Role of Primary Care Provider in Inflammatory Bowel Disease

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Objectives

- Review Inflammatory Bowel Disease presentation of Crohn’s and Ulcerative Colitis
- Discuss goals of treatment in IBD
- Review outpatient preventive care for Inflammatory Bowel Disease patients.
- Review Inpatient management of patient with inflammatory bowel disease
Inflammatory Bowel Disease

- **Is NOT**
  - An Allergy
  - An immune deficiency

- **Is**
  - Inflammatory activated immune system in the intestinal tract
  - Chronic – last a long time (maybe lifetime)
  - Treatable
Current Etiologic Hypothesis for IBD

- Genetic Susceptibility
- Immune Response
- Environmental Factors
  - Microbial flora
  - Lack of infections (Hygiene Hypothesis)

IBD
Incidence IBD < 1960
Incidence 1980-2008
Inflammatory Bowel Disease (IBD)

- Approximately 1.4 million Americans have IBD
- 70,000 new cases each year
Onset of IBD
What is Ulcerative Colitis?

- Inflammatory bowel disease involving the large intestine (colon and rectum)
- Variable extent of large bowel involvement
- Almost always starts in the rectum and may involve more bowel or progress proximally
- Major symptoms usually come from the inflamed rectum
- Disease is characterized in most patients by active inflammation alternating with periods of quiescence (remission)
Ulcerative colitis location and extent

- Proctitis: 28%
- Left-sided Disease: 25%
- Pancolitis: 47%
Presentation of UC

- Symptoms depending on extent and severity of inflammation
- Bloody diarrhea
- Abdominal cramping
- Tenesmus – fecal urgency
- Systemic symptoms, fever, decreased stamina, weight loss
Natural history of UC

- Disease progress in 54% of patients within 5 years of diagnosis
- Complications highest among pancolitis patients
- 20-38% ultimate require proctocolectomy
- Increased risk of colon cancer
MILD
<4 stools/day ± blood
Normal ESR
No signs of toxicity

MODERATE
≥ 4 stools/day
Minimal signs of toxicity

SEVERE
>6 bloody stools/day +
Fever, tachycardia, anemia, or ↑ ESR

FULMINANT
>10 stools/day, continuous bleeding, toxicity, abdominal tenderness/distension, transfusion requirement, colonic dilation on x-ray

What is Crohn’s disease?

• Inflammatory bowel disease involved the entire GI tract (mouth to anus)
• Disease is characterized in most patients by patchy inflammation which alternates between periods of active disease and periods of quiescence.
• Inflammation is full-thickness
• Fistulas and strictures occur
• Symptoms depend on extent and severity of disease
Crohn’s disease location and extent

- Mouth to Stomach: 6%
- Colitis 32%
- Ileocolitis 45%
- Ileitis 22%

Need ref
Clinical presentation of Crohn’s disease

- Ileocecal disease: abdominal pain, diarrhea, fever
- Colonic disease: bloody diarrhea, weight loss, fever
- Perianal disease: pain, fistulae, fissures
Clinical Criteria for Crohn’s Disease Activity

- Mild to moderate disease
  - Ambulatory, no abdominal tenderness, painful mass, or obstruction

- Moderate to severe disease
  - Unresponsive to treatment for mild to moderate disease with prominent fever, weight loss, anemia, abdominal pain and tenderness or intermittent nausea or vomiting

- Severe fulminant disease
  - Persistent symptoms on corticosteroids or with high fever, rebound tenderness, cachexia or abscess
### Difference between Ulcerative Colitis vs. Crohn’s Disease

<table>
<thead>
<tr>
<th></th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distribution</td>
<td>Continuous, symmetric, and diffuse distribution</td>
<td>Distribution is often discontinuous and asymmetric with skipped segments and normal intervening mucosa</td>
</tr>
<tr>
<td>Depth of Inflammation</td>
<td>Mucosal/submucosal inflammation</td>
<td>Mucosal, submucosal, and/or transmural inflammation</td>
</tr>
<tr>
<td>Site</td>
<td>Colon affected exclusively</td>
<td>May affect any part of GI tract</td>
</tr>
<tr>
<td>Rectal Involvement</td>
<td>Almost always involves the rectum</td>
<td>Relative rectal sparing may be present</td>
</tr>
</tbody>
</table>

What is clinical remission?

- A) Getting rid of all inflammation
- B) Achieving symptom relief
- C) Curing the disease
- D) Decrease symptoms
What drug classes are available for treatment?

- Aminosalycilates
- Immunomodulators
- Biologics
- Non-TNF Biologics
- Steroids
Induction Therapy

- Induction
  - Achieve quick treatment response and clinical remission
  - Decided based on severity of disease
- Options
  - Aminosalicylates
  - Steroids
  - Anti-TNF Agents (Biologics)
Maintenance Therapy

- Maintenance
  - Prevents relapses and maintains long term clinical remission
  - Therapy depends on severity of disease
  - Corticosteroid sparing therapy

- Options
  - Aminosalycilates
  - Immunomodulators
  - Anti-TNF Agents (Biologics)
  - Non-TNF Biologics
Goals of Therapy

- Establish and maintain symptom control (clinical remission)
- Control inflammation
- Prevent flare-ups of disease (maintain remission)
- Reduce complications
- Reducing the need for surgery
- Improve quality of life
- In children facilitating normal growth
Crohn’s Disease: 1960’s historical perspective

Treatment limited to sulfasalazine and prednisone. No need for algorithm, because limited options available.
We have come along way.
Principles of IBD Treatment

- Since it’s an autoimmune condition most cases are treated with immunosuppressant.
- Mild cases can be treated with non-immunosuppressant's.
- Steroids are temporary and do not make inflammation better.
Serious Potential Adverse Effects From Prolonged Corticosteroid Therapy

Adverse effect

Infection
Hypertension
Diabetes
Osteonecrosis
Osteoporosis
Myopathy
Cataracts
Glaucoma
Psychosis

Use of corticosteroids in IBD should *always* have an effective exit strategy.

Lichtenstein GR et al. ACG 2008;Abstract 14
Sandborn WJ. *Can J Gastroenterol.* 2000;14(suppl C):17C-22C
Biologics

Chimeric monoclonal antibody (75% human IgG₁ isotype)

Human recombinant antibody (100% human IgG₁ isotype)

Humanized Fab’ fragment (95% human IgG₁ isotype)

Infliximab

Adalimumab

Certolizumab Pegol
TNF inhibitors Mechanism of Action

• Interfere with body inflammatory response targeting specific cytokines
• Targeted treatment as opposed to corticosteroids provide more general suppression
• Work by binding and preventing activity of tumor necrosis factor alpha (TNF-alpha)
Selective anti-adhesion molecules: Rationale

- Brain
- Bone marrow
- Gut
- MadCAM-1
- a4b7
- VCAM-1
- a4b1
- endothelium
- leukocyte
- integrins
- addressins
- natalizumab
- Vedolizumab, rhuMab-beta7
- PF-00547659
- CCR9
- vercirron
Conventional and evolving treatment strategies in CD

Ordás I et al. Gut 2011
The impact of CE studies: SONIC:
Corticosteroid-Free Clinical Remission at Week 50

Patients with CRP $\geq 0.8$ mg/dL and Lesions on Baseline Endoscopy*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percent of Patients (%)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZA+ placebo</td>
<td>22.7</td>
<td>0.002</td>
</tr>
<tr>
<td>IFX + placebo</td>
<td>41.5</td>
<td>0.016</td>
</tr>
<tr>
<td>IFX + AZA</td>
<td>50.0</td>
<td>0.354</td>
</tr>
</tbody>
</table>

* Patients who did not enter the study extension were treated as nonresponders

AZA=azathioprine; IFX=infliximab

Mucosal Healing and Time to Colectomy in Infliximab-treated Patients: Endoscopy Subscore

Preventive care Recommended?

- 26yo with newly diagnosed Crohn’s disease with ileal and perianal disease starting TNF therapy
- What preventive measures would you recommend?
Risk of Infection in IBD

- Infections are the most common significant adverse event among immunosuppressed patients with IBD.
- Risk of serious infection increases with the number of immunosuppressive therapies.
  - Steroids
- Many infections are preventable with routine preventive immunizations.
Serious Infection Risk with TNF-α vs. non-biologics

Table 2. Initiation of TNF-α Antagonists and Risk of Serious Infections

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Events, No.</th>
<th>Person-Years, No.</th>
<th>Rate, per 100 Person-Years</th>
<th>Hazard Ratio (95% CI) for Propensity Score-Matched Cohorts</th>
<th>Adjusted Hazard Ratios (95% CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonbiologic regimens</td>
<td>326</td>
<td>4192</td>
<td>7.78</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>TNF-α antagonists</td>
<td>497</td>
<td>6089</td>
<td>8.16</td>
<td>1.05 (0.91-1.21)</td>
<td>1.05 (0.91-1.21)</td>
</tr>
<tr>
<td>Baseline glucocorticoid use, prednisone equivalents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>&gt;0-&lt;5 mg/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.32 (1.10-1.58)</td>
</tr>
<tr>
<td>5-10 mg/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.78 (1.47-2.15)</td>
</tr>
<tr>
<td>&gt;10 mg/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.95 (2.41-3.61)</td>
</tr>
</tbody>
</table>

Grijalva et al JAMA 2011 306(21):2331-2339
Vaccination

- Goal: prevent infections in a population that is often immunocompromised
  - Influenza and pneumococcal pneumonia are the most common vaccine preventable illnesses in adults
- Standard recommended immunization scheduled for adults should be adhered to
- At diagnosis, all adults should have review of immunization history, with catch up vaccination given as needed
- Exceptions
  - Live virus vaccines
    - Contraindicated with immunosuppression
      
Patients with IBD are under-vaccinated

- 169 patients surveyed at Tertiary IBD Center
- 98% reported current or past immunosuppressant use
- 28% received regular influenza shots
- 9% had pneumococcal vaccination
- 45% tetanus vaccine in past 10 years
- Most common reason for non-immunization
  - Lack of awareness (49%)

Melmed Am J Gastroenterol 2006;101:1834-40
Immunization of IBD Patients

- All patients should get influenza vaccination
- All patients should get vaccinated with pneumococcal vaccine
  - Patient on Immunosuppression should receive new 13 serotype followed by 23 serotype vaccine
- Young males and females vaccinated for HPV.

Invasive Pneumococcal Disease

- S. Pneumonia is a leading cause of sepsis, pneumonia, meningitis, and otitis media
- At risk: Immunosuppression, Comorbidities
- Booster after 5 years

www.cdc.gov
Increased risk of Pneumonia in IBD

Retrospective national cohort
108, 604 IBD vs. 434,416 non IBD

Response to pneumococcal vaccine

- Patients on anti-TNF + immunomodulator therapy have significantly lower response to pneumococcal vaccination compared with IBD and healthy controls.

Melmed Amj 2010 jan 105(1) 148-54.
ACIP & IDSA Recommendation

- PPSV23 vaccine (polysaccharide) should be given to ALL patients and repeat in 5 years
- PCV 13 (conjugated) vaccine should be given to all patients with current or planned immunosuppression
  - At least 8 weeks before or at least 1 year after PPSV23 (vaccine)
IDSA 2013 Recommendations

- Patient on low dose immunosuppression can receive Zoster vaccination
- such as low-dose prednisone (<2 mg/kg; maximum ≤20 mg/day), MTX (≤0.4 mg/kg/week), azathioprine (≤3 mg/kg/day), and 6-mercaptopurine (≤1.5 mg/kg/day)
Other pearls from the IDSA Guidelines

- How long do you have to wait to start immune suppression after a live virus vaccine?
  - At least 4 weeks

- NEVER give live influenza*, MMR or yellow fever if immune suppressed

- Household contacts
  - CAN receive: MMR, rotavirus for infants, Varicella/Zoster (but watch for lesions), yellow fever, oral typhoid
  - CANNOT receive: live influenza, live polio
Risk of Herpes Zoster ("shingles") is increased in IBD

- Case control study, GPRD 1988-1997
  - 7823 (Crohn’s), 11,930 (UC), and 79,563 (control)
- Incidence of HZV is about 1.5x higher in IBD
- Risk increases with immunosuppression
  - Corticosteroids OR 1.5 (1.1 – 2.2)
  - AZA/6MP OR 3.1 (1.7 – 5.6)

Gupta, Lautenbach, and Lewis. *Gastroenterology* 2006
Zoster in IBD increases with Age
Varicella and Zoster vaccines in immune suppressed patients

- Varicella vaccination safe and effective in children with HIV
- Pediatric IBD patients from Boston Children’s → varicella vaccination in immunosuppressed kids was safe and effective
- 463,541 Medicare beneficiaries with various inflammatory disorders (subgroup on biologics)
  - No cases of HZV infection in biologic-treated patients who received Zoster vaccine
  - Zoster Vaccine was protective HR 0.61 (95% CI, 0.52-0.71)

Smoking Cessation in IBD Patients

- Crohn’s and UC patient should be counseled to quit.
- Increased prevalence of Crohn’s disease in smokers
- Crohn’s disease patients who are smokers
  - More severe ileal disease,
  - Increased risk of frequent flares,
  - An increased need for steroids and immunomodulators
  - Higher rates of surgery
Smoking cessation is crucial aspect in the management of Crohn’s patients that if often overlooked

- Decreased risk of relapse
- Decreases need for steroids or immunomodulators
Bone Health In IBD Patients

- IBD patients have increased risk of osteoporosis and osteopenia
  - Risk factors: BMI, steroids, severity of intestinal inflammation, dietary habits
- Evaluate patients on greater than 10mg for 60 days
  - Bone density evaluation
  - Vitamin D
- IBD patients are under screened 23%
Non-Melanoma Skin Cancer

• Most common in industrialized nations
• 100 increased risk in solid organ transplant.
• Do Immunomodulators increase the risk of skin cancer?
• Do Anti-TNF increase the risk of skin cancer?
# Thiopurines and non-melanoma skin cancer

## Table. Risk of NMSC Among IBD Patients Exposed to Thiopurines

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of IBD Patients</th>
<th>NMSC-Specific Design</th>
<th>Definition of Thiopurine Exposure</th>
<th>Risk of NMSC</th>
<th>Possible Biases</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong and Kriker, 2001²</td>
<td>Cohort: 15 471</td>
<td>Nested case-control</td>
<td>General Practice Research Database: prescription for thiopurine before cancer diagnosis</td>
<td>OR, 0.99</td>
<td>95% CI, 0.35-2.81</td>
<td>B</td>
</tr>
<tr>
<td>Long et al, 2010⁷</td>
<td>Cohort: 53 377</td>
<td>Nested case-control</td>
<td>Outpatient pharmacy claims: recent or persistent thiopurine prescription</td>
<td>OR, 0.99</td>
<td>95% CI, 0.35-2.81</td>
<td>B</td>
</tr>
<tr>
<td>van Schaik et al, 2011⁸</td>
<td>2887</td>
<td>Retrospective cohort</td>
<td>Health claim review: 50 mg thiopurines daily for 6 mo</td>
<td>HR, 0.85</td>
<td>95% CI, 0.51-1.41</td>
<td>B</td>
</tr>
<tr>
<td>Peyrin-Biroulet et al, 2011⁵</td>
<td>19 486</td>
<td>Prospective cohort</td>
<td>Gastroenterologist report: exposure to thiopurines, past or ongoing</td>
<td>Past use: HR, 3.9; 95% CI, 1.3-12.1 Ongoing use at NMSC diagnosis: HR, 5.9; 95% CI, 2.1-16.4</td>
<td>Surveillance bias inherent to study design</td>
<td>B</td>
</tr>
<tr>
<td>Singh et al, 2011⁴</td>
<td>Cohort: 96 18 (2037 with NMSC, each matched to 4 case-controls)</td>
<td>Nested case-control</td>
<td>Database: ≥2 prescriptions for thiopurines</td>
<td>OR, 2.17</td>
<td>95% CI, 1.24-3.81</td>
<td>A</td>
</tr>
<tr>
<td>Setshedi et al, 2012⁹</td>
<td>1084</td>
<td>Retrospective cohort</td>
<td>Patient medical, pharmacy, or laboratory records: note of thiopurine use</td>
<td>OR, 5.0</td>
<td>95% CI, 1.1-22.8 P &lt; .05</td>
<td>B</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; IBD, inflammatory bowel disease; NMSC, nonmelanoma skin cancer; OR, odds ratio.
## Risk of NMSC in IBD patients exposed to biologics

<table>
<thead>
<tr>
<th></th>
<th>Biologic</th>
<th>Risk estimate</th>
<th>Biologics increase the risk of NMSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long et al, CGH 2010</td>
<td>IFX/ ADA in CD</td>
<td>Recent use (&lt;90 days): 1 OR 2.07 (95%CI 1.28-3.33)</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Persistent use (&gt;365 days): 1 OR 2.18 (95%CI 1.07-4.46)</td>
<td></td>
</tr>
<tr>
<td>Long et al, Gastroenterology 2012</td>
<td>IFX/ ADA/CZP in IBD</td>
<td>Any use 1 OR 1.14 (95%CI 0.95-1.36)</td>
<td>NO</td>
</tr>
<tr>
<td>Burmester et al, Ann Rheum Dis 2013</td>
<td>ADA in CD</td>
<td>SIR 2.29 (95%CI 1.44-3.47)</td>
<td>YES</td>
</tr>
</tbody>
</table>

1 – adjusted OR
Take-home messages regarding skin cancer

- Thiopurines increase the risk of developing skin cancer
  - 2-fold increased risk of NMSC (persisting after withdrawal)
  - Probably no increased risk of melanoma

- Biologics may increase the risk of NMSC
- Recommend routine skin exams
- Recommend preventive measures
  - Sunscreen
  - Avoid excessive use tanning beds
Cumulative risk of developing Colorectal Cancer in UC Historical Meta-analysis

Risk of CRC in IBD is elevated
Inflammation of the colon is the key factor

<table>
<thead>
<tr>
<th>Site</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CD</td>
<td>2.5</td>
<td>1.3-4.7</td>
</tr>
<tr>
<td>Colon</td>
<td>4.5</td>
<td>1.3-14.9</td>
</tr>
<tr>
<td>Ileum</td>
<td>1.1</td>
<td>0.8-1.5</td>
</tr>
</tbody>
</table>

Canavan C et. al. *Aliment Pharmacol Ther* 2006: 23, 1097
Colorectal cancer screening in Inflammatory Bowel Disease: The role of Chromoendoscopy

- Spraying of dye in the colon
- Two main uses in IBD Surveillance
  - Improve detection of subtle colonic lesions (increase sensitivity of surveillance)
  - Once lesion detected-to aid in differentiating between neoplastic and non-neoplastic based on crypt architecture and modified pit pattern
61 yold Crohn's Colitis
Inpatient Management and Goals of Hospitalization

1) Assess disease activity
2) Monitor for complications
3) Apply medical treatment or surgery
4) Exclude infections
IBD Hospital readmission

- Readmission significant burden to health care system
- Readmission associated with
  - Incorrect discharge instructions
  - Outpatient follow up scheduled
- 25.7% of patients all cause 30 day readmission
Determine the need for admission?

- 30yold male with ulcerative colitis present with worsening diarrhea and abdominal pain. Getting worse even though on Prednisone 40mg.
- ESR 13, CRP 1, WBC 5.9, Hg 12.4, Platelet 277
Fecal biomarkers

- **Fecal Calprotectin**
  - Calcium binding neutrophilic cytosolic protein
  - Stable for 1 week
  - 5-7 days to process
  - Increase with NSAIDS
  - Value given

- **Fecal Lactoferrin**
  - Iron binding protein neutrophil derived
  - Stable 48+ hours
  - Measure of mucosal inflammatory activity
  - Increase with NSAIDS use
Worsening diarrhea?

- 30 year old female with UC admitted with bloody diarrhea, abdominal pain and weight loss. She feels this a typical flare and just needs IV steroids. What is your next step?

1. IV steroids
2. NPO
3. Clostridium difficile
4. Remicade
Unique Risk Factors for CDI in IBD Patients

- Younger age
- No antibiotic exposure
- Outpatient acquisition
- More commonly seen in UC and Crohn’s colitis

C. difficile Colonization Rates Higher in IBD Patients

- IBD patients in remission vs. healthy adults
- No exposure to antibiotics, steroids, immunomodulators, hospitalizations

<table>
<thead>
<tr>
<th>Study group</th>
<th>No. of participants</th>
<th>Male/female</th>
<th>No. (%) of C. difficile positive</th>
<th>No. (%) of toxin positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic healthy adult</td>
<td>99</td>
<td>38/61</td>
<td>2 (2.0)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>IBD patients</td>
<td>122</td>
<td>48/74</td>
<td>13 (10.7)</td>
<td>10 (8.2) *P=0.02</td>
</tr>
<tr>
<td>With ulcerative colitis</td>
<td>64</td>
<td>23/41</td>
<td>7 (10.9)</td>
<td>6 (9.4) *P=0.015</td>
</tr>
<tr>
<td>With Crohn’s disease</td>
<td>58</td>
<td>25/33</td>
<td>6 (10.3)</td>
<td>4 (6.9) *P=0.06</td>
</tr>
</tbody>
</table>

CDI-IBD Patients Have Worse Outcomes

- Population based retrospective study based on discharge diagnosis (2003)

- Primary outcome: in-hospital mortality

- CDI-IBD 2804, CDI 44,400, IBD 77,366

- Compared to non IBD CDI patients; IBD patients with CDI had:
  - 2x greater mortality
  - 6x more likely to undergo bowel surgery
  - 3x longer length of stay
  - 3x more likely to require TPN
  - 2x more likely to require blood transfusions

Ananthakrishnan AN, McGinley EL, Binion DG. Excess hospitalization burden associated with Clostridium difficile in patients with inflammatory bowel disease. Gut. 2008 Feb;57(2):205-10
Cases: Severe, hospitalized UC

- 24 y man admitted with severe UC, failing oral steroids x 10 days
  - 8-12 bloody BM/day, Hgb 9.0, ESR =40
  - No fever or toxic signs
  - No personal or family history of thrombosis
  - Nonsmoker, no recent travel

Which DVT prophylaxis is most appropriate?
1. Ambulation along
2. Compression stockings
3. Leg compression devices
4. Subcutaneous heparin 5000 U three times daily
Risk of VTE in IBD

- Large European and North American studies shown 2-3 fold increase in VTE
- 50% of thrombosis in IBD have no identifiable risk factor
Why are IBD patients at Risk?
Virchow Triad

Hypercoagulable state

- Inflammation
- Thrombocytosis
- Surgery
- Cigarette smoking
- Corticosteroids
- Antiphospholipid antibody
- Hyperhomocysteinemia

DVT

- Inflammation
- IV catheter

Venous stasis

- Dehydration
- Immobilization

Endothelial injury
Increased Risk compared to controls

Table 1. Risk of thromboembolic events in IBD patients relative to non-IBD patients

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of study patients</th>
<th>Patients and setting</th>
<th>Primary outcome</th>
<th>Risk measure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IBD</td>
<td>Non-IBD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernstein et al. (1)</td>
<td>5,529</td>
<td>~55,000</td>
<td>Hospitalized patients (Manitoba, Canada)</td>
<td>Hospitalization for VTE</td>
</tr>
<tr>
<td>Grainge et al. (2)</td>
<td>13,756</td>
<td>71,672</td>
<td>Ambulatory and hospitalized patients (U.K.)</td>
<td>All VTEs</td>
</tr>
<tr>
<td>Huerta et al. (3)</td>
<td>NA</td>
<td>NA</td>
<td>Ambulatory and hospitalized patients (U.K.)</td>
<td>All VTEs</td>
</tr>
<tr>
<td>Nguyen and Sam (5)</td>
<td>116,842</td>
<td>522,703</td>
<td>Hospitalized patients (U.S.A.)</td>
<td>All VTEs</td>
</tr>
<tr>
<td>Miehsler et al. (4)</td>
<td>618</td>
<td>618</td>
<td>Ambulatory and hospitalized patients (Austria)</td>
<td>All VTEs</td>
</tr>
<tr>
<td>Novacek et al. (6)</td>
<td>86</td>
<td>1,255</td>
<td>Ambulatory and hospitalized patients (Austria)</td>
<td>Recurrent VTEs</td>
</tr>
</tbody>
</table>

 Murthy SK, Am J Gastroenterol 2011; 106:713–718
Disease flare increase VTE Risk

VTE risk between 13,756 IBD and 71,672 nonIBD
UK Primary care database

<table>
<thead>
<tr>
<th>Risk of VTE</th>
<th>Risk per 1000 p-y</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD overall</td>
<td>2.6</td>
</tr>
<tr>
<td>IBD flare</td>
<td>10</td>
</tr>
<tr>
<td>Ambulatory flare</td>
<td>6.4</td>
</tr>
<tr>
<td>Hospitalized flare</td>
<td>37.5</td>
</tr>
</tbody>
</table>

Grainge et al, Lancet 2010
VTE Risk in Ambulatory IBD flare
VTE Risk in hospitalized non-IBD
VTE Risk in IBD Hospitalized

**Ten Thousand People**
- pictures to help you see your odds
Increased Hospital Mortality

- National inpatient sample database of 522,000 non IBD compared to 116,000 IBD
- Inpatients with IBD who had a VTE had a 2.5 higher mortality compared to non IBD VTE related hospitalization

Nguyen  Am J Gastroenterol 2008 Sep 103(9)
Risk of Recurrent VTE in IBD

- 1255 non-IBD subjects with unprovoked VTE
  - Matched to 116 with history of VTE (86 were unproved)

- After 5 years, and adjustment for cofounders
  - Risk of recurrent VTE was higher in IBD
  - HR 2.5 (1.4, 4.2)
Are Patients with IBD at “high risk of bleeding”?

- Prophylactic doses of these medications appear safe to use
- Meta-analysis of 8 RCT, 454 subjects
- Safety
- No increased bleeding risk

Shen, J. Aliment Pharmacol Ther. 2007 Sep
## Recommendations

**TABLE 1. Recommendations From Major Organizations Regarding Thromboprophylaxis for Inpatients With IBD**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Organization</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geerts et al(^{18})</td>
<td>American College of Chest Physicians</td>
<td>Prophylaxis with LMWH, LDUH, or fondaparinux for patients with IBD</td>
</tr>
<tr>
<td>Kombluth and Sachar(^{19})</td>
<td>American College of Gastroenterology</td>
<td>Prophylaxis with heparin for patients with UC</td>
</tr>
<tr>
<td>Mowat et al(^{20})</td>
<td>British Society of Gastroenterology</td>
<td>Prophylaxis with heparin for patients with UC</td>
</tr>
<tr>
<td>Travis et al(^{21})</td>
<td>European Crohn’s and Colitis Organization</td>
<td>Prophylaxis with heparin for patients with UC</td>
</tr>
<tr>
<td>Van Assche et al(^{22})</td>
<td>European Crohn’s and Colitis Organization</td>
<td>Prophylaxis for patients with Crohn disease</td>
</tr>
</tbody>
</table>

LDUH, low-dose unfractionated heparin.
Sequential compression devices

- ACP recommended in those with contra-indication to pharmacological therapy
- Patient adherence might be lower due to increase bowel movements
Is outpatient heparin prophylaxis indicated?

- NO

- Not in outpatients, unless another reason
  - “Prophylaxis would be needed for 312 to prevent one person developing venous thromboembolism” – G. Nguyen, Lancet
Pneumocystis Jirocevi Pneumonia

- PJP risk in solid organ transplant 5-15% absence of prophylaxis
- Are IBD patient at increased risk due to immunosuppression?
- Who will benefit from prophylaxis?
Increased Risk of Pneumocystis Jiroveci Pneumonia Among Patients with Inflammatory Bowel Disease.

- Risk based on immunosuppression
  - Immunosuppressed 32/100,000
  - 5.5/100,000 not immunosuppressed.
- NNT 3750 to prevent one case of PCP in IBD population
Summary: Take Home Points

- We are never going to prevent all infections
- But, we have an opportunity to prevent serious infectious complications by thoughtful patient selection and vaccination
- Perform skin exams in immunosuppressed IBD population
- PJP prophylaxis is low yield in IBD population
- Evaluate IBD patients with diarrhea for Clostridium difficile.
- Provide Pharmacological prophylaxis for inpatients with IBD.
THANK YOU

- Questions?
  - fcaldera@medicine.wisc.edu

- New Multi-Disciplinary IBD clinic
  - complicated patients seen by
    - IBD specialist
    - Colorectal Surgeon.
    - Ostomy nurse