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**METABOLIC BONE  
DISEASE IN  
GASTROENTEROLOGY:  
A SHORT POEM**

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Disclosures

- ⦿ NONE!
- ⦿ I am responsible for the opinions expressed during this presentation.

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Non – PMO bone disease

- ⦿ Almost every chronic disease will have a bone manifestation
- ⦿ Wide range of pathophysiologies
- ⦿ Pharmacotherapies very limited in mechanism of action
- ⦿ Barely have enough data for PMO management

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### A POEM for you

- ⊙ P = practical problems
- ⊙ O = observations already made
- ⊙ E = extrapolations from other data
- ⊙ M = ministrations (what to do)

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### Observations: IBD

- ⊙ Low BMD<sup>1</sup>
- ⊙ Select individuals lose bone mass<sup>2</sup>
  - Older age, GC use
- ⊙ May have higher fracture risk<sup>3</sup>
  - Many uncontrolled variables
  - Many small studies (n < 500)
  - Wide confidence intervals
  - Fractures not clearly related to BMD<sup>4</sup>

1. Clin Gastroenterol Hepatol 2006;4:152  
2. Calcif Tissue Int 2012;91:356  
3. Gastroenterology 2003;125:1591  
4. Aliment Pharmacol Ther 2002;16:1519

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### Observations: IBD - 2

- ⊙ Low vitamin D levels<sup>1</sup>
- ⊙ Low vitamin K levels<sup>2</sup>
- ⊙ Systemic inflammation may increase bone resorption<sup>3</sup>
- ⊙ Hypogonadism may modulate bone status<sup>4</sup>

1. Pediatrics 2006;118:1950  
2. Osteoporosis Int 2009;20:935  
3. Nat Rev Drug Dis 2012;11:234  
4. Alimentary Pharm Ther 1998;21

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### Observations - celiac

- Associated with low BMD<sup>1</sup>
- Possible increased fracture risk<sup>2</sup>
- Associated with low vitamin D

1 - Scand J Gastroenterol 2000;3:274  
2 - Aliment Pharmacol Ther 2007;25:273

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### Observations - CLD

- Have low BMD
- Can have high bone remodelling rates
- May have higher risk of fractures
- May have bone loss, fractures post transplant

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### Observations - bariatric surgery

- Bone loss occurs: ? Unloading effect vs malabsorption
- Some bone mineral issues develop
- Some bone mineral issues resolve
- May not be associated with higher fracture rates

BMJ 2012;345:e5085

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### Observations - intervention

- ◎ Small studies
  - Bisphosphonates for PBC (2011)
    - N= 207 from 6 pooled studies (no effect)
  - HRT in PBC (2011)
    - N= 47 from 2 pooled studies
- ◎ Primary outcome is BMD change
  - Not recognized as a valid endpoint in drug registration trials
- ◎ Duration 0.5 - 4 years

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### Observations - guidelines

- ◎ BSG 2007
  - Majority of recommendations are grade C/D
  - Grade A/B recommendations are extrapolations from menopausal OP
- ◎ AGA 2002
  - All GI specific recommendations are grade D
- ◎ WGO 2004
  - Recapitulates ACR guidelines

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### Extrapolations from PMO

- ◎ Intervention decisions based primarily upon fracture risk
  - FRAX
  - Age, sex, BMI, steroid use, smoking, EtOH, rheumatoid arthritis, fam hx, prior fracture, BMD
  - Addition of BMD adds very little in many cases
  - Many people with low BMD are low fracture risk (mid-term)
  - Many people with "normal" BMD are high fracture risk (mid-term)

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### Extrapolation of FRAX to GI

- ⊙ Increased statistical difficulty of a regression equation that can account for all additional IBD-related variables
- ⊙ "IBD" may not confer increased fracture risk after FRAX variables considered<sup>1</sup>
- ⊙ Remember that "IBD" not a homogeneous diagnosis!

JBMR 2013;5:1007

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### Extrapolation of FRAX to GI

- ⊙ Problem: spectrum effect of risk factors
- ⊙ Problem: IBD only?
- ⊙ Problem: age < 45
- ⊙ Problem: you will never treat anyone <60
- ⊙ Problem: BMD will decline
- ⊙ Question: is "some" bone loss the "cost" of having IBD?

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### Extrapolation of intervention studies

- ⊙ Post-menopausal women, older men
- ⊙ Young women (even GIO): no # data
- ⊙ "perimenopausal" prevention study: 6 yrs alendronate, no # benefit.

JCEM 2004;89:4879-85.

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### Extrapolation problems

- ⊙ Bisphosphonates are not always benign
- ⊙ Duration of therapy now a big issue
- ⊙ “easy to start.....but then what?”

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### Atypical Fractures of the Femoral Diaphysis in Postmenopausal Women Taking Alendronate



"Atypical # on BP"

"Atypical # with NO BP"

64% have involvement of contralateral,  
76% have prodromal symptoms of thigh pain, weakness (usually dismissed)

NEJM 2008;358:12

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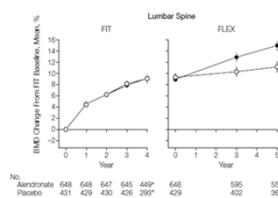
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### Effects of Continuing or Stopping Alendronate After 5 Years of Treatment



JAMA. 2006;296:2927-2938

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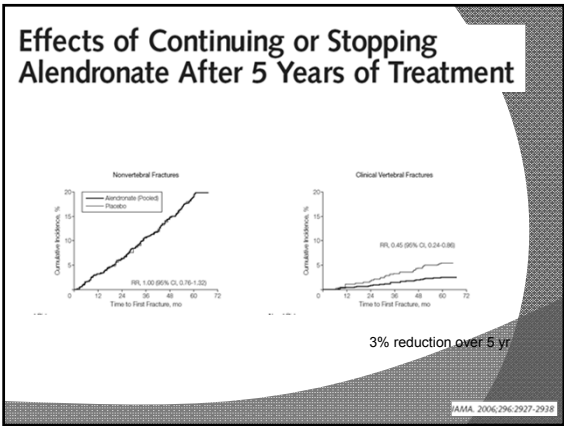
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### Practical problems from lack of evidence.....

- Should bisphosphonate therapies be limited to 5 years?
- ? “drug holiday”?
- If so, how long?
- Are there any patient factors that modulate the length of therapy or drug holiday?
- What if glucocorticoids ongoing?

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### Ministrations

- We screen because we can
- Abnormalities are often present
- Drugs are available
- Is it that simple?

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### A realistic expectation of GI?

- ⦿ Are you really taking this on or advising the GP?
- ⦿ Multi-factorial risk assessment
- ⦿ Fracture risk estimation
- ⦿ Discussion of evidence limitations
- ⦿ Pt counseling about interventions
- ⦿ Management of insurance issues
- ⦿ Management of adverse effects
- ⦿ Interpretation of change over time
- ⦿ Define parameters of treatment success/cessation
- ⦿ A simile: NAFLD and the endocrinologist

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### My Grade D recommendations

- ⦿ Try to understand the pathophysiology:
  - High turnover, low turnover, rate of loss
  - Expected course of disease
- ⦿ Make up a fracture risk estimate
- ⦿ Always fix the fixable:
  - Gonadal status consideration
  - Vitamin D
  - Lifestyle factors

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### My **grade D** recommendations: drugs

- ⦿ Any PMF or man > 65 – counsel per PMO +/- steroids (recommendation to GP!)
- ⦿ Any GI disease with true fragility fracture, strong consideration of Rx, esp if on steroids
- ⦿ **If no fractures AND pre-menopausal/young:**
- ⦿ IBD > 1 yr, active or steroid using, DXA and discussion of Rx
- ⦿ IBD 6-12 months active or steroid using consider DXA
- ⦿ Active/steroid using IBD <6 months, not your problem
- ⦿ Celiac, PBC, short gut, CLD – risk factor “notification”
- ⦿ Pre-transplant – MBC assessment

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## A real poem

An endocrinologist from Calgary  
Gets tired of treating disease;  
He'd much rather hang with the colonoscopy crowd  
'Cause they get to go to Louise!

Thank You  
gakline@ucalgary.ca

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## Perturbations in the evidence base

- Disease-specific descriptions of the natural hx of bone complications
- Disease specific estimates of fracture burden
  - Controlled for known co-factors / severity
  - Controlled for age
  - Controlled for time course
- Benefits from interventions
- Adverse effects
- Cost – benefits
- Value of screening protocols

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