

Osteoarthritis, classification, prevalence and risk factors

Zeeshan Anjum and Syed Rizwan Abbas*

Department of Biotechnology; University of Azad Jammu and Kashmir; Pakistan

Abstract

Purpose of study:

This study was aimed to make a comprehensive review over prevalence of osteoarthritis and risk factors associated with it and to relate the latest findings with it.

Summary:

Osteoarthritis is the major chronic disease causing disability. Patients suffering from it feel pain and become unable to walk or work. Mostly affected joints were hip, knee, hand and foot. Its classification and phenotypes were also discussed. Recent studies also agreed that obesity and aging are the major risks for the prevalence of osteoarthritis. Malnutrition and socio-economic condition also has impact on disease prevalence along with heredity factors. Occupation with severe workload on joints and injuries increase risk of osteoarthritis. Females are getting this disease more compared to men. Diagnosis methods are progressing and MRI is more helpful in diagnosis. Osteoarthritis showed increase in prevalence during previous years. Person level and joint level risks studies were also reviewed.

Keywords: Osteoarthritis; prevalence

Introduction

Osteoarthritis is a common disease of joints causing heavy burden as it causes pain and discomfort to the patient. The patient becomes unable to move or perform its daily life activities. Osteoarthritis is affecting all the countries poor and rich and affecting the daily life of people. This paper is aimed to analyze the epidemiology of arthritis in different regions and also discuss its risk factors. Recent reviews on osteoarthritis are also taken in consideration. (Allen, 2015, zhang, 2010, litwic, 2013, Johnson, 2014, Neogi, 2013, silverwood, 2014). Risk factors are divided into categories person level risk factors, joint level risk factors and genetic risk factors nearly similar to other study (Allen, 2015).

Definition and classification of arthritis:

Osteoarthritis is degenerative disease of joints involving cartilage damage and also damage to surrounding tissues. Damage to articular cartilage, weakening of muscles and synovial inflammation may also be involved. (Hutton CW, 1989). Articular damage and osteoarthritis are the major causes of pain and disability in middle age and in old people. Although the mechanism of osteoarthritis cause is poorly understood still age related changes are also responsible for progressive development of osteoarthritis. (Buckwalter, 1997). Most common and major cause of disability among adults is caused by arthritis. (song, 2006, Lawrence, 2008, CDC, 2010, McDonough *et al*, 2010, Johnson *et al*, 2014). In young it is mostly caused by sports injury. (Roos *et al*, 2005). Osteoarthritis can be defined by three ways 1) pathologically 2) radiographically 3) clinically. Most common method used for radiographic definition is Kellgren-Lawrence

(K/L) radiographic scheme. In this method joint scoring is in five levels from 0 to 4 based on presence of a definite osteophyte, joint space narrowing, sclerosis, cyst forming and presence of deformity. (Zhang *et al*, 2010). Joint space width measurement is used for epidemiological and clinical studies of osteoarthritis. (Altman *et al*, 2004, Brandt *et al*, 2002). A better method is use of magnetic resonance imaging for better visualization of joint structures. (Hernborg *et al*, 1977, Ahlback *et al*, 1968).

For clinical diagnosis of osteoarthritis American college of rheumatology (ACR) is used for knee (Altman *et al*, 1986) for hip (Altman *et al*, 1991) and for hand (Altman *et al*, 1990). All the people having radiographic signs don't have clinical sign symptoms so data based on clinical signs and data based on radiographic study may be different from each other (Hannan *et al*, 2000). Recent studies shows modest agreement between radiographic, clinical and self-reported osteoarthritis as 39(66%) out of 59 clinical cases of osteoarthritis also showed radiological agreement (Parsons, 2015).

Epidemiology:

Osteoarthritis may develop in any joint but it is commonly found in knee, hip, hand and facet joints. According to an estimate of 2005 in United States 26 million people are affected by arthritis of some kind. (Lawrence, 2008). In Canada it is estimated that from 2010 to 2031 will increase from 13.6% to 18.6% and total direct cost will increase from \$2.9 billion to \$7.6 billion. (Sharif, 2015). The incidence of osteoarthritis is found more in women as compared to men. This incidence increases over 50 and starts decrease after 80 years. The facts show that knee osteoarthritis cases are highest (240/100,000 persons/year), hand osteoarthritis intermediate (100/100,000 persons/year) and it was lowest for hip osteoarthritis (88/100,000 persons/year) (Oliveria *et al*, 1995). Consultation for osteoarthritis in England is reported 8.6/1000 persons above age of 15 in men and 10.8/1000 in women. The incidence is also increased between 2003 and 2010. Incidence sharply increased between age of 45 to 64 years peaking at 75 to 84 years. (Yu *et al*, 2015). Prevalence of osteoarthritis in Ireland population above 50 was found overall 12.9% and 17.9% in women while in men it was 9.4%. Prevalence increased with increase in age. Above age of 80 it became double as compared to what found between 50 to 60 years. (French *et al*, 2015).

Hip Osteoarthritis:

Hip arthritis is less common form of osteoarthritis. It is 1.4% in Asia, 2.8% in Africa, 10.1% in Europe and 7.2% in North America. (Felson, 1987). In Korean population older than 65 hip osteoarthritis is found 2 % (15/686). (Cho *et al*, 2015). In another recent study it showed that 19.6% in radiographic and 4.2% in symptomatic. It also showed that men have higher prevalence in men in radiographic not symptomatic osteoarthritis. (Kim, 2014). Radiographically hip osteoarthritis is associated with the increased risk of mortality by all causes and also by cardiovascular diseases in white women. (Barbour *et al*, 2015). However investigations by another study showed that there is no significance correlation. Further studies are required in this regard (Hoeven *et al.*, 2014).

Knee Osteoarthritis:

Knee osteoarthritis according to Framingham study prevalence of knee osteoarthritis diagnosed by radiographic in participants above 45 years is 19.2% and above 80 years figure reached to 43.7%. Dutch public health institute data shows that knee osteoarthritis in men is 15.6% and 30.5% in women above age of 55 years. (Bijlsma, 2007). Another radiographic study in Korea showed knee osteoarthritis up to 38 % (265/696) in individuals above 65 years of age. Obesity was related to it. (Cho, 2015). In Malmö and Sweden among age of 56 to 84 years prevalence of radiographic knee osteoarthritis was 25.4% and symptomatic knee osteoarthritis was 15.4%. (Turkiewicz, 2014). Knee osteoarthritis and frailty are associated with function limitation problems with the age. Frailty is found more associated with the knee

osteoarthritis as compared to other types of osteoarthritis. (Misra, 2014). Data from china indicated that prevalence of knee osteoarthritis is two or times greater than Framingham osteoarthritis studies (Fransen, 2011). Five phenotypes are identified in knee osteoarthritis depending on clinical characteristics. These phenotypes are 1) minimal joint disease phenotype, 2) strong muscle strength phenotype, 3) severe radiographic osteoarthritis phenotype, 4) obese phenotype, and 5) depressive mood phenotype. (Esch *et al*, 2015).

Hand Osteoarthritis:

Symptomatic hand joint osteoarthritis is defined as if you have both symptoms and radiographic evidence for the presence of osteoarthritis. In the survey conducted the presence of symptomatic osteoarthritis of hand was higher in women (26.2%) as compared to men (13.4%) in subjects aged between 72 to 100 years. (Zhang, 2002). In another study it is reported that hand osteoarthritis is found more in women (67%) compared to men (54%) for at least one hand in subjects of age above 55 years. Weak association also found between hand osteoarthritis and pain/disability. (Dahaghin *et al*, 2005). Another study in United States indicated that in US every 1 out of 12 older people have symptomatic hand osteoarthritis. In first metacarpal deformity women were more (24.3%) compared to men (10.3%). (Dillon *et al*, 2007). Symptomatic hand osteoarthritis was also found associated with increased risk of coronary heart diseases while there was no relation found between coronary heart disease and radiographic hand osteoarthritis. (Haughen *et al*, 2015). According to a study burden due to hand osteoarthritis is affecting a major part of population under 60 years of age. (Wilder *et al*, 2006). Hand osteoarthritis (60%) was 2nd to spine osteoarthritis (66%) in Korean community of above 65 years and aging was also found associated with it. (Cho *et al*, 2015). A comparison showed black women (25.5%) have more cases of hand osteoarthritis as compared to white females (19.2%). (Sowers *et al*, 2000).

Foot Osteoarthritis

By data it is evident that many of the obese people suffer from foot osteoarthritis or they are at risk of developing it. (Mickle *et al*, 2015). A detailed review has also been published on foot osteoarthritis which stated that most studies are focused on radiographic study and its prevalence is between 0.1 to 61 % depending on age, sex and joints under focus. (Kalichman, 2014). Three distinct classes of foot osteoarthritis have been identified. First one is no or minimal foot osteoarthritis in 64% cases, isolated 1st MTPJ osteoarthritis in 22% and polyarticular foot osteoarthritis in 15% cases. (Rathod *et al*,2015).

In England a postal survey from adults of 50 or above resulted 72% response out of 26,705 mails and approximately 50% were suffering with disabling osteoarthritis of some kind out of four joints i.e., hip, knee, hand or foot.(Thomas *et al*, 2014).

Health care facilities database was used by many recent studies (Moriatis, 2014, Rahman, 2014, Prieto-Alhambra, 2014, Turkiewicz, 2014). Data is showing that incidence of osteoarthritis is increasing 2.3 to 3.3% per year from 2000/2001 to 2008/2009. (Rahman, 2014).

Risk Factors for osteoarthritis:

Person level risk factors

1) Age:

Age is major risk factor for the arthritis. (Felson *et al*, 2000, Lawrence, 2008). Increase in age is positively related to risk of osteoarthritis. (Johnson *et al*, 2014, Neogi *et al*, 2013).

2) Sex:

Osteoarthritis is more prevalent in females as compared to males. (Srikanth *et al*, 2005, Allen *et al*, 2015).

3) Socio-economic status:

There is increased risk of disease with lower socio-economic status. (Allen *et al*, 2015).

4) Genetic Factor:

Hereditary character is considered very strong in development of osteoarthritis. Identification of genes associated with osteoarthritis can help to understand it further. Studies showed that micro RNA miR-127-5p under expression was observed in knee osteoarthritis and there was also an increased expression of MMP-13. (Arellano *et al*, 2015). Weak association of *ERα XbaI* polymorphism and osteoarthritis is also shown in European people by a study. (Ren *et al*, 2015). Family History like knee replacement therapy is also a contributing factor according to recent research. (Pan *et al*, 2014). Family history also contributed to knee joint space narrowing. (Khan *et al*, 2015).

5) Obesity:

Obesity is observed as a major factor in all the cases. (Allen *et al*, 2015, Batis, 2015, Forrester, 2015, Lee, 2015). Obesity increases the osteoarthritis risk in both knee and hand. Adipokines are known to disturb the homeostasis of joint tissues increasing the chances of osteoarthritis. Adipokines are secreted by adipose tissues. (Fu *et al*, 2015). With 5 kg weight loss 50% decrease in risk of symptomatic knee osteoarthritis. (Felson *et al*, 1992). Reduction of systemic levels of inflammation (C-reactive protein (CRP) and interleukin-6 (IL-6)) in obese people were achieved by loss of 5 KG body weight. (Beavers, 2015). According to study body fat and waist to hip ratio is associated with the knee osteoarthritis however weakly associated with hip osteoarthritis. (Allen *et al*, 2015).

5) Nutrition and Vitamin:

Diet is directly linked to the obesity and also has an impact on aging that's why an important role has in osteoarthritis. (Davidson *et al*, 2015). Result of 4 month dietary plan of Mediterranean type significantly improved the perceptual markers of osteoarthritis. (Davison *et al*, 2014). Diet low in vitamin D and Vitamin C is also a possible risk for knee osteoarthritis. Some food products are useful for osteoarthritis. (Sanghi *et al*, 2015). It is also shown in a study that vitamin K is also associated with osteoarthritis and women having low plasma PK plasma PK were more prone to progression of articular cartilage and meniscus damage. (Shea, 2015).

6) Bone mass and Bone mass:

High bone mass is directly linked with the osteoarthritis of hip and knee and high bone mass is associated with bone sclerosis so hypertrophic phenotype will be suggested. (Allen *et al*, 2015)

7) Smoking:

Smoking protects from the osteoarthritis according to some studies (Leung *et al*, 2014, Felson, 2015) but another study doubts and states that this may be false. (Hui *et al*, 2011).

JOINT ASSOCIATED RISK

1) Bone/Joint Shape:

A recent study shows that proximal shapes were different among osteoarthritis and normal person among male. (Nelson *et al*, 2014, Wise *et al*, 2014). Reduced femoral offset, more valgus neck shaft angle, increased hip height center and increased abductor angle are found associated with osteoarthritis. (Allen *et al*, 2015). Mild and moderate osteoarthritis grades were associated with dorsal wedging of third tarsal bone while plantar wedging was associated with severe cases. (Sprackman *et al*, 2015). Subcondral bone early changes may predict the phenotype of osteoarthritis and help the clinician. (Brentano *et al*, 2015).

2) Injury:

Injury is the one of the most important risks for the osteoarthritis especially for knee causing meniscal damage, rupture of anterior cruciate ligament, or direct injury of articular cartilage. (Allen *et al*, 2015). In a study the knee osteoarthritis was high among patients with constructed cruciate ligament injury.

(Nordenvall, 2014). Occupational knee osteoarthritis and previous history of knee injury are two most important factors. (Dulay *et al*, 2015). Patient with reconstructed cruciate ligament must manage weight avoid excessive loading to remain protected from osteoarthritis. (Simon *et al*, 2015).

3) Muscle Mass and Muscle strength:

Muscle weakness may cause osteoarthritis. Specific role of muscle mass and muscle strength is still unclear. (Allen *et al*, 2015). Women with more fat in intramuscular areas were found having pain. (Runhaar *et al*, 2014).

4) Joint load and alignment:

Knee alignment is the main prediction sign for the osteoarthritis. (Sharma *et al*, 2010). Most of the literature suggests that knee alignment is very important with regard to osteoarthritis. (Allen *et al*, 2015, Johnson *et al*, 2014, Neogi *et al*, 2013, Zhang *et al*, 2011). But still the findings are not regular. (Tanamas *et al*, 2009). Malalignment of metatarsophalangeal joint was linked with the osteoarthritis of metatarsal joint as well as knee joint and hip joint osteoarthritis. (Allen *et al*, 2015).

5) Occupation and Activities:

Previous studies (Allen *et al*, 2015, Johnson *et al*, 2014) showed that occupations involved in extreme pressure and joint activity are linked with osteoarthritis while moderate level activity is not linked with it. About hip osteoarthritis and occupation a comprehensive study is also present. (Harris *et al*, 2015).

6) Other joint level risks:

Leg length inequality was also reported to have some link but more study on it is needed. (Harvey *et al*, 2010). Crepitus in women was associated with the osteoarthritis. Infrapatellar fat pad was also significantly and beneficially associated with the knee osteoarthritis. (Allen *et al*, 2015).

Conclusion

Osteoarthritis is a major chronic disease especially higher in women. Osteoarthritis major target joints are hand, hip, knee and foot joint. Current methods for its diagnose are clinical method, radiographic and Magnetic resonance imaging. Its probability increases with the increase in age and severe physical activity, diet low in vitamin D and Vitamin C, Obesity, injury, repaired cruciate ligament, low bone mass. Smokers and people with good muscle strength have low chances of developing osteoarthritis. Future research should pay attention toward relationship between these risk factors especially on age and obesity. A Future research for a balanced diet to avoid obesity and provide sufficient nutrients and vitamins could help to decrease its incidence.

References

- Allen, K. D., & Golightly, Y. M. (2015). Epidemiology of osteoarthritis: state of the evidence. *Current opinion in rheumatology*, 27(3), 276.
- Zhang, Y., & Jordan, J. M. (2010). Epidemiology of osteoarthritis. *Clinics in geriatric medicine*, 26(3), 355-369.
- Litwic, A., Edwards, M. H., Dennison, E. M., & Cooper, C. (2013). Epidemiology and burden of osteoarthritis. *British medical bulletin*, lds038.
- Johnson, V. L., & Hunter, D. J. (2014). The epidemiology of osteoarthritis. *Best Practice & Research Clinical Rheumatology*, 28(1), 5-15.
- Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum Dis Clin North Am*. 2013;39:1–19.
- Silverwood V, Blagojevic-Bucknall M, Jinks C, et al. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2014

- Hutton, C. W. (1989). Osteoarthritis: the cause not result of joint failure?. *Annals of the rheumatic diseases*, 48(11), 958-961.
- Buckwalter, J. A., & Mankin, H. J. (1997). Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. *Instructional course lectures*, 47, 487-504.
- Song J, Chang RW, Dunlop D. Population impact of arthritis on disability in older adults. *Arthritis Rheum.* 2006;55:248–255
- Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. *Arthritis Rheum.* 2008;58:26–35.
- Centers for Disease Control and Prevention. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation: United States, 2007–2009. *MMWR Morb Mortal Wkly Rep.* 2010;59:1261–1265.
- McDonough CM, Jette AM. The contribution of osteoarthritis to functional limitations and disability. *Clin Geriatr Med Aug.* 2010;26:387–399.
- Roos, E. M. (2005). Joint injury causes knee osteoarthritis in young adults. *Current opinion in rheumatology*, 17(2), 195-200.
- Altman RD, Bloch DA, Dougados M, et al. Measurement of structural progression in osteoarthritis of the hip: the Barcelona consensus group. *Osteoarthritis Cartilage* 2004;12(7):515–24
- Brandt KD, Mazuca SA, Conrozier T, et al. Which is the best radiographic protocol for a clinical trial of a structure modifying drug in patients with knee osteoarthritis? *J Rheumatol* 2002;29(6): 1308–20.
- Hernborg JS, Nilsson BE. The natural course of untreated osteoarthritis of the knee. *Clin Orthop* 1977;123:130–7
- Ahlback S. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968 277:7–72
- Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., ... & Wolfe, F. (1986). Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis & Rheumatism*, 29(8), 1039-1049.
- Altman, R., Alarcon, G., Appelrouth, D., Bloch, D., Borenstein, D., Brandt, K., ... & Wolfe, F. (1991). The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis & Rheumatism*, 34(5), 505-514.
- Altman, R., Alarcon, G., Appelrouth, D., Bloch, D., Borenstein, D., Brandt, K., ... & Wolfe, F. (1990). The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis & Rheumatism*, 33(11), 1601-1610.
- Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. *J Rheumatol* 2000;27(6):1513–7
- Parsons, C., Clynes, M., Syddall, H., Jagannath, D., Litwic, A., van der Pas, S., ... & Edwards, M. H. (2015). 038. How Well Do Radiographic, Clinical and Self-Reported Diagnoses of Knee Osteoarthritis Agree? Findings from the Hertfordshire Cohort Study. *Rheumatology*, 54(suppl 1), i63-i64.
- Sharif, B., Kopec, J., Bansback, N., Rahman, M. M., Flanagan, W. M., Wong, H., ... & Anis, A. (2015). Projecting the direct cost burden of osteoarthritis in Canada using a microsimulation model. *Osteoarthritis and Cartilage*.
- Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis Rheum* 1995;38(8):1134–41
- Yu, D., Peat, G., Bedson, J., & Jordan, K. P. (2015). Annual consultation incidence of osteoarthritis estimated from population-based health care data in England. *Rheumatology*, kev231.

- French, H. P., Galvin, R., Horgan, N. F., & Kenny, R. A. (2015). Prevalence and burden of osteoarthritis amongst older people in Ireland: findings from The Irish Longitudinal Study on Ageing (TILDA). *The European Journal of Public Health*, ckv109.
- Felson, D. T. (1987). Epidemiology of hip and knee osteoarthritis. *Epidemiologic reviews*, 10, 1-28.
- Cho, H. J., Morey, V., Kang, J. Y., Kim, K. W., & Kim, T. K. (2015). Prevalence and Risk Factors of Spine, Shoulder, Hand, Hip, and Knee Osteoarthritis in Community-dwelling Koreans Older Than Age 65 Years. *Clinical Orthopaedics and Related Research*®, 1-8.
- Kim, C., Linsenmeyer, K. D., Vlad, S. C., Guermazi, A., Clancy, M. M., Niu, J., & Felson, D. T. (2014). Prevalence of radiographic and symptomatic hip osteoarthritis in an urban United States community: the Framingham osteoarthritis study. *Arthritis & Rheumatology*, 66(11), 3013-3017.
- Barbour, K. E., Lui, L. Y., Nevitt, M. C., Murphy, L. B., Helmick, C. G., Theis, K. A., ... & Cauley, J. A. (2015). Hip osteoarthritis and the risk of all-cause and disease-specific mortality in older women: Population-based cohort study. *Arthritis & Rheumatology*.
- Hoeven, T. A., Leening, M. J. G., Bindels, P. J., Castaño-Betancourt, M., van Meurs, J. B., Franco, O. H., ... & Bierma-Zeinstra, S. M. (2015). Disability and not osteoarthritis predicts cardiovascular disease: a prospective population-based cohort study. *Annals of the rheumatic diseases*, 74(4), 752-756.
- Bijlsma, J. W. J., & Knahr, K. (2007). Strategies for the prevention and management of osteoarthritis of the hip and knee. *Best Practice & Research Clinical Rheumatology*, 21(1), 59-76.
- Turkiewicz A, Gerhardsson de Verdier M, Engstrom G, et al. Prevalence of knee pain and knee OA in southern Sweden and the proportion that seeks medical care. *Rheumatology (Oxford)* 2014
- Misra, D., Felson, D. T., Silliman, R. A., Nevitt, M., Lewis, C. E., Torner, J., & Neogi, T. (2015). Knee osteoarthritis and frailty: findings from the Multicenter Osteoarthritis Study and Osteoarthritis Initiative. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 70(3), 337-342.
- Fransen, M., Bridgett, L., March, L., Hoy, D., Penserga, E., & Brooks, P. (2011). The epidemiology of osteoarthritis in Asia. *International journal of rheumatic diseases*, 14(2), 113-121.
- Van der Esch, M., Knoop, J., van der Leeden, M., Roorda, L. D., Lems, W. F., Knol, D. L., & Dekker, J. (2015). Clinical phenotypes in patients with knee osteoarthritis: a study in the Amsterdam osteoarthritis cohort. *Osteoarthritis and Cartilage*, 23(4), 544-549.
- Dahaghin, S., Bierma-Zeinstra, S. M., Ginai, A. Z., Pols, H. A. P., Hazes, J. M. W., & Koes, B. W. (2005). Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study). *Annals of the rheumatic diseases*, 64(5), 682-687.
- Dillon, C. F., Hirsch, R., Rasch, E. K., & Gu, Q. (2007). Symptomatic hand osteoarthritis in the United States: prevalence and functional impairment estimates from the third US National Health and Nutrition Examination Survey, 1991–1994. *American Journal of Physical Medicine & Rehabilitation*, 86(1), 12-21.
- Haugen, I. K., Ramachandran, V. S., Misra, D., Neogi, T., Niu, J., Yang, T., ... & Felson, D. T. (2015). Hand osteoarthritis in relation to mortality and incidence of cardiovascular disease: data from the Framingham Heart Study. *Annals of the rheumatic diseases*, 74(1), 74-81.
- Wilder, F. V., Barrett, J. P., & Farina, E. J. (2006). Joint-specific prevalence of osteoarthritis of the hand. *Osteoarthritis and cartilage*, 14(9), 953-957.
- Sowers, M., Lachance, L., Hochberg, M., & Jamadar, D. (2000). Radiographically defined osteoarthritis of the hand and knee in young and middle-aged African American and Caucasian women. *Osteoarthritis and cartilage*, 8(2), 69-77.
- Mickle, K. J., & Steele, J. R. (2015). Obese older adults suffer foot pain and foot-related functional limitation. *Gait & posture*.

- Kalichman L, Hernandez-Molina G. Midfoot and forefoot osteoarthritis. *Foot*. 2014;24:128–134.
- Rathod, T., Marshall, M., Thomas, M. J., Menz, H. B., Myers, H. L., Thomas, E., ... & Roddy, E. (2015). Investigation of potential phenotypes of foot osteoarthritis: Cross-sectional analysis from the Clinical Assessment Study of the Foot. *Arthritis care & research*.
- Thomas E, Peat G, Croft P. Defining and mapping the person with osteoarthritis for population studies and public health. *Rheumatology (Oxford)* 2014;53:338–345
- Moriatis Wolf J, Turkiewicz A, Atroshi I, Englund M. Prevalence of doctor-diagnosed thumb carpometacarpal joint osteoarthritis: an analysis of Swedish healthcare. *Arthritis Care Res*. 2014;66:961–965
- Rahman MM, Cibere J, Goldsmith CH, et al. Osteoarthritis incidence and trends in administrative health records from British Columbia, Canada. *J Rheumatol*. 2014;41:1147–1154
- Prieto-Alhambra D, Judge A, Javaid MK, et al. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. *Ann Rheum Dis*. 2014;73:1659–1664
- Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med* 2000;133(8):635–46
- Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. *Arthritis Rheum*. 2008;58:26–35.
- Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage* 2005;13(9):769–81.
- Arellano, R. D. P. V., Argüello, J. R. A., Morán Martínez, J., Garcia Marin, A. Y., Gonzalez Galarza, F. F., Guzman, D. G., & Sánchez, J. L. C. (2015). Brief Review of Genomics in Osteoarthritis. *International Journal of Orthopaedics*,2(4), 341-346.
- Ren, Y., Tan, B., Yan, P., You, Y., Wu, Y., & Wang, Y. (2015). Association between polymorphisms in the estrogen receptor alpha gene and osteoarthritis susceptibility: a meta-analysis. *BMC musculoskeletal disorders*, 16(1), 44.
- Pan F, Ding C, Winzenberg T, et al. The offspring of people with a total knee replacement for severe primary knee osteoarthritis have a higher risk of worsening knee pain over 8 years. *Ann Rheum Dis*. 2014
- Batsis, J. A., Zbehlik, A. J., Scherer, E. A., Barre, L. K., & Bartels, S. J. (2015). Normal Weight with Central Obesity, Physical Activity, and Functional Decline: Data from the Osteoarthritis Initiative. *Journal of the American Geriatrics Society*, 63(8), 1552-1560.
- Forrester, K., Taufiq, F., & Samuels, J. (2015). Comparison of knee osteoarthritis treatment in the non-obese vs obese populations across different medical specialties. *Osteoarthritis and Cartilage*, 23, A202.
- Lee, S., Kim, T. N., Kim, S. H., Kim, Y. G., Lee, C. K., Moon, H. B., ... & Yoo, B. (2015). Obesity, metabolic abnormality, and knee osteoarthritis: A cross-sectional study in Korean women. *Modern Rheumatology*, 25(2), 292-297.
- Fu, Y., & Griffin, T. M. (2015). Obesity, Osteoarthritis and Aging: The Biomechanical Links. In *The Mechanobiology of Obesity and Related Diseases*(pp. 181-201). Springer International Publishing.
- Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. *Ann Intern Med* 1992;116(7): 535–9.
- Beavers, K. M., Beavers, D. P., Newman, J. J., Anderson, A. M., Loeser, R. F., Nicklas, B. J., ... & Messier, S. P. (2015). Effects of total and regional fat loss on plasma CRP and IL-6 in overweight and obese, older adults with knee osteoarthritis. *Osteoarthritis and Cartilage*, 23(2), 249-256.

- Davidson, R. K., & Clark, I. M. (2015). Dietary intervention for osteoarthritis: Clinical trials after the 'Bone and Joint Decade'. *Nutrition Bulletin*, 40(3), 203-210.
- Davison, G., Dyer, J. R., Marcora, S. M., & Mauger, A. R. (2015). The efficacy of a Mediterranean type diet on symptoms of osteoarthritis—a pilot study. *Proceedings of the Nutrition Society*, 74(OCE1), E142.
- Sanghi, D., Mishra, A., Sharma, A. C., Raj, S., Mishra, R., Kumari, R., ... & Srivastava, R. N. (2015). Elucidation of Dietary Risk Factors in Osteoarthritis Knee—A Case-Control Study. *Journal of the American College of Nutrition*, 34(1), 15-20.
- Shea, M. K., Kritchevsky, S. B., Hsu, F. C., Nevitt, M., Booth, S. L., Kwok, C. K., ... & Study, H. A. (2015). The association between vitamin K status and knee osteoarthritis features in older adults: The Health, Aging and Body Composition Study. *Osteoarthritis and Cartilage*, 23(3), 370-378.
- Leung YY, Ang LW, Thumboo J, et al. Cigarette smoking and risk of total knee replacement for severe osteoarthritis among Chinese in Singapore: the Singapore Chinese health study. *Osteoarthritis Cartilage*. 2014;22:764–770.
- Felson, D. T., & Zhang, Y. (2015). Smoking and osteoarthritis: a review of the evidence and its implications. *Osteoarthritis and Cartilage*, 23(3), 331-333.
- Hui M, Doherty M, Zhang W. Does smoking protect against osteoarthritis? Meta-analysis of observational studies. *Ann Rheum Dis*. 2011;70:1231–1237.
- Nelson AE, Liu F, Lynch JA, et al. Association of incident symptomatic hip osteoarthritis with differences in hip shape by active shape modeling: the Johnston County Osteoarthritis Project. *Arthritis Care Res*. 2014;66:74–81.
- Wise BL, Kritikos L, Lynch JA, et al. Proximal femur shape differs between subjects with lateral and medial knee osteoarthritis and controls: the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2014;22:2067–2073.
- Sprackman, L., Dakin, S. G., May, S. A., & Weller, R. (2015). Relationship between the shape of the central and third tarsal bones and the presence of tarsal osteoarthritis. *The Veterinary Journal*, 204(1), 94-98.
- Funck-Brentano, T., & Cohen-Solal, M. (2015). Subchondral bone and osteoarthritis. *Current opinion in rheumatology*, 27(4), 420-426.
- Nordenvall R, Bahmanyar S, Adami J, et al. Cruciate ligament reconstruction and risk of knee osteoarthritis: the association between cruciate ligament injury and posttraumatic osteoarthritis. a population based nationwide study in Sweden, 1987–2009. *PLoS One*. 2014;9:e104681.
- Dulay, G. S., Cooper, C., & Dennison, E. M. (2015). Knee pain, knee injury, knee osteoarthritis & work. *Best Practice & Research Clinical Rheumatology*.
- Simon, L. S. (2015). OARSI Clinical Trials Recommendations: An abbreviated regulatory guide to the clinical requirements for development of therapeutics in osteoarthritis. *Osteoarthritis and Cartilage*, 23(5), 674-676.
- Runhaar J, van Middelkoop M, Reijman M, et al. Malalignment: a possible target for prevention of incident knee osteoarthritis in overweight and obese women. *Rheumatology (Oxford)* 2014;53:1618–1624.
- Sharma L, Song J, Dunlop D, et al. Varus and valgus alignment and incident and progressive knee osteoarthritis. *Ann Rheum Dis*. 2010;69:1940–1945.
- Harris, E. C., & Coggon, D. (2015). HIP osteoarthritis and work. *Best Practice & Research Clinical Rheumatology*.
- Harvey WF, Yang M, Cooke TD, et al. Association of leg-length inequality with knee osteoarthritis: a cohort study. *Ann Intern Med*. 2010;152:287–295