Bone Health and IBD

Ashwin N Ananthakrishnan, MD, MPH
Associate Professor of Medicine
Massachusetts General Hospital
Harvard Medical School

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Bone Health in IBD
Objectives

- Prevalence of osteoporosis and fracture in IBD
- Assessment of Bone Health
- Management of osteoporosis in IBD
- Role of vitamin D in the management of IBD

Bone Health in IBD

Prevalence of Osteoporosis

- Prevalence of osteoporosis in IBD: 3-42%
  - Depends on population (age, disease features)
  - Mode of assessment (DXA vs. clinical assessment)

- Systematic review: 12 studies, 3,661 patients with IBD
    - All IBD: 2-16%
      - Crohn's disease: 7-15%
      - Ulcerative colitis: 2-9%
    - General population: 3-10%

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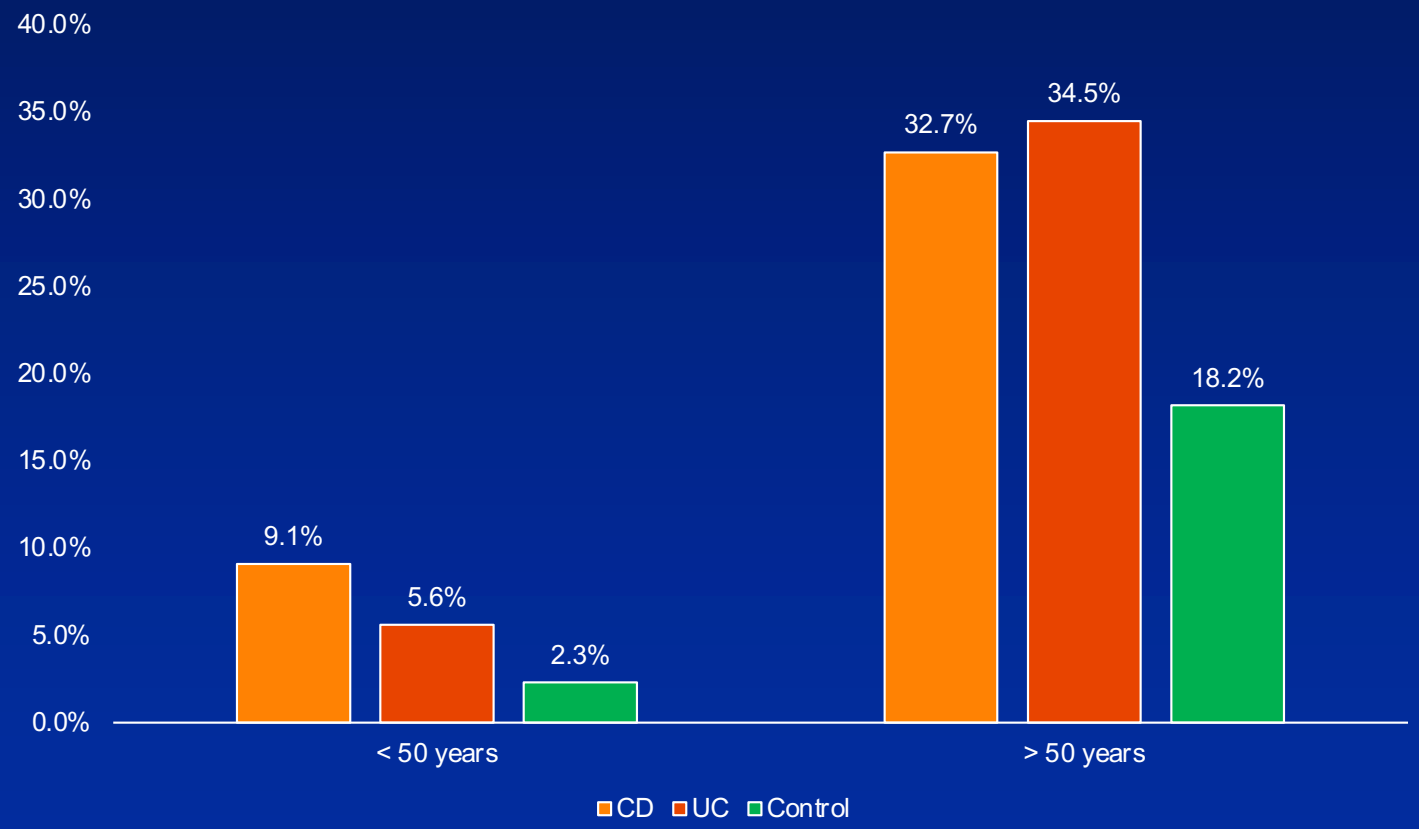
Prevalence of Osteoporosis

- Population-based cohort in Denmark (2003-04) of 513 patients with IBD (213 CD / 300 UC)
- 62% received a cumulative dose of prednisone ≥500mg/day.



- Osteoporosis may also be common in patients with newly diagnosed IBD with 0-5%

Lo B. Journal of Crohn's and Colitis, 2020, 904–914

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Systematic review of osteoporosis

- Systematic review of 16 studies examining bone mineral density in patients with IBD
  - Patients with IBD have lower BMD at the femoral neck as well as lumbar spine

	Change vs. controls	P-value
Femoral Neck		
BMD	-0.04g/cm2	0.001
Z-score	-0.45	< 0.00001
Total Femur		
BMD	-0.08g/cm2	< 0.00001
Z-score	-1.01	0.07
Lumbar Spine		
BMD	-0.06g/cm2	0.001
Z-score	-0.52	< 0.00001

Szafors P. Osteoporos Int . 2018 Nov;29(11):2389-2397.

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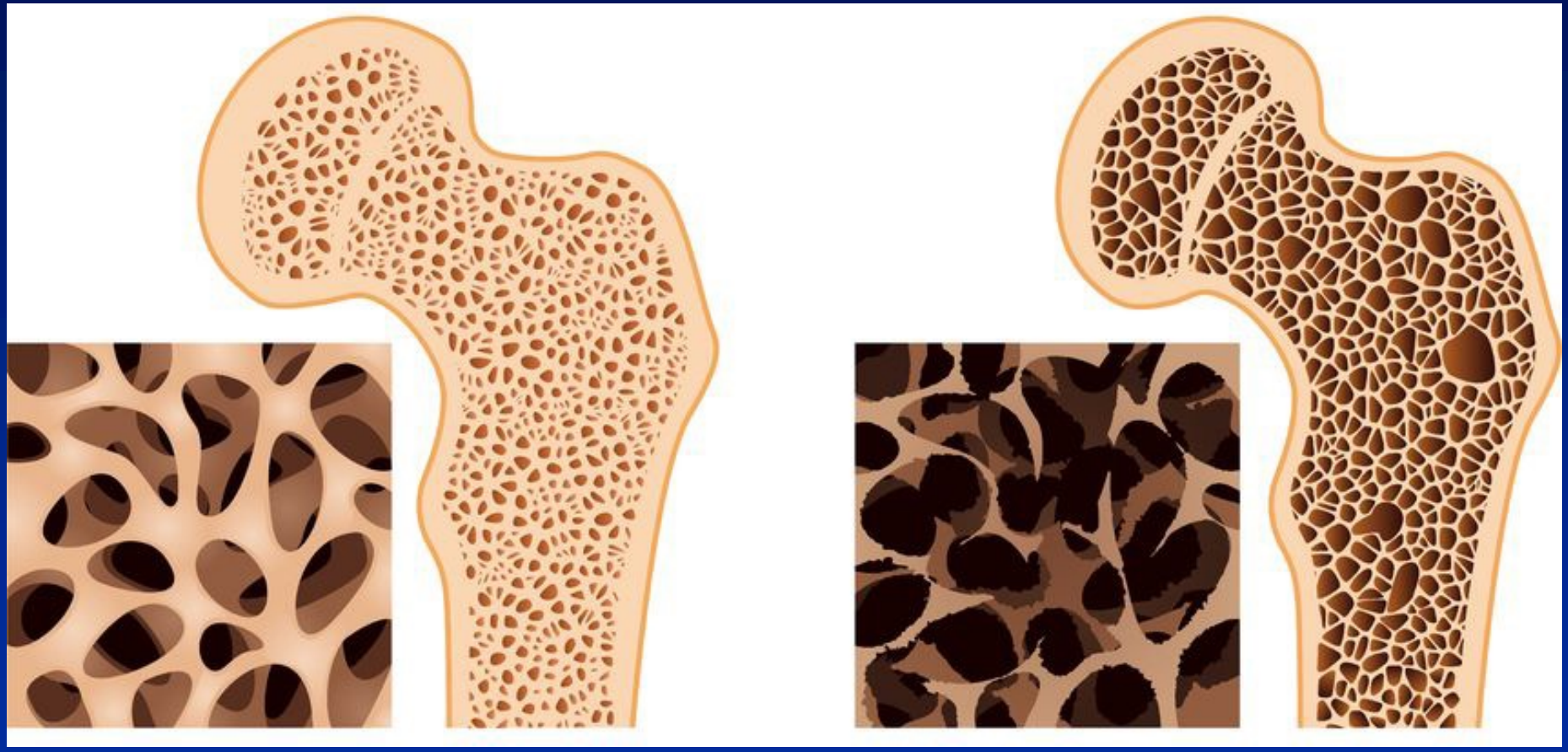
Osteoporosis



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Fracture Risk in IBD

- Data from Korean National Health Insurance Claims (2007-16)
- Fracture incidence over 7 years compared in 18,228 patients with IBD compared to 186,871 controls.

	All patients	Steroid users
General Population	1.0	1.0
IBD	1.24	1.37
UC	1.16	1.33
CD	1.56 Vertebral: 1.88 Hip: 0.95	1.50

Ahn HJ. Clin Gastroenterol Hepatol . 2022 May;20(5):e1022-e1039.

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Risk Factors for osteoporosis

- Female gender
- Older age
- Family history of osteoporosis
- Low body mass index
- Shorter Height
- Ethnicity (Caucasian and Asian)
- Smoking
- Excess alcohol intake

Karnsund S. World J Gastroenterol . 2020 Sep21;26(35):5362-5374.

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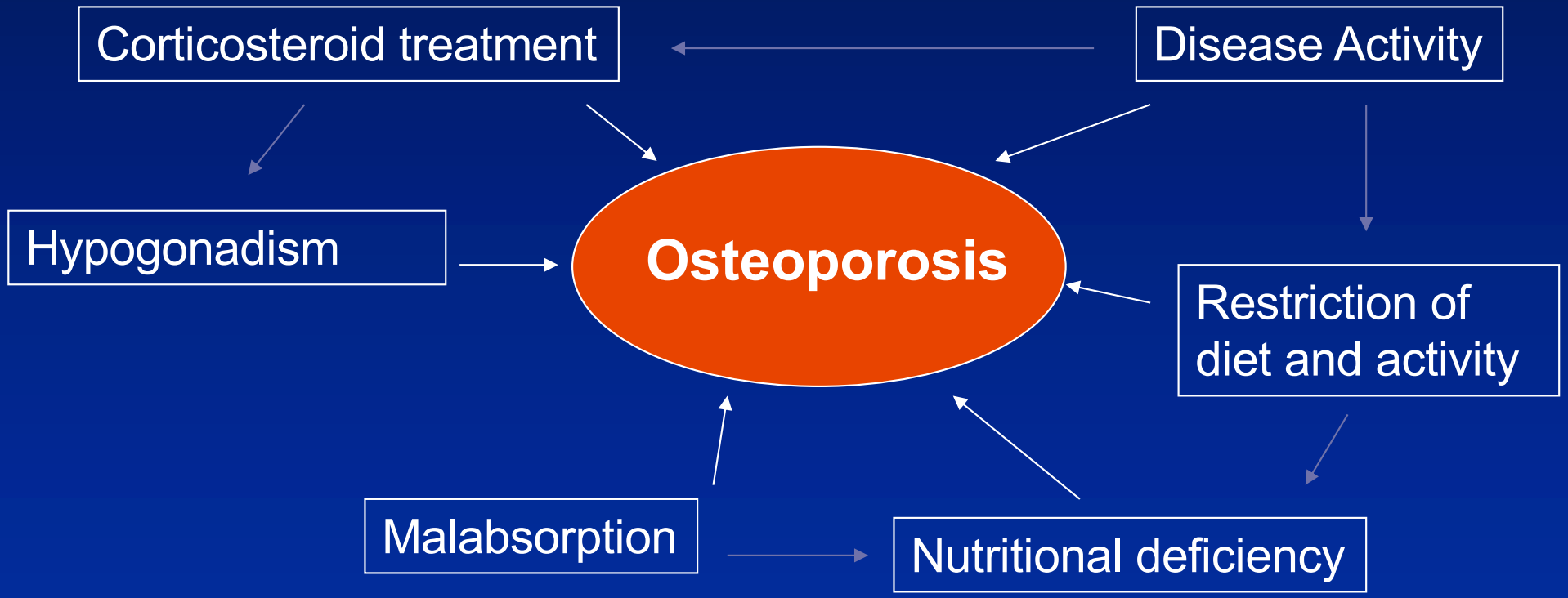
Risk factors for osteoporosis in IBD



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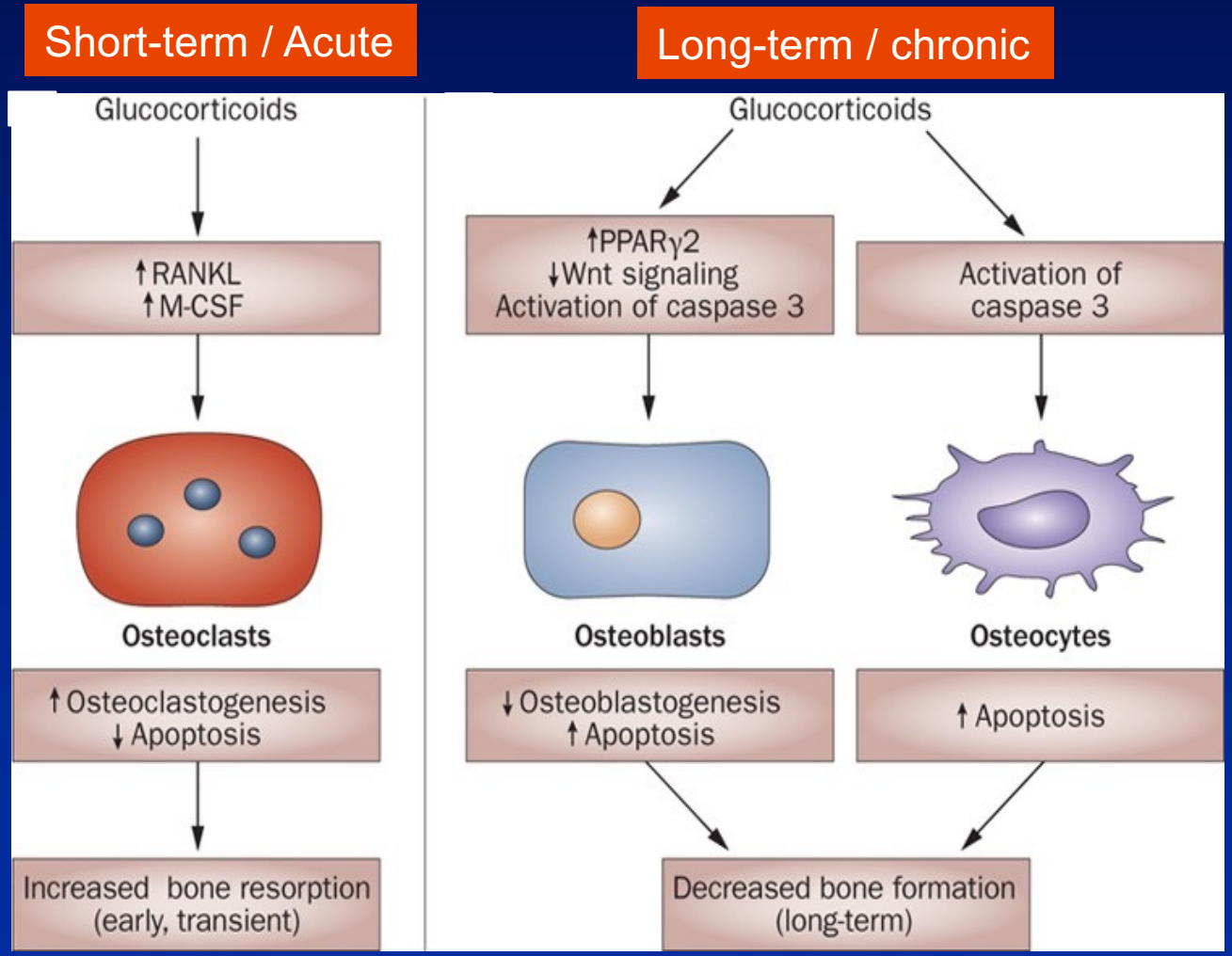
Steroid-induced osteoporosis

- Steroid-induced osteoporosis occurs in 2 phases



Compston J. Nat Rev Rheumatol 6, 82–88 (2010)

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Steroid-induced osteoporosis

- Steroids also decrease intestinal calcium absorption resulting in increase PTH and increased resorption
- Fractures may be noted in as many as 30-50% of steroid users
- Increase in fracture risk can be noted with as low as 2.5-7.5mg/day of prednisone use or within 30 days of use
- Incidence of fracture is higher with higher dose, longer duration, and advanced age.

Compston J. Nat Rev Rheumatol 6, 82–88 (2010)

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Assessment of Bone Health: Who?

- Recommendations for screening:
  - Women > 65 years
  - Men > 70 years
  - Adults with fracture > 50 years
  - Any adult with fracture not caused by severe trauma
  - Younger women with fracture risk similar to a 65 year old
  - Adults with a condition or medication use that increases fracture risk
    - Prednisone-equivalent > 7.5mg/day for > 3 months

Farraye FA. Am J Gastroenterol . 2017 Feb;112(2):241-258.

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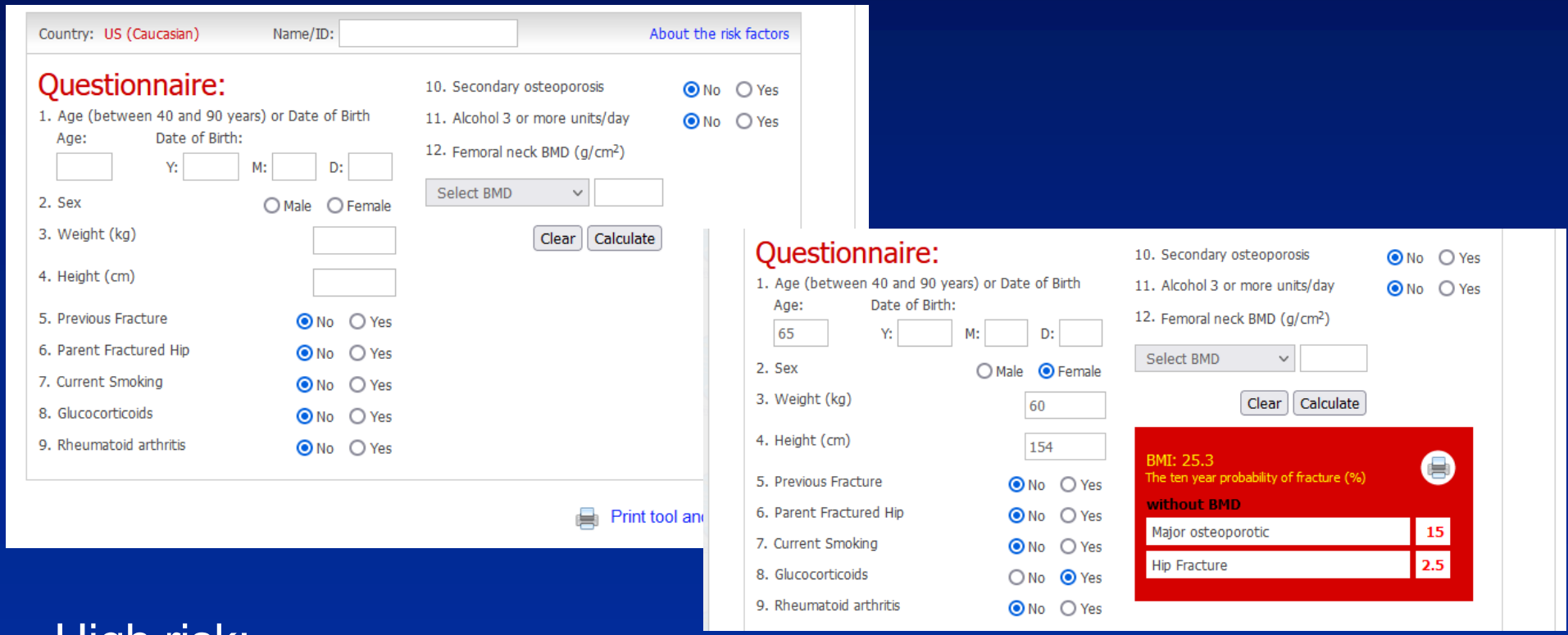
Assessment of Bone Health: Who?

- The FRAX tool calculates the 10-yr probability of hip fracture and major osteoporosis-related fracture



High risk:

- ≥20% for major FF (or)
- ≥ 3% for hip FF

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Assessment of Bone Health: How?

- Dual Energy x-ray absorptiometry
  - Most widely used
  - Measures bone mineral content (BMC) and bone area (BA)
  - BMD = BMC / BA (in g/cm2)

Sites of measurement:

- Lumbar Spine
- Proximal femur
- Femur neck

Diagnosis	T-score
Normal	> -1.0
Low Bone mass	Between -1.0 and -2.5
Osteoporosis	≤-2.5
Severe osteoporosis	≤-2.5 and fragility fracture

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Secondary Osteoporosis

- Chronic conditions that contribute to accelerated bone loss

Endocrine or metabolic causes

Acromegaly
Anorexia nervosa
Athletic amenorrhea
Diabetes mellitus (type 1)
Hemochromatosis
Hyperadrenocorticism
Hyperparathyroidism
Hyperprolactinemia
Thyrotoxicosis

Collagen/genetic disorders

Ehlers-Danlos syndrome
Glycogen storage diseases
Homocystinuria
Hypophosphatasia
Marfan syndrome
Osteogenesis imperfecta

Medications

Cyclosporine (Sandimmune)
Excess thyroid hormone
Glucocorticoids
GnRH agonists
Methotrexate (Rheumatrex)
Phenobarbital
Phenothiazines
Phenytoin (Dilantin)
Heparin, prolonged treatment

Nutritional

Alcoholism
Calcium deficiency
Chronic liver disease
Gastric operations
Malabsorption syndromes
Vitamin D deficiency

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Non-Pharm Treatment of ostoeporosis

- Maintain sufficient calcium and vitamin D intake
  - Target serum vitamin D: 30-50ng/mL
    - Daily supplementation of > 400-800 IU
  - Calcium intake 1000-1200mg daily
    - Preferably through diet
    - Calcium supplementation in non-institutionalized adults is not supported by evidence
- Reduce intake of caffeine ≤ 4 cups of coffee / day
- Smoking cessation
- Reduce alcohol consumption < 2 drinks / day
- Fall Risk assessment
- Physical Therapy and Exercise

Coronado-Zarco. R. Osteoporos Sarcopenia . 2019 Sep;5(3):69-77.

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Exercise and BMD

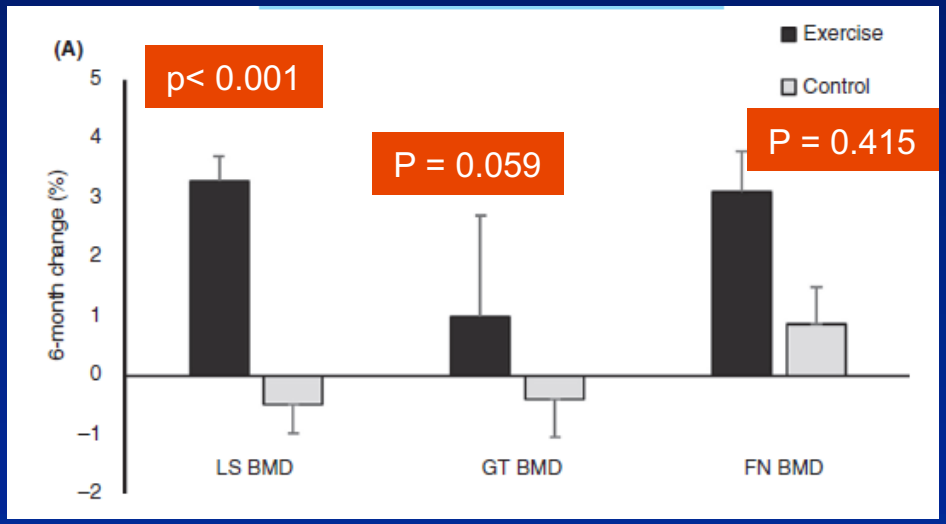
- 117 patients with CD were randomized to low-impact exercise or control for 12 months
- Overall cohort: No difference in BMD in exercise group and controls.
- Fully compliant cohort: Exercise was associated with increase in BMD
  - Increases in BMD were significantly related to the number of exercise sessions completed (femoral neck; r = 0.28 p = 0.04). .

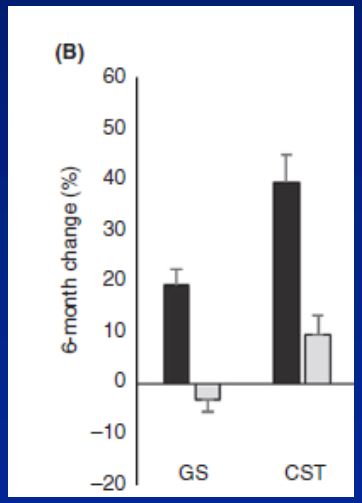
	Compliers	Control	% difference	P-value
Femoral neck	+3.5%	+0.5%	+2.99%	0.19
Lumbar spine	+2.97	+0.7%	+2.2%	0.30
Trochanter	+7.7%	+3.1%	+4.7%	0.02

Robinson RJ. Gastroenterology . 1998 Jul;115(1):36-41.

Bone Health in IBD
Exercise and BMD

- 47 patients with CD were assigned to exercise (combined impact and resistance training, 3 60min session/week) x 6 months) or usual care
  - BMD values were superior in the exercise group with statistical significance at lumbar spine





The exercise group also had superior values muscle function outcomes

- Grip strength (GS)
- Chair stand test

Jones K. Aliment Pharmacol Ther . 2020 Sep;52(6):964-975.

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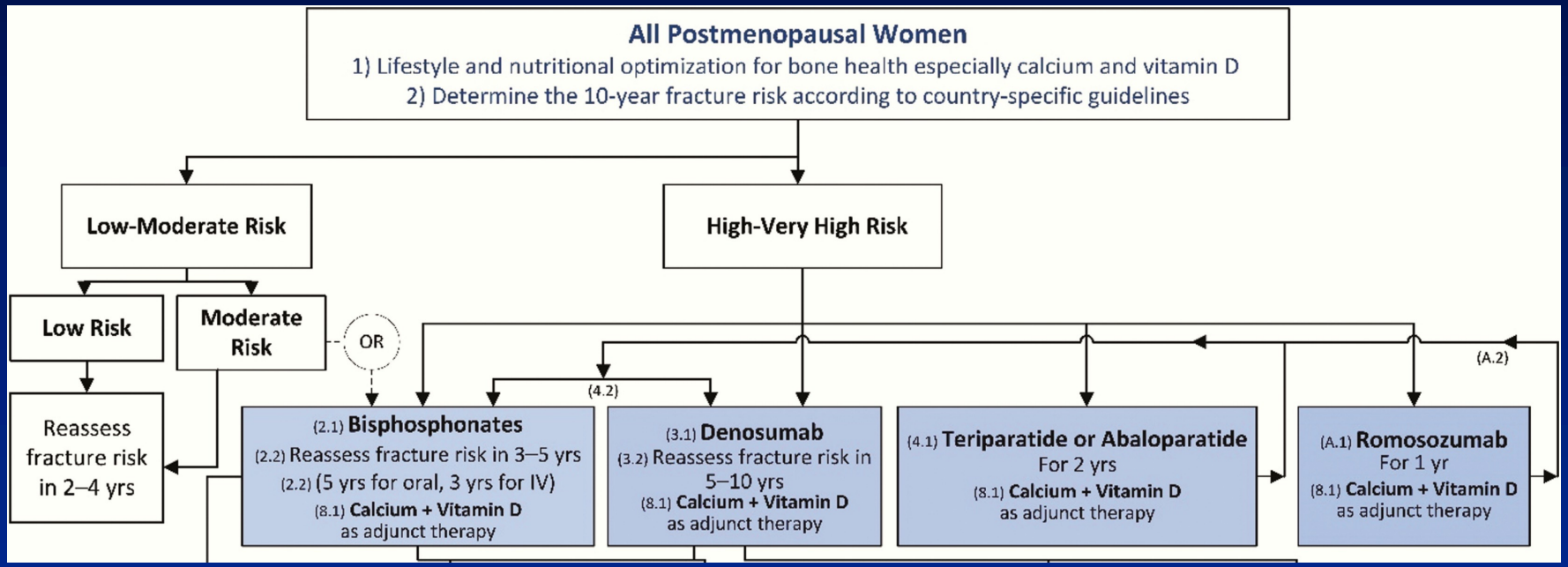
Pharmacologic Treatment



Bisphosphonates
Anti-resorptive
Reduce osteoclast number and function

Denosumab
Anti-resorptive
Monoclonal antibody that inhibits RANKL
Reduces osteoclast number, turnover, and function

Teriparatide
Form of PTH
Aids in bone formation
Should only be used for 2 years
Abaloparatide: PTH analogue

Romosozumab
Inhibits sclerostin and activates the Wnt pathway promoting bone formation

Shoback D. J Clin Endocrinol Metab, 105(3): 2020, 587–594

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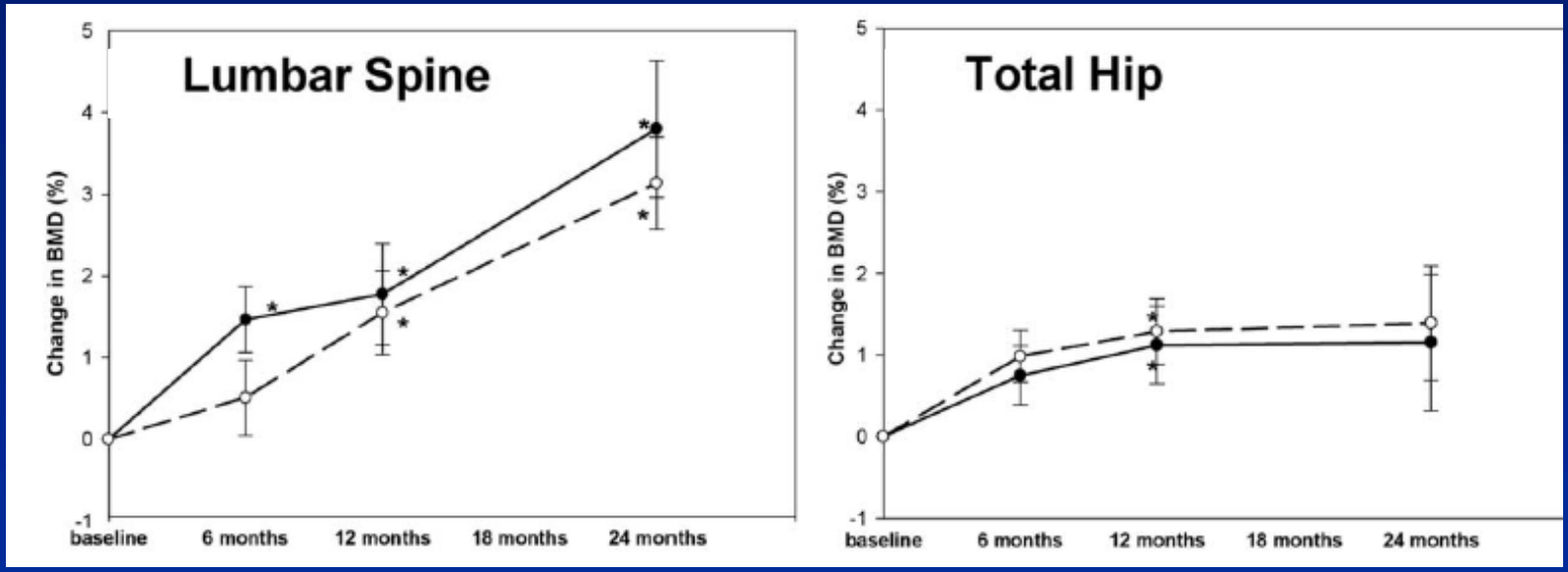
Calcium and vitamin D

- 154 patients with CD with decreased BMD were randomized to etidronate (400 mg orally) (or not) for 14 days;
- All received daily calcium 500mg and vitamin D 400 IU x 76 days.
- This cycle was repeated x 8 over 2 years



The increase in bone mineral density was similar in each treatment group.

Siffledeen JS. Clin Gastroenterol Hepatol . 2005 Feb;3(2):122-32.

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Calcium and vitamin D

- 205 CD patients:
  - In osteopenic patients: Supplemental vitamin D (800 IU) and Calcium (500-1000 mg) were prescribed.

- Among those with a second BMD in 4 years: Increase in mean BMD
  - L spine: +0.76% (95%CI: -2.63%; +3.87%)
  - Hip: +0.43% (95%CI: -2.65% ; +1.11%)

Bakker SF. J Crohns Colitis . 2013 Jun;7(5):377-84.

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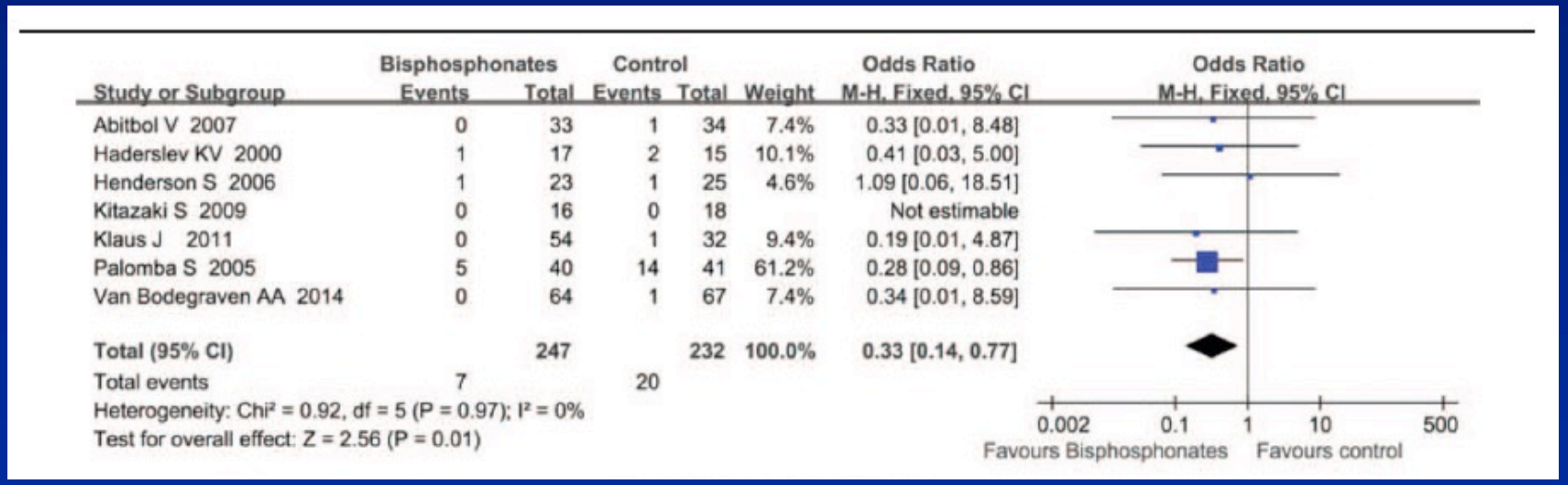
Treatment of Osteoporosis in IBD

- Meta-analysis of bisphosphonates in IBD
  - 13 RCTs (923 patients (482 bisphosphonates, 441 control))
  - Treatment improved bone density at hip and T spine and reduced fracture risk
  - No increase in adverse effects



Study or Subgroup	Bisphosphonates Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abitbol V 2007	0	33	1	34	7.4%	0.33 [0.01, 8.48]
Haderslev KV 2000	1	17	2	15	10.1%	0.41 [0.03, 5.00]
Henderson S 2006	1	23	1	25	4.6%	1.09 [0.06, 18.51]
Kitazaki S 2009	0	16	0	18		Not estimable
Klaus J 2011	0	54	1	32	9.4%	0.19 [0.01, 4.87]
Palomba S 2005	5	40	14	41	61.2%	0.28 [0.09, 0.86]
Van Bodegraven AA 2014	0	64	1	67	7.4%	0.34 [0.01, 8.59]
Total (95% CI)		247		232	100.0%	0.33 [0.14, 0.77]
Total events	7		20			

Heterogeneity: Chi² = 0.92, df = 5 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)

Yao L. Medicine (Baltimore) . 2017 Jan;96(3):e5861.

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Steroid-induced osteoporosis prevention

- Lowest dose, shortest duration, steroid-sparing regimens when able
- Topical therapy > enteral or parenteral glucocorticoids
- Weight bearing exercises to prevent both loss and muscle atrophy
- Avoid smoking and excess alcohol
- Fall prevention measures

- Calcium (1000-1200mg/day) and vitamin D (600-800IU/day)
  - Meta-analysis of 5 trials: Improvement in BMD, no difference in fracture risk.

- Consider pharmacologic therapy if high fracture risk in post-menopausal women and men > 40 years

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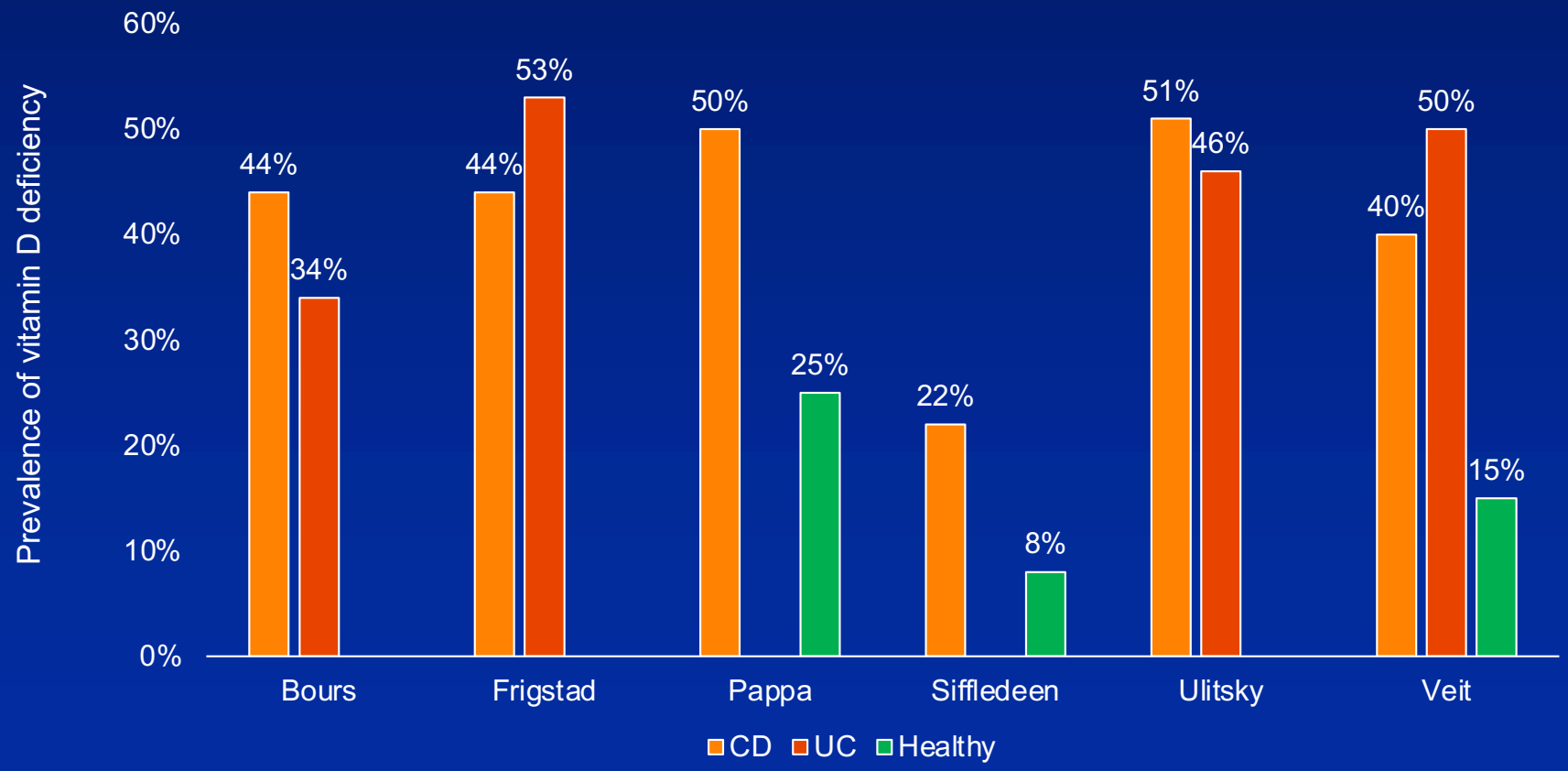
Vitamin D and IBD

- The Institute of Medicine defines vitamin D deficiency as 25-OH-D less than 20 ng/mL (50 nmol/L)* (> 30ng/ml or 75 nmol / L is considered adequate)
  - *Based on skeletal effects of vitamin D



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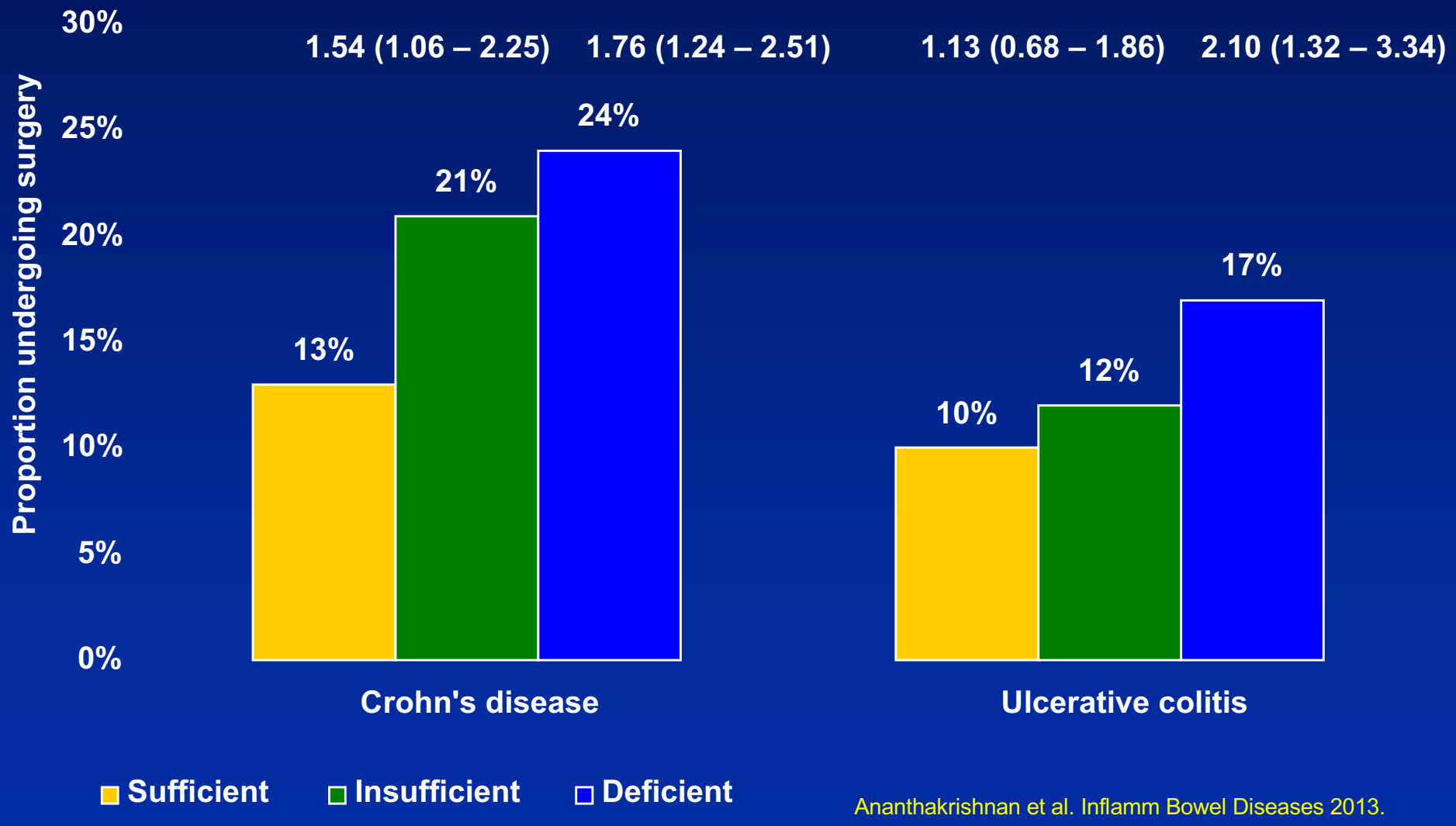
Vitamin D and IBD: Observational data

- In observation studies, vitamin D deficiency is associated with more severe disease in IBD



Ananthakrishnan et al. Inflamm Bowel Diseases 2013.

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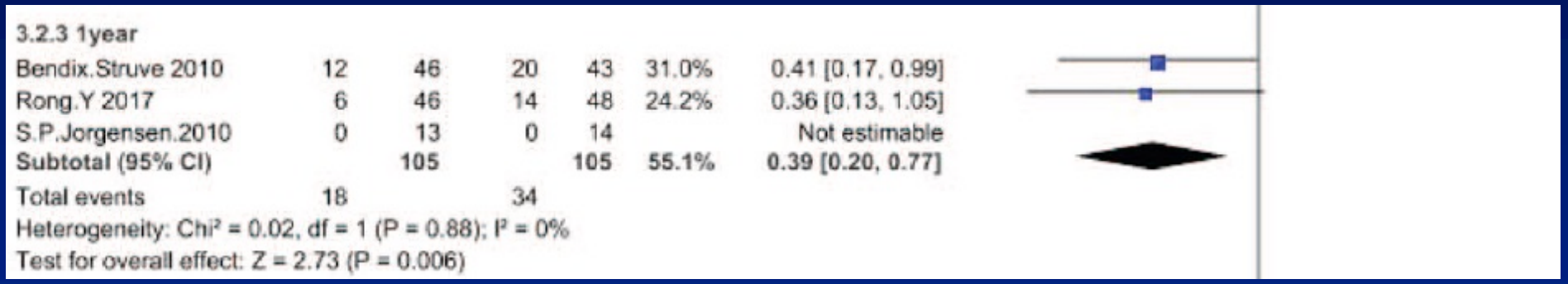
Vitamin D and IBD: Interventions

- Initial studies promising showed reduced rates of relapse in patients treated with vitamin D



3.2.3 1year						
Bendix.Struve 2010	12	46	20	43	31.0%	0.41 [0.17, 0.99]
Rong.Y 2017	6	46	14	48	24.2%	0.36 [0.13, 1.05]
S.P.Jorgensen.2010	0	13	0	14		Not estimable
Subtotal (95% CI)		**105**		**105**	**55.1%**	**0.39 [0.20, 0.77]**
Total events	18		34			

Heterogeneity: $Chi^2 = 0.02$, df = 1 (P = 0.88); $I^2 = 0\%$

Test for overall effect: Z = 2.73 (P = 0.006)

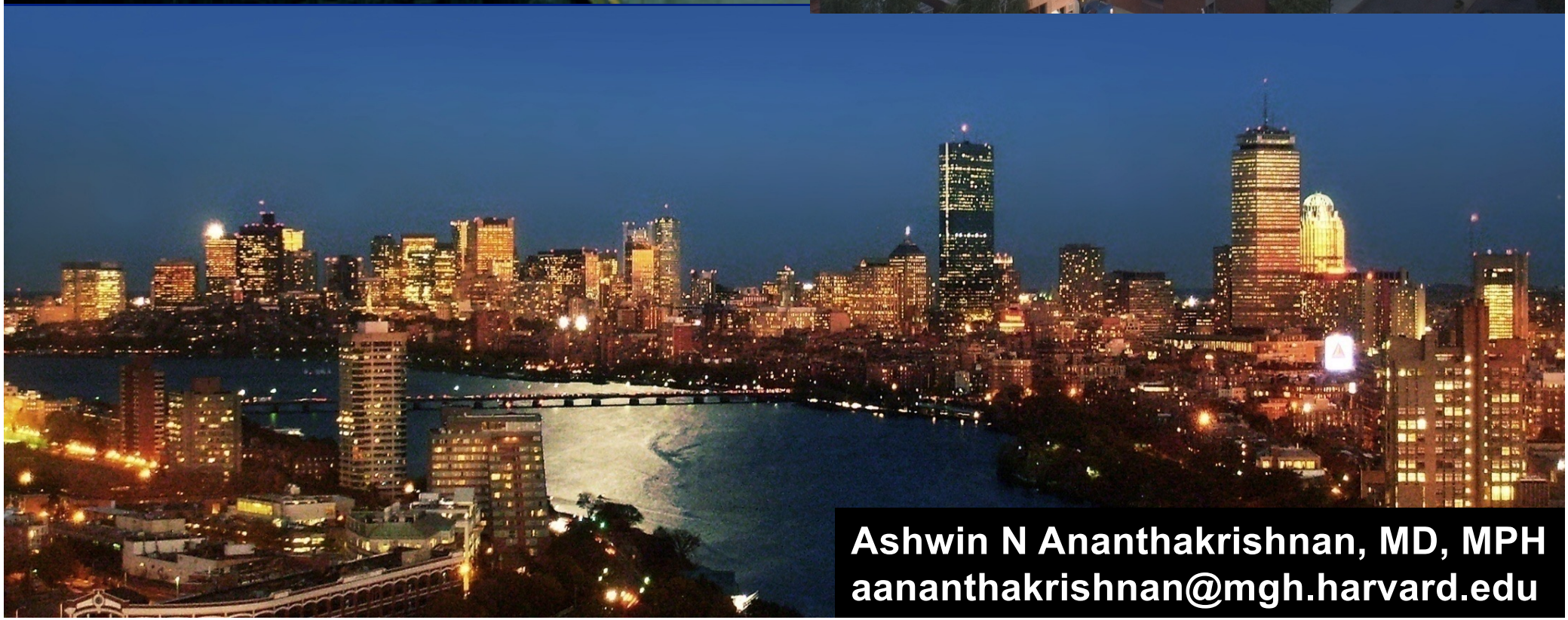
- More recent pooled analysis of 17 trials with 1127 patients with IBD
  - Oral vitamin D supplementation
    - Increased serum vitamin D levels (12.15 ng mL^{-1};)
    - Reduced C-reactive protein levels (SMD -0.33)
    - Did not decrease ESR or disease activity index
    - Did not decrease rates of relapse (RR 0.59; 95% CI 0.19, 1.86)

Li J. Medicine (Baltimore). 2018 Nov;97(46):e12662.
Guo Y. Food Funct . 2021 Sep 7;12(17):7588-7606

Bone Health in IBD

Conclusions

- Suboptimal bone health can have profound consequenecs on patients with IBD, particularly the IBD
- Treating clinicians should routinely incorporate assessment of bone health in the management of patients with IBD
- Improving bone health importantly allows optimization of functional capacity



Ashwin N Ananthakrishnan, MD, MPH
aananthakrishnan@mgh.harvard.edu