



Advancing NIH Research on the Health of Women: A 2021 Conference

Chronic Debilitating Conditions on Women: Sex and Gender Impact on Osteoarthritis

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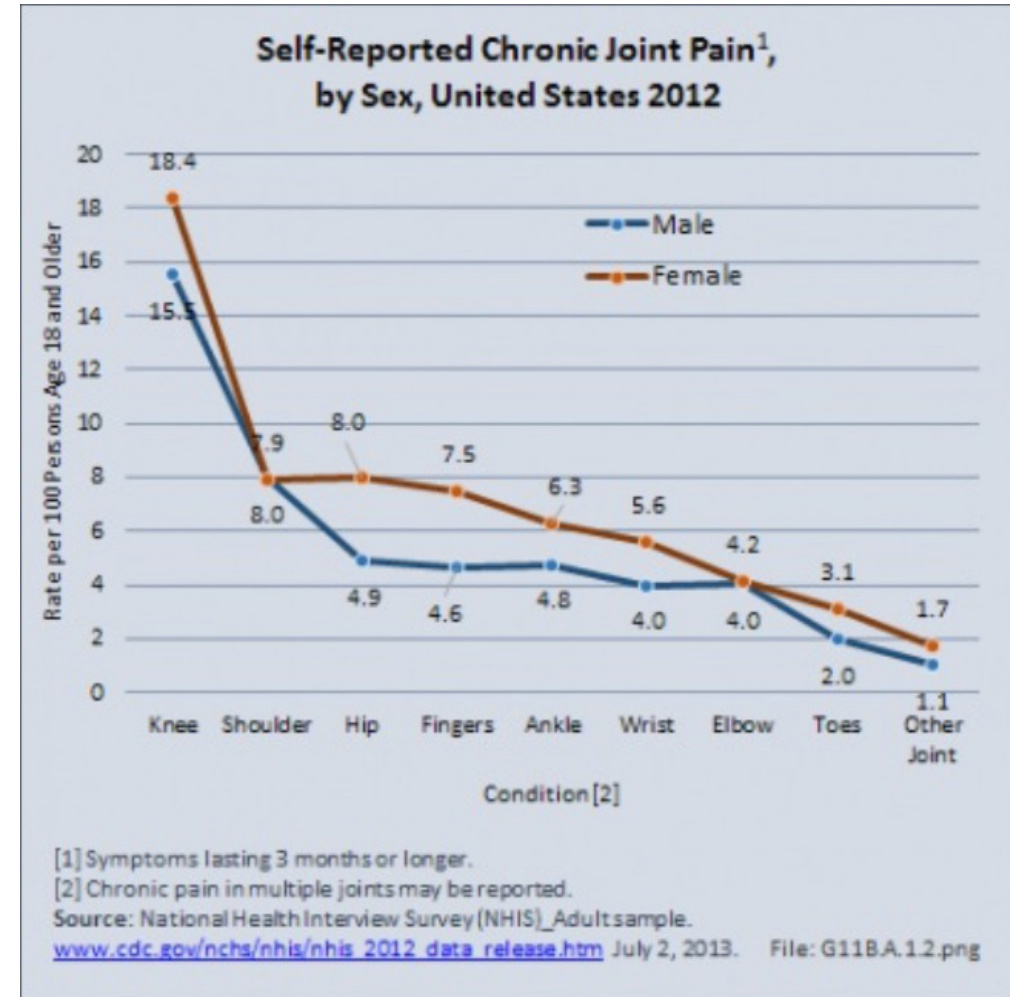
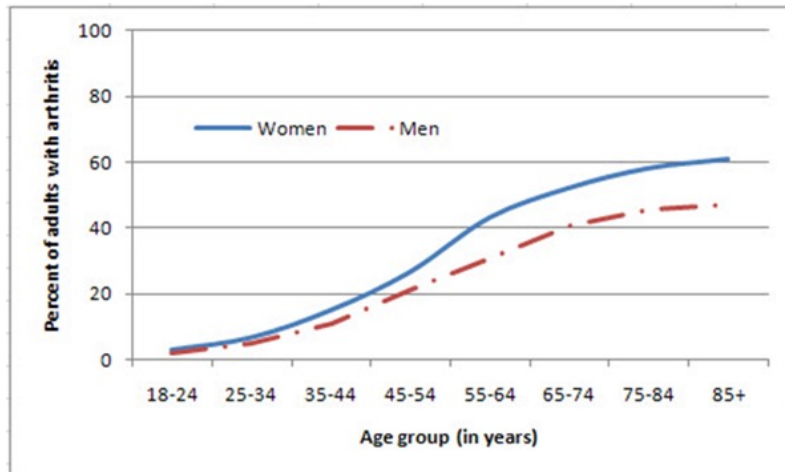
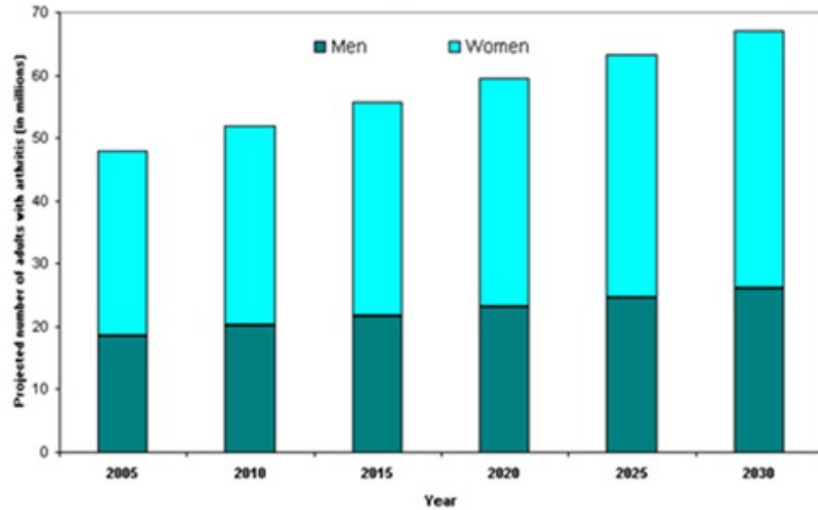
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Osteoarthritis Prevalence

Arthritis is expected to affect millions more people in the coming years.

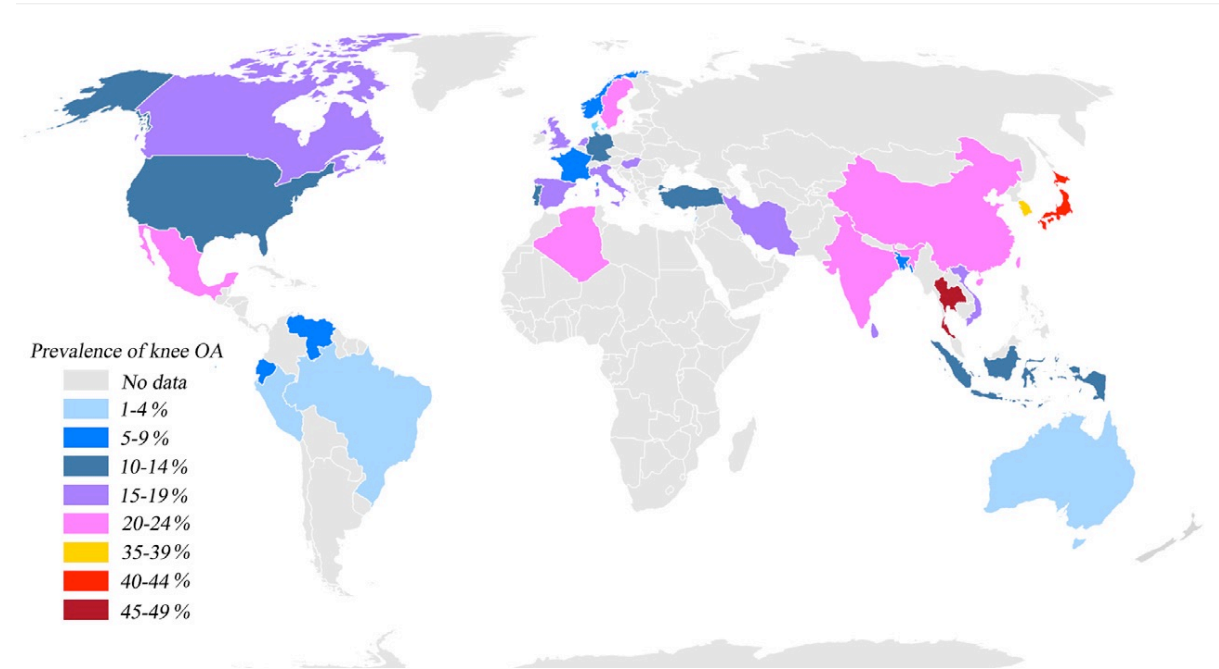


Burden of Musculoskeletal Conditions in the US, 2015

Knee OA Prevalence

- Meta-analysis with ~3.7 million people
- Rates increase with age
- US about 130 per 10,000 person-years
- Ratios of prevalence, incidence females to males 1.69/1.39

Cui et al *E Clin Med* 2020



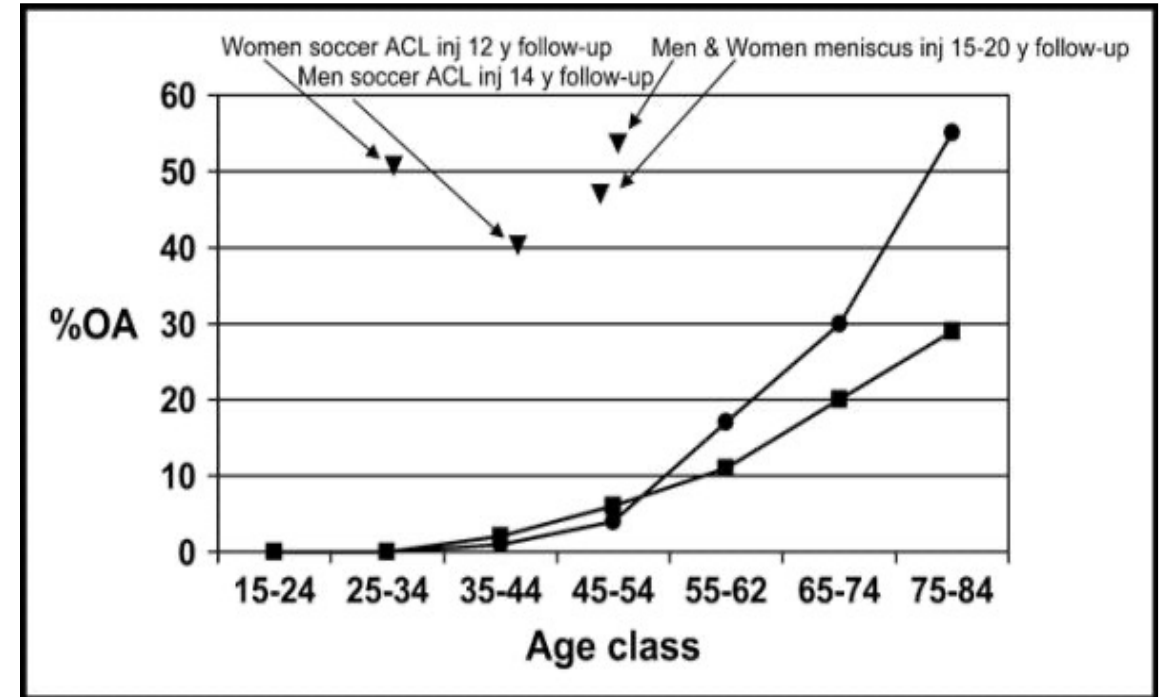
Sex/Gender-Specific Knee OA Risk Factors

- Acquired
injury
patterns of overuse
- Inherent
anatomy
gait pattern
impact of estrogen
muscle strength
- Inflammatory response (to injuries, obesity, OA)



Joint Injury

- Higher risk in women (especially ACL)
- Significantly higher risk of OA in younger people after knee injury-even with reconstruction
- Earlier among women than men with ACL injuries



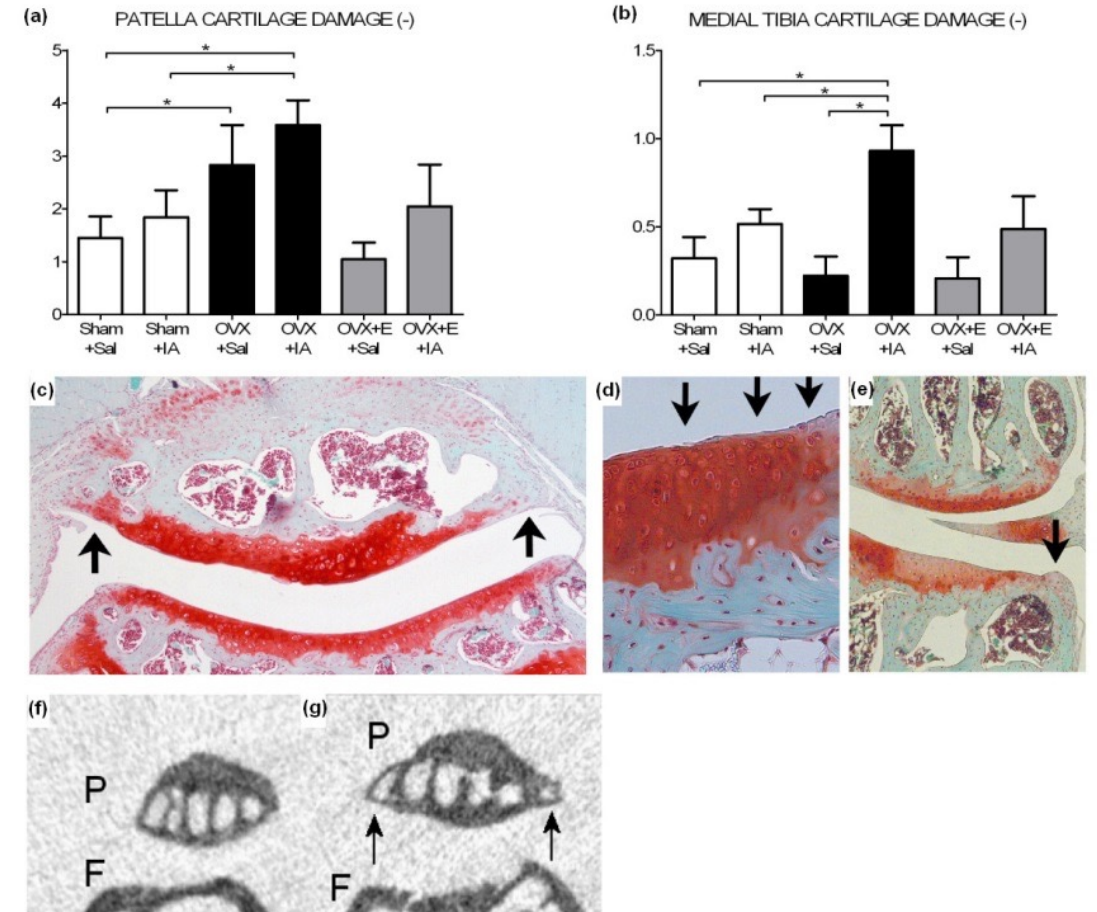
Knee OA-Anatomic Risk Factors

- Larger Q-angle
- Foot pronation
- Increased femoral anteversion
- Genu valgum
- External tibial torsion
- Tibia vara
- Generalized ligamentous laxity
- Tight lateral patellar retinaculum
- Patella alta
- Shallower femoral notch
- Narrower patella



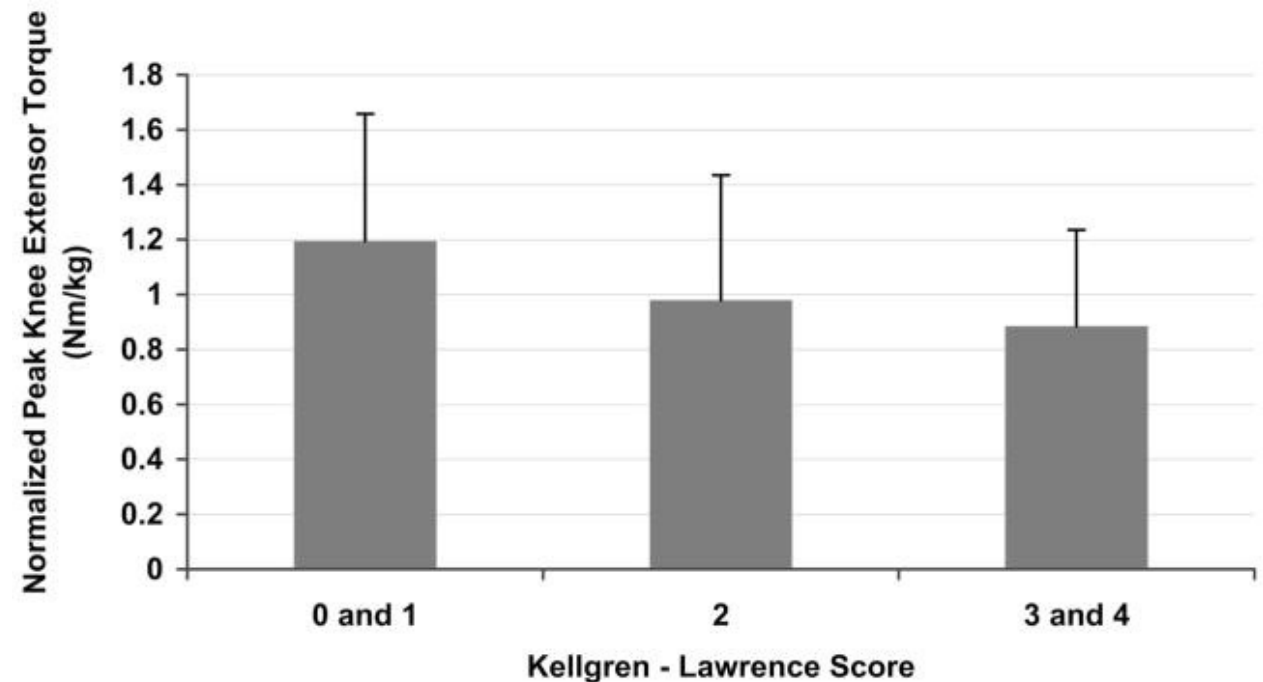
Effects of Estrogen

- Mice with model of induced OA
- Ovariectomy increased degree of cartilage injury
- Due to loss of bone or direct effect on cartilage?
- Does this translate to joint issues for women after menopause?



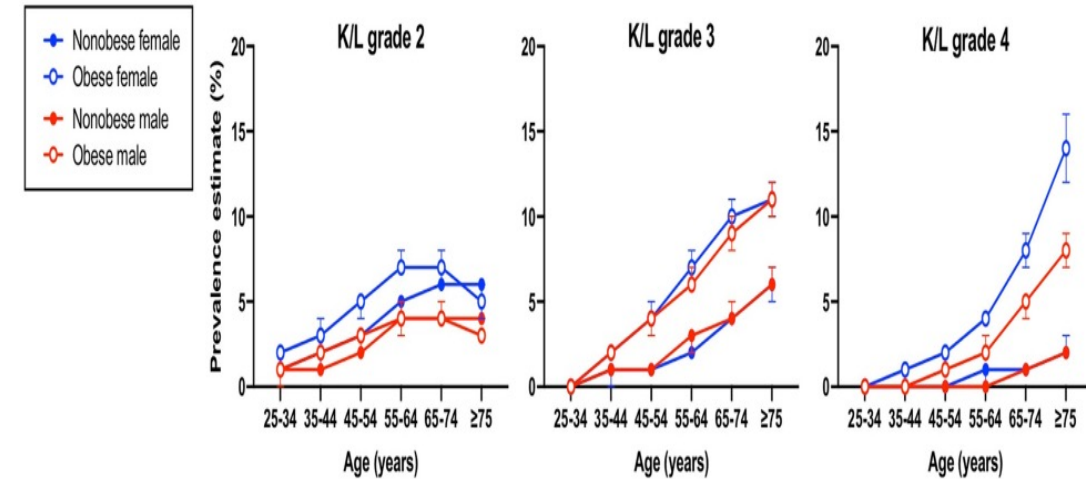
Muscle Strength

- Quads strength in women was higher in those without OA or few radiographic changes
- Only ½ with OA had OA-related pain
- Impact of strength on development of OA?



Impact of/Response to Obesity

- More than only increased cartilage loads (increased risk of hand OA)
- Women more likely to demonstrate association between metabolic syndrome and symptomatic OA
- Effect of obesity was greater in women than men for more severe knee OA (K/L grade 2 and 4)
- Link between obesity and OA may be mediated by leptin, especially for women



Sex/Gender Impact on Pain

Sex-Based

- Genetic
- Neurochemical
- Impact of sex steroids
- Systems level (e.g., inflammation, cortical connectivity, midbrain-brainstem connectivity)
- Psychologic (e.g., depression, anxiety)

Gender-based

- Psychosocial (e.g., coping, self-efficacy)
- Sociocultural (e.g., gendered expectations, gender role)
- Experiential (e.g., abuse, IPV, familial history)

Knee OA Treatment

Non-Surgical

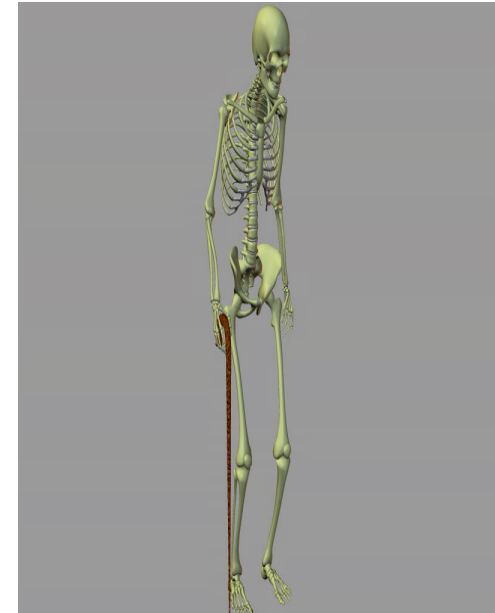
- Women more likely (than men) to be treated in the 12 months prior to surgery with
 - opioids
 - non-opioids
 - injections
 - physical therapy

Bawa et al *J of Arthroplasty* 2016

Pre-operative Function

- Patients with end-stage OA and waiting for TKA/THA
- Women with significantly poorer health-related QOL scores, self-efficacy (confidence in management of pain, fatigue, etc), and function

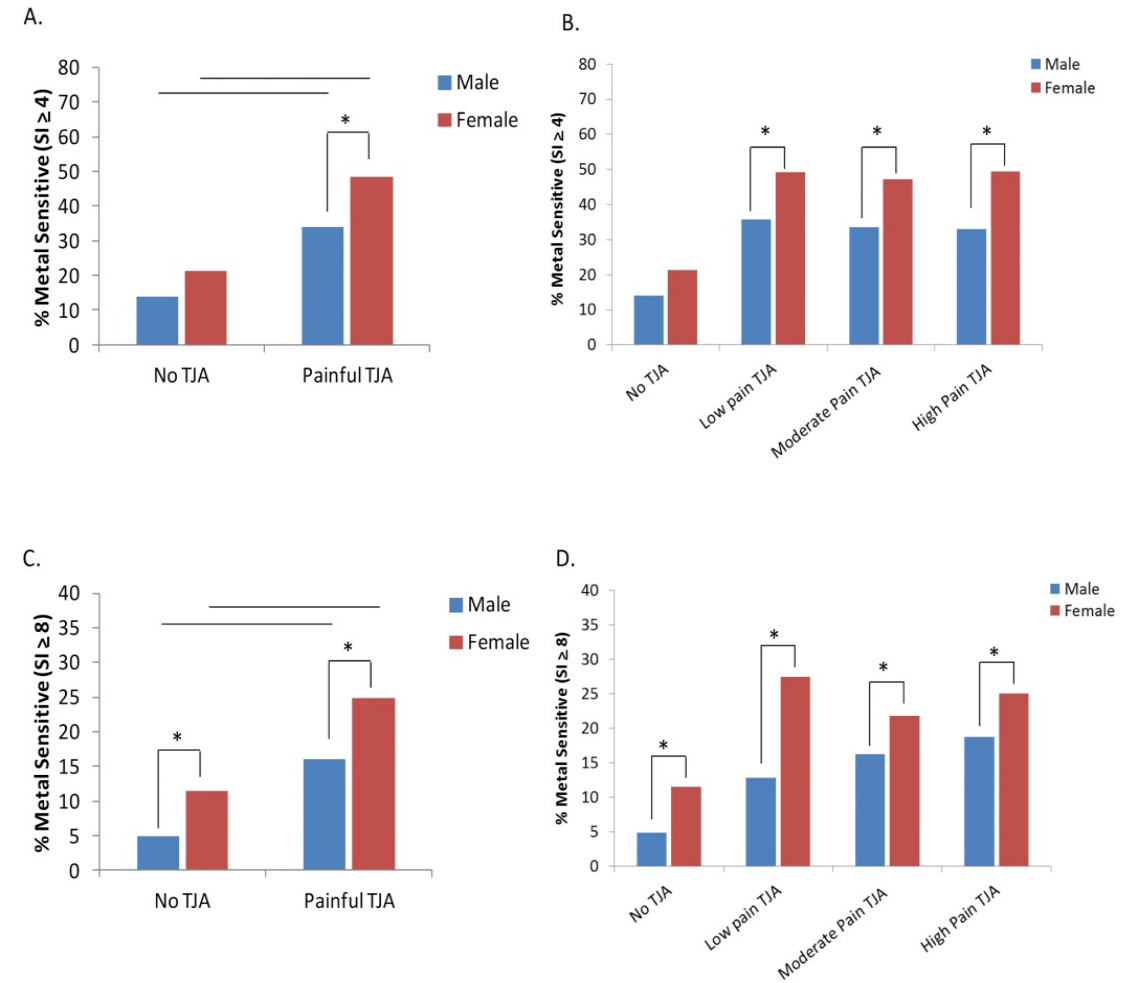
Ackerman et al *Arthritis Rheum* 2005



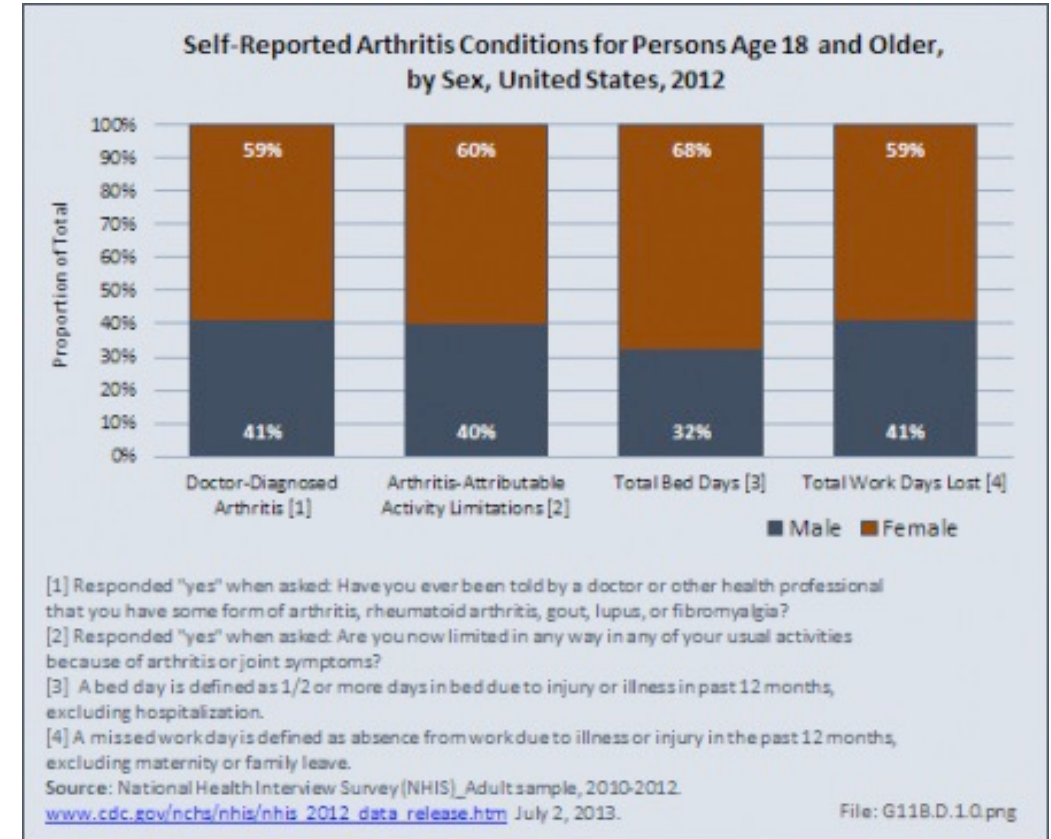
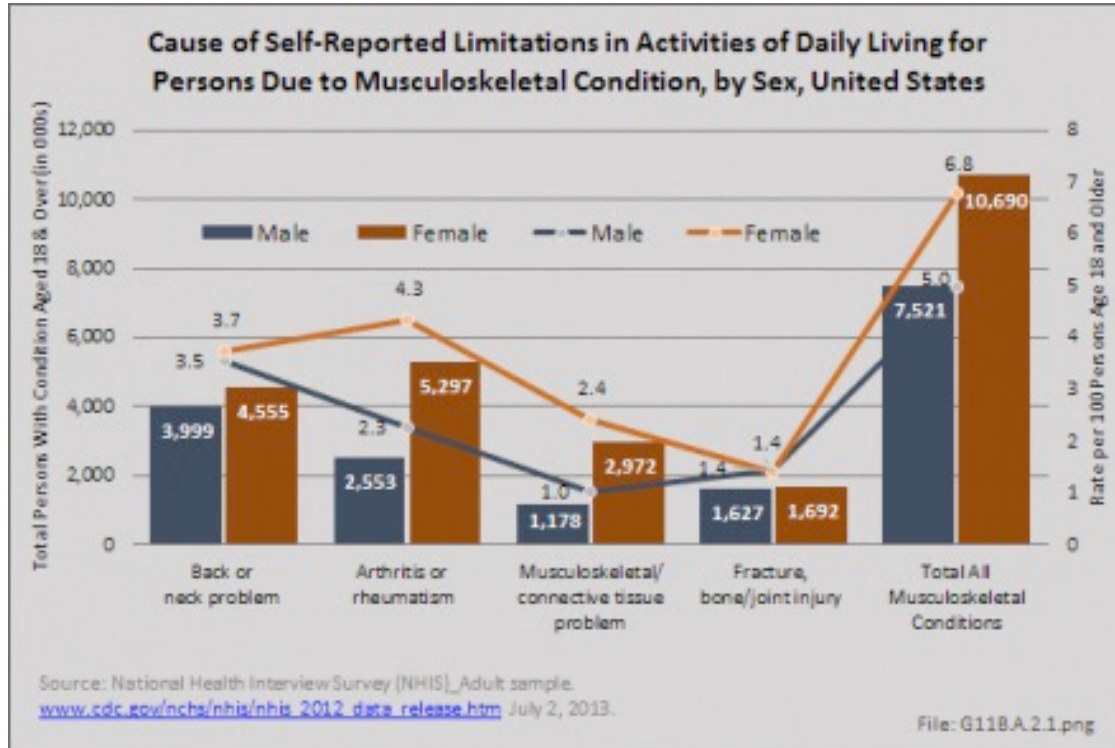
Metal Hypersensitivity

- Pts referred with painful joint replacements
- Women had higher levels of pain than men
- Women had higher rates and severity of metal sensitization

Caicedo et al *JBJS* 2017



Quality of Life/Disability



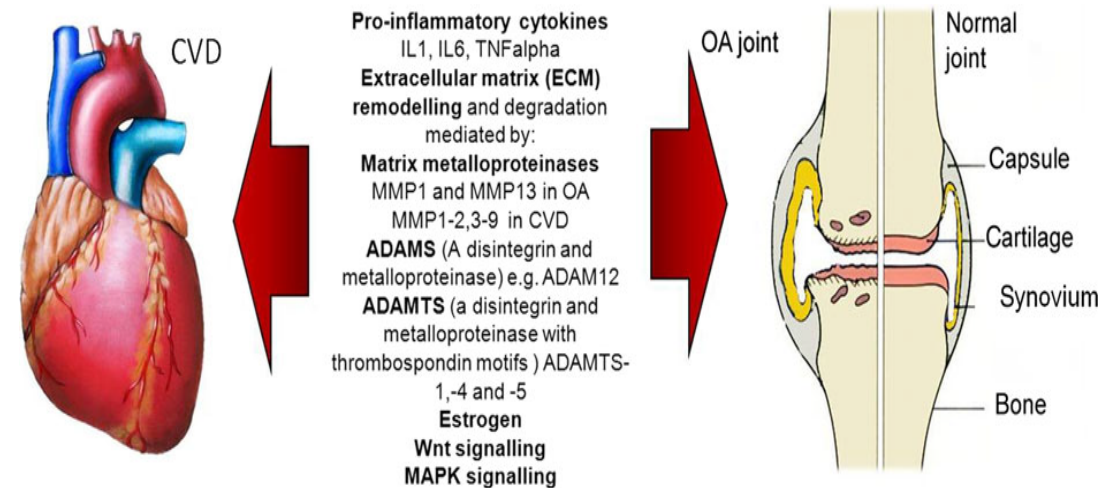
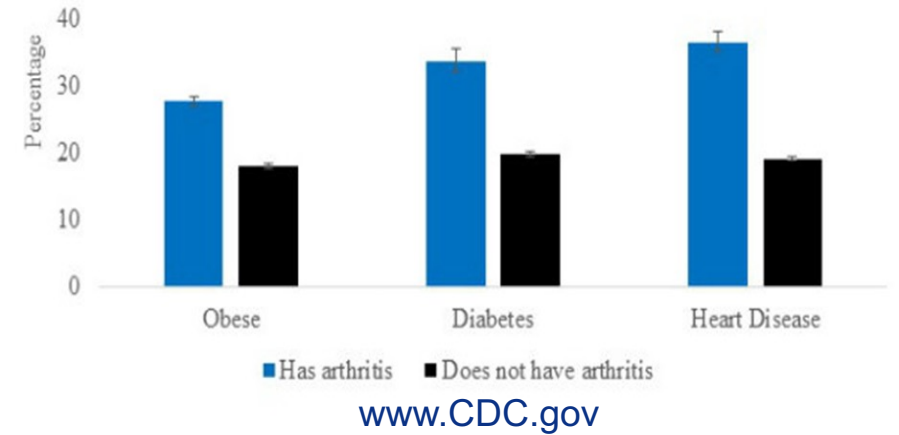
Burden of Musculoskeletal Conditions in the US 2015

OA and Co-morbidities

- HTN, depression, COPD most common co-morbidities for women and men with OA
- Prevalence of each additional condition more common among women
- Women had higher number of co-morbidities

Marshall et al *BMJ Open* 2019

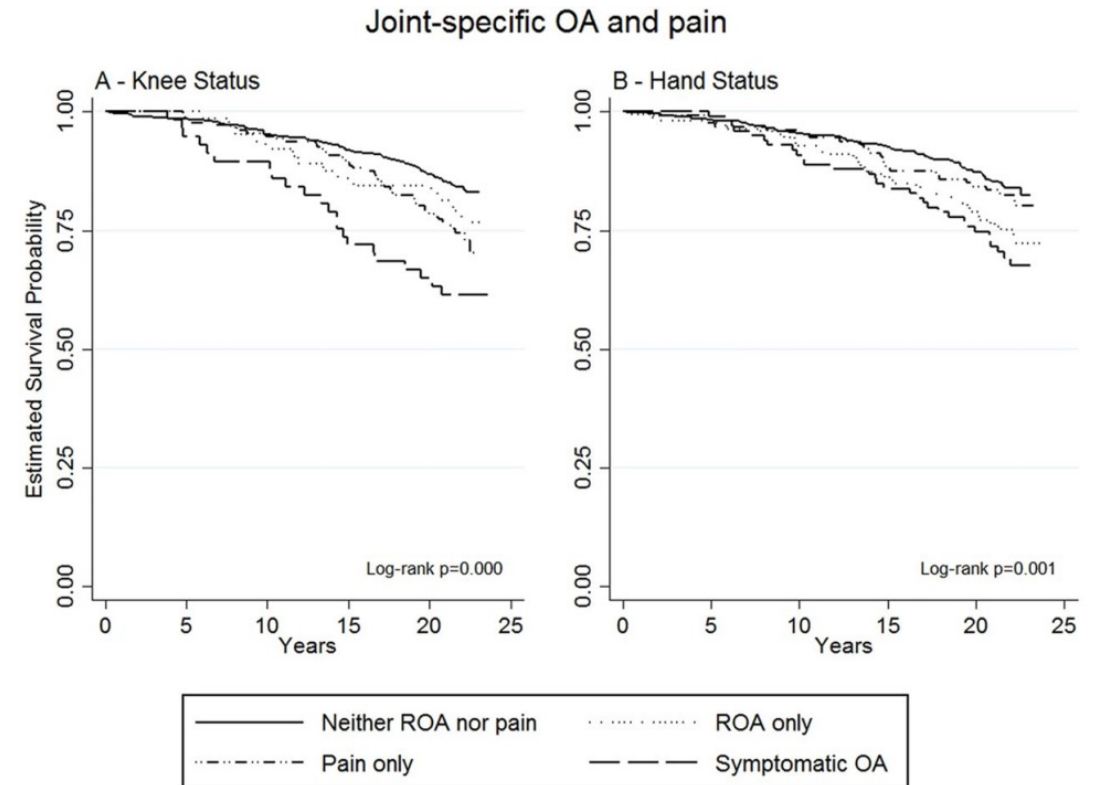
Age-Adjusted Percentage of Doctor-Diagnosed Arthritis Among Adults, by Obesity, Diabetes, and Heart Disease Status — National Health Interview Survey, United States, 2013–2015



Fernandes et al *Eur J Clin Invest* 2015

Women, Knee OA, and Mortality

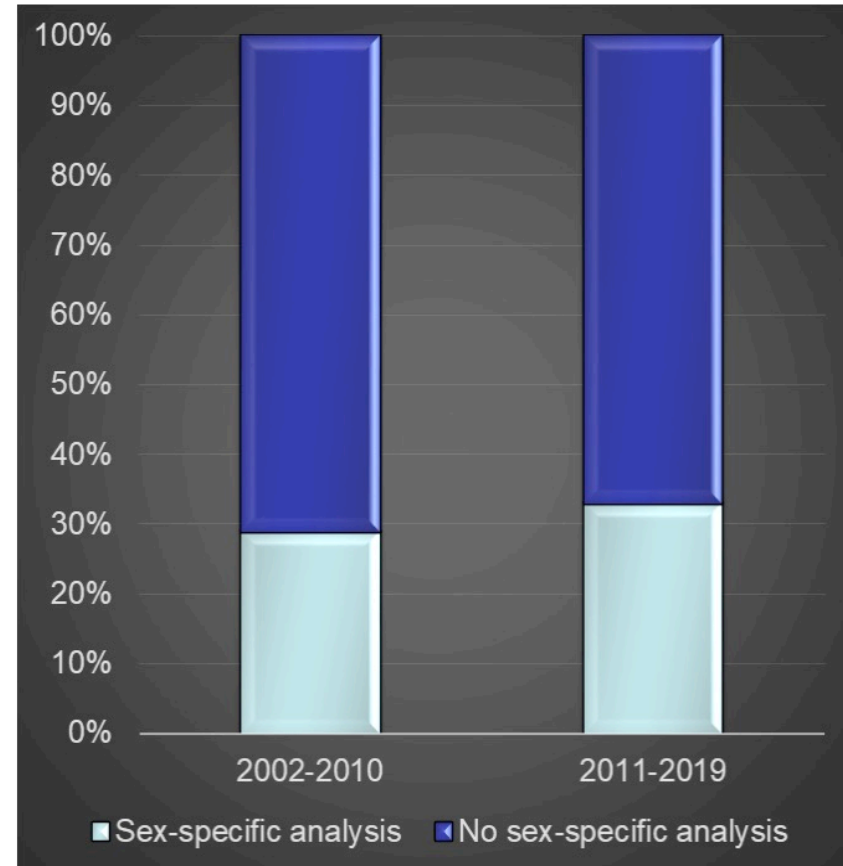
- Increased CVD-related and all-cause mortality for those with OA of the knee
- Women with knee pain and no ROA had a 49% increased risk of dying from all-cause mortality (compared with those with no knee pain/no ROA)
- Women with painful knee ROA had a 97% increase in mortality risk
- Greatest increase in mortality from CVD conditions (pain only HR=3.25, pain and ROA HR=4.19)
- Related to the presence of knee pain, not only radiographic degenerative changes (no increased mortality among those with only radiographic changes)
- No similar findings for those with hand OA



Reported Results Based on Sex

- Evaluation of literature for rotator cuff injuries and OA of the knee
- 31% reported sex-specific analysis
- 30-40% reported based on sex for knee OA studies
- No change over time

Stumpff et al *JWH* 2020



Future Directions

Continued exploration of the impact of sex/gender on OA

- onset/risk factors/early diagnosis
- prevention
- response to treatment
- impacts on function, co-morbidities, mortality

Requires

- disaggregation of data based on sex/gender
- targeted research/funding regarding OA among women, given differing risks/contributing factors
- enhanced health education in sex/gender to train next generations of clinicians and researchers

Thank You!

