Inflammation of the joints, or arthritis, is one of the leading causes of pain and disability for adults living in the U.S., affecting over 20% of the population.(1) There are several types of arthritis that can also cause systemic inflammation, organ damage and loss of function. (1) Osteoarthritis and rheumatoid arthritis are two of the most common types of arthritis, (with the prevalence of OA being much higher), which can have similar presentations despite differing etiologies.(2,3) The myriad social and economic ramifications of these diseases include increased healthcare costs, work limitations, and increased risk of falls and fall-related injuries.(1,4) As one of the leading causes of chronic pain, arthritis is typically treated by opioid analgesics; however, as of 2015, the US Dept. of Health and Human Services declared an opioid epidemic due the high prevalence of prescription drug abuse.(5) These facts highlight the importance of non-pharmacological, evidence-based treatment for arthritis. In response to the opioid epidemic, the American Physical Therapy Association launched a campaign called Choose PT to promote physical therapy as a profession which is dedicated to providing safe and effective interventions for chronic pain.(6) With regard to physical therapy, the purpose of this paper is to discuss the mechanism, examination, presentation, prevention, and intervention of joint damage associated with both osteoarthritis and rheumatoid arthritis.

Both osteoarthritis and rheumatoid arthritis cause inflammation of synovial joints and subsequent damage to articular cartilage and surrounding tissue.(7) However, the mechanism by which damage occurs differs between them. Osteoarthritis describes inflammation that arises from wear and tear on cartilaginous tissue covering the surfaces of bone, while rheumatoid arthritis describes an autoimmune disease which causes inflammation of the synovium, leading to subsequent damage of articular cartilage and bone.(7) As a result of chronic inflammation, an individual with OA or RA experiences pain, swelling, redness, and stiffness of synovial joints.(7)

During physical therapy examination of individuals presenting with painful, swollen joints, there are several factors that differentiate osteoarthritis and rheumatoid arthritis. Prevalence of both is higher in women compared to men and both can affect individuals across the lifespan.(8) However, due to its degenerative nature, osteoarthritis typically develops gradually after continuous wear upon joints, and therefore, the incidence is higher in adults over the age of 50.(9) Osteoarthritis can occur prematurely in younger individuals as a result of trauma, infection or avascular necrosis of subchondral bone.(10)

Rheumatoid arthritis manifests rather quickly; however, the exact cause is unknown.(8) There are several genetic and environmental risk factors that have been identified, including modifiable and non-modifiable factors.(8) Genetics play a role in both diseases, with genes influencing an estimated 20 – 35% of knee OA and almost 50% of hip and hand OA.(11) Studies have shown that genes linked with several other autoimmune diseases have strong associations with rheumatoid arthritis, which aligns with findings that show co-occurrence of multiple autoimmune diseases.(12)

Modifiable risk factors vary between rheumatoid arthritis and osteoarthritis and can be used to guide examination as well as prevention and intervention. Smoking is the strongest modifiable risk factor for rheumatoid arthritis; research suggests that individuals with a history of smoking have about twice (1.3 to 2.4 times) the risk of developing RA than those who refrain from tobacco use.(8) There is mixed evidence regarding the association between hormones and RA risk, especially when examining women's reproductive and menstrual history.(13) Rheumatoid arthritis is also associated with several comorbidities, including cardiovascular disease, infections, mental health disorders and cancer.(14) Modifiable risk factors for osteoarthritis include obesity, previous joint injury or trauma, structural malalignment, muscle

weakness, and occupations which involve repetitive motions or heavy lifting.(2,11) Comorbidities for osteoarthritis include obesity, heart disease and diabetes.(2)

Rheumatoid arthritis and osteoarthritis also present differently radiographically. Joints affected by rheumatoid arthritis have loss of bone surrounding the joint, which means the bone appears more radiolucent on imaging.(15) This periarticular osteoporosis is one of four radiographic findings present in the varying stages of the disease and can be used for diagnosis. The remaining three include fusiform soft-tissue swelling, diffuse loss of interosseous space, and marginal erosion of bone.(15) In contrast to rheumatoid arthritis, osteoporotic joints have increased bone density, appearing more radiopaque on imaging. Bone remodeling, joint space narrowing and osteophytes (also known as bone spurs) are other common radiographic findings. There is no erosion or cysts present in OA.(2,16)

Over time, the presence of inflammation in both diseases leads to damage of articular cartilage and eventually bony erosion. Structurally, however, this damage of intra-articular tissues presents differently. Figure 1 and 2 presents images of the varying levels of pathological changes that occur with rheumatoid arthritis and osteoarthritis.(15,17) In a normal joint, the synovial membrane surrounds the joint and contacts the surfaces of the two bones on either side at the site where articular cartilage stops.(15) At the onset of rheumatoid arthritis, the synovial membrane becomes inflamed. This acute synovitis results in intra-articular edema (increase in synovial fluid), redness (vascular congestion) and the initiation of scar tissue formation (presence of fibrin).(15) Due to the inflammation, there is accumulation of red and white blood cells, as well as plasma.(15) One radiographic finding, fusiform soft-tissue swelling, is a result of this increase in inflammation and effusion within the intra-articular space in addition to edema of the surrounding soft-tissues (capsular distension).(15) Periarticular osteoporosis is a common

radiographic finding in individuals with rheumatoid arthritis; however, it depends on their baseline bone density.(15) For instance, adult men who are physically active will have less risk of this occurrence than adult women, who are already at risk for osteoporosis due other factors.(15) At slightly later stages, if the synovial membrane continues to be inflamed, it will extend itself across the joint space overlying the articular cartilage of the two bones, as seen in Figure 5.(15) Not only does this decrease the interosseous space, but also leads to chondral defects and eventually erosion.(15) The destruction of the articular cartilage, and the extension of the inflamed membrane above the point where cartilage ends, leads to the fourth radiographic finding, bony erosion.(15) If the joint is left untreated, chronic inflammation promotes accumulation of fibrin, eventually leading to fibrous ankyloses.(15) Subchondral and synovial cysts are fairly common manifestation of RA as well and can be seen radiographically; they form in subchondral bone in response to increased fluid for the purpose of decreasing intra-articular pressure.(15)

The mechanism by which osteoarthritis destroys articular cartilage is different than rheumatoid arthritis. Articular cartilage is responsible for distributing force from high loads, decreasing contact force from low loads, reducing friction with joint movement and for shock absorption during repetitive loading.(15) It is aneural and avascular, meaning that joint sensation (i.e. pain) does not originate directly from AC, and its ability to repair itself is diminished due to lack of blood flow.(2) Repair is also diminished due to the low metabolic activity of chondrocytes, which are the cells which form cartilage.(18) Excessive contact pressures destroy articular cartilage; contact pressure is influenced by contact forces (amount of loading), contact area (location of loading), as well as speed of loading, and duration of loading.(18) With too much contact pressure, the cartilage becomes rough and coarse, eventually developing crevices

or cracks and finally degenerating completely or breaking off into the intra-articular space.(15) When this happens, chondral defects and particles inflame the synovium, and cause pain, redness, and edema.(2) Radiographically, joint space narrowing and loss of interosseous space is observed as a result of progressive loss of cartilage, resulting in direct bone on bone contact in later stages of the disease.(15) After chondral degeneration, two different bone pathologies can present including eburnation and formation of cysts.(15) Eburnation is a term describing the increase in bone density of subchondral bone when exposed to high contact pressures.(19) Because bone is so dynamic, it responds to loading by building more bone; therefore, in areas in which articular cartilage had disintegrated, bone becomes harder and even more damage and pain can occur when the bone surfaces rub together.(18) Similar to RA, subchondral cysts can develop under the part of the bone subjected to excessive contact pressure.(15) Again, the cause is uncertain but could be due to high intra-articular pressures which promote extrusion of synovial fluid into the bone.(15) Osteophytes, while less common, develop in response to excess subchondral bone formation.(15) Osteophytes, degradation of articular cartilage, and intra-articular inflammation can all cause crepitus, catching, joint tenderness and effusion and eventual subluxation and deformity.(20)

The progression of various pathologies outlined above suggest that joints affected by rheumatoid arthritis and osteoarthritis will be swollen, red, stiff, and painful as a result of inflammation. How can rheumatoid arthritis and osteoarthritis be differentially diagnosed? Through laboratory tests, biologic markers such as rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA) can be used for diagnosis and prognosis.(21) RF and ACPA are proteins found in the blood and can be used as diagnostic tests due to their high association with autoimmune diseases, like RA.(22) Being positive for RF (and especially when high levels are

present), there is a greater risk for complications and manifestations that indicate more severe rheumatoid arthritis progression.(21) Individuals with osteoarthritis characteristically do not have positive tests for rheumatoid factor.(16) If they do have RF factor present, it is typically due to other chronic inflammatory diseases associated with older age.(16) Having positive tests for antibodies against cyclic citrullinated peptides (CCP) suggests the presence of autoimmune responses for diagnosis of several diseases.(21) For RA, presence of anti-CCP antibodies also indicates more rapid progression of disease.(21) C-reactive protein (CRP), and ESR (erythrocyte sedimentation rate) are also two objective measures for predicting joint damage, as elevated levels predict higher levels of radiographic erosive progression.(21) Both CRP and ESR are also indicators of inflammation and are present in the blood of individuals with several other types of chronic disease. Research is conflicting and inconclusive regarding the presence of CRP and ESR in osteoarthritis.

There are several distinctive clinical characteristics that differentiate RA from other rheumatic conditions, like osteoarthritis. Superficially, joints afflicted by OA incur swelling that is hard and “bony” with palpation; in contrast, joints afflicted by RA are typically soft and “boggy”.(16) RA joints are also characterized by tenderness.(16) Rheumatoid arthritis is known as a type of polyarthritis, which classifies it as affecting more than five joints, whereas osteoarthritis typically occurs at individual joints in response to overuse or other musculoskeletal impairment.(13) The likelihood of receiving a diagnosis of RA increases with the number of small joints involved, compared with osteoarthritis, which typically affects larger, weight-bearing joints (i.e. knee and hip). While RA can affect the knee and hip, and osteoarthritis can affect small joints in the hand, the progression and presentation of pain differs. For example, OA affects the carpometacarpal joint most prominently in the hand, whereas RA does not.(16)

Presentation of symptoms can also be a distinguishing factor between the two diseases. Researchers created a valid clinical prediction rule for patients with rheumatoid arthritis with the purpose of identifying individuals with nonspecific arthritis that may progress to RA.(22) Figure 3 details the CPR which involves variables including age, female sex, distribution of affected joints, morning stiffness, number of tender and swollen joints, presence of rheumatoid factor and anti-citrullinated protein antibody, as well as C-reactive protein and ESR levels.(22) Inflammatory arthritis typically involves joints in the wrist and hand.(16) The most commonly involved joints in RA include the metacarpophalangeal joints and proximal interphalangeal joints.(16) Osteoarthritis, however, typically affects the distal interphalangeal joints.(16) While RA is stereotypically thought to be symmetrical in nature, this is not always the case.(16) Osteoarthritis only presents symmetrically if malalignments, high loads or repetitive loading scenarios afflict bilateral joints similarly.(16) Morning stiffness is very common and can last over an hour and is usually a result of rest overnight.(16) In contrast, stiffness of joints is not necessarily characteristic of osteoarthritis.(16) While stiffness from RA is usually worse after not moving the joint for long periods of time, stiffness from OA is usually worse after the joint has had to move excessively during the day or after activity.(16) If individuals with OA have morning stiffness, it usually lasts less than 30 minutes, which helps to distinguish between RA stiffness which is long-lasting.(16)

Unlike osteoarthritis, which is a degenerative disease of the joints, RA is an autoimmune disease with other systemic symptoms that can include fatigue, weakness, muscle soreness, low-grade fever and weight loss.(22) Due to the presence of systemic inflammation, rheumatoid arthritis can affect several other organs and bodily systems, including the cardiopulmonary, integumentary, nervous, and musculoskeletal systems as well as the individual’s eyes.(22)

Cardiovascular disease is prevalent in individuals with rheumatoid arthritis, who have a higher risk of developing coronary artery disease, especially if other risk factors are present such as a history of smoking (which is already a risk factor for RA).(22) The leading cause of death in patients with RA is accelerated atherosclerosis, which is why hypertension and hypocholesteremia are important to control.(22) Pleural effusion, pulmonary nodules and interstitial lung disease are all possible secondary pulmonary conditions that can affect individuals with this disease; rheumatoid lung disease may be due to a possible association with rheumatoid factor which is an antibody that attacks healthy tissue, not just intra-articular tissue.(22) Rheumatoid nodules are firm lumps that can form underneath the skin at various joints, most commonly at the olecranon and metacarpophalangeal joints.(22,23) They occur in about 20% of patients and are thought to be a result of excessive pressure or trauma, are usually non-tender and are composed of inflammatory tissue.(23,24) In patients with osteoarthritis, Heberden's nodes can develop at distal interphalangeal joints, which are idiopathic bony enlargements which are thought to occur in response to destruction of underlying existing subchondral bone after articular cartilage has been worn away.(10) These osteophytes extend proximally, resembling the wings of a sea-gull, which is clinically noted as the sea-gull sign.(15) Heberden's nodes are 10 times more likely to occur in women than men.(17) Both cervical myelopathy and neuropathy can manifest in individuals with rheumatoid arthritis; carpal tunnel and foot drop are common and subluxation of C1-C2 can cause cord compression.(22) The eyes of those with RA can develop scleritis, conjunctivitis, or ulcerative keratitis, however, these are rare.(22) Osteoarthritis does not involve the eyes; however, it can develop in the spine, especially the lumbar spine as this it is a weight bearing area.(2)

There are a range of musculoskeletal tissues that can be affected by rheumatoid arthritis including bone, bursa, tendon, ligament, capsule, and articular cartilage.(15) Due to the bone erosion and subsequent osteoporosis that can occur with inflammation of the synovial membrane, insufficiency stress fractures are another complication of RA.(15) This risk becomes exacerbated with disuse and presence of corticosteroids, which are a viable treatment and can cause further destruction of connective tissue like bone.(15,18) To differentiate RA from other rheumatic diseases, RA results in bony erosion while systemic lupus erythematosus (SLE) does not.(15) Chronic inflammatory diseases can both increase bone resorption and decrease bone formation, which doubles the risk of developing osteoporosis.(25) Additionally, inflamed, painful joints can cause disuse atrophy of bone and surrounding tissue leading to loss of functional movement.(25)

Bursa, tendon, and ligament that are peripheral to synovial joints can often become inflamed as well.(15) Bursa can fill with fluid, contributing to pain and tenderness in the area. (15) Common areas for inflamed bursa include the retrocalcaneal, subacromial and olecranon bursa.(15) Tendonitis and tenosynovitis can occur, especially at on the dorsum of the hand and foot.(15) Similar to capsular tissue, ligaments can be overly stretched due to the presence of chronic edema within the intra-articular space.(15) This ligament laxity can cause subluxation; for example, atlantoaxial subluxation in the cervical spine can potentially lead to cervical myelopathy.(15) Angular deformities can also occur in response to tendinous and ligamentous impairments.(15) Commonly seen deviations include ulnar deviation of metacarpophalangeal joints, fibular deviation of metatarsophalangeal joints, as well as boutonniere and swan-neck deformities in the phalanges.(15) Subluxations and angular deviations contribute to damage of the articular cartilage and erosion of underlying bone.(15)

Pain for individuals with RA is a result of inflammation of the synovium; however, that pain will increase with bony erosion. Therefore, interventions to prevent further damage should focus on reducing inflammation of the joint and protection of articular cartilage in order to indirectly protect subchondral bone. To combat inflammation, the first-line treatment for rheumatoid arthritis is DMARDS (Disease-Modifying Antirheumatic Drugs) which work to block the inflammatory cascade.(22) These drugs are most successful when initiated in early stages of the disease to prevent further damage to intra-articular tissue.(22) Total joint replacement may be necessary for patients who have extensive joint damage in later stages of the disease.(22) For osteoarthritis, pain control is typically the primary treatment; for instance, NSAIDs, corticosteroids (oral or injection), and opioid analgesics have all be used to reduce inflammation and pain.(26) Physical therapy and exercise can be interventions for both of these diseases.(27) Physical therapists can strengthen muscles, improve joint range of motion, reduce swelling and edema, improve balance and increase functional mobility.(27)

Prevention of these diseases can focus on addressing modifiable risk factors as stated previously. For rheumatoid arthritis, cessation of smoking, controlling hypertension and other comorbidities can be beneficial. In addition, anti-inflammatory diets such as Mediterranean diets have had anecdotal success.(22) Manageable risk factors for osteoarthritis include obesity, malalignment, muscle weakness, protection from injury and modification of activity or occupations.(2,11) Exercise is a viable treatment for either disease and has been shown to improve quality of life for patients with RA.(22) Physical therapists should take a holistic approach for treatment of individuals with rheumatoid arthritis and osteoarthritis to not only address pain, but also impact comorbidities, extra-articular manifestations, systemic inflammation, and quality of life.

FIGURE 1: Rheumatoid Arthritis Disease Progression

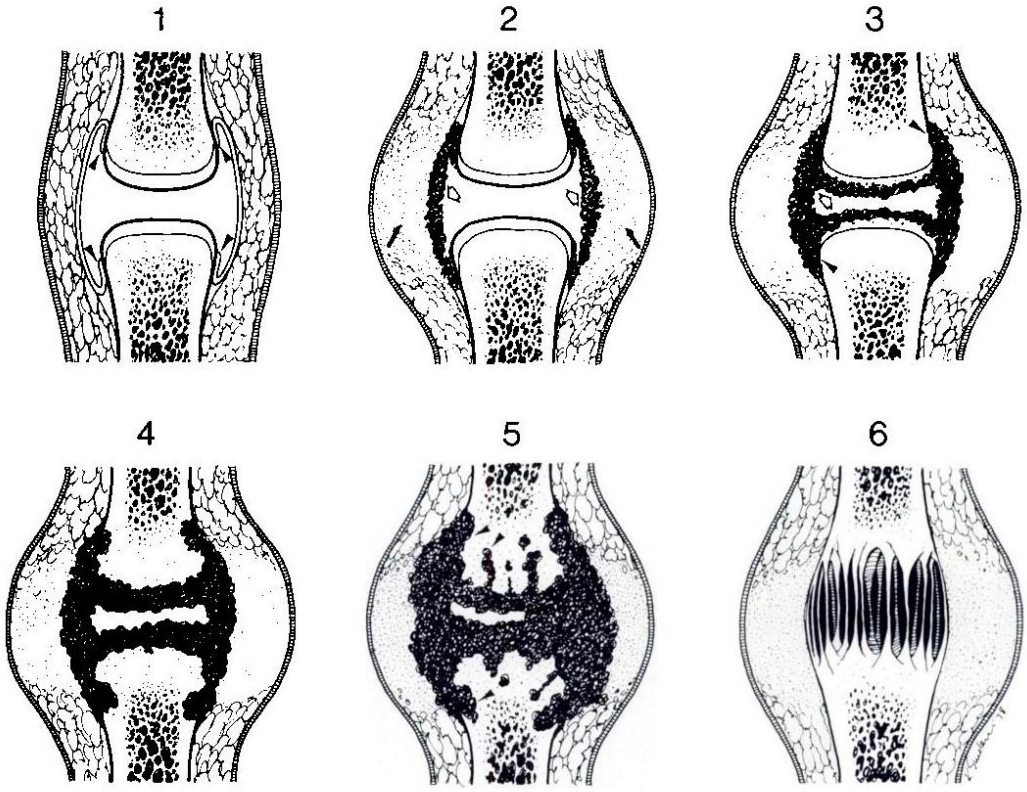

Fig. 5.—Rheumatoid arthritis: pathologic overview.
1, Normal joint. Observe articular cartilage and synovial membrane. At edges of articulation (*arrowheads*), synovium abuts on bone that does not possess protective cartilage.
2, Very early abnormalities of rheumatoid arthritis consist of synovial proliferation (*open arrows*), soft-tissue edema (*solid arrows*), and osteoporosis.
3, Slightly later stage. Inflamed synovial tissue or pannus (*arrow*) extends across cartilaginous surface, leading to chondral erosion. Capsular distension, soft-tissue edema, and osteoporosis are seen. Small osseous erosions at margins of joint are apparent (*arrowheads*).
4 and *5*, More advanced stages. Large marginal and central erosions and cysts are noted (*arrowheads*).
6, Advanced rheumatoid arthritis. Fibrous ankylosis of the joint dominates.

FIGURE 2: Osteoarthritis Disease Progression

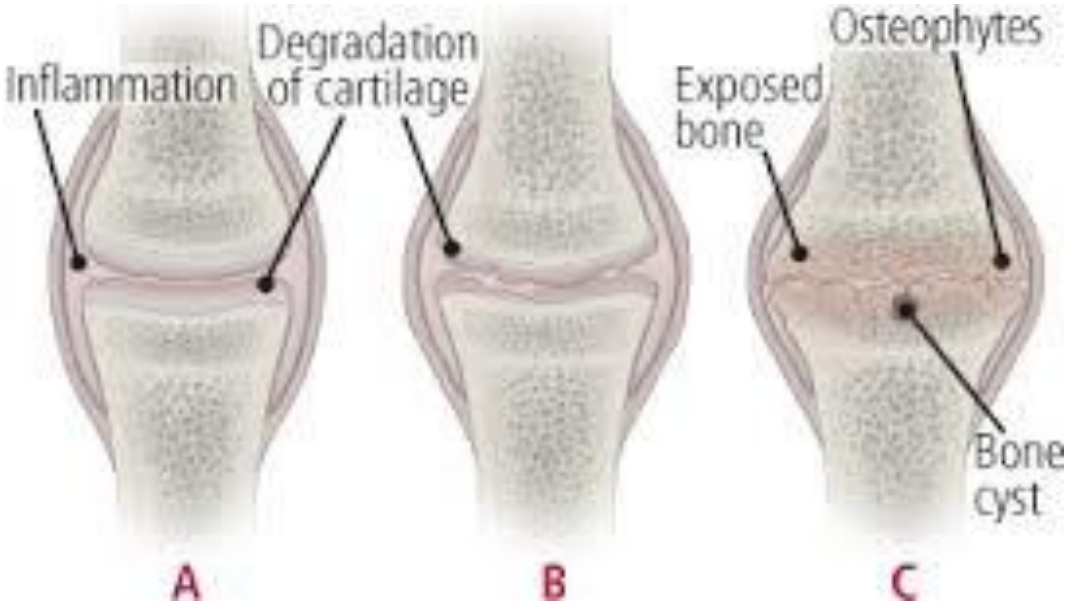

FIGURE 3: Clinical Prediction Rule

Patient Characteristics				**Points**
Age				Years x 0.02
Female sex				1.0
Distribution of affected joints (pts may receive points for more than one item)				
• Small joints of hands or feet				0.5
• Symmetric				0.5
• Upper extremities				1.0
• Upper and lower extremities				1.5
Score for morning stiffness on a 100-mm visual analog scale				
• 26 to 90 mm				1.0
• >90 mm				2.0
Number of tender joints				
• Four to 10				0.5
• ≥ 11				1.0
Number of swollen joints				
• Four to 10				0.5
• ≥ 11				1.0
C-reactive protein level				
• 5 to 50 mg per L				0.5
• ≥ 51 mg per L				1.5
Positive for rheumatoid factor				1.0
Positive for anti-citrullinated protein antibody				2.0
Total:				
Scoring: Rounded to the nearest number ending in 0 or 0.5				
Score	# with RA	# without RA	Likelihood ratio	Percentage with RA at one year
0 to 3.5	0	109	0	0
3.51 to 6.5	41	214	0.42	16
6.51 to 8.5	71	53	3.0	57
=8.5	63	11	12.7	85

References

1. Centers for Disease Control and Prevention (CDC). Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation--United States, 2010-2012. MMWR Morb Mortal Wkly Rep. 2013 Nov 8;62(44):869–873.
2. Osteoarthritis (OA) | Arthritis | CDC [Internet]. [cited 2016 Dec 7]. Available from: http://www.cdc.gov/arthritis/basics/osteoarthritis.htm
3. Sacks JJ, Luo Y-H, Helmick CG. Prevalence of specific types of arthritis and other rheumatic conditions in the ambulatory health care system in the United States, 2001-2005. Arthritis Care Res (Hoboken). 2010 Apr;62(4):460–464.

4. Gabriel SE, Crowson CS, Campion ME, O'Fallon WM. Indirect and nonmedical costs among people with rheumatoid arthritis and osteoarthritis compared with nonarthritic controls. J Rheumatol. 1997 Jan;24(1):43–48.
5. About the Epidemic | HHS.gov [Internet]. [cited 2016 Dec 7]. Available from: http://www.hhs.gov/opioids/about-the-epidemic/
6. Choose Physical Therapy Over Opioids for Pain Management - #ChoosePT - MoveForward [Internet]. [cited 2016 Dec 7]. Available from: http://www.moveforwardpt.com/choose-physical-therapy-over-opioids-for-pain-management-choosept
7. Arthritis Types | Arthritis | CDC [Internet]. [cited 2016 Dec 7]. Available from: https://www.cdc.gov/arthritis/basics/types.html
8. Epidemiology of the Rheumatic Diseases - Alan J. Silman; Marc C. Hochberg - Oxford University Press [Internet]. [cited 2016 Dec 8]. Available from: https://global.oup.com/academic/product/epidemiology-of-the-rheumatic-diseases-9780192631497?cc=us&lang=en&
9. Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. Clin Orthop Relat Res. 2004 Oct;(427 Suppl):S6–15.
10. Kellgren JH, Moore R. Generalized osteoarthritis and Heberden's nodes. Br Med J. 1952 Jan 26;1(4751):181–187.
11. Felson DT. Risk factors for osteoarthritis: understanding joint vulnerability. Clin Orthop Relat Res. 2004 Oct;(427 Suppl):S16–21.
12. Cojocaru M, Cojocaru IM, Silosi I. Multiple autoimmune syndrome. Maedica. 2010 Apr;5(2):132–134.
13. CDC C for DC and P. Rheumatoid Arthritis (RA) [Internet]. 2016 [cited 2016 Dec 8]. Available from: http://www.cdc.gov/arthritis/basics/rheumatoid.htm
14. Mikuls TR, Saag KG. Comorbidity in rheumatoid arthritis. Rheum Dis Clin North Am. 2001 May;27(2):283–303.
15. Resnick D. Common disorders of synovium-lined joints: pathogenesis, imaging abnormalities, and complications. AJR Am J Roentgenol. 1988 Dec;151(6):1079–1093.
16. Diagnosis and differential diagnosis of rheumatoid arthritis [Internet]. [cited 2016 Dec 9]. Available from: http://www.uptodate.com/contents/diagnosis-and-differential-diagnosis-of-rheumatoid-arthritis
17. What is Osteoarthritis? - Symptoms & Information - Patient Education Center [Internet]. [cited 2016 Dec 9]. Available from: http://www.patienteducationcenter.org/articles/osteoarthritis-2/
18. Gross MT. Articular Cartilage: Composition, Structure, Function, Mechanical Properties, and Healing.
19. Eburnation | definition of eburnation by Medical dictionary [Internet]. [cited 2016 Dec 10]. Available from: http://medical-dictionary.thefreedictionary.com/eburnation
20. Buckwalter JA, Martin JA. Osteoarthritis. Adv Drug Deliv Rev. 2006 May 20;58(2):150–167.
21. Biologic markers in the diagnosis and assessment of rheumatoid arthritis - UpToDate [Internet]. [cited 2016 Dec 9]. Available from: https://www.uptodate.com/contents/biologic-markers-in-the-diagnosis-and-assessment-of-rheumatoid-arthritis?source=see_link

22. Wasserman AM. Diagnosis and management of rheumatoid arthritis. Am Fam Physician. 2011 Dec 1;84(11):1245–1252.
23. NRAS - National Rheumatoid Arthritis Society [Internet]. [cited 2016 Dec 9]. Available from: http://www.nras.org.uk/rheumatoid-nodules
24. Wolff M, Memon AA, Chalmers JP, Sundquist K, Midlöv P. Yoga's effect on inflammatory biomarkers and metabolic risk factors in a high risk population - a controlled trial in primary care. BMC Cardiovasc Disord. 2015 Aug 19;15:91.
25. Hardy R, Cooper MS. Bone loss in inflammatory disorders. J Endocrinol. 2009 Jun;201(3):309–320.
26. Clinical Practice Guidelines Osteoarthritis [Internet]. [cited 2016 Dec 10]. Available from: http://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Osteoarthritis
27. Physical Activity for Arthritis | Basics | Arthritis [Internet]. [cited 2016 Dec 10]. Available from: http://www.cdc.gov/arthritis/basics/physical-activity-overview.html