Falls, Falls Injuries, Knee Osteoarthritis, Opioid Analgesia, Pain, Treatment.

indicated or pursued, less than optimal results have emerged as evidenced by the increasing and anticipated 2050 prevalence of the disease <sup>[1]</sup>. In particular, as opposed to the possible influences of clinical signs, body mass or joint range of motion <sup>[2]</sup>, the use of a group of narcotic medications classed as opioids to quell pain may simultaneously encourage joint overuse and injurious movement impacts, gait and balance impairments. The chronic usage of opioids may also have serious cognitive effects that impact muscle reflexes adversely with possible destabilization of the affected joint during weight bearing, as well as injuries attributable to stumbling and muscle mass losses <sup>[3,4]</sup>. In addition to inducing mobility impairments including walking and stair climbing <sup>[5]</sup> and more pain <sup>[6]</sup> this series of events can potentially exacerbate the need for more frequent high doses of opioid based drugs.

In light of the aging of society, and the immense public health burden attributable to knee osteoarthritis in its own right, this mini review sought to examine what researchers have found over time when they have examined if chronic opioid usage is indicated or not for averting painful knee osteoarthritis and its oftentimes progressive joint damage. This area of inquiry does seem to be uncertain at best, but of great clinical and economic importance in the sphere of aging societies. In this regard, Krebs, *et al.* <sup>[7]</sup> reported the adjusted risk of falling did not differ significantly between opioid use and non-use groups, but did not specifically assess cases with knee osteoarthritis. They did however note physical performance was worse at baseline for the opioid use group that may or may not be relevant without further clarifying research. Another view is that caution is advised in the context of advocating the use of opioids in the elderly knee osteoarthritis case due to its possible impact on falls, fractures, and progressively disabling functional impairments among those with persistent pain as implied by Lo-Ciganic, *et al.* <sup>[8]</sup> and van Schoor, *et al.* <sup>[9]</sup>.

Unfortunately, knee osteoarthritis, the joint most often affected by disabling pain, could serve to engender a state of muscular weakness and inflammation as well as more pain and injury risk if the joint is not adequately protected from excess impacts <sup>[10,11]</sup>. Moreover, based on a reasonably voluminous literature on the impact of knee osteoarthritis on walking ability, and the fact that walking speed is found to be valid predictor of future osteoarthritis disability among older adults as well as falls, a linkage between possible usages of opioid type

drugs and falls cannot be refuted. In addition to a role for chronic opioid use in disrupting mobility patterns and exacerbating knee osteoarthritis falls risk, this risk is likely to increase if unaddressed and in light of the notable increase in opioid usage among older adults and others in the last several years it is bound to affect untold numbers of older adults in the future in the absence of careful preventive intervention <sup>[12]</sup>. Indeed even if opioids relieve pain temporarily, their overall impact on balance proficiency may yet induce falls even after knee replacement surgery <sup>[2]</sup> especially among those cases who present with concurrent cardiovascular pathology that may be dependent on narcotics <sup>[13]</sup>.

Drawn largely from the PUBMED database, the world's largest research repository, it was hoped the overview might provide the interested reader with a general perspective of current observations and trends in this regard, plus data and proposals worthy of further consideration and study. The possibility that the presence of any opioid associated impact on knee osteoarthritis falls risk, while conceptually and empirically supported to some degree, is not widely studied or accepted by all as a potent falls mediator or moderator in older knee osteoarthritis cases, although often the focus of therapeutic endeavors to quell pain is a possible highly valuable clinically salient pain attribute in its own right.

#### **METHOD:**

To obtain salient information on the above mentioned topic, the electronic data source known as PUBMED was carefully searched, and the selected articles were confirmed as those of key import after conducting a further scan of PubMed Central, and GOOGLE Scholar databases. The key time period of interest searched ranged from January 1, 2010- January 10, 2024. Applied were the key words, Falls, Opioids, Older Adults, Knee Osteoarthritis. Articles assessed were largely limited to those examining some form of narcotic as related to pain of knee osteoarthritis and falls risk. Excluded were other falls correlates, and those focusing on other forms of osteoarthritis and younger populations under the age of 60 years. In light of the limited number of topical studies, only a narrative overview was deemed plausible. A descriptive overview is provided, as there is an obvious lack of robust research in this realm. No form of invasive intervention was examined and the focus was on the community dwelling older adult, rather than the institutional setting

The generic term ‘opioids’ was used regardless of the type of narcotic in question such as Codeine, ‘Oxycodone’, Percoset, or ‘Tramadol’, among others. The impact of multiple medications when combined with opioid usage is not examined or discussed.

#### RESULT:

In addition to a wealth of data showing knee joint osteoarthritis is highly disabling, additional data have frequently alluded to a possible wide array of opioid induced risk factors for poor health if used for any extended duration<sup>[14]</sup>. A disease associated with a wide array of highly destructive local joint features including joint inflammation, instability, and a significant falls risk. Knee osteoarthritis often induces considerable bouts of chronic intractable neuropathic type pain in many cases and engenders a distressing physical and emotional state that is highly challenging to alleviate or reverse. As well as feeling overwhelmed due to possible related declines in general health, vitality, and mobility, the older adult may thus feel helpless and depressed and unmotivated to move. As a result, individuals with this disease have a high risk of incurring a poor life quality, and often a much reduced functional and self-care capacity, as well as a possible loss of independence. In addition, as outlined in a recent related review utilizing data sourced from the Osteoarthritis Initiative that included 1,019 adults diagnosed as having osteoarthritis between the, ages of 45 to 64, the prevalence of self-reported falls in the past 12 months was reported to be 43.7 % (445/1,019) and could add to the many challenges already experienced. While factors influential in this regard were having a higher depression score, being White/Caucasian and having a higher rather than lower educational attainment level, opioids, known to have a possible highly salient bearing on falls and falls injury risk<sup>[15,16]</sup> as well as on recurrent falls were not discussed. In addition, whether adults older than 65 would portray the same features as those 45 to 65 years of age or younger cannot be estimated, but should be examined rather than overlooked in the future<sup>[17]</sup>. Indeed, a study of older adults with painful osteoarthritis published in 2013 was able to show narcotic analgesic prescriptions to be significantly associated with a greater risk of falls and fractures than other non-narcotic medications, thus of possible significance to the knee osteoarthritis case<sup>[18]</sup>.

In another report, Kim, *et al.*<sup>[19]</sup> who examined how people with osteoarthritis define falls, and related

factors that contributed to their fall experiences, the researchers concluded that falls are common and warrant attention to avert the possible impact on activity and life quality. They suggested that psychological factors contributing to the fear of falling and decreased participation in daily activities may be increasing the subject’s falls risk, but did not mention the use of chronic opioid medications, a possible salient contributor that has been put forth as a serious falls risk factor in those deemed to be elderly<sup>[20-22]</sup>, as well as those older adults undergoing elective surgery<sup>[23]</sup>. Similarly, even though a substantive rate of almost 20 % of 4,990 participants older than 50 years of age were found to have a fall history in the past 12 months, with 10.1 % reporting more than two fall events, osteoarthritis and subjective imbalance, opioids were not mentioned as risk factors<sup>[24]</sup>.

However, in addition to lab evidence that opioids can have a toxic effect on articular cartilage chondrocytes<sup>[25]</sup> and that a high percentage of opioid users are older adults with osteoarthritis<sup>[26]</sup> who may not benefit markedly from opioid narcotic use<sup>[27]</sup>, their effect on possible falls alone, for example due to their impact on dizziness<sup>[28]</sup> may induce, provoke or magnify exposure of the affected joint [s] to injuries that further reduce mobility and independence, and that may warrant hospital admission, a need for home health care or discharge to a nursing home<sup>[29]</sup>. In addition to possibly having no significant impact on neuropathic type pain<sup>[30]</sup> and fractures<sup>[31]</sup>, other unwanted outcomes that may arise in the face of persistent opioid usage are falls that raise the risk for joint dislocations, joint injuries other than dislocations, brain injuries, lacerations, internal injuries, dehydration, muscle wasting, and pressure sores due to "long lie times" and pain. Fear of falling and dependence all of which can ensue post an acute or incident fall as well as recurrent falls may result in a spiral of enormous ongoing physical, social, and morbidity costs. These possible outcomes may well prevail or be heightened in the case of an already debilitated knee osteoarthritis case and possibly where multiple joints are affected by the disease. There may also be an induced increase in the pain experience over time, in absence of progression pathology as a result of opioid tolerance and negatively impacted neural responses<sup>[31]</sup>. Even if surgery to replace the painful joint with a metal prosthesis is undertaken, chronic opioid users are observed to exhibit more suboptimal outcomes than those who do not use these pain remedies<sup>[33,34]</sup>.

Thus, other than primary prevention of knee osteoarthritis, falls, and/or opioid reliance, what is needed here is more data to allow for concerted global effort to offset the current challenges of opioid addictions that may accompany efforts to relieve knee osteoarthritis pain. Based on emerging evidence, younger opioid users who have fallen may be an important group to examine periodically, educate about their risk for fall induced knee joint structural damage and a cycle of functional challenges, and pain if they continue their opioid dependence. Until then, based on what we do know, it seems plausible to believe practitioners can greatly help avert this possible downward spiral of events in the context of current health practices. They could do this by dedicated efforts to place a strong focus on opportunities to employ safe forms of pain relief and encourage joint protection and disease associated self-efficacy attributes for increasing the pain threshold. Training their team members to conduct medication assessments and provide careful instructions about their falls risks, especially among those deemed obese or frail, who may fall and sustain a severe injury due to poor bone health. As well, an effort to foster the subject's overall wellbeing, including efforts to optimize their cardiovascular health, their balance capacity, sleep quality and mental health status in parallel with judicious usage of any necessary medication regimens appears desirable <sup>[19,20,28]</sup>.

To foster evidence that can help to better employ future deep learning intelligence based clinical applications in this realm, as well as a more profound evidence base for practice and policy making, it is accepted that these aforementioned issues that are not well covered in the current literature should be subject to more careful scrutiny and validation processes in the future. In the interim, current data are however, generally consistent with those assessed in 2015, that has indicated there is a modest to high incremental risk for falling in older adults with osteoarthritis symptoms and that symptomatic knee osteoarthritis is as important risk factor for falls <sup>[35]</sup>, especially in the face of severe unrelenting pain <sup>[20]</sup>. To avoid incurring a fall requiring emergency visits, and either opioid initiation or persistent usage those cases with a high pain sensitivity profile should be targeted accordingly <sup>[36]</sup>. This is because it appears there is a substantive risk for incurring an injurious fall or multiple falls and worse osteoarthritis outcome if the older adult sufferer becomes dependent on opioids to offset their pain <sup>[37]</sup>.

Van Schoor, *et al.* <sup>[9]</sup> who strove to examine whether low physical performance, low physical activity and use of pain medication are falls mediators, found the use of opioids and analgesics mediated the associations between clinical osteoarthritis and (recurrent) falls, while physical performance and physical activity did not. Silverman, *et al.* <sup>[38]</sup> that assessed the frequency, as well as the treatment characteristics, and risk factors associated with falls or fractures among patients with osteoarthritis taking opioids found falls and fractures impose a major clinical burden on patients if used to a chronic extent for osteoarthritis-related pain management. This may be due to both cognitive as well as gait related modifications and should be examined further <sup>[39]</sup> especially to identify age-associated impacts as related to falls and subsequent pain <sup>[40]</sup>. As per Taqi, *et al.* <sup>[41]</sup> who noted analgesics are consistently associated with an increased risk of falls within one year of knee joint osteoarthritis diagnosis, those who use analgesics should be targeted for fall prevention programs/interventions as early as possible. Moreover, even if this idea is not strongly evident, reviewing the current data concerning falls factors among knee osteoarthritis sufferers, the presence of pain is strongly supported <sup>[10]</sup> even if narcotic intake is not a mentioned determinant <sup>[42]</sup> or believed to have no adverse impact on a bilateral knee replacement procedure <sup>[43]</sup>.

The risk of falls alone is, however, increasingly deemed relevant to consider among supporters of those older adults who want to live out their lives in their own homes in the community, and where many adults with or at risk for knee osteoarthritis may fall quite frequently <sup>[43]</sup>. Moreover, even if this risk is modest at best- that attributable to narcotic excesses should not be overlooked as a mechanism that explains findings of worse baseline as well as more rapid progressive joint changes, pain, and worse subjective symptoms in users compared to non users <sup>[44]</sup>. Recurrent falls are also quite evident in cases with knee osteoarthritis and may be caused by a failure to examine medication profiles carefully in selected cases <sup>[8,45]</sup>. In particular older adults taking multiple medications should be examined because many are abusing opioids and are at high risk for falling <sup>[35]</sup> and if found to be on potentially risky regimens, there appears to be an urgent need to act to modify the patient's medication usage more strategically at the outset. At the same time, fostering a greater reliance on joint protection, as well as standard physical therapies and others with fewer known side effects may not only quell

pain, but may successfully help to minimize falls, as well as pain, and their immense collective personal and healthcare costs. Research that carefully analyzes these options, including economic analyses may be helpful here, as may educational and marketing to make known the possible widespread adverse influence of excess opioid usage among older adults with or without knee osteoarthritis who may request their provider provide these potentially risky narcotics.

Indeed, tentative results have suggested an increased risk of falls, fall injuries, and fractures does tend to exist among older adults who use opioid drugs that warrants validation among samples that more closely represent older community dwelling adults using objective standardized and uniformly applied measurements and instruments, and more elaborate end points overextended time periods of study.

In the interim, since multiple findings point to a consistent negative influence of opioid usage on falls frequency in older adults<sup>[46,47]</sup> Yoshikawa, *et al.*<sup>[48]</sup> imply caution is advised regarding the extended usage of opioids for purposes of alleviating knee osteoarthritis pain among older adults at high risk for falls<sup>[47, 48]</sup>. This is indicated both before as well after any knee joint replacement surgery<sup>[49]</sup>. Moreover, even if only a small percentage of knee osteoarthritis cases do actually use opioids on a consistent basis, their costly often long term side-effects alone may prove devastating<sup>[35,50]</sup>.

## DISCUSSIONS:

Overwhelming evidence continues to show that osteoarthritis, a complex joint disease which frequently affects the knee joints of older adults, induces inordinate degrees of intractable pain and immense societal and human costs, despite decades of research<sup>[51]</sup>. In particular, many reports speak to the immense pain and disease associated with disability of knee osteoarthritis and a need to reduce or eliminate remedial correlates of the disease, of which various health behaviors have been increasingly discussed as possible mediators that may be amenable to various forms of prevention or counter therapy.

One area of concern is the finding that cases with knee osteoarthritis may be exposed to excess joint damage and debility due to injurious falls that may heighten and perpetuate a cycle of its disabling symptoms, joint destruction, and inflammation responses. In particular, falls may prove potent disablers in their own right and

among those fall, a fair percentage may be found to have or be using varying doses of opioids on a consistent basis to quell pain or have recently begun an opioid associated regimen<sup>[16]</sup>. While not clear cut to any degree, as many factors may cause falls in addition to evidence indicating users of opioids tend to exhibit more distress and pain than non users<sup>[44]</sup>, it does appear older adults with a knee osteoarthritis diagnosis may fall more frequently than anticipated if opioid usage is chronic, rather than eliminated or minimized, consequent to its central nervous system as well as its systemic impacts. This appears consistent with what we have learned over the past few years about knee osteoarthritis, as well as knowledge of the multiple neural pathways affected by this disease, plus the possible adverse impact of opioids on the timing and magnitude of inherent protective mechanisms, among other factors that influence joint viability and vulnerability.

Fortunately, management approaches that are non-invasive do exist, and include, but are not limited to concentrated efforts to maximize muscle balance and reaction time, joint support, and walking ability rather than opioid dependence<sup>[52]</sup>. In addition the judicious use of non steroidal anti-inflammatory drugs, joint-friendly medicinal plants, and nutraceuticals, and the application of stringent guidelines for opioid usage in selected cases may be valuable<sup>[28,32,55]</sup>. Other non invasive approaches that may be amenable to the community dwelling older adult with knee osteoarthritis as well as favorably impactful and possibly disease modifying as well are tailored efforts directed by a skilled and insightful medical team toward improving overall health, stress coping ability, and pain self-efficacy<sup>[53]</sup>. These ideas are summarized below and may be applied alone or in combination and tailored to the client's needs, goals, and extent of pathology with the expectation of improving overall health and alleviating pain and narcotic dependence.

In sum, due to the high risk of older adults with knee osteoarthritis incurring multiple devastating impacts consequent to a falls injury, including increases in pain and joint dysfunction of the affected knee, among other health impacts, especially among chronic opioid users<sup>[8]</sup>, carefully prescribed measures for relieving knee osteoarthritis pain are clearly indicated. This potential for opioids to induce a falls injury and excess knee pathology thereafter is not just a theoretical idea, but one that poses an immense threat to life among many older opioid dependent knee osteoarthritis cases if

unaddressed. In this regard, clinicians as well as researchers can undoubtedly play a key role in helping to more carefully delineate the relationship of painful knee osteoarthritis, chronic opioid use and falls injuries risk as applied to different osteoarthritis subgroups, by developing improved pharmacologic pain alleviation approaches for older adults, by education in pharmacies, and by posing novel research questions and designs that can be translated into practice and policy realms in a timely manner in light of the increased opioid usage by older adults, plus the global synthetic opioid epidemic of much more potent Fentanyl and its ease of access. Additionally, funders can help to provide support and resources to those efforts that are put forth to monitor the legislation governing opioid usage, while carefully examining the precise role of other potentially modifiable co-existing knee osteoarthritis pain risk factors possibly amenable to non toxic forms of remediation or palliation not highlighted in the literature. These may include the interaction between frailty as well as obesity, sarcopenia, fatigue, depression, and erroneous health beliefs about both osteoarthritis as well as falling outcomes. Opioid education and carefully targeted usage under the guidance of the primary health provider, plus family education, can potentially help to counter any tendency of an older adult with osteoarthritis knee pain towards additive usage.

### CONCLUSIONS:

The results of this current exploration pertaining to opioid usage for purposes of pain control at the knee joint in the context of osteoarthritis among older adults, while limited, clearly tends to show:

Opioids can mediate, moderate or have a causative role in fostering progressive knee joint attrition due to its potential impact on the risk of falling and falls injuries in vulnerable older adults.

Efforts to improve conservative management and if necessary opioid withdrawal approaches or the implementation of carefully targeted opioid dosage selection applied in a timely manner may be helpful in averting injurious falls, especially recurrent falls that are observed in a sizable number of older knee osteoarthritis cases.

Further careful and comprehensive robust studies of how to limit knee osteoarthritis pain and falling risk through improved pharmacologic as well as non-pharmacological approaches are highly indicated along with comprehensive risk assessments, individualized

multidimensional treatment and management plans, and education to reduce joint impact and pain.

It is also concluded that until more knowledge is acquired, it appears reasonable to suggest that to reduce the chances of possible opioid related falls injuries among older knee osteoarthritis cases with joint instability and one or more chronic health issues, interventions to carefully monitor a patient's daily opioid drug usage pattern both before and after surgery are also clearly imperative.

To this end, primary care providers, pharmacists, allied health workers, and surgeons can help by providing ongoing clear consultative assistance, educational materials, therapy directives, and resources to foster osteoarthritis self-management and self-efficacy for pain control, including menus of the many possible non narcotic pain reducing approaches that abound and home safety directives.

Policy makers and legislators can enforce or modify existing regulations and should be included in efforts to save possible lives and enormous societal and elder care costs.

### ACKNOWLEDGEMENT:

Authors wish to thank KYDSCTS College of Pharmacy for providing the facility to complete this review study.

### REFERENCES:

1. GBD 2021 Osteoarthritis Collaborators. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet. Rheumatol*, 2023; 5(9): e508-e522.
2. Frattura DL, Giorgio, *et al*. Risk of falls in patients with knee osteoarthritis undergoing total knee arthroplasty: a systematic review and best evidence synthesis. *J Orthopaedics*, 2018; 15(3): 903-908.
3. Amann, Markus, *et al*. Opioid-mediated muscle afferents inhibit central motor drive and limit peripheral muscle fatigue development in humans. *J Physiol*, 2009; 587(1): 271-283.
4. Tsonga, Theano, *et al*. Analyzing the history of falls in patients with severe knee osteoarthritis. *Clin Orthop Surg*, 2015; 7(4): 449-456.
5. Boudreau RM, *et al*. Central nervous system medication use and incident mobility limitation in community elders: the Health, Aging, and Body Composition study. *Pharmacoepidemiol Drug Saf*, 2009; 18(10): 916-922.
6. Iijima H, Aoyama T. Increased recurrent falls

- experience in older adults with coexisting of sarcopenia and knee osteoarthritis: a cross-sectional study. *BMC Geriatr*, 2021; 21(1): 698.
7. Krebs, Erin E, *et al.* Association of opioids with falls, fractures, and physical performance among older men with persistent musculoskeletal pain. *J Gen Intern Med*, 2016; 31(5): 463-469.
  8. Lo-Ciganic WH, *et al.* Analgesic use and risk of recurrent falls in participants with or at risk of knee osteoarthritis: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*, 2017; 25(9): 1390-1398.
  9. Schoor V, *et al.* Clinical osteoarthritis of the hip and knee and fall risk: The role of low physical functioning and pain medication. *Semin Arthritis Rheum*, 2020; 50(3): 380-386.
  10. Manlapaz, Donald G, *et al.* Risk factors for falls in adults with knee osteoarthritis: a systematic review. *PM R*, 2019; 11(7): 745-757.
  11. Use of opioids to control arthritis pain under scrutiny. Increase in falls, fractures in older adults attributed to narcotic painkillers, such as oxycodone, Vicodin or Percocet. *Duke Med Health News*, 2013; 19(5): 7.
  12. Gerlach LB, *et al.* Opioids and other central nervous system-active polypharmacy in older adults in the United States. *J Am Geriatr Soc*, 2017; 65(9): 2052-2056.
  13. Aparasu RR, Chatterjee S. Use of narcotic analgesics associated with increased falls and fractures in elderly patients with osteoarthritis. *Evid based Med*, 2014; 19(1): 37-38.
  14. Fuggle N, *et al.* Safety of opioids in osteoarthritis: outcomes of a systematic review and meta-analysis. *Drugs Aging*, 2019; 36: 129-143.
  15. Dufort A, Zainab S. Problematic opioid use among older adults: epidemiology, adverse outcomes and treatment considerations. *Drugs Aging*, 2021; 38(12): 1043-1053.
  16. Söderberg KC, Lucie L, Jette M. Newly initiated opioid treatment and the risk of fall-related injuries: a nationwide, register-based, case-crossover study in Sweden. *CNS Drugs*, 2013; 27: 155-161.
  17. Ofori-Asenso R, *et al.* Prevalence and correlates of falls in a middle-aged population with osteoarthritis: Data from the Osteoarthritis Initiative. *Health Soc Care Community*, 2021; 29(2): 436-444.
  18. Rolita L, *et al.* Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. *J Am Geriatr Soc*, 2013; 61(3): 335-340.
  19. Kim J, Kharma F. Fall experiences from the perspectives of people with osteoarthritis: in their own words. *Disabil Rehabil*, 2024; 46(1): 77-85.
  20. Deyo RA, *et al.* Opioids for low back pain. *BMJ*, 2015; 350: g6380.
  21. Guan, Q, *et al.* Opioid initiation and the hazard of falls or fractures among older adults with varying levels of central nervous system depressant burden. *Drugs Aging*, 2022; 39(9): 729-738.
  22. Gray SL, *et al.* Association between medications acting on the central nervous system and fall-related injuries in community-dwelling older adults: a new user cohort study. *J Gerontol: Series A*, 2020; 75(5): 1003-1009.
  23. Santosa KB, *et al.* Higher amounts of opioids filled after surgery increase risk of serious falls and fall-related injuries among older adults. *J Gen Intern Med*, 2020; 35: 2917-2924.
  24. Delbari A, *et al.* Prevalence, complications, and risk factors of falls and fear of falling among older adults; based on Ardakan Cohort Study on Aging (ACSA). *Arch Acad Emerg Med*, 2023; 12(1): e9-e13.
  25. Abrams GD, Wenteh C, Jason LD. *In vitro* chondrotoxicity of nonsteroidal anti-inflammatory drugs and opioid medications. *Am J Sports Med*, 2017; 45(14): 3345-3350.
  26. Thorlund JB, *et al.* Opioid use in knee or hip osteoarthritis: a region-wide population-based cohort study. *Osteoarthritis Cartilage*, 2019; 27(6): 871-877.
  27. Avouac J, *et al.* Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. *Osteoarthritis and Cartilage*, 2007; 15(8): 957-965.
  28. D'Arcy, Yvonne, *et al.* Treating osteoarthritis pain: mechanisms of action of acetaminophen, nonsteroidal anti-inflammatory drugs, opioids, and nerve growth factor antibodies. *Postgrad Med*, 2021; 133(8): 879-894.
  29. Gammel LB, *et al.* Controlled substance use and clinical outcomes of elderly patients after a fall. *Cureus*, 2022; 14(2): e22356.
  30. Gaskell H, *et al.* Oxycodone for neuropathic pain in adults. *The Cochrane Database of Systematic Reviews*, 2016; 7(7): CD010692.
  31. Lee M, *et al.* A comprehensive review of opioid-

- induced hyperalgesia. *Pain Physician*, 2011; 14(2): 145.
32. Xie J, *et al.* Association of Tramadol v/s. Codeine prescription dispensation with mortality and other adverse clinical outcomes. *JAMA*, 2021; 326(15): 1504-1515.
  33. Dragos D, *et al.* Phytomedicine in joint disorders. *Nutrients*, 2017; 9(1): 70.
  34. Doré AL, *et al.* Lower-extremity osteoarthritis and the risk of falls in a community-based longitudinal study of adults with and without osteoarthritis. *Arthritis Care Res*, 2015; 67(5): 633-639.
  35. Bloomer A, *et al.* Balancing safety, comfort, and fall risk: an intervention to limit opioid and benzodiazepine prescriptions for geriatric patients. *Geriatr Orthop Surg Rehabil*, 2022, 13: 21514593221125616.
  36. Virnes RE, *et al.* Opioids and falls risk in older adults: a narrative review. *Drugs Aging*, 2022; 39(3): 199-207.
  37. Seppala LJ, *et al.* Fall-risk-increasing drugs: a systematic review and meta-analysis: III. Others. *J Am Med Dir Assoc*, 2018; 19(4): e1-372.e8.
  38. Silverman S, *et al.* Clinical and economic burden of prescribing tramadol and other opioids for patients with osteoarthritis in a commercially insured population in the United States. *Pain*, 2022; 163(1): 75-82.
  39. Henriksen M, *et al.* Opioid-induced reductions in gait variability in healthy volunteers and individuals with knee osteoarthritis. *Pain Med*, 2019; 20(11): 2106-2114.
  40. Cordovilla-Guardia S, *et al.* Association of benzodiazepines, opioids and tricyclic antidepressants use and falls in trauma patients: conditional effect of age. *PloS One*, 2020; 15(1): e0227696.
  41. Taqi A, *et al.* Current use of analgesics and the risk of falls in people with knee osteoarthritis: a population-based cohort study using primary care and hospital records. *Osteoarthr Cartil Open*, 2021; 3(2): 100165.
  42. Wilfong JM, Perruccio AV, Badley EM. Examination of the increased risk for falls among individuals with knee osteoarthritis: a Canadian longitudinal study on aging population based study. *Arthritis Care Res*, 2023; 75(11): 2336-2344.
  43. Bieganowski T, *et al.* Opioid consumption and mobilization in staged bilateral total joint arthroplasty: did we learn our lesson the first time? *J Arthroplasty*, 2024; 39(1): 49-53.
  44. Bodden J, *et al.* Opioid users show worse baseline knee osteoarthritis and faster progression of degenerative changes: a retrospective case-control study based on data from the Osteoarthritis Initiative (OAI). *Arthritis Res Ther*, 2021; 23(1): 146.
  45. Aspinall SL, *et al.* Central nervous system medication burden and risk of recurrent serious falls and hip fractures in veterans affairs nursing home residents. *J Am Geriatr Soc*, 2019; 67(1): 74-80.
  46. Rat A, *et al.* Antihypertensive, anticholinergic, and opioid drugs impact fall events differently in patients with knee and/or hip osteoarthritis: a five-year follow-up of the khoala cohort. *HAL Open Access*, 2023.
  47. Losina E, *et al.* Opioid use among medicare beneficiaries with knee osteoarthritis: prevalence and correlates of chronic use. *Arthritis Care Res*, 2023; 75(4): 876-884.
  48. Yoshikawa A, *et al.* Opioid use and the risk of falls, fall injuries and fractures among older adults: a systematic review and meta-analysis. *J Gerontol A*, 2020; 75(10): 1989-1995.
  49. Ebata N, *et al.* Use of analgesics before and after total joint replacement in working-age Japanese patients with knee and hip osteoarthritis: a retrospective database study. *Asia-Pac J Sports Med Arthrosc*, 2023; 35: 1-8.
  50. Driest VD, Jacoline J, *et al.* Opioid prescriptions in patients with osteoarthritis: a population-based cohort study. *Rheumatol*, 2020; 59(9): 2462-2470.
  51. Gress K, *et al.* Treatment recommendations for chronic knee osteoarthritis. *Best Practice & Research Clinical Anaesthesiology*, 2020; 34(3): 369-382.
  52. Busse JW, *et al.* Guideline for opioid therapy and chronic noncancer pain. *CMAJ*, 2017; 189 (18): E659-E666.
  53. Gérard B, *et al.* How to treat chronic pain in rheumatic and musculoskeletal diseases (RMDs) - A pharmacological review. *Joint Bone Spine*, 2024; 91(1): 105624.
  54. Sethi V, *et al.* Model-based meta-analysis supporting the combination of acetaminophen and topical diclofenac in acute pain: a therapy for mild-to-moderate osteoarthritis pain? *Pain Therapy*, 2024; 13: 145-159.



55. Wang Z, *et al.* Medicinal plants and their secondary metabolites in alleviating knee osteoarthritis: a systematic review. *Phytomed*, 2022; 105: 154347.

**Conflict of Interest:** None

**Source of Funding:** Nil

**Paper Citation:** Ingale AS\*, Patil PR. Knee Osteoarthritis, Falls, and Opioids: Interactions and Recommendations. *J Pharm Adv Res*, 2024; 7(2): 2079-2087.