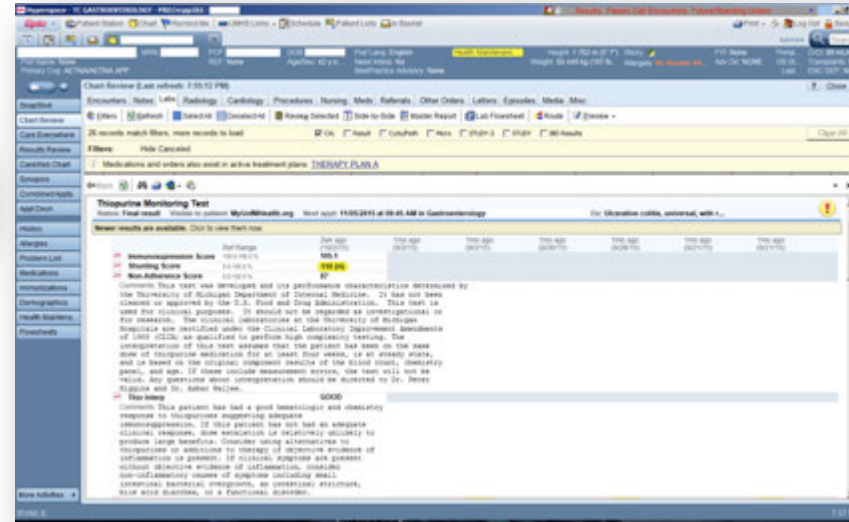# Health Maintenance in Inflammatory Bowel Disease

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Treatment of Intestinal Damage is a Major Focus of IBD Management

# Some Important Issues Can Be Easy to Overlook

Preventing Avoidable Infections by Vaccination

PCPs and GI Docs Need to Work Together

- 52% of GI docs assess vaccination status among IBD patients

- 64% believe PCP should determine which vaccinations to give

- 83% believe that PCPs should administer the vaccines

- GI offices may not stock all vaccinations

- Knowledge regarding live vaccines among GI docs was also poor

Wassan. *IBD* 2011

Fatal Illnesses are Preventable with Vaccination in IBD

IBD Patients at Risk of Preventable Illness
and Vaccination Rates in United States

Adapted from Melmed, AJG 2006
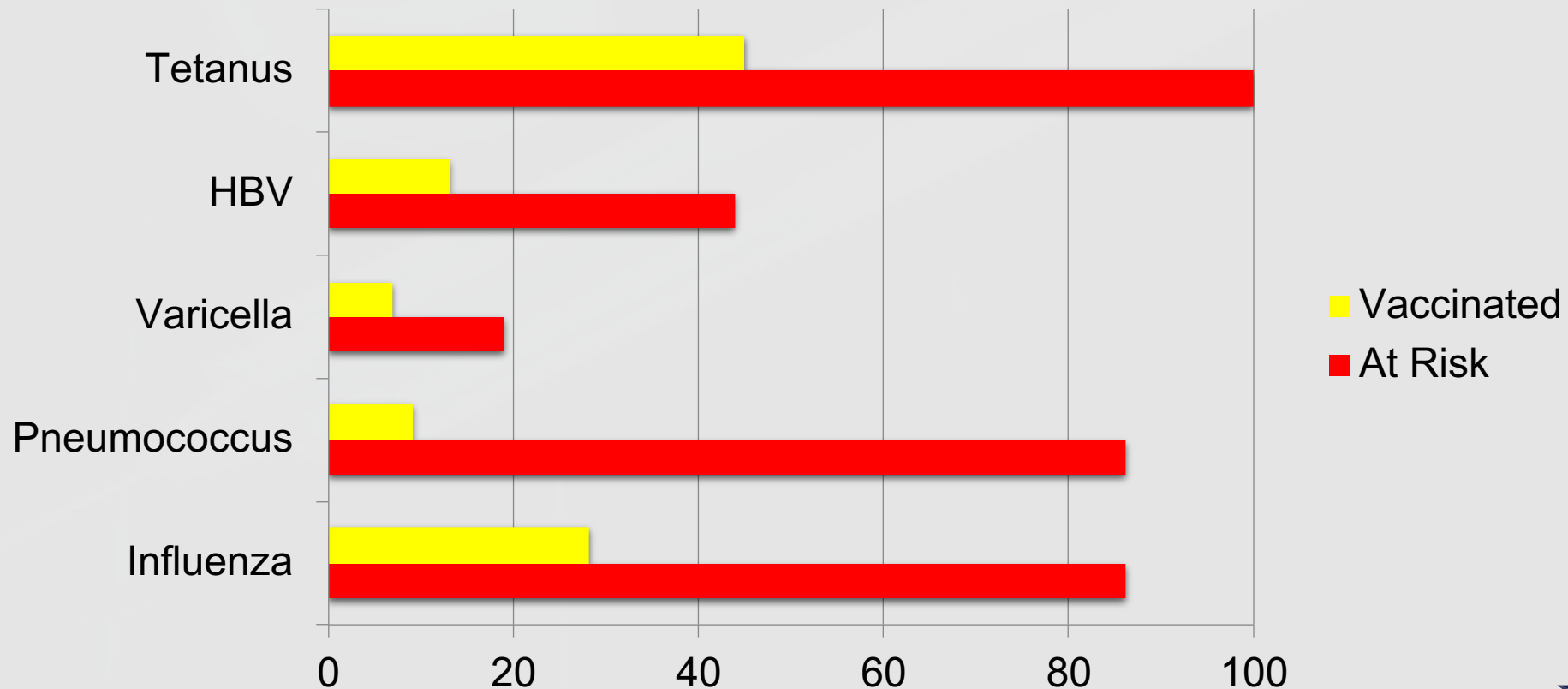
Definition of Immunosuppressed IBD Patient

Any of these Criteria

- Anti-TNF use within 3 months

- Thiopurine use within prior 3 months

- Methotrexate use within prior 3 months

- Corticosteroids >20mg for 2 weeks

- Severe protein-calorie malnutrition

- Combined variable immunodeficiency (CVID)

Live Vaccine List

- Nasal Influenza

- ~~Zostavax (Shingles)~~

- Rotavirus (oral)

- Varicella

- MMR

- Polio (oral)

Vaccinating Immunosuppressed IBD Patients

Inactive / Heat-killed Vaccines:
- Safe for use in immunosuppressed
- Not associated with increased disease activity
- May have diminished response to vaccination

Confirm protective titers

Live Attenuated Vaccines:
- ***Not recommended*** in immunosuppressed
- Give Live vaccination 6 weeks before immunosuppression
- Safe for family members to use live vaccines.

Pneumococcal Pneumonia

- Increased risk of pneumonia in IBD, further increased with use of immunosuppression

- Options:
  - Pneumococcal-13 valent (PCV-13)
  - Pneumococcal-23 valent (PCV-23)

- Timing/Order:
  - On immunosuppression: PCV-13 then 8 weeks later, PCV-23
  - Not on immunosuppression: PCV-13 then 1 year later, PCV-23

Pneumococcal Vaccine Timing

- If already given PCV-23, then PCV-13 1 year later in all patients

- Repeat PCV-23 in 5 years and then again at 65

- Give prior to immunosuppression

Melmed, AJG 2010
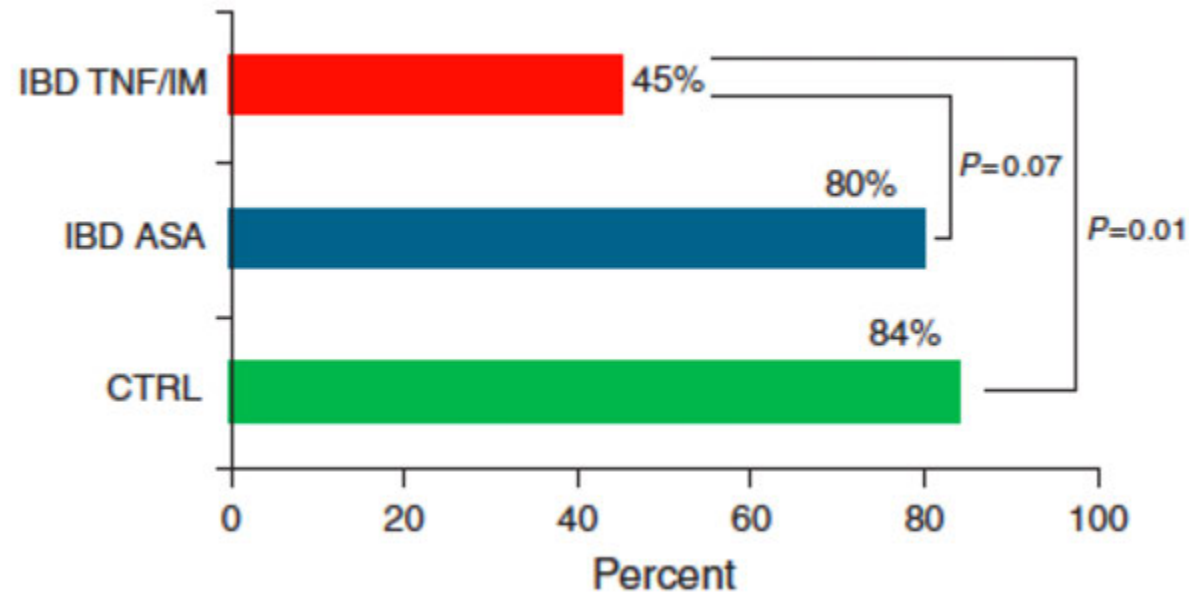
Shingles Incidence Increased in IBD
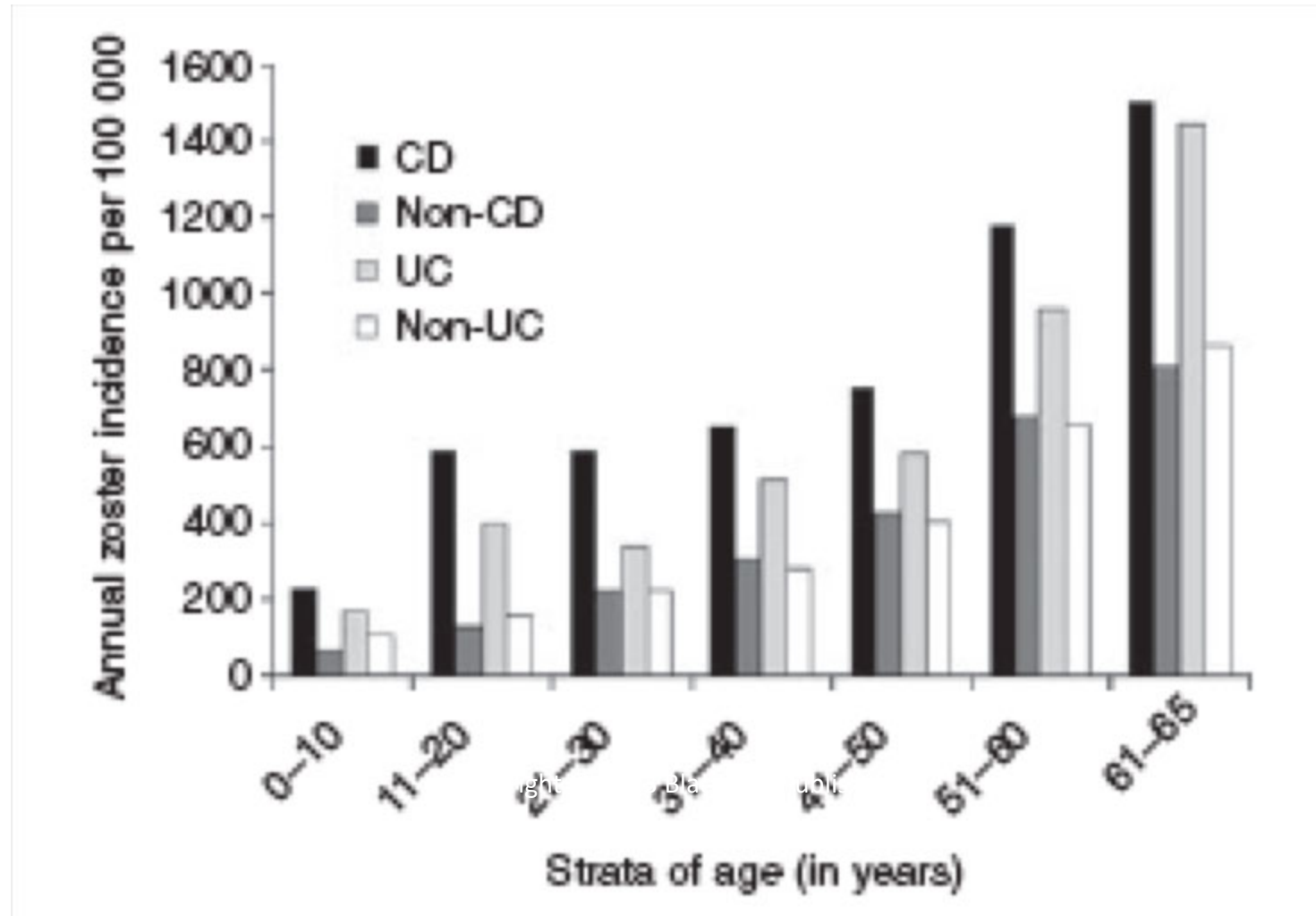
Shingles Increased by Immunosuppression

Medication	IBD overall (n = 13 129)	
	Crude OR, 95% CI	Adjusted OR, 95% CI
Any use in prior 120 days*		
5-ASA	1.20 (1.09–1.32)	1.08 (0.97–1.19)
Biologic	2.57 (2.13–3.10)	1.81 (1.48–2.21)
Thiopurine	2.28 (2.00–2.60)	1.85 (1.61–2.13)
Corticosteroid	2.53 (2.22–2.87)	1.73 (1.51–1.99)

Medication	IBD overall (n = 13 129) adjusted OR, 95% CI
Any use in prior 120 days	
Thiopurine*	1.86 (1.61–2.15)
Biologic†	1.83 (1.44–2.31)
Combination‡	3.29 (2.33–4.65)

- In particular, shingles risk is higher on one of newest drugs, tofacitinib
- 5% of patients receiving this drug for UC in studies developed Zoster
- Highest risk: >65 and prior anti-TNF use

Winthrop. IBD 2018

Shingrix (recombinant shingles vaccine)

- 2 vaccines, separated by 2-6 months
- Preferred vaccine for shingles
- All adults over age of 50
- >90% effective in preventing shingles and post-herpetic neuralgia

Hepatitis B

- Reactivation can lead to lethal infection among patients on immunosuppression (not just anti-TNFs)

- Response rate to vaccination is 50-60%

- Anti-TNF users with lower response rates

- Check titers after series and re-vaccinate if not >10 IU/L

Gisbert, AJG 2012

Other Vaccines

- Influenza yearly intramuscular

- TD (q10 years) with TDaP substituted once for pertussis coverage

- HPV: both genders between 11-26

Cancer Surveillance

Colon Cancer Risk in IBD

TABLE 2. Reported Colorectal Cancer Risk in Patients with IBD

IBD Type (Study References); Subgroup Analysis	No. of Patients	PYAR[a]	Observed CRC	Pooled SIR	95% CI	I^2 (%)
IBD[2,7,8,16,22,34,35,37,65]; population-based	13,010	259,266	210	1.7	1.2–2.2	64
IBD[20,21,30,31]; referral center	2098	29,799	57	6.9	4.1–9.7	43
UC[2,7,8,16,34,35,37,65]; population-based	8964	161,154	188	1.7	1.03–2.4	73
UC[21,30,31]; referral center	1585	22,375	48	8.3	5.9–10.7	0
CD[7,8,22]; population-based	4046	98,112	22	1.7	1.01–2.5	0
CD[20]; referral center	513	7424	9	4.4	1.5–7.2	NA

Risk Factors

- Extent of Disease

- Duration of Disease

- Primary sclerosing cholangitis (PSC): ***annual colonoscopy*** (14-31% develop colorectal cancer)

- Severity of Inflammation

- Pseudopolyps

Surveillance Intervals

- Restage disease extent after 8 years

- Among those with extensive disease, q1-2 year colonoscopy with surveillance biopsies

- Exception: Annual colonoscopy in PSC patients

- SCENIC guidelines: chromoendoscopy is "suggested" (conditional recommendation, low quality evidence)
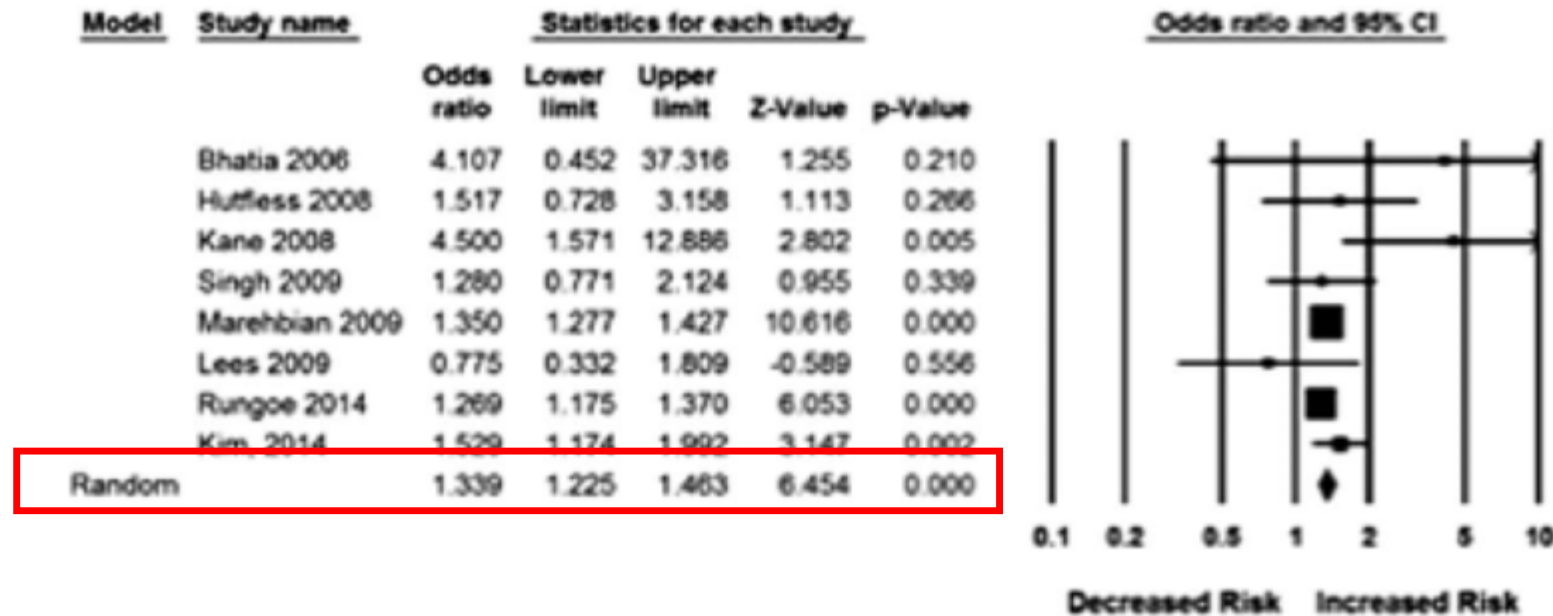
Medication-Related Skin Cancer Risk

	Melanoma	NMSC
	Relative Risk (95% CI)	
5-ASA	0.98 (0.63–1.53)	1.01 (0.90–1.13)
Biologic	**1.88 (1.08–3.29)**	1.16 (0.95–1.41)
Thiopurine	0.92 (0.53–1.59)	**1.85 (1.66–2.05)**

- Combination therapy - **NMSC x3.2 RR**
- Advocate sun protection
- Routine dermatology evaluation for immunosuppressed

Long et al, Gastro 2012

Cervical Dysplasia Risk

Risk of Cervical Cancer/Dyplasia in IBD Patients on Immunosuppression

Model	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	Bhatia 2006	4.107	0.452	37.316	1.255	0.210
	Hutfless 2008	1.517	0.728	3.158	1.113	0.266
	Kane 2008	4.500	1.571	12.886	2.802	0.005
	Singh 2009	1.280	0.771	2.124	0.955	0.339
	Marehbian 2009	1.350	1.277	1.427	10.616	0.000
	Lees 2009	0.775	0.332	1.809	-0.589	0.556
	Rungoe 2014	1.269	1.175	1.370	6.053	0.000
	Kim 2014	1.529	1.174	1.992	3.147	0.002
Random		1.339	1.225	1.463	6.454	0.000

Meta Analysis

- ACOG recommends annual pap smears for patients who are immunosuppressed

Allegretti et al, IBD 2015

Venous Thromboembolism (VTE) More Common in IBD
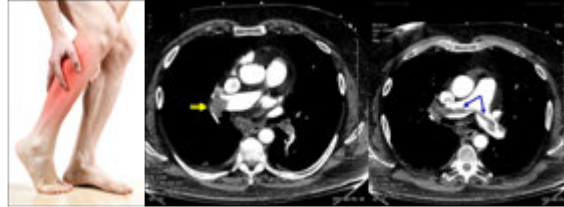
Study	No. of study patients		Primary outcome	Risk measure (95% CI)
	IBD	*Non-IBD*		
Bernstein *et al.*	5,529	~55,000	Hosp. for VTE	IRR 3.47 (2.94, 4.09)
Grainge *et al.*	13,756	71,672	All VTEs	HR 3.4 (2.7, 4.3)
Nguyen *et al.*	116,842	522,703	All VTEs	OR 1.85 (1.70, 2.01)
Miehsler *et al.*	618	618	All VTEs	OR 3.6 (1.7, 7.8)

- IBD has 2.5x mortality from VTE

How Do Medications Impact VTE in IBD?

n=15,000 IBD patients
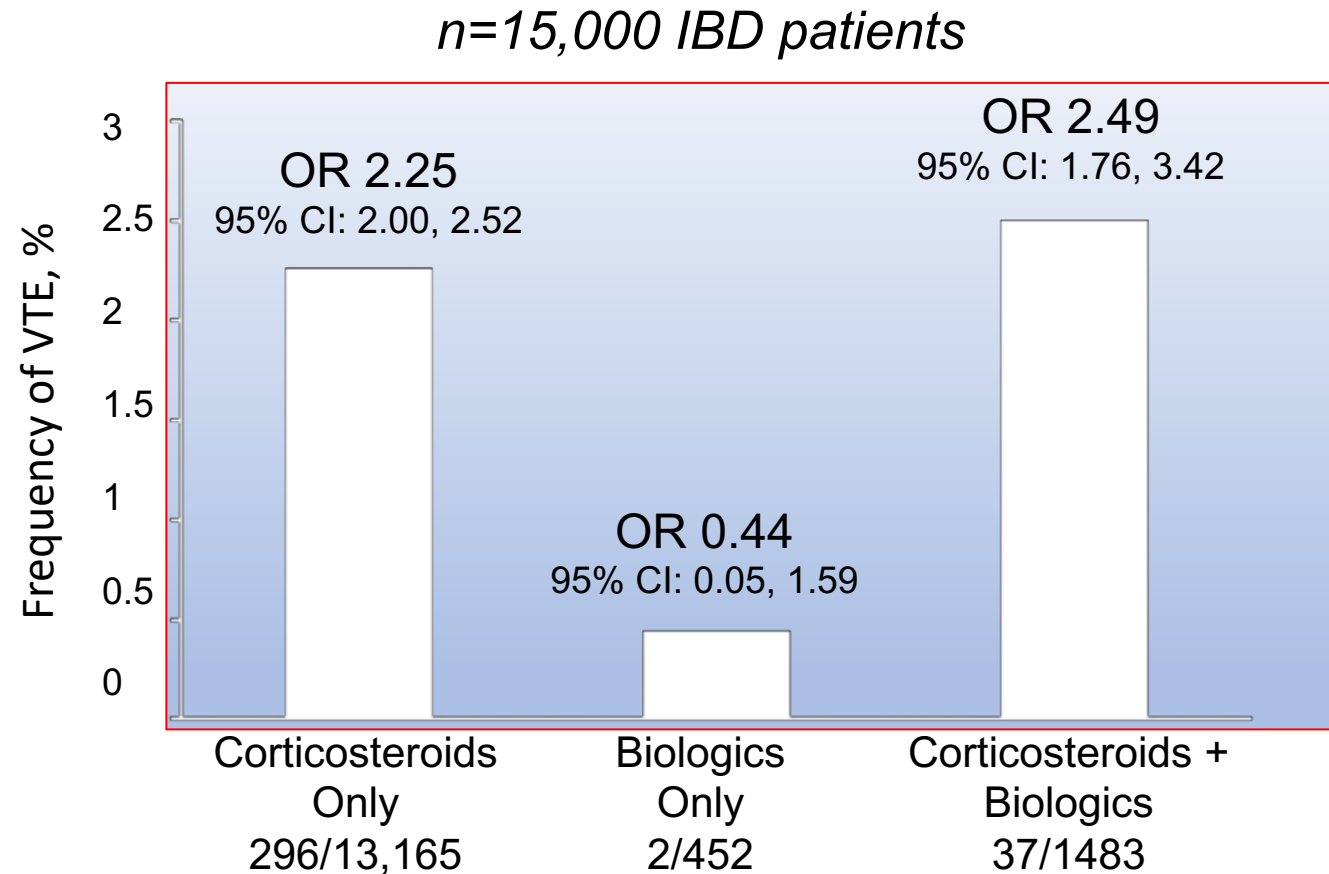
- Steroids effect is dose-dependent (>20mg OR 3.33)
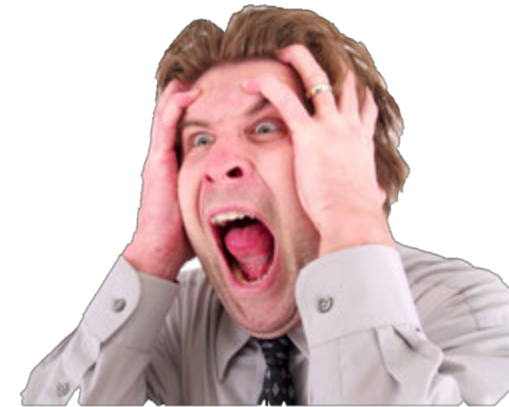
Higgins et al, CGH 2015

Are We Doing Enough to Prevent VTE in IBD?

VTE Prophylaxis Order Written in 24h: 49%
Total Heparin Doses Administered: 41%
Prophylaxis Orders Were Appropriate: 37.5%
GI Consultants Recc on VTE prophylaxis: 15%

Overall Adequate VTE prophylaxis: 7%

Avoiding Prophylaxis
- Hematochezia (OR 3.5, p=0.002)
- Active Flare (OR 2.9, p=0.005)
- Use of Biologic (OR 2.4, p=0.03)

Osteoporosis and Fracture are More Prevalence in IBD

- Osteoporosis prevalence is 18-42%
- Fracture risk 40% greater than general population
- Early Bone Densitometry Recommended (AGA)

-Steroid Use >3 months

-Inactive disease with steroid use >1 year in past 2 years

-Post-menopausal women

-Males >50 years old

- History of vertebral fractures

Only 23% of IBD patients had recommended osteoporosis screening

1. Bernstein et al. Gastro 2003
2. Ali et al. Am J Med 2009.

Mineral and Vitamin Deficiencies in IBD

Vitamin D has an important role in IBD

Low Vitamin D associated with:
- More surgeries (OR 1.76, 95%CI 1.24-2.51)
- More hospitalization (OR 2.07, 95%CI 1.59-2.68)
- Less Flares in RCT of VitD vs. Placebo (13% vs. 29%)

Plasma 25-OH Vitamin D Level Ranges:
- *Deficient*: <20 ng/mL
- *Insufficient*: 20-30 ng/mL
- *Sufficient*: >30 ng/mL

Vitamin D Requirements:
IBD with *insufficient* levels need 2000-5000 IU D3 daily
IBD with *deficient* levels need 50,000 IU D2 weekly x 12wks

1. Ananthakrishnan IBD 2013.
2. Burstein, NutJ 2014

Anemia is Common in IBD

34-80% of All IBD Patients are Anemic
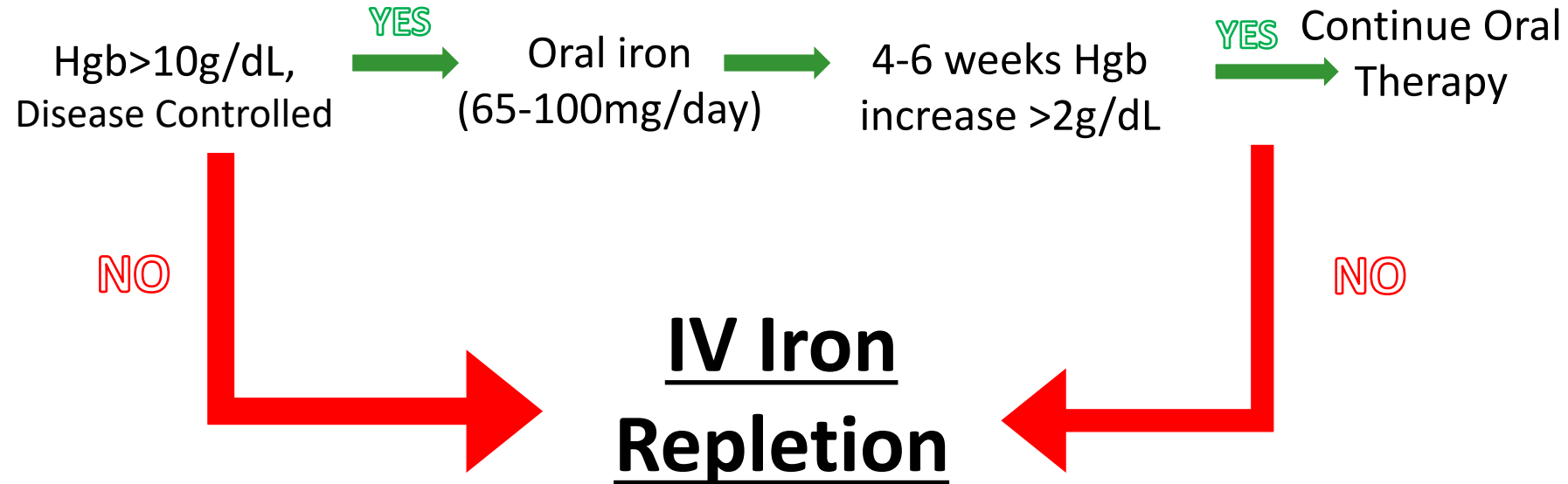
HGB : Males <13g/dL

HGB : Females <12g/dL

Ferritin: <30ug/L ** Acute Phase Reactant

MCV: Unreliable (40% Normal MCV)

- **Iron Deficiency : 90% of all cases**
- Anemia of Chronic Disease : 10-30% of cases
- Occasional: B12, Folate, Medication Induced

Goodhand et al. IBD 2012
Reinisch et al. JCC 2013
Gasche et al. Gut 2004

Iron Deficiency Anemia Treatment in IBD

Hgb>10g/dL, Disease Controlled → **YES** → Oral iron (65-100mg/day) → 4-6 weeks Hgb increase >2g/dL → **YES** → Continue Oral Therapy

NO → **IV Iron Repletion** ← **NO**

Fixed Dosing for IV Iron Requirement

Hgb (g/dL)	<70 kg	>=70 kg
>10	1000mg	1500mg
<10	1500mg	2000mg

Stein et al. Ann Gastro 2013

Health Maintenance Checklist

- Cornerstoneshealth.org

Thank you!

Q&A/Panel Discussion

Drs. Echavarria, Coss & Govani

15 Minute Break