

Original Research Paper

Relationship between body mass index (BMI), stage of knee osteoarthritis, and pain severity

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Abstract

The prevalence of knee osteoarthritis has increased significantly over recent decades. Osteoarthritis causes pain, swelling, stiffness, loss of function, and decreased quality of life (QoL). Although evidence suggests that increased BMI contributes to both the development and severity of knee OA, research examining the relationship between BMI, OA stage, and the degree of knee pain remains limited, highlighting the need for further investigation. This study aims to determine the relationship between BMI, the stage of knee osteoarthritis, and the degree of pain in patients with knee OA. This research is an analytical observational study with a cross-sectional design, utilizing secondary data (patient medical records). We conducted sample selection using purposive sampling. Data analysis: descriptive analysis, Chi-Square test, and logistic regression. A total of 101 respondents participated in the study, with the majority had a normal BMI (52.5%), had mild-to-moderate knee OA (56.4%), and reported mild pain (52.5%). There was a significant relationship between BMI and the stage of knee osteoarthritis with the degree of pain (p-value <0.05), with odds ratios (OR) for BMI and OA stage at 3.93 and 3.96, respectively. This indicates that higher BMI and more advanced OA stage are associated with a greater degree of knee pain in patients. Weight loss is an effective strategy to reduce mechanical stress on joints and decrease inflammatory mediators, thereby lowering chronic inflammation and alleviating pain. Further research on effective management strategies for knee OA is essential to help reduce the disease burden and improve the QoL of knee OA patients.

Keywords: body mass index; genu osteoarthritis; knee osteoarthritis; level of pain; stage of knee OA

1. Introduction

Osteoarthritis (OA) is a condition characterized by tissue damage to the cartilage that lines the bones, causing the bones to frequently come into direct contact during movement. Osteoarthritis mainly attacks joint cartilage, causing pain, swelling, stiffness and even loss of function that has the potential to cause disability (Cai *et al.*, 2021; Hunter & Bierma-Zeinstra, 2019; Jang *et al.*, 2021) and a decline in quality of life (Kawano *et al.*, 2015; Mahir *et al.*, 2016; Shalhoub *et al.*, 2022). Osteoarthritis can affect small, medium, and large joints. However, the joints that feel the most pain are the joints that bear the weight of the body such as the hands, spine in the lower lumbar, pelvis, and knees. The knee is the joint most susceptible to osteoarthritis (OA) (Smith *et al.*, 2021). The prevalence of knee OA has significantly increased over the decades due to factors such as aging, obesity and other risk factors (Cui *et al.*, 2020; Palazzo *et al.*, 2016). In 2020, global prevalence estimates for knee OA were approximately 16% in individuals over 15 years and 22.9% in those over 40 years (Cui *et al.*, 2020). Knee osteoarthritis, also known as osteoarthritis genu, generally affects women over 60 years old, with a prevalence of 13% in women and 10% in men (Primorac *et al.*, 2020).

Overweight and obesity are significant risk factors for knee OA, influencing both its development and severity. Overweight and obesity are classified based on BMI. Being overweight adds extra stress to the joints that hold the weight of the body. The results of systematic reviews and meta-analyses reported that overweight and obesity increased the risk of knee OA by about 2.5 times and 4.6 times, respectively (Zheng & Chen, 2015).



According to D'Amen *et al.* (2021), joint pain, limitations in a person's ability to perform activities, and signs of inflammation are symptoms of osteoarthritis (OA). Pain in osteoarthritis is one of a person's responses to show that tissue damage will occur, especially in the joints. Pain is the cause of decreased functional activity in individuals who experience OA. Pain in OA, especially in the knee joint, develops slowly and gradually. The degree of pain is objective and certainly different for each patient. There are several ways to assess the degree of pain in OA patients such as the Visual Analog Scale (VAS)/Numeric Rating Scale (NRS) and WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index). The use of NRS is easier to use than WOMAC because it can easily interpret the results while for WOMAC it is sometimes difficult to interpret the results (Tiofunda & Friska, 2020).

Although evidence suggests that increased BMI contributes to both the development and severity of knee OA (Park *et al.*, 2023; Samma *et al.*, 2021; Shumnalieva *et al.*, 2023; Zheng & Chen, 2015), research examining the relationship between BMI, OA stage and the degree of knee pain remains limited, more research is needed to evaluate the specific relationship between the three factors. It is important to develop more effective prevention and treatment strategies for patients with knee OA. This study aims to determine the relationship between BMI and knee osteoarthritis stage and the degree of pain of knee osteoarthritis patients.

2. Research Methods

This research is an analytical observational study with a cross-sectional design. The research was conducted at the Dr. Soeharso Orthopedic Hospital Surakarta. The study utilized secondary data from patient medical records (RM) of knee OA patients, which included information on name, gender, BMI, stage of knee OA, degree of pain in knee OA, and coexisting conditions. The sampling technique used is purposive sampling with following inclusion criteria: patients diagnosed with unilateral genotype osteoarthritis who have undergone a radiological examination and received radiology readings. Meanwhile, the exclusion criteria include patients with knee/genu osteoarthritis who have fractures or dislocations evident in x-ray images, patients with osteomyelitis, and patients with incomplete data. The sample in this study consists of 101 respondents.

BMI data is obtained from BMI calculation based on weight and height recorded in the medical records. The body mass index is categorized into two groups : normal BMI (<25kg/m²) and abnormal (≥25 kg/m²). The assessment of knee OA stages is conducted by interpreting the radiological data in the medical records. The stages of knee OA are categorized as light-moderate (1-2), characterized by the presence of a few osteophytes and osteophytes in two locations within one joint, and severe (3-4), indicated by moderate to numerous osteophytes with no joint gaps. The degree of knee OA pain is assessed using the Visual Analog Scale (VAS) which has been recorded in the medical records. OA pain is categorized into two levels: mild (1-3) and severe (7-10). Data analysis used was univariate analysis (descriptive analysis), bivariate analysis (Chi-Square test) and multivariate analysis (logistic regression). This research has undergone an ethical review process by the Health Research Ethics Commission (KEPK) of Moewardi Hospital with the number: 1860 / X / HREC / 2023.

3. Results and Discussion

3.1.Characteristics of Respondents

Almost three-quarters of the respondents in the study were female (72.3%), with the majority falling into the late elderly group (56-65 years old) (77.2%). Hypertension is the most common comorbidity among respondents (66.3%). More than half of the respondents (52.5%) had a normal BMI (<25kg/m²). The majority of respondents exhibited mild-moderate knee OA (stages 1-2), and reported mild pain (1-3) at rates of 56.4% and 52.5%, respectively. The complete characteristics of the respondents are presented in Table 1 below.

Table 1. Characteristics of Respondents

Variable	Frequency (n)	Percentage (%)
Gender		
Male	28	27.7
Female	73	72.3
Total	101	100
Age		
Early elderly (46-55th)	23	22.8
Late elderly (56-65th)	78	77.2
Total	101	100
Comorbidities		
Diabetes	21	20.8
Kidney problems	4	4.0
Heart problems	9	8.9
Hypertension	67	66.3
Total	101	100
BMI		
Normal (<25kg/m ²)	53	52.5
Abnormal (≥25 kg/m ²)	48	47.5
Total	101	100
Stage of Knee OA		
Mild – Moderate (1-2)	57	56.4
Severe (3-4)	44	43.6
Total	101	100
Degree of pain		
Mild (1-3)	53	52.5
Severe (7-10)	48	47.5
Total	101	100

The majority of respondents in this study were female (72.3%). [Graham *et al.* \(2023\)](#) reported that from 2001 to 2018, there was a decrease in the percentage of knee osteoarthritis (OA) in women by 4.5% (from 65.3% to 60.8%). However, overall, knee OA patients were predominantly women. Meanwhile, in men, the percentage of knee OA has significantly increased by 4.6% over the last three decades (from 34.6% to 39.2%). Women are at greater risk of developing knee OA than men, which is influenced by a combination of hormonal, biological, genetic, and lifestyle factors ([Segal *et al.*, 2024](#); [Szilagy *et al.*, 2022](#)). Hormonal factors play an important role in the development of knee osteoarthritis (OA) in women, especially during and after menopause. Decreased estrogen levels are the main factors affecting the increased prevalence and severity of OA among postmenopausal women ([Dennison, 2022](#); [Mei *et al.*, 2022](#)).

Knee osteoarthritis generally occurs after age 40 ([Dong *et al.*, 2023](#)) and significantly increases the risk of knee OA at age 50 ([Ackerman *et al.*, 2017](#)). In this study, we found that more than three-quarters (77.2%) of the respondents belonged to the late elderly group (ages 56-65). Although knee OA is more prevalent among the elderly, younger individuals can also be affected. A cohort-prospective study conducted by [Graham *et al.* \(2023\)](#) reported a 16.5% increase in knee OA cases among patients aged 18-44 years from 2001-2018. According to [Ackerman *et al.* \(2017\)](#), injuries and obesity contribute to the rising prevalence of knee OA in younger populations. Additionally, an unhealthy diet – characterized by high consumption of processed foods rich in sugar, salt, and fat, and low in fiber ([Canhada *et al.*, 2020](#); [Gomes *et al.*, 2022](#); [Hall *et al.*, 2019](#); [Machado *et al.*, 2020](#); [Nardocci *et al.*,](#)

2019) – and lack of physical activity (Guddal *et al.*, 2020; Kurdaningsih *et al.*, 2016; Suza *et al.*, 2020) are also contributing factors to the increase in obesity among younger individuals.

Some studies have confirmed that obesity is a risk factor for knee OA (Reyes *et al.*, 2016; Salis & Sainsbury, 2023; L. Zhang *et al.*, 2023). Compared to populations with a normal BMI, obesity increases the risk of knee OA by 2.5 to 4.6 times, with each increase in BMI of 5 kg/m² corresponding to a 35% increase in the risk of knee OA (Zheng & Chen, 2015). According to Thijssen *et al.* (2015), the load on the knee joint increases with weight gain, leading to cartilage damage, which is a major contributor to the high-incidence of knee OA. Additionally, metabolic disorders and inflammatory responses associated with obesity are also believed to play a role in the development of OA (Han *et al.*, 2019).

Osteoarthritis often occurs alongside various comorbidities, especially among older adults. The prevalence and impact of these comorbidities are significant, as they can worsen the symptoms and functional limitations associated with OA. We found that more than two-thirds of respondents (67%) had hypertension, followed by diabetes (20.8%), heart disorders (8.9%), and kidney disorders (4%). The results align with previous studies indicating that 54.6% of OA patients have at least one comorbidity (Marshall *et al.*, 2019). Marshall *et al.* (2019) also identified hypertension, depression, and chronic obstructive pulmonary disease (COPD) as the most common comorbidities among OA patients, with 40% of OA patients experiencing a combination of these conditions.

3.2. The Relationship between BMI, Stage of knee OA, and Degree of Mild Knee OA Pain

Based on Table 2, it is evident that 77.3% of respondents with normal BMI reported mild knee OA pain. In contrast, 60.4% of respondents with an abnormal BMI experienced severe pain. The results of the Chi-Square test indicated a significant relationship between BMI and the degree of pain in knee osteoarthritis patients (p-value 0.001, which is less than 0.05). These findings are consistent with a previous study by Raud *et al.* (2020), which reported that higher BMI values were associated with higher pain scores. Additionally, Landsmeer *et al.* (2018) reported that a high BMI contributes directly to the development and severity of patellofemoral pain, as well as to cartilage defects and the development of synovitis, by 62% and 18%, respectively.

Table 2. The Relationship between BMI, Stage of Knee OA, and Degree of knee OA Pain

	Degree of Knee OA pain				Total		p-Value
	Mild		Severe		n	%	
	n	%	n	%			
BMI							
Normal	41	77.3	12	22.7	53	100	0.001
Abnormal	12	25	36	60.4	75	100	
Stage of Knee OA degree							
Mild – Moderate	43	75.3	14	24.7	57	100	0.000
Severe	10	22.7	34	77.2	44	100	

An increase in BMI leads to a reduction in the mass of the intrapatellar fat pad (IFP). The decrease in IFP occurs due to changes in adipocyte size, which decreases the regulation of adipogenesis in the IFP and leads to an inflammatory process in the joints, resulting in increased joint pain (Berenbaum *et al.*, 2017). An increase in BMI is also correlated with the severity of knee OA (Brasnjevic, 2016; Mutiwara, 2016). Mutiwara (2016) research stated that an increase in BMI causes the risk of joint damage in individuals suffering from knee osteoarthritis, triggering pain stimulation.

It is found that 75.3% of respondents with mild-moderate stage OA had mild pain, while over three-quarters (77.2%) of respondents with severe knee OA experienced severe pain as well. The results of

bivariate analysis showed that there was a significant relationship between the stage of OA and the degree of pain in knee OA patients (p -value $0.00 < 0.05$). Previous results showed similar findings that an increase in the severity of knee OA was positively correlated with an increase in knee pain (Weiss, 2014). According to Wang *et al.* (2017), the enlargement of subchondral bones and the formation of osteophytes cause the gaps in the joints to narrow and the nerves to become depressed, which has an impact on the onset of pain. The process starts from proteolysis which causes the thinning of cartilage, then fibrosis occurs accompanied by the release of proteoglycan so that collagen breaks into the synovial fluid causing an inflammatory response in the synovial which stimulates the production of macrophages so that this condition causes pain stimulation in the cartilage.

Table 3 below explains that there is a significant relationship between BMI and stage of knee OA with pain degree in patients with knee osteoarthritis (p -value, which is less than 0.05). The higher the BMI and stage of knee OA, the more severe the degree of pain felt by knee OA patients. The value of the determination coefficient or R square in this study is 0.377. This figure means that Body Mass Index (BMI) and the stage of knee OA have a joint influence on the variable of pain degree in knee OA patients by 37.7%.

Table 3. Multivariate Analysis

Variable	coefficient	P Value	Exp (B)	Negelkerke R Square
BMI	1.370	0.032	3.935	
OA stage	1.377	0.032	3.963	0.377

The odds ratio (OR) value for the relationship between BMI and pain severity in this study was 3.93. This explains that individuals with a high BMI are 3.93 times more likely to experience more severe pain compared to those with a normal BMI. These results reported a significant positive association between obesity (in this case measured through BMI) and the degree of knee OA pain. Almost similar to this study, a study on BMI and pain degree with knee OA stage reported that there was a significant relationship between BMI and knee OA stage, as well as pain degree and knee OA stage (Samma *et al.*, 2021). The findings confirm that as BMI increases, the stage of knee OA becomes higher. In addition, a higher stage of knee OA is associated with a higher degree of pain.

Some previous literature mentioned that an increase in BMI (obesity) can lead to increase pain in knee OA patients. Obesity causes increased pressure on joints, especially weight-bearing joints such as knees. Any increase in BMI can increase the risk of knee OA by 35% (Zheng & Chen, 2015). This additional load causes damage to cartilage and other joint structures, which contributes to the development of pain. An increase in BMI also increases the occurrence of inflammation in OA (T. Wang & He, 2018). An increase in BMI can lead to changes in adipose tissue, including increased production of pro-inflammatory cytokines such as leptin, TNF- α , IL-6, and IL-1 β . Increased levels of these cytokines can trigger and worsen inflammatory processes in the joints, which contribute to pain (Darbandi *et al.*, 2023).

Meanwhile, the odds ratio (OR) for the relationship between the stage of knee OA and the degree of pain in this study was 3.96. This explains that individuals with severe knee OA are 3.96 times more likely to experience severe pain compared to those with stage mild to moderate OA. These results reported a significant positive relationship between the stage of knee OA and the degree of knee OA pain. The results of the study by Weiss (2014) show similar results. The results of the ANCOVA double regression showed that although the severity of OA was taken into account, subjects with a higher BMI reported more pain than subjects with a lower BMI (Weiss, 2014). Severe knee osteoarthritis causes narrowing of joint gaps, large additional bone growth (osteophytes), increased bone hardness (bone sclerosis), and the occurrence of bone deformities. This supports that OA with severe stages causes an increase in the degree of pain in the knee joint. Community-based studies stated that approximately

40% to 80% of OA patients who were detected severely radiographically had a correlation with increased pain intensity (Lakkireddy, 2015).

Losing weight will be the most effective strategy to reduce mechanical stress on the joints and lower inflammatory mediators, which in turn helps decrease chronic inflammation (Bartels *et al.*, 2014). People with a high BMI are more likely to develop metabolic syndrome, which is characterized by the occurrence of several risk factors simultaneously (such as hypertension and high cholesterol), type 2 diabetes, or coronary heart disease (Dickson *et al.*, 2019; Rahmawati *et al.*, 2024; Ying *et al.*, 2022; S. Zhang *et al.*, 2024). Chronic lesions are affected by microinflammation (contributing to the onset and continuation of knee OA correlated with insulin resistance levels) (Duclos, 2016) and insulin resistance (related to location and percentage of fat mass) (Lalia *et al.*, 2016). Reducing fat mass can be a key factor in lowering micro-inflammation and the clinical impact of knee OA.

4. Conclusion

There is a significant relationship between BMI and the stage of knee osteoarthritis, as well as the degree of pain experienced by patients. Higher BMI and more advanced stages of knee OA are associated with greater levels of pain. Specifically, individuals with a high BMI are 3.93 times more likely to experience severe pain compared to those with a normal BMI. Additionally, individuals with severe knee OA are 3.96 times more likely to experience more severe pain compared to those with mild to moderate OA. Weight loss is an effective strategy to reduce mechanical stress on the joints and lower inflammatory mediators, which in turn can decrease chronic inflammation and pain. Further research on effective management strategies for knee OA is needed to alleviate the disease burden and improve the quality of life for patients.

Reference

- Ackerman, I. N., Kemp, J. L., Crossley, K. M., Culvenor, A. G., & Hinman, R. S. (2017). Hip and Knee Osteoarthritis Affects Younger People, Too. *Journal of Orthopaedic & Sports Physical Therapy*, 47(2), 67–79. <https://doi.org/10.2519/jospt.2017.7286>
- Bartels, E. M., Christensen, R., Christensen, P., Henriksen, M., Bennett, A., Gudbergesen, H., Boesen, M., & Bliddal, H. (2014). Effect of a 16 weeks weight loss program on osteoarthritis biomarkers in obese patients with knee osteoarthritis: A prospective cohort study. *Osteoarthritis and Cartilage*, 22(11), 1817–1825. <https://doi.org/10.1016/j.joca.2014.07.027>
- Berenbaum, F., Griffin, T. M., & Liu-Bryan, R. (2017). Metabolic Regulation of Inflammation in Osteoarthritis. *Arthritis & Rheumatology* (Hoboken, N.J.), 69(1), 9–21. <https://doi.org/10.1002/art.39842>
- Brasnjevic. (2016). Association of Body Mass Index and Waist Circumference With Severity of Knee Osteoarthritis. *Acta Reumatologica Portuguesa*, 3(2), 1–18.
- Cai, X., Yuan, S., Zeng, Y., Wang, C., Yu, N., & Ding, C. (2021). New Trends in Pharmacological Treatments for Osteoarthritis. *Frontiers in Pharmacology*, 12, 645842. <https://doi.org/10.3389/fphar.2021.645842>
- Canhada, S. L., Luft, V. C., Giatti, L., Duncan, B. B., Chor, D., Fonseca, M. de J. M. da, Matos, S. M. A., Molina, M. D. C. B., Barreto, S. M., Levy, R. B., & Schmidt, M. I. (2020). Ultra-processed foods, incident overweight and obesity, and longitudinal changes in weight and waist circumference: The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *Public Health Nutrition*, 23(6), 1076–1086. <https://doi.org/10.1017/S1368980019002854>
- Cui, A., Li, H., Wang, D., Zhong, J., Chen, Y., & Lu, H. (2020). Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *eClinicalMedicine*, 29. <https://doi.org/10.1016/j.eclinm.2020.100587>

- D'Amen, B., Socci, M., & Santini, S. (2021). Intergenerational caring: A systematic literature review on young and young adult caregivers of older people. *BMC Geriatrics*, 21(105), 1–17.
- Darbandi, M., Shadmani, F. K., Miryan, M., Ghalandari, M., Mohebi, M., Jam, S. A., & Pasdar, Y. (2023). The burden of osteoarthritis due to high Body Mass Index in Iran from 1990 to 2019. *Scientific Reports*, 13(1), 11710. <https://doi.org/10.1038/s41598-023-37780-z>
- Dennison, E. M. (2022). Osteoarthritis: The importance of hormonal status in midlife women. *Maturitas*, 165, 8–11. <https://doi.org/10.1016/j.maturitas.2022.07.002>
- Dickson, B. M., Roelofs, A. J., Rochford, J. J., Wilson, H. M., & De Bari, C. (2019). The burden of metabolic syndrome on osteoarthritic joints. *Arthritis Research & Therapy*, 21(1), 289. <https://doi.org/10.1186/s13075-019-2081-x>
- Dong, Y., Yan, Y., Zhou, J., Zhou, Q., & Wei, H. (2023). Evidence on risk factors for knee osteoarthritis in middle-older aged: A systematic review and meta analysis. *Journal of Orthopaedic Surgery and Research*, 18, 634. <https://doi.org/10.1186/s13018-023-04089-6>
- Duclos, M. (2016). Osteoarthritis, obesity and type 2 diabetes: The weight of waist circumference. *Annals of Physical and Rehabilitation Medicine*, 59(3), 157–160. <https://doi.org/10.1016/j.rehab.2016.04.002>
- Gomes, C. S., Mendes, L. L., Vieira, M. A., Costa, M. A., & Melendez, G. V. (2022). Spatial distribution of sedentary behavior and unhealthy eating habits in Belo Horizonte, Brazil: The role of the neighborhood environment. *Ciencia & Saude Coletiva*, 27(4), 1503–1512. <https://doi.org/10.1590/1413-81232022274.47232020>
- Graham, J., Novosat, T., Sun, H., Piper, B. J., Boscarino, J. A., Kern, M. S., Hayduk, V. A., Beck, C., Robinson, R. L., Casey, E., Hall, J., Dorling, P., & Wright, E. (2023). Medication use and comorbidities in an increasingly younger osteoarthritis population: An 18-year retrospective open-cohort study. *BMJ Open*, 13(5), e067211. <https://doi.org/10.1136/bmjopen-2022-067211>
- Guddal, M. H., Stensland, S. Ø., Småstuen, M. C., Johnsen, M. B., Heuch, I., Zwart, J.-A., & Storheim, K. (2020). Obesity in Young Adulthood: The Role of Physical Activity Level, Musculoskeletal Pain, and Psychological Distress in Adolescence (The HUNT-Study). *International Journal of Environmental Research and Public Health*, 17(12), 4603. <https://doi.org/10.3390/ijerph17124603>
- Hall, K. D., Ayuketah, A., Brychta, R., Cai, H., Cassimatis, T., Chen, K. Y., Chung, S. T., Costa, E., Courville, A., Darcey, V., Fletcher, L. A., Forde, C. G., Gharib, A. M., Guo, J., Howard, R., Joseph, P. V., McGehee, S., Ouwerkerk, R., Raising, K., ... Zhou, M. (2019). Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. *Cell Metabolism*, 30(1), 67–77.e3. <https://doi.org/10.1016/j.cmet.2019.05.008>
- Han, W., Aitken, D., Zheng, S., Wang, B., Wluka, A. E., Zhu, Z., Blizzard, L., Wang, X., Winzenberg, T., Cicuttini, F., Jones, G., & Ding, C. (2019). Higher Serum Levels of Resistin Are Associated With Knee Synovitis and Structural Abnormalities in Patients With Symptomatic Knee Osteoarthritis. *Journal of the American Medical Directors Association*, 20(10), 1242–1246. <https://doi.org/10.1016/j.jamda.2019.07.001>
- Hunter, D. J., & Bierma-Zeinstra, S. (2019). Osteoarthritis. *Lancet (London, England)*, 393(10182), 1745–1759. [https://doi.org/10.1016/S0140-6736\(19\)30417-9](https://doi.org/10.1016/S0140-6736(19)30417-9)
- Jang, S., Lee, K., & Ju, J. H. (2021). Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. *International Journal of Molecular Sciences*, 22(5), 19–26.
- Kawano, M. M., Araújo, I. L. A., Castro, M. C., & Matos, M. A. (2015). Assessment of quality of life in patients with knee osteoarthritis. *Acta Ortopedica Brasileira*, 23(6), 307–310. <https://doi.org/10.1590/1413-785220152306150596>

- Kurdaningsih, S., Sudargo, T., & Lusmilasari, L. (2016). Physical activity and sedentary lifestyle towards teenagers' overweight/obesity status. *International Journal of Community Medicine and Public Health*, 630–635. <https://doi.org/10.18203/2394-6040.ijcmph20160623>
- Lakkireddy. (2015). Correlation Among Radiographic, Arthroscopic and Pain Criteria For The Diagnosis Of Knee Osteoarthritis. *Journal of Clinical and Diagnostic Research: JCDR*, 5(2), 9–18.
- Lalia, A. Z., Dasari, S., Johnson, M. L., Robinson, M. M., Konopka, A. R., Distelmaier, K., Port, J. D., Glavin, M. T., Esponda, R. R., Nair, K. S., & Lanza, I. R. (2016). Predictors of Whole-Body Insulin Sensitivity Across Ages and Adiposity in Adult Humans. *The Journal of Clinical Endocrinology and Metabolism*, 101(2), 626–634. <https://doi.org/10.1210/jc.2015-2892>
- Landsmeer, M. L. A., De Vos, B. C., Van Der Plas, P., Van Middelkoop, M., Vroegindewij, D., Bindels, P. J. E., Oei, E. H. G., Bierma-Zeinstra, S. M. A., & Runhaar, J. (2018). Effect of weight change on progression of knee OA structural features assessed by MRI in overweight and obese women. *Osteoarthritis and Cartilage*, 26(12), 1666–1674. <https://doi.org/10.1016/j.joca.2018.08.006>
- Machado, P. P., Steele, E. M., Levy, R. B., da Costa Louzada, M. L., Rangan, A., Woods, J., Gill, T., Scrinis, G., & Monteiro, C. A. (2020). Ultra-processed food consumption and obesity in the Australian adult population. *Nutrition & Diabetes*, 10(1), 39. <https://doi.org/10.1038/s41387-020-00141-0>
- Mahir, L., Belhaj, K., Zahi, S., Azanmasso, H., Lmidmani, F., & El Fatimi, A. (2016). Impact of knee osteoarthritis on the quality of life. *Annals of Physical and Rehabilitation Medicine*, 59, e159. <https://doi.org/10.1016/j.rehab.2016.07.355>
- Marshall, D. A., Liu, X., Barnabe, C., Yee, K., Faris, P. D., Barber, C., Mosher, D., Noseworthy, T., Werle, J., & Lix, L. (2019). Existing comorbidities in people with osteoarthritis: A retrospective analysis of a population-based cohort in Alberta, Canada. *BMJ Open*, 9(11), e033334. <https://doi.org/10.1136/bmjopen-2019-033334>
- Mei, Y., Williams, J. S., Webb, E. K., Shea, A. K., MacDonald, M. J., & Al-Khazraji, B. K. (2022). Roles of Hormone Replacement Therapy and Menopause on Osteoarthritis and Cardiovascular Disease Outcomes: A Narrative Review. *Frontiers in Rehabilitation Sciences*, 3. <https://doi.org/10.3389/fresc.2022.825147>
- Mutiwara, E. (2016). Hubungan Indeks Massa Tubuh dengan Derajat Kerusakan Sendi pada Pasien Osteoarthritis Lutut di RSUP Dr. M. Djamil Padang. *Jurnal Kesehatan Andalas*, 5(2), 1–9.
- Nardocci, M., Leclerc, B.-S., Louzada, M.-L., Monteiro, C. A., Batal, M., & Moubarac, J.-C. (2019). Consumption of ultra-processed foods and obesity in Canada. *Canadian Journal of Public Health = Revue Canadienne De Sante Publique*, 110(1), 4–14. <https://doi.org/10.17269/s41997-018-0130-x>
- Palazzo, C., Nguyen, C., Lefevre-Colau, M.-M., Rannou, F., & Poiraudreau, S. (2016). Risk factors and burden of osteoarthritis. *Annals of Physical and Rehabilitation Medicine*, 59(3), 134–138. <https://doi.org/10.1016/j.rehab.2016.01.006>
- Park, D., Park, Y.-M., Ko, S.-H., Hyun, K.-S., Choi, Y.-H., Min, D.-U., Han, K., & Koh, H.-S. (2023). Association of general and central obesity, and their changes with risk of knee osteoarthritis: A nationwide population-based cohort study. *Scientific Reports*, 13(1), 3796. <https://doi.org/10.1038/s41598-023-30727-4>
- Primorac, D., Molnar, V., Rod, E., Jeleč, Ž., Čukelj, F., Matišić, V., Vrdoljak, T., Hudetz, D., Hajsok, H., & Borić, I. (2020). Knee Osteoarthritis: A Review of Pathogenesis and State-Of-The-Art Non-Operative Therapeutic Considerations. *Genes*, 11(8), 10.3390/genes11080854.
- Rahmawati, N. D., Andriani, H., Wirawan, F., Farsia, L., Waits, A., & Karim Taufiqurahman, K. A. (2024). Body mass index as a dominant risk factor for metabolic syndrome among Indonesian

- adults: A 6-year prospective cohort study of non-communicable diseases. *BMC Nutrition*, 10(1), 43. <https://doi.org/10.1186/s40795-024-00856-8>
- Raud, B., Gay, C., Guiguet-Auclair, C., Bonnin, A., Gerbaud, L., Pereira, B., Duclos, M., Boirie, Y., & Coudeyre, E. (2020). Level of obesity is directly associated with the clinical and functional consequences of knee osteoarthritis. *Scientific Reports*, 10(1), 3601. <https://doi.org/10.1038/s41598-020-60587-1>
- Reyes, C., Leyland, K. M., Peat, G., Cooper, C., Arden, N. K., & Prieto-Alhambra, D. (2016). Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. *Arthritis & Rheumatology (Hoboken, N.J.)*, 68(8), 1869–1875. <https://doi.org/10.1002/art.39707>
- Salis, Z., & Sainsbury, A. (2023). Association Between Change in Body Mass Index and Knee and Hip Replacements: A Survival Analysis of Seven to Ten Years Using Multicohort Data. *Arthritis Care & Research*, 75(6), 1340–1350. <https://doi.org/10.1002/acr.25021>
- Samma, L., Rasjad, C., Prihantono, Seweng, A., Haryasena, Latief, J., Bausat, A., Mustari, M. N., & Kusuma, M. I. (2021). Correlation between Body Mass Index (BMI), Visual Analogue Scale (VAS) score and knee osteoarthritis grading. *Medicina Clínica Práctica*, 4. <https://doi.org/10.1016/j.mcpsp.2021.100228>
- Segal, N. A., Nilges, J. M., & Oo, W. M. (2024). Sex differences in osteoarthritis prevalence, pain perception, physical function and therapeutics. *Osteoarthritis and Cartilage*, 32(9), 1045–1053. <https://doi.org/10.1016/j.joca.2024.04.002>
- Shalhoub, M., Anaya, M., Deek, S., Zaben, A. H., Abdalla, M. A., Jaber, M. M., Koni, A. A., & Zyoud, S. H. (2022). The impact of pain on quality of life in patients with osteoarthritis: A cross-sectional study from Palestine. *BMC Musculoskeletal Disorders*, 23(1), 248. <https://doi.org/10.1186/s12891-022-05207-x>
- Shumnalieva, R., Kotov, G., & Monov, S. (2023). Obesity-Related Knee Osteoarthritis—Current Concepts. *Life*, 13(8), 1650. <https://doi.org/10.3390/life13081650>
- Smith, S. R., Katz, J. N., Collins, J. E., Solomon, D. H., Jordan, J. M., Suter, L. G., Yelin, E. H., David Paltiel, A., & Losina, E. (2021). Cost-Effectiveness of Tramadol and Oxycodone in the Treatment of Knee Osteoarthritis. *Arthritis Care & Research*, 2(1), 234–242.
- Suza, D. E., Miristia, V., & Hariati, H. (2020). Physical Activities and Incidence of Obesity among Adolescent in Medan, Indonesia. *Open Access Macedonian Journal of Medical Sciences*, 8(E), 198–203. <https://doi.org/10.3889/oamjms.2020.4225>
- Szilagyi, I. A., Waarsing, J. H., van Meurs, J. B. J., Bierma-Zeinstra, S. M. A., & Schiphof, D. (2022). A systematic review of the sex differences in risk factors for knee osteoarthritis. *Rheumatology (Oxford, England)*, 62(6), 2037–2047. <https://doi.org/10.1093/rheumatology/keac688>
- Thijssen, E., van Caam, A., & van der Kraan, P. M. (2015). Obesity and osteoarthritis, more than just wear and tear: Pivotal roles for inflamed adipose tissue and dyslipidaemia in obesity-induced osteoarthritis. *Rheumatology (Oxford, England)*, 54(4), 588–600. <https://doi.org/10.1093/rheumatology/keu464>
- Tiofunda, B. N., & Friska, W. I. (2020). Gambaran derajat nyeri pada pasien osteoarthritis genu di Rumah Sakit Royal Taruma Jakarta Barat. *Tarumanagara Medical Journal*, 2(2), 372–377.
- Wang, T., & He, C. (2018). Pro-inflammatory cytokines: The link between obesity and osteoarthritis. *Cytokine & Growth Factor Reviews*, 44, 38–50. <https://doi.org/10.1016/j.cytogfr.2018.10.002>
- Wang, Y., Yu, D., Liu, Z., Zhou, F., Dai, J., Wu, B., Zhou, J., Heng, B. C., Zou, X. H., & Ouyang, H. (2017). Exosomes From Embryonic Mesenchymal Stem Cells Alleviate Osteoarthritis Through Balancing Synthesis And Degradation Of Cartilage Extracellular Matrix. *Stem Cell Research & Therapy*, 8(1), 1–13.

- Weiss, E. (2014). Knee osteoarthritis, body mass index and pain: Data from the Osteoarthritis Initiative. *Rheumatology* (Oxford, England), 53(11), 2095–2099. <https://doi.org/10.1093/rheumatology/keu244>
- Ying, M., Hu, X., Li, Q., Dong, H., Zhou, Y., & Chen, Z. (2022). Long-term trajectories of BMI and cumulative incident metabolic syndrome: A cohort study. *Frontiers in Endocrinology*, 13. <https://doi.org/10.3389/fendo.2022.915394>
- Zhang, L., Zhang, W., Wu, X., Cui, H., Yan, P., Yang, C., Zhao, X., Xiao, J., Xiao, C., Tang, M., Wang, Y., Chen, L., Liu, Y., Zou, Y., Zhang, L., Yang, Y., Yao, Y., Li, J., Liu, Z., ... Jiang, X. (2023). A sex- and site-specific relationship between body mass index and osteoarthritis: Evidence from observational and genetic analyses. *Osteoarthritis and Cartilage*, 31(6), 819–828. <https://doi.org/10.1016/j.joca.2023.02.073>
- Zhang, S., Wang, D., Zhao, J., Zhao, H., Xie, P., Zheng, L., Sheng, P., Yuan, J., Xia, B., Wei, F., & Zhang, Z. (2024). Metabolic syndrome increases osteoarthritis risk: Findings from the UK Biobank prospective cohort study. *BMC Public Health*, 24(1), 233. <https://doi.org/10.1186/s12889-024-17682-z>
- Zheng, H., & Chen, C. (2015). Body mass index and risk of knee osteoarthritis: Systematic review and meta-analysis of prospective studies. *BMJ Open*, 5(12), e007568. <https://doi.org/10.1136/bmjopen-2014-007568>