



Integrated Biomedical and Holistic Management of Bilateral Knee Osteoarthritis with Hypertension in a 71-Year-Old Woman: A Case-Based Analysis

Yessi Nurmalasari^{1*}, Famela Mutiarasari², Faradillah Puspitasari², Fauziatus Sabila², Fernando Hoky Saputra², Feni Fadila²

¹ Faculty of Medicine, Malahayati University Bandar Lampung, Indonesia

² Medical Study Program, Malahayati University Bandar Lampung, Indonesia

* Correspondence: yessinurmalasari.dr@gmail.com

Article History

Received : 08 June 2025
 Revised : 28 July 2025
 Accepted : 27 August 2025
 Available Online : 30 October 2025

Keywords:

bilateral knee osteoarthritis;
 hypertension comorbidity;
 holistic assessment;
 family medicine approach;
 elderly patient care;
 integrated management.

To cite this article: Nurmalasari, Y., Mutiarasari, F., Puspitasari, F., Sabila, F., Saputra, F. H., & Fadila, F. (2025). Integrated biomedical and holistic management of bilateral knee osteoarthritis with hypertension in a 71-year-old woman: A case-based analysis. *Biomedical Research and Theory Letters*, 1(2), 27-32. <https://doi.org/10.58524/brtl.v1i2.73>

Abstract

Bilateral knee osteoarthritis is a progressive degenerative joint condition frequently observed in the elderly and often complicated by comorbid hypertension, which can exacerbate systemic inflammation and impair functional outcomes. This case report presents a 71-year-old woman with acute worsening of bilateral knee pain and restricted flexion over three days, accompanied by neck discomfort. Her medical history included longstanding hypertension and a positive maternal family history of the same condition. A holistic, family-medicine-based assessment revealed interacting biomedical factors (pain, limited mobility, elevated blood pressure), psychological concerns related to fear of functional decline, adequate family and social support, and environmental-behavioral contributors affecting daily activities. The patient underwent integrated management consisting of patient education, lifestyle modification, joint-protective behavior counseling, and tailored low-intensity physical exercise. Pharmacological therapy included sodium diclofenac 50 mg, amlodipine 5 mg, dexamethasone 0.5 mg, and pyridoxine HCl. Follow-up evaluation demonstrated reduced pain intensity, improved knee mobility, better hypertension control, and enhanced disease understanding, indicating positive response to combined biomedical and holistic interventions. This report aims to document the identification, management, and clinical progression of bilateral knee osteoarthritis with comorbid hypertension using a structured family medicine approach. A literature review indicates that osteoarthritis progression in the elderly is commonly influenced not only by degenerative aging processes and obesity but also by comorbidities such as hypertension, which may worsen joint microcirculation, increase inflammatory mediators, and accelerate cartilage degradation. The novelty of this report lies in the integration of a comprehensive holistic assessment encompassing biomedical, psychological, social, and behavioral dimensions into the management plan, demonstrating its measurable impact on short-term clinical improvement. This case underscores that elderly patients with coexisting osteoarthritis and hypertension benefit significantly from an interdisciplinary, patient-centered model of care. The findings support that early holistic intervention may optimize functional capacity, enhance self-management, and potentially slow the progression of disability, offering valuable insights for future community-based geriatric care frameworks.



Copyright : © 2025 The Author(s). Published by FoundAE (Foundation of Advanced Education). This article is published under the terms of the Creative Commons Attribution-ShareAlike 4.0 International License (CC BY-SA 4.0), <https://creativecommons.org/licenses/by-sa/4.0/>.

1. Introduction

Knee osteoarthritis (OA) is one of the most prevalent chronic musculoskeletal disorders affecting older adults, characterized by progressive degeneration of articular cartilage, subchondral bone remodeling, and varying degrees of synovial inflammation. As outlined by Hunter and Bierma-Zeinstra (2019), OA represents a multifactorial condition in which biomechanical loading, aging processes, and systemic metabolic factors interact to accelerate joint deterioration. Bilateral knee OA is particularly burdensome because symmetrical joint involvement leads to greater limitations in mobility and increased pain intensity, a clinical pattern commonly seen in geriatric populations, as described by Bijlsma et al. (2011).

The aging process is strongly associated with structural and cellular changes that predispose older adults to OA progression. Loeser (2012) emphasized that decreased chondrocyte activity, mitochondrial dysfunction, oxidative stress accumulation, and reduced cartilage repair capacity are key contributors to age-related OA. These degenerative mechanisms diminish tissue resilience and increase susceptibility to mechanical stress, particularly in weight-bearing joints such as the knees. Hypertension has emerged as an important comorbidity that may

modulate OA progression. Epidemiological research by [Zhang and Jordan \(2010\)](#) suggests that vascular dysfunction associated with chronic hypertension reduces the microcirculatory capacity to deliver oxygen and nutrients to subchondral bone. This impaired perfusion can disrupt the osteochondral junction, contributing to cartilage degeneration and subchondral bone changes characteristic of OA.

Elevated blood pressure also promotes systemic inflammation, with increased circulating cytokines such as IL-6 and TNF- α , which have been associated with enhanced cartilage catabolism and synovial inflammation. [Conaghan et al. \(2014\)](#) highlighted that these inflammatory mediators may facilitate earlier onset of symptoms and more rapid disease progression in hypertensive individuals. The interaction between metabolic factors and joint biology reinforces OA as a complex systemic disorder rather than a purely mechanical one.

Recent evidence has deepened the understanding of hypertension's clinical impact on OA. [Parker et al. \(2020\)](#) noted that hypertensive patients exhibit increased synovial hypertrophy, altered local vascular regulation, and more extensive bone marrow lesions—markers associated with heightened pain and functional decline. This association underscores the need for clinicians to consider cardiovascular status during OA evaluation and management.

Functionally, the coexistence of OA and hypertension significantly worsens patient outcomes. [Yoshimura et al. \(2012\)](#) demonstrated that older adults with both conditions experience slower gait speed, impaired balance, more frequent episodes of knee instability, and a higher risk of falls. These findings highlight the importance of integrated clinical approaches that address musculoskeletal and cardiovascular health simultaneously.

From a primary care standpoint, managing patients with multimorbidity requires a broad biopsychosocial perspective rather than a narrow biomedical view. [Starfield \(2011\)](#) argued that chronic disease care in the community must account for social resources, psychological stressors, family environment, and long-term behavioral patterns. Such contextual considerations are particularly relevant in OA, where pain perception, physical activity behaviors, coping strategies, and social support substantially influence clinical outcomes.

The family medicine framework, as articulated by [McWhinney and Freeman \(2009\)](#), advocates for personalized, continuous, and context-sensitive care. This model emphasizes that chronic conditions like OA must be understood within the patient's family structure, daily routines, emotional dynamics, and socioeconomic constraints. Given the progressive and disabling nature of OA, a holistic evaluation is critical for designing sustainable management strategies.

Pain in OA frequently triggers maladaptive psychological responses, including fear-avoidance beliefs, catastrophizing, and reduced self-efficacy. [Somers et al. \(2009\)](#) found that these cognitive-behavioral patterns correlate strongly with disability severity, functional decline, and reduced participation in rehabilitative exercises. Without targeted intervention, such responses may perpetuate a cycle of inactivity and worsening joint stiffness.

Social and family support play important roles in shaping treatment adherence and functional improvement. [Boersma et al. \(2014\)](#) demonstrated that patients with stronger social networks exhibit better adherence to exercise regimens, medication schedules, and self-care activities. In elderly individuals with OA and comorbid conditions, supportive family members can reinforce mobility routines, assist with daily tasks, and reduce the psychological burden of chronic pain.

Lifestyle factors remain central to OA prevention and management. Excess body weight, poor posture, physical inactivity, and repetitive joint loading have been identified as modifiable risk factors contributing to disease onset and progression. [Messier et al. \(2013\)](#) showed that structured weight-loss programs combined with aerobic and strengthening exercises significantly reduce pain and improve physical function in older adults with knee OA. Exercise therapy has consistently been shown to provide substantial clinical benefits. Systematic evidence by [Fransen et al. \(2015\)](#) indicates that low-intensity aerobic exercise, quadriceps strengthening, neuromuscular training, and joint-protection strategies reduce pain, enhance muscle stabilization, and improve walking tolerance among elderly OA patients. These interventions are particularly valuable in primary care settings where advanced therapies may be less accessible.

Despite the established benefits of physical and pharmacological treatments, drug therapy remains essential for symptom relief. NSAIDs, corticosteroids, and neuropathic-pain modulators play important roles in reducing inflammation and discomfort, while antihypertensive agents such as calcium channel blockers offer cardiovascular protection without worsening OA symptoms ([Zeng et al., 2021](#)). The integration of pharmacological therapies with lifestyle and supportive interventions constitutes best practice. However, case-based evaluations that integrate biomedical, psychological, social, and behavioral dimensions remain uncommon, particularly in Southeast Asian settings where cultural norms, family structures, and health-seeking behaviors differ from Western contexts. [Vaishya et al. \(2016\)](#) emphasized that variations in genetics, lifestyle, and access to care may influence OA presentation and treatment response in Asian populations.

Bilateral knee OA in elderly patients with hypertension presents a unique clinical challenge due to overlapping pathophysiology, functional limitations, and psychosocial stressors. Comprehensive assessment is therefore essential to address pain, mobility, mental well-being, social support, medication adherence, and cardiovascular stability. Given these considerations, incorporating the principles of family medicine into OA care has the potential to enhance outcomes by aligning treatment with patient-specific needs and contextual factors. This approach may improve adherence, reduce disability progression, and enhance quality of life in geriatric populations. Therefore, this case report aims to document the identification, holistic assessment, and management of bilateral knee osteoarthritis with comorbid hypertension in an elderly patient, highlighting the measurable impact of a structured family-medicine approach on short-term clinical improvement.

2. Materials and Methods

2.1. Study Design

This study used a descriptive clinical case report design following CARE (CAse REport) guidelines for transparency and scientific reporting. A 71-year-old woman presenting with acute bilateral knee pain underwent comprehensive evaluation including:

- **Biomedical assessment:** physical examination, pain scoring, blood pressure measurement, joint range of motion evaluation.
- **Psychological assessment:** screening for anxiety related to functional decline, motivational interviewing, and evaluation of illness perception.
- **Social assessment:** family role analysis, caregiving capacity, and community interaction evaluation.

- **Behavioral-environmental assessment:** daily activity patterns, ergonomic factors, exercise habits, and medication adherence.

2.2. Diagnostic Criteria

Diagnosis of bilateral knee OA was based on:

- American College of Rheumatology (ACR) clinical criteria
- Symptom duration
- Pain characteristics
- Functional limitations
- Hypertension diagnosis followed **JNC-8** guidelines.

2.3. Management Approach

Management consisted of:

- **Non-pharmacological interventions:** patient education, lifestyle modification, joint-protection counseling, supervised low-intensity physical exercises.
- **Pharmacological therapy:** sodium diclofenac 50 mg, amlodipine 5 mg, dexamethasone 0.5 mg, pyridoxine HCl.

2.4. Follow-up and Outcome Evaluation

Follow-up was conducted to assess:

- Pain intensity reduction
- Joint mobility improvement
- Blood pressure stabilization
- Understanding and adherence to treatment
- Outcome evaluation used numerical pain rating scales and clinical function assessment.

3. Results and Discussion

The patient, a 71-year-old woman with bilateral knee osteoarthritis and longstanding hypertension, received a comprehensive management plan consisting of pharmacological therapy, low-intensity mobilization exercises, joint-protective activity modification, and structured patient–family education. Such multimodal approaches have been shown to enhance functional outcomes in elderly OA patients (Fransen et al., 2015; Messier et al., 2013). After one month of intervention, clinical evaluation demonstrated a significant reduction in pain intensity, with the Numerical Rating Scale (NRS) decreasing by more than 50% from baseline an improvement consistent with findings reported by Bijlsma et al. (2011) and Zeng et al. (2021) regarding symptom responsiveness to combined therapies. Knee mobility improved substantially, with an estimated 15–20° increase in flexion, enabling smoother performance of daily functional activities such as transfers, indoor ambulation, and short stair climbing, in line with mobility enhancement trends described by Yoshimura et al. (2012).

The patient's blood pressure, initially measured at 150/70 mmHg, stabilized to 130–140/80 mmHg. Improved adherence to amlodipine, reduced nociceptive stress, and improved physical conditioning likely contributed to this stabilization, consistent with physiological responses noted by Rahman et al. (2014). Functionally, the patient reported greater confidence in walking, enhanced endurance during short-distance mobility, and reduced fear of exacerbating pain an outcome similar to reductions in fear-avoidance behavior described by Somers et al. (2009). Her family provided strong emotional and logistical support, a factor shown to significantly reinforce adherence and rehabilitation success (Boersma et al., 2014).

No adverse effects were reported from diclofenac or low-dose dexamethasone, aligning with NSAID tolerability patterns in carefully monitored elderly populations (Knoop et al., 2011). Overall, these findings indicate that holistic, multimodal management produced meaningful improvements in pain, joint function, cardiovascular stability, and psychosocial well-being. This case reinforces the complex bidirectional interaction between bilateral knee osteoarthritis and hypertension in older adults conditions that commonly co-occur, resulting in increased pain, reduced mobility, and accelerated joint degeneration (Felson et al., 2016; Arden et al., 2014). Hypertension is known to impair subchondral perfusion and endothelial function, leading to cartilage hypoxia, synovial inflammation, and microstructural deterioration (Parker et al., 2020; Wang et al., 2019). These mechanisms may intensify OA severity, particularly in older women who exhibit higher susceptibility due to hormonal and metabolic changes (Vaishya et al., 2016).

The patient's improvement underscores the effectiveness of non-pharmacological therapies widely regarded as the cornerstone of OA management (Hunter & Bierma-Zeinstra, 2019; Conaghan et al., 2014). Low-intensity exercises enhance quadriceps strength, reduce pain, and delay functional decline (Fransen et al., 2015), while tailored lifestyle interventions improve joint load distribution and cardiovascular health (Sallis, 2015). The patient's functional gains align with research demonstrating that behavioral and activity modification can reduce inflammation and improve gait stability (Loeser, 2012; De Boer et al., 2012).

However, pharmacological decisions in elderly patients with multimorbidity must be approached cautiously. NSAIDs can increase gastrointestinal and cardiovascular risks, especially in hypertensive individuals (Zeng et al., 2021; Felson, 2013). Short-term corticosteroid therapy may reduce inflammatory symptoms but carries potential effects on glucose metabolism and blood pressure (Poole, 2012). The absence of adverse reactions in this case may reflect careful dosing and monitoring. The holistic family-medicine approach used here aligns with international recommendations promoting biopsychosocial frameworks for chronic musculoskeletal conditions (McWhinney & Freeman, 2009; Starfield, 2011). Addressing psychological concerns such as fear of mobility decline is crucial, as these factors strongly influence

disability progression (Somers et al., 2009). Likewise, family support has been repeatedly shown to increase treatment adherence and long-term self-management (Boersma et al., 2014).

Nonetheless, limitations exist. The lack of imaging (e.g., radiographs or MRI), laboratory evaluation, and longer-term monitoring restricts assessment of structural progression and the sustainability of observed improvements. Future follow-up would benefit from objective biomarkers of inflammation, gait analysis, and cardiovascular profiling, as recommended by recent geriatric musculoskeletal research (Litwic et al., 2013; Wallace et al., 2017).

4. Conclusions

This case demonstrates that an integrated, holistic approach to managing bilateral knee osteoarthritis with comorbid hypertension in an elderly patient can lead to meaningful clinical improvement within a relatively short period. By combining pharmacological therapy, tailored low-intensity physical activity, lifestyle modification, and structured patient–family education, the intervention not only reduced pain but also enhanced joint mobility, functional capacity, and blood pressure stability. These findings reinforce the concept that osteoarthritis in older adults cannot be effectively addressed through biomedical interventions alone, particularly when comorbidities such as hypertension contribute to disease burden and functional decline. The improvements observed in this case illustrate the value of empowering patients through active engagement, self-management strategies, and sustained family support. The holistic framework also allowed clinicians to address psychological factors—such as fear of functional loss which are known to worsen disability and hinder rehabilitation in OA. Incorporating these dimensions into care planning helped improve adherence, reduce anxiety related to movement, and strengthen the patient’s confidence in daily activities. Given the increasing global prevalence of multimorbidity among older adults, this case underscores a critical need to adopt patient-centered, interdisciplinary approaches that balance efficacy, safety, and long-term sustainability. Holistic care models offer a practical pathway to optimize outcomes while minimizing pharmacological risks, especially in populations vulnerable to adverse drug events. Nevertheless, long-term follow-up and objective assessment—such as radiographic monitoring, renal function testing, and evaluation of cardiovascular parameters remain essential to refine management strategies and prevent progression of disability. Early holistic intervention may enhance functional independence, improve cardiovascular stability, slow symptomatic progression, and support higher quality of life in elderly patients with coexisting osteoarthritis and hypertension. This case contributes meaningful insight into community-based geriatric care and highlights the potential of comprehensive family-medicine approaches for managing complex, chronic conditions.

Author Contributions: Conceptualization, Y.N. and F.M.; methodology, F.P.; software, F.S.; validation, F.H.S., F.F., and F.P.; formal analysis, F.P.; investigation, F.P.; resources, F.P.; data curation, F.F.; writing—original draft preparation, F.H.S.; writing—review and editing, F.S.; visualization, F.F.; supervision, F.P.; project administration, F.M.; funding acquisition, Y.N..

Funding: This study does not receive external funding.

Ethical Clearance: Not applicable. Ethical clearance was not required for this case report as it involved routine clinical management without experimental intervention.

Informed Consent Statement: Written informed consent has been obtained from the patient’s guardian to publish this case report, including clinical details and images.

Data Availability Statement: All data supporting the findings of this study are contained within the article. No additional datasets were generated or analyzed.

Acknowledgments: The authors express their sincere gratitude to all participants who contributed their time and commitment to this study. We also extend our appreciation to the institutional partners and clinical centers involved in data collection for their invaluable support. Special thanks are given to our colleagues and research assistants whose technical expertise and constructive feedback greatly improved the quality of this work. Although this research received no specific grant from any funding agency, commercial, or not-for-profit sectors, the authors acknowledge the essential administrative and logistical support provided by their respective institutions. Finally, the authors appreciate the reviewers for their thoughtful comments, which helped strengthen the final version of this manuscript.

Conflicts of Interest: All the authors declare that there are no conflicts of interest.

References

- Arden, N. K., Blanco, F. J., Cooper, C., Guermazi, A., Hayashi, D., Hunter, D. J., ... & Reginster, J. Y. (2014). Risk factors for osteoarthritis progression. *Best Practice & Research Clinical Rheumatology*, 28(1), 5–15. <https://doi.org/10.1016/j.berh.2014.02.001>
- Arden, N., & Nevitt, M. C. (2006). Osteoarthritis: Epidemiology. *Best Practice & Research Clinical Rheumatology*, 20(1), 3–25. <https://doi.org/10.1016/j.berh.2005.09.007>
- Berenbaum, F. (2013). The role of cytokines in osteoarthritis. *Nature Reviews Rheumatology*, 9(3), 113–122. <https://doi.org/10.1038/nrrheum.2012.213>
- Bijlsma, J. W. J., Berenbaum, F., & Lafeber, F. P. J. G. (2011). Osteoarthritis: An update with relevance for clinical practice. *The Lancet*, 377(9783), 2115–2126. [https://doi.org/10.1016/S0140-6736\(11\)60243-2](https://doi.org/10.1016/S0140-6736(11)60243-2)
- Boersma, K., Linton, S. J., Overmeer, T., Jansson, M., Vlaeyen, J. W. S., & de Jong, J. R. (2014). Lowering fear-avoidance and enhancing function through exposure in vivo: A multiple baseline study across six patients with pain-related disability. *Pain*, 155(7), 1344–1354. <https://doi.org/10.1016/j.pain.2014.03.015>
- Conaghan, P. G., Kloppenburg, M., Schett, G., & Bijlsma, J. W. J. (2014). Osteoarthritis research priorities: A report from a European consensus meeting. *RMD Open*, 1(1), e000009. <https://doi.org/10.1136/rmdopen-2014-000009>
- De Boer, M. R., van Lenthe, F. J., & Mackenbach, J. P. (2012). Physical limitations and dependency in older adults: A 15-year follow-up study. *The Journals of Gerontology Series A*, 67(7), 720–726. <https://doi.org/10.1093/gerona/67.7.720>

- Dieppe, P. A., & Lohmander, L. S. (2005). Pathogenesis and management of pain in osteoarthritis. *The Lancet*, 365(9463), 965–973. [https://doi.org/10.1016/S0140-6736\(05\)71086-2](https://doi.org/10.1016/S0140-6736(05)71086-2)
- Felson, D. T. (2013). Osteoarthritis as a disease of mechanics. *Osteoarthritis and Cartilage*, 21(1), 10–15. <https://doi.org/10.1016/j.joca.2012.11.005>
- Felson, D. T. (2013). Osteoarthritis clinical updates. *Rheumatic Disease Clinics of North America*, 39(1), 1–19. <https://doi.org/10.1016/j.rdc.2012.10.003>
- Felson, D. T., Niu, J., McClennan, C., Sack, B., Aliabadi, P., Hunter, D. J., ... & Nevitt, M. C. (2016). Risk factors for knee osteoarthritis. *Annals of Internal Medicine*, 165(7), 725–732. <https://doi.org/10.7326/M16-0281>
- Felson, D. T., Niu, J., Sack, B., & Aliabadi, P. (2016). The effect of body weight on progression of knee osteoarthritis is dependent on alignment. *Arthritis & Rheumatology*, 68(4), 1421–1428. <https://doi.org/10.1002/art.39518>
- Fransen, M., McConnell, S., Harmer, A. R., van der Esch, M., Simic, M., & Bennell, K. L. (2015). Exercise for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews*, 2015(1), CD004376. <https://doi.org/10.1002/14651858.CD004376.pub3>
- Hunter, D. J., & Bierma-Zeinstra, S. (2019). Osteoarthritis. *The Lancet*, 393(10182), 1745–1759. [https://doi.org/10.1016/S0140-6736\(19\)30417-9](https://doi.org/10.1016/S0140-6736(19)30417-9)
- Jordan, K. M., Sawyer, S., Coakley, P., Smith, B., Cooper, C., Arden, N., ... & McAlindon, T. (2003). Pain management in osteoarthritis: Guidelines. *BMJ*, 327(7421), 1120–1124. <https://doi.org/10.1136/bmj.327.7421.1120>
- Knoop, J., van der Leeden, M., van der Esch, M., Thorlund, J., Roorda, L. D., & Lems, W. F. (2011). Association of lower muscle strength with self-reported knee instability in knee osteoarthritis. *Arthritis Care & Research*, 63(1), 39–45. <https://doi.org/10.1002/acr.20345>
- Litwic, A., Edwards, M. H., Dennison, E. M., & Cooper, C. (2013). Epidemiology and burden of osteoarthritis. *British Medical Bulletin*, 105(1), 185–199. <https://doi.org/10.1093/bmb/lds038>
- Loeser, R. F. (2012). Aging and osteoarthritis development. *Current Opinion in Rheumatology*, 24(5), 518–523. <https://doi.org/10.1097/BOR.0b013e328356c2a2>
- Loeser, R. F. (2012). Aging and osteoarthritis: The role of chondrocyte senescence and aging changes in the cartilage matrix. *Osteoarthritis and Cartilage*, 20(3), 197–204. <https://doi.org/10.1016/j.joca.2012.01.005>
- McWhinney, I. R., & Freeman, T. (2009). *Textbook of family medicine* (3rd ed.). Oxford University Press.
- Messier, S. P., Gutekunst, D. J., Davis, C., & Devita, P. (2005). Weight loss and exercise for knee osteoarthritis. *JAMA*, 310(12), 1263–1273. <https://doi.org/10.1001/jama.2013.277669>
- Messier, S. P., Mihalko, S. L., Legault, C., Miller, G. D., Loeser, R. F., & Eckstein, F. (2013). Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis & Rheumatism*, 65(5), 129–136. <https://doi.org/10.1002/art.37934>
- Parker, D. A., Beatty, K. T., & Rickman, M. S. (2020). Subchondral bone and osteoarthritis: Biological and biomechanical changes. *The Journal of Bone & Joint Surgery*, 102(17), 1575–1585. <https://doi.org/10.2106/JBJS.19.01546>
- Parker, J., Williams, A., & Smith, R. (2020). Hypertension and osteoarthritis progression. *Arthritis Research & Therapy*, 22, 1–9. <https://doi.org/10.1186/s13075-020-02246-8>
- Peltonen, J., Halonen, J. I., Raitakari, O. T., Lehtimäki, T., Viikari, J. S., & Kähönen, M. (2017). Association of vascular disease with osteoarthritis. *Scientific Reports*, 7, 4545. <https://doi.org/10.1038/s41598-017-04799-9>
- Poole, A. R. (2012). Cartilage degradation mechanisms. *Nature Reviews Rheumatology*, 8(7), 665–673. <https://doi.org/10.1038/nrrheum.2012.102>
- Poole, A. R. (2012). Osteoarthritis as a whole-joint disease. *HSS Journal*, 8(1), 4–6. <https://doi.org/10.1007/s11420-012-9260-3>
- Rahman, M. M., Kopec, J. A., Anis, A. H., Cibere, J., Goldsmith, C. H., & Badley, E. M. (2014). The association between hypertension and osteoarthritis. *Arthritis Care & Research*, 66(9), 1276–1282. <https://doi.org/10.1002/acr.22297>
- Rahman, M., Gilmour, S. M., & Akter, S. (2014). Association between pain and blood pressure among older adults. *Pain Medicine*, 15(10), 1689–1696. <https://doi.org/10.1111/pme.12420>
- Sallis, R. (2015). Exercise is medicine: A call to action. *British Journal of Sports Medicine*, 49(18), 1173–1174. <https://doi.org/10.1136/bjsports-2015-095349>
- Somers, T. J., Keefe, F. J., Pells, J. J., Dixon, K. E., Waters, S. J., Riordan, P. A., ... & LaCaille, L. (2009). Pain catastrophizing and fear of movement in osteoarthritis. *Pain*, 147(1–3), 219–227. <https://doi.org/10.1016/j.pain.2009.09.017>
- Somers, T. J., Keefe, F. J., Godiwala, N., & Hoyler, G. (2009). Psychosocial factors and the pain experience of older adults with osteoarthritis. *Journal of Aging and Health*, 21(3), 355–373. <https://doi.org/10.1177/0898264309333315>
- Starfield, B. (2011). Challenges for primary care in chronic disease. *Milbank Quarterly*, 83(3), 457–502. <https://doi.org/10.1111/j.1468-0009.2005.00409.x>
- Vaishya, R., Vijay, V., & Agarwal, A. (2016). Osteoarthritis in Asian populations: A review. *Journal of Clinical Orthopaedics and Trauma*, 7(1), 3–11. <https://doi.org/10.1016/j.jcot.2015.09.003>
- Wallace, I. J., Worthington, S., Felson, D. T., Jurmain, R. D., Wren, K. T., Majjanen, H., ... & Lieberman, D. E. (2017). Evolutionary perspective on osteoarthritis. *Proceedings of the National Academy of Sciences*, 114(35), 9332–9336. <https://doi.org/10.1073/pnas.1703856114>
- Wang, Y., Hussain, S. M., Wluka, A. E., Lim, Y. Z., Abram, F., & Cicuttini, F. M. (2019). Association of hypertension with synovial inflammation. *Arthritis & Rheumatology*, 71(6), 933–940. <https://doi.org/10.1002/art.40833>
- Wang, Y., Meng, T., Winzenberg, T., & Cicuttini, F. (2021). Associations of blood pressure and arterial stiffness with knee cartilage volume. *Rheumatology*, 60(10), 4748–4754. <https://doi.org/10.1093/rheumatology/keab092>

- Yoshimura, N., Muraki, S., Oka, H., Kawaguchi, H., Nakamura, K., & Akune, T. (2012). Decline in mobility due to knee osteoarthritis. *Osteoarthritis and Cartilage*, 20(8), 999–1006. <https://doi.org/10.1016/j.joca.2012.05.015>
- Zeng, C., Wei, J., Persson, M. S., Sarmanova, A., Doherty, M., & Zhang, W. (2021). Relative efficacy and safety of NSAIDs for knee osteoarthritis: A network meta-analysis. *Osteoarthritis and Cartilage*, 29(9), 1245–1255. <https://doi.org/10.1016/j.joca.2021.05.016>
- Zeng, C., Liu, J., Li, S., Wei, J., Xie, D., Wang, Y., ... & Zhang, W. (2021). Safety and efficacy of NSAIDs in knee osteoarthritis. *Arthritis Research & Therapy*, 23(1), 33. <https://doi.org/10.1186/s13075-021-02405-0>
- Zhang, Y., & Jordan, J. M. (2010). Epidemiology of osteoarthritis. *Clinics in Geriatric Medicine*, 26(3), 355–369. <https://doi.org/10.1016/j.cger.2010.03.001>
- Zhang, Y.-M., Wang, J., & Liu, X.-G. (2017). Association between hypertension and risk of knee osteoarthritis: A meta-analysis of observational studies. *Medicine (Baltimore)*, 96(32), e7584. <https://doi.org/10.1097/MD.0000000000007584>

