Obesity and Musculoskeletal/Rheumatologic Disease: "Working Out" The Causes

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Why give this talk?

- The importance of obesity in rheumatologic disease is underestimated
- Observed Paradox: The more prevalent a disease is, the less it is discussed/treated, e.g., OA vs. SLE
- Treating the cause of disease is almost always preferable to treating the sequela

Objectives

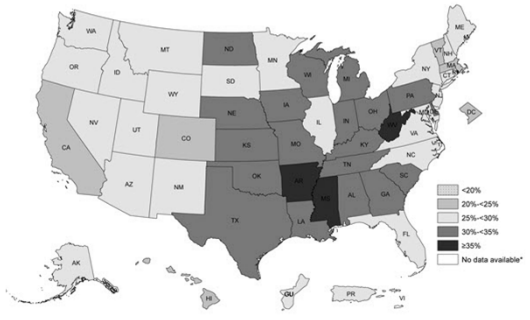
1. Recognize the prevalence of obesity in the US population
2. Identify obesity as a risk factor for musculoskeletal and rheumatologic disease
3. Evaluate the evidence for weight loss as a treatment adjunct for musculoskeletal and rheumatologic disease

Prevalence of Obesity in the U.S.

- Obesity is a problem THROUGHOUT the U.S.
- Over one third (34.9% / 78.6 million) of U.S. adults are obese
- In 2014, no state had a prevalence of obesity less than 20%.

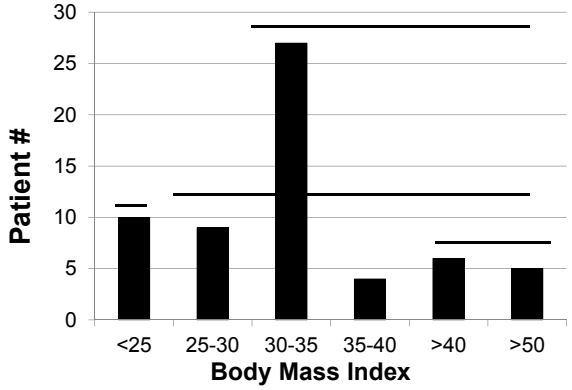
- 5 states and the District of Columbia had a prevalence of obesity between 20% and <25%.
- 23 states, Guam and Puerto Rico had a prevalence of obesity between 25% and <30%.
- 19 states had a prevalence of obesity between 30% and <35%.
- 3 states (Arkansas, Mississippi and West Virginia) had a prevalence of obesity of 35% or greater.
- The Midwest had the highest prevalence of obesity (30.7%), followed by the South (30.6%), the Northeast (27.3%), and the West (25.7%)

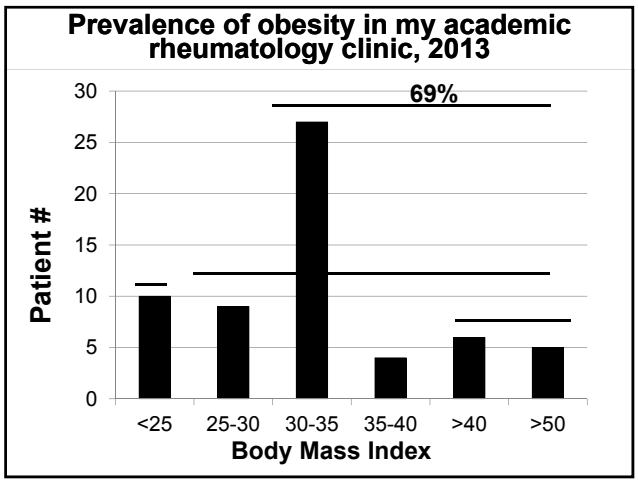
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2014



CDC.gov

Prevalence of obesity in my academic rheumatology clinic, 2013




Prevalence of obesity in my academic rheumatology clinic, 2013
Patient #
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69%
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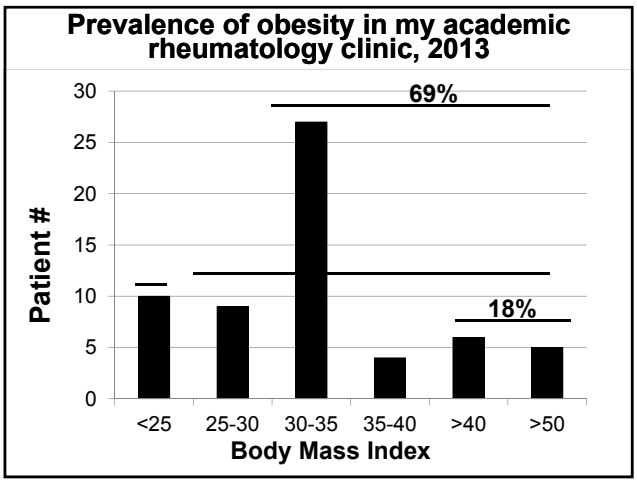
Body Mass Index


Prevalence of obesity in my academic rheumatology clinic, 2013
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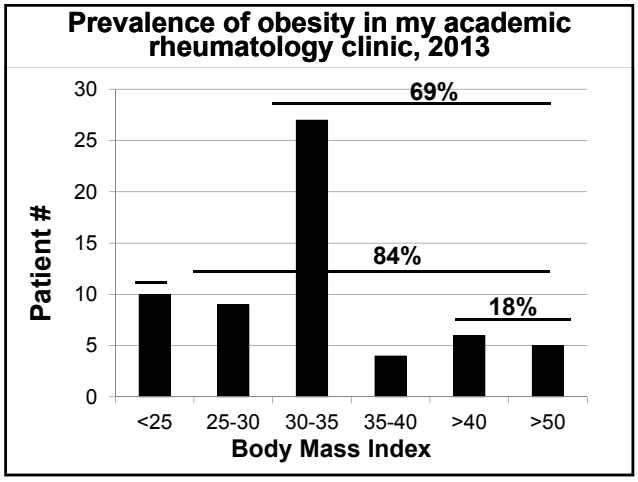
Body Mass Index


Prevalence of obesity in my academic rheumatology clinic, 2013
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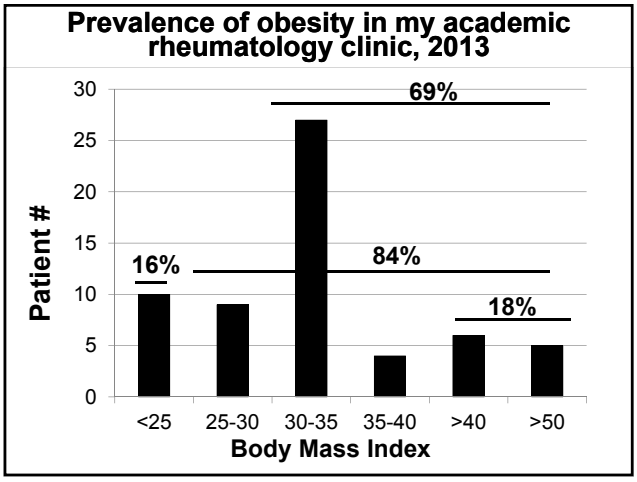
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Body Mass Index

Healthcare Costs of Obesity

- 1998: medical costs of obesity estimated to be as high as $78.5 billion
  - Half financed by Medicare and Medicaid.
- The increased prevalence of obesity is responsible for almost $40 billion of increased medical spending through 2006
- Medical costs of obesity could have risen to $147 billion per year by 2008.

[*Health Affairs* 28, no. 5 (2009): w822–w831 (published online 27 July 2009; 10.1377/hlthaff.28.5.w822)]

Obesity and Musculoskeletal/Rheumatologic Disease

- Obesity and risks of Autoimmune Disease
  - RA
  - Psoriatic Arthritis
- Obesity and acute phase reactants
- OA
- Chronic back pain
- Chronic pain

[Gout, MS, others not discussed]

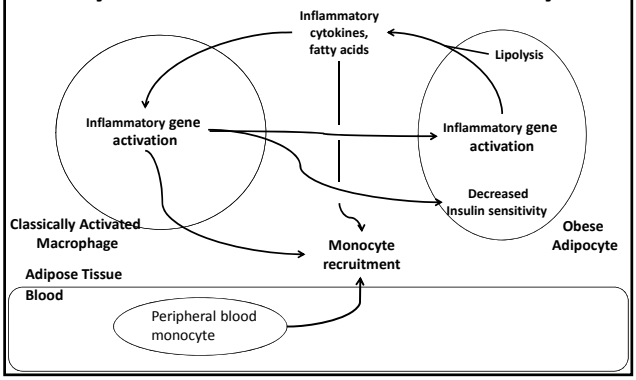
Obesity and Autoimmune Disease

- The incidence of autoimmune disease may be slowly rising
- Significant changes in western dietary habits have led to the parallel rise in obesity
- White adipose tissue (WAT; i.e. "fat") secretes adipokines and inflammatory cytokines.
  - Inflammatory adipokines: leptin, resistin and visfatin = increase in obesity
  - Anti-inflammatory adipokines: adiponectin = decrease in obesity

Mechanism of Obesity's association with Autoimmune Disease

- Proposed mechanism: metabolic inflammation may contribute to autoimmunity and/or to chronic disease (metabolic syndrome, HTN, HL, DM, etc.)
- Other potential contributing factors:
  - Vitamin D deficiency
  - Alteration of gut microbiome
  - Dysreguation of T helper (Th)17/T-regulatory cell (Treg)balance
- Other diseases associated with obesity: MS, Type I DM, Hashimoto's, IBD

Adipose tissue macrophages promote systemic inflammation in obesity



Obesity as a risk factor for RA?

- The role of obesity in RA is controversial
- Most studies report a higher risk of developing RA in obese individuals with an odds ratio ranging from 1.2 to 3.4
  - Anti-CCP antibody (ACPA)-negative RA
- Increased RA disease severity correlates with pro-inflammatory adipokine levels
- Decreased treatment efficacy
- The prevalence of obesity in RA is variable (18% to 31%)

BMI and Relative Risk of RA

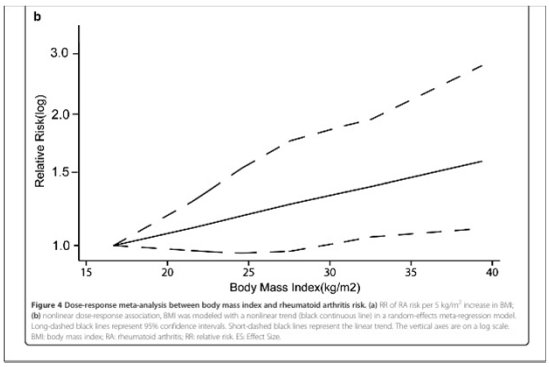


Figure 4 Dose-response meta-analysis between body mass index and rheumatoid arthritis risk. (a) RR of RA risk per 5 kg/m² increase in BMI; (b) nonlinear dose-response association, BMI was modeled with a nonlinear trend (black continuous line) in a random-effects meta-regression model. Long-dashed black lines represent 95% confidence intervals. Short-dashed black lines represent the linear trend. The vertical axes are on a log scale. BMI: body mass index; RA: rheumatoid arthritis; RR: relative risk. ES: Effect Size.

Qin et al. Arthritis Research & Therapy (2015) 17:86
DOI 10.1186/s13075-015-0601-x

Counterpoints: Obesity as a RA Risk

- BMI may be protective of RA incidence in men, not not in women (mechanism?)
- Not all weight loss in RA is good weight loss—sarcopenia and chachexia

Decreased treatment efficacy due to obesity in RA

- Obesity may be associated with a worse therapeutic response
- negative association between BMI and response to anti-TNFα therapies, notably infliximab, in RA, psoriatic arthritis and ankylosing spondylitis
- no impact on response to rituximab

Does weight loss improve RA?

- Understudied
- J Sparks, *et al*, May 2015: retrospective cohort study involving 53 RA patients who underwent bariatric surgery,
  - Post-bariatric surgery, significant improvements in:
    - RA disease activity
    - serum inflammatory markers
    - RA-related medication usage.
- One year after bariatric surgery, only 6% had moderate/high RA disease activity compared to 57% at baseline ($P<0.001$).

Arthritis Care & Research DOI 10.1002/acr.22629

Does weight loss improve RA?

- Lost a mean of 41 kg, corresponding to 70% mean excess weight loss.
- Improvements NOT related to more aggressive medical management, as RA-related medication usage significantly decreased after bariatric surgery, with 98% on medications at baseline compared to only 66% one year after surgery.

Arthritis Care & Research DOI 10.1002/acr.22629

Obesity as a risk for psoriatic arthritis (PsA)

- >50% of PsA patients are overweight or obese
- Obesity is considered a risk factor for PsA
- Impacts disease activity and response to therapy
- Eder *et al* 2014:
  - obesity is associated with a lower probability of achieving sustained remission, irrespective of therapy.

- Di Minno *et al* 2014:
  - obesity = independent risk factor for not achieving minimal disease activity (MDA) in 24 months of follow-up (hazard ratio 4.90, 95% confidence interval (CI) 3.04–7.87)
- Does weight loss improve odds of reaching MDA?
  - Weight loss of 5% or more = higher likelihood of achieving MDA (odds ratio (OR) 4.20, 95% CI 1.82–9.66)
- Methotrexate use in PsA: obesity is a risk factor for liver fibrosis in patients with psoriasis and PsA
- Current recommendations: weight loss may improve disease outcomes and decrease risk of therapy

Obesity and acute phase reactants

- ESR and CRP can be elevated in obese patients
  - Obese population = higher ESR/CRP levels compared to age and gender matched non-obese
- Adipose tissue as a "pro-inflammatory" organ
- Connection between obesity and metabolic disease? (HTN, HL, DM, etc.)
  - Worse outcomes associated with obesity-driven systemic inflammation

Obesity as a risk for Osteoarthritis

- Obesity = single most important risk factor for the incidence of severe knee OA
- Best studied association
- Obesity is also a risk factor for:
  - OA progression
  - Receiving a knee replacement
- Increased odds ratios of knee (2.81) and hand (2.59) OA
  - although no increased risk of hip OA (1.11)

Mechanism of association between Obesity and OA

- Prevailing Theory: mechanical hypothesis
  - excessive weight increases joint loading, "wear and tear"
  - Elevated BMI increases strain on medial and lateral parts of the knee and alters gait
  - However: Obesity is also a risk factor for OA in non–weight-bearing joints, like hand and wrist.
- Modern Theory: Adipose tissue is an endocrine organ
  - Systemic adipokines, cytokines promote systemic low-grade inflammation.
  - Disturbed lipid metabolism
- Hypothesis: systemic factors of obesity influence OA outcomes

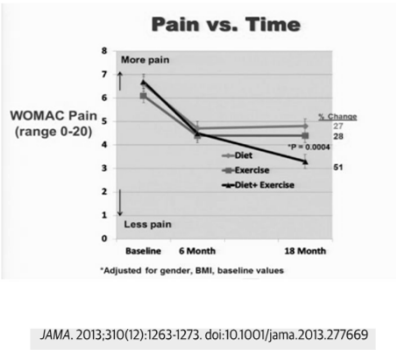
Obesity adversely affects joint replacement outcomes

- 104,000 TJA procedures performed in Canada in 2012–2013:
  - 40 % of total hip and 60 % of total knee patients were obese
- Increased peri- and post-operative complications and slower functional improvement post-op
- Increased risk of surgical complications including infection, thromboembolic events, long-term prosthetic survivorship, component malposition, and prosthesis loosening and dislocation

Obesity adversely affects joint replacement outcomes

- Obese patients are less healthy for major surgery: age, diabetes, coronary artery disease, hyperlipidemia, hypertension and sleep apnea
- Current guidelines universally recommend weight loss prior to undergoing elective joint replacement

Does Weight Loss Improve OA Outcomes? IDEA Trial (Messier, *et al* JAMA 2013)



JAMA. 2013;310(12):1263-1273. doi:10.1001/jama.2013.277669

- 454 patients randomized to three treatment groups
- Groups:
  - 1. exercise alone
  - 2. diet alone
  - 3. diet + exercise
- All lost 5-10% weight
- 6mo: 30% improvement
- 18mo: 50% improvement in diet + exercise group
- Recommendations for OA treatment include diet and exercise
- Both are "strongly recommended" in 2012 ACR guidelines

Obesity as a risk for chronic back pain

- Higher rate of non-radiating and non-specific low back pain in obese men
- The prevalence of low back pain increases as BMI rises:
  - <3% normal BMI range report low back pain in the past 3 months
  - 7.7% of obese and 11.6% of morbidly obese individuals reported low back
  - Linear increment of chronic pain cases as BMI increases in large population studies in the US

Obesity and chronic low back pain

- Obesity = risk for low back pain adolescents (regardless of gender)
- Obesity may decrease effectiveness of conservative therapy for LBP
- Reduction in obesity may improve outcomes
- Obesity with LBP: increased disability, higher pain severity, and worse functional capacity
- Degenerative disk disorder (DDD) more frequent in obese population
  - The severity of DDD positively correlates with BMI.

- Vicious cycle: pain with activity leads to less movement, less movement facilitates disability and deconditioning, deconditioning facilitates worsening musculoskeletal damage and sedentary lifestyle promotes obesity and chronic disease which worsens pain

Obesity as a risk for chronic pain

- Obesity is significantly associated with persistent pain complaints (odds ratio =1.89, 95% confidence interval, 1.56–2.30)
- Dose response of BMI to rates of recurring pain:
  - Overweight (BMI 25-29.9) = 20% greater rates of recurring pain
  - Class I obesity (BMI 30-34.9) = 68% greater rates of recurring pain
  - Class II obesity (BMI 35-39.9) = 136% greater rates of recurring pain
  - Class III obesity (BMI 40+, morbid obesity) = 254% greater rates of recurring pain
- Similar rates of recurrent pain in adolescents and children

Obesity results in poor chronic pain outcomes

- Obesity is associated with various pain diagnoses including low back pain, headaches, fibromyalgia/chronic widespread pain, pelvic pain, neuropathic pain and abdominal pain
- Fibromyalgia and obesity:
  - Several studies demonstrate that the majority of patients with fibromyalgia are overweight or obese
  - Higher mean BMI in fibromyalgia patients compared to the pain-free individuals

Chronic pain promotes Obesity

- Weight gain may occur as a result of chronic pain
  - Chronic pain is one of the major self-identified causes of weight gain
  - Frustration may lead to overeating.
  - Sedentary lifestyle, poor sleep, and side effects of pain medications may also contribute to weight gain

Does bariatric surgery improve chronic pain?

- YES
  - Bariatric surgery in morbidly obese: 5% weight loss at 3mo already associated with significant reductions in low back and knee pain
  - @ 1yr follow up = 27% reduction in weight, associated with 68% of the patients reporting improvements in pain
  - Reduced headache and migraine frequency following bariatric surgery

Does non-surgical weight loss reduce chronic pain?

- YES
  - Much less weight loss than bariatric approaches
  - Diet and exercise improve pain in OA patients (IDEA trial)
  - Fibromyalgia improves with non-surgical weight loss
  - Dieting with weight loss is associated with chronic pain improvements, but lost with return to normal diet

Summary

1. Obesity is a complex, highly prevalent and expensive problem for the U.S.
2. Obesity represents a risk for the onset of and worsening outcomes with a number of autoimmune and musculoskeletal diseases
3. Weight loss can improve outcomes in musculoskeletal and rheumatologic disease
4. Educating patients on the role of obesity in rheumatologic disease may preserve rheumatologic and musculoskeletal health

Case 1

- 35yo woman presents with activity-worsened knee, lateral hip and ankle pain present for 2-3+ years
- c/s: ANA is 1:40, r/o rheum dz?
- Exam: BMI 43, no overt inflammatory arthritis, no crepitus, normal ROM
- Normal chem 10, cbc, lfts, ESR 34, CRP 13.5
- X-rays: mild medial joint space loss b/l knees, ankles unremarkable.

Case 1 Questions to Consider:

- What is the biggest risk to this patient's health?
- Does the ANA aid in diagnosis/prognosis?
- Does the sed rate/CRP aid in diagnosis/prognosis?
- What is the most likely etiology of this patient's pain?
- What is the recommended course of treatment?

Case 2

- 65yo man presents for evaluation of 7yrs of chronic knee pain, L > R in severity, occasional locking, taking Tylenol for pain
- c/s: evaluate/treat knee pain
- Exam: BMI 35, diffuse crepitus and moderate cold effusion L > R, quadriceps atrophy (mild) b/l, diffuse mild deconditioning
- Labs: normal chem 10, cbc, lfts
- X-rays: moderate to severe tricompartmental OA changes in the L > R knees

Case 2 Questions to Consider

- What is this patient's diagnosis?
- What is the most appropriate next step in his management?
- What is the role of weight loss in his management?
- What weight loss strategies should be pursued?
- Are there concerns regarding exercise for this patient?

Case 3

- 25yo woman presents for evaluation of pain, swelling in her hands and wrists with morning stiffness lasting 3 months
- c/s: RF 225, CCP negative, eval for RA
- Exam: BMI 34, synovitis throughout the MCPs, wrists, MTPs, ankles associated with tenderness.
- Labs: sed rate 74, CRP 29, hgb 11.1, plts 450k,

Case 3 Questions to Consider

- What is this patient's diagnosis?
- What is the most appropriate next step in her management?
- What is the role of her weight in the development of her diagnosis?
- What should her rheumatologist be aware of regarding her treatment relative to her obesity?
- What is the role of weight loss in her management plan?

Future Considerations

1. As the obesity epidemic worsens, we may see a higher prevalence of rheumatologic and musculoskeletal disease
2. Transition to population health/value-based healthcare delivery will likely change the interaction of primary physician and specialist
3. Recognizing the role of obesity in the prevalence of common musculoskeletal (and less common rheumatologic disease) will be vital in common clinical practice

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