MANAGING COMMON GI PROBLEMS IN STUDENT HEALTH CLINICS

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University of Vermont
NECHA 2014

*no affiliations to disclose

Objectives: evaluation & treatment of

Upper GI problems
1. Gastroesophageal Reflux disease (GERD)
2. Peptic ulcer disease (PUD)
3. Functional Dyspepsia (FD) (or the condition formerly known as NUD...nonulcer dyspepsia)

Lower GI problems
4. Celiac disease
5. Lactose intolerance
6. Irritable bowel syndrome (IBS)
   • Inflammatory bowel diseases (IBD)
     •Crohn’s
     •Ulcerative colitis

What do we mean by dys-pepsi-a?

Dyspepsia

- Greek: dys = “bad” or “difficult” + pepsis = “digestion”
- Sensation of pain or discomfort in the upper abdomen; it often is recurrent. It may be described as indigestion, gassiness, early satiety, postprandial fullness, gnawing, or burning
- Types/syndromes
  - GERD: heartburn
  - PUD: ulceration of stomach or duodenum
  - FD: without evidence of an organic disease that is likely to explain the symptoms
  - (rarely) cancer

GastroEsophageal Reflux Disease

GERD

- What is it?
  - Regurgitation of stomach contents into the esophagus leading to mucosal changes and/or symptoms of heartburn
- Prevalence
  - Very common in US
    - 44% adults experience monthly sx; 14% weekly; 7% daily
    - 22% of any college students, and weekly sx in 7% in one Pakistani study

Gastroenterology 2002; 122:1500
J Pak Med Assoc 2010; 60:147
GERD: history & physical

Symptoms
• Retrosternal burning
• Regurgitation, sour taste
• Atypical sx:
  - Cough, laryngitis, sore throat
  - Tob, ETOH, meds = risk fx
• Obesity = risk fx

Red flag sx: significant wt loss; dysphagia, persistent vomiting; +FHx gastroesophageal malignancy

Exam
• Usually negative
• Neither sensitive or specific findings to aid in dx

GERD: accuracy of symptoms

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief from PPIs</td>
<td>78</td>
<td>54</td>
<td>1.7</td>
<td>0.41</td>
</tr>
<tr>
<td>Heartburn</td>
<td>68</td>
<td>52</td>
<td>1.42</td>
<td>0.62</td>
</tr>
<tr>
<td>Acid regurgitation</td>
<td>50</td>
<td>52</td>
<td>1.25</td>
<td>0.77</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>54</td>
<td>47</td>
<td>1.01</td>
<td>0.98</td>
</tr>
<tr>
<td>Clinician gestalt</td>
<td>59</td>
<td>83</td>
<td>3.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

GERD: Diagnostic tests

GERD: accuracy of tests

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole challenge*</td>
<td>78</td>
<td>85</td>
<td>5</td>
<td>0.3</td>
</tr>
<tr>
<td>pH probe**</td>
<td>80</td>
<td>73</td>
<td>3</td>
<td>0.3</td>
</tr>
<tr>
<td>Endoscopy/EGD***</td>
<td>30</td>
<td>78</td>
<td>1.4</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Clinician’s subjective sense of GERD, and response to tx are the best to rule in GERD

*Gastroenter 1998; 115:42
**Ann Surg 1984; 200:724
***Dig Dis Sci 2000; 45: 217

GERD: treatment options

• Lifestyle modification
  - Altered diet—avoid ETOH, caffeine, acidic foods, peppermint
  - Mechanical—staying upright 3+hr post prandial, loose clothing, smaller meals, elevate head o’ bed for nighttime sx
  - Discontinue tobacco use
  - Lose weight
• Motility agents (cisapride, metoclopramide)
• Antacid medications
  - Calcium carbonate and carafate less effective than other meds; consider for adjunctive tx
  - H2 Blockers
  - Proton pump inhibitors
• Surgical interventions
  - Reserved for truly recalcitrant cases

A comment about PPIs

• PPIs more effective than H2Bs (NNT=3)
  - Though 75% of people w/ mild to moderate GERD effectively tx w/ H2Bs; 50% of those w/ severe GERD
• Within class, meds equivalent efficacy
• Long-term use of PPIs demonstrated to be safe
  - Millions of patients over last few decades
  - Tiny increased risk of pneumonia (NHH=449/yr)
  - Long-term, high dose PPI -> slight incr risk of hip fx n osteoporosis (OR 2.6)
Undifferentiated Dyspepsia (aka nonGERD dyspepsia)

Dyspepsia w/o GERD
- Peptic ulcer disease (PUD)
- H pylori infection (85% DU, 75% GU)
- Chronic NSAID use (includes asa, COX2 inhib)
- ETOH, tobacco, social stressors
- Functional dyspepsia (aka nonulcer dyspepsia, NUD)
  - Diagnosis of exclusion; must rule out other causes
  - ~70% of those presenting w/ dyspepsia have no organic cause found on testing

Prevalence
- Dyspepsia—16.3% US adult population (meta-analysis)*
- PUD—6.8% US adult population**
- Limited data on college population: ~9% in one Chinese study***

*Am J Managed Care 2011; 17: 3449
**Vital Health Stat 2005; 10:; www2.niddk.nih.gov
***PLoS ONE 2013; 8: e54183

Dyspepsia: history & physical

Symptoms
- Epigastric pain/discomfort, nausea, early satiety, bloating
- Sx sit more predictive of PUD:
  - Alleviation w/ food
  - Nighttime sx
  - Episodic pain

Exam
- Often normal
- Possible epigastric tenderness

Red Flag Sx: new onset sx >55yo; wt loss >5%; jaundice; palpable mass; GI bleed or anemia

H&P Accuracy: dyspepsia → PUD

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food reduces pain</td>
<td>39</td>
<td>88</td>
<td>3.25</td>
<td>0.69</td>
</tr>
<tr>
<td>Episodic pain</td>
<td>80</td>
<td>65</td>
<td>2.30</td>
<td>0.31</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>88</td>
<td>62</td>
<td>1.8</td>
<td>0.52</td>
</tr>
<tr>
<td>Tenderness, deep palpation</td>
<td>52</td>
<td>27</td>
<td>0.71</td>
<td>1.78</td>
</tr>
<tr>
<td>Tenderness, light palpation</td>
<td>4</td>
<td>75</td>
<td>0.16</td>
<td>1.3</td>
</tr>
<tr>
<td>Clinician Gestalt</td>
<td></td>
<td></td>
<td>2.2</td>
<td>0.45</td>
</tr>
</tbody>
</table>

JAMA 2006; 295: 1566-76. LOE 1

H&P Accuracy: dyspepsia → FD

<table>
<thead>
<tr>
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<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenderness, deep palpation</td>
<td>77%</td>
<td>38%</td>
<td>1.24</td>
<td>0.61</td>
</tr>
<tr>
<td>Tenderness, light palpation</td>
<td>20%</td>
<td>81%</td>
<td>1.10</td>
<td>0.99</td>
</tr>
<tr>
<td>Clinical gestalt</td>
<td>1.90</td>
<td>0.40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Bottomline: individual sx, signs and even clinician impression insufficient in distinguishing PUD from FD

Dyspepsia: diagnosing PUD

1. Empiric treatment (aka clinical dx only)
2. Test and treat strategy (H pylori) (NNT = 8)
3. Double contrast Upper GI Barium (UGI)
4. Endoscopy

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGI</td>
<td>74</td>
<td>93</td>
<td>10.7</td>
<td>0.27</td>
</tr>
<tr>
<td>EGD</td>
<td>95</td>
<td>98</td>
<td>41.3</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Kil Scan J Gastro 1980; 15:39
Which dx approach to take?

- Test & treat strategy is most cost-effective*
  - Demo’d if prevalence rate of H.Pylori >10%
  - US & Canada ~25-30% **
  - Most other countries much higher (Mexico 70-90%; Asia 50-80% Middle East 80-90%)

- In dyspepsia with +H.Pylori, eradication treatment→sx resolution (NNT=6)***
  - Endoscopy is the gold standard
  - If red flag sx’s or no response to eradication tx, consider EGD
  - In areas with limited specialty services, UGI option for primary care settings

*AGA guidelines; **UpToDate; ***Arch Int Med 2011; 171: 1929

Testing for H Pylori

Testing H.Pylori

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea breath test</td>
<td>89</td>
<td>100</td>
<td>178</td>
<td>0.1</td>
</tr>
<tr>
<td>Blood antigen</td>
<td>90</td>
<td>90</td>
<td>9.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Serum antibody</td>
<td>81</td>
<td>88</td>
<td>7.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Gatta Gut 2006; 55:487
Gastro 1996; 109: 136
Gastro 1998; 33: 364
Dig Dis Sci 1998; 43:193
Dig Dis Sci 1999; 44:2303

PUD treatment = H Pylori eradication

- In dyspepsia with +H.Pylori, eradication tx x 4-8 weeks
- Stop treatment; re-initiate prn
- Consider other cause; consider referral to GI
- Repeat H.Pylori testing (stool or breath)
- Re-treat H.Pylori with different regimen
- Consider empiric PPI x 8 wk vs referral to GI for EGD
- Age >55, or red flag sx’s present
  - Refer to GI for EGD
- Clinical impression = GERD
  - Trial of PPI
- Age >55 or red flag sx’s present
  - Refer to GI for EGD, or consider Barium Swallow

FD treatment

- Dietary changes—no data to support
  - Though reasonable to recommend avoiding triggering foods, weight loss if obese
- H2Blockers and PPIs are effective
  - Double dosing not superior to standard dosing
  - PPIs not superior to H2Bs
  - Tricyclic antidepressants effective, if comorbid anxiety or depression (NNT=3)
- Other non-pharm options w/ limited but supportive data
  - CBT small benefit, but short duration
  - Acupuncture superior to sham-acupuncture in one RCT
  - Hypnotherapy

Upper GI syndrome algorithm
Celiac disease

• What is it?
  - Genetically-based, immune-mediated response to gluten causing small bowel malabsorption
  - HLA types DQ2 & DQ8
  - Prevalence 0.8-1% U.S. population
  - Similar rates worldwide, with exception of East Asia and sub-Saharan Africa
  - Blacks, Asians & nonwhite Hispanics rates about ½ of Whites

Celiac: History & Physical

Symptoms
  - bloating, flatulence, chronic diarrhea &/or constipation, abdominal pain
  - classic GI sx → 2.3 fold increase in dx vs general pop
  - limited benefit

Exam
  - skin manifestation: dermatitis herpetiformis
  - possible weight loss

Celiac: Value of symptoms

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx since childhood</td>
<td>35</td>
<td>89</td>
<td>3.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Flatulence/gas</td>
<td>76</td>
<td>43</td>
<td>1.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>20</td>
<td>81</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>71</td>
<td>21</td>
<td>0.9</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Celiac: Diagnostic Tests

- IgA anti-tissue transglutaminase
- IgA anti-endomysial antibody
  - Lack of gluten exposure→false negative testing
- IgA deficiency→false negative

- No longer used anti-gliadin

- Definitive dx = resolution of sx on gluten free diet
- Gold Standard= biopsy (small bowel or skin if DH)
Celiac: Test accuracy

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endomysial antibody</td>
<td>87</td>
<td>99</td>
<td>87</td>
<td>0.1</td>
</tr>
<tr>
<td>Tissue Transglutaminase antibody (tTG)</td>
<td>87</td>
<td>97</td>
<td>29</td>
<td>0.1</td>
</tr>
<tr>
<td>Gladin peptide antibody IgG</td>
<td>88</td>
<td>94</td>
<td>15</td>
<td>0.1</td>
</tr>
</tbody>
</table>

JAMA 2010; 303:1743
LOE 1a

Celiac: Treatment

Celiac: bottomline

- H&P not helpful enough to make dx—though useful to consider in patients with chronic lower GI complaints
- Blood tests required:
  - Transglutaminase Ab (anti-tTG) &/or Endomysial Ab (anti-EM)
  - Test while consuming gluten; consider IgA at time of testing
- If +, gluten free diet, for life
- Likely scope w/ bx not necessary
  - Reserve for those with
    - No or incomplete response to treatment
    - Red flag sx

Most of these improve/resolve with adherence to gluten-free diet

Celiac: Special Considerations

- Dermatological Manifestation
  - Dermatitis herpetiformis

- Nutritional deficiencies
  - anemia
  - folate
  - Vit D
  - Vit D with hypocalcemia → osteopenia/porosis

- Risk of certain cancers increased
  - adenocarcinoma of small intestines, non-Hodgkins lymphoma

- Some association with
  - infertility, other autoimmune disorders, liver disease

Celiac: Eating gluten-free

Wt In the bag: 3
1. Wheat
   - Breads, cereals, pasta, sauces, salad dressings
2. Barley
   - Malt, food coloring, BEER!
3. Rye
   - Triticale

Most of these improve/resolve with adherence to gluten-free diet

Lactose Intolerance

Lactose Intolerance

• What is it?
  - Syndrome of GI sx following the ingestion of lactose
  - Severity will depend of amt of lactose consumed, level of lactase deficiency
  - Cause: lactase deficiency, primary vs secondary (acquired); genetic LI (rare), developmental LI

• Prevalence
  - Primary lactase deficiency: 70-75% world pop
    - in N America: Native Americans 79%; Blacks 75%; Hispanics 51%; Whites 21%
  - Self reported LI ~12%
  - ~10% prevalence in one Ohio State study

• Cause: lactase deficiency, primary vs secondary (acquired); genetic LI (rare), developmental LI

Lactose info vs Milk Allergy

• Enzyme deficiency limiting absorption of mild sugars
• GI sx only
• More often begins in adolescence/young adulthood

• IgE mediated response to milk proteins
• Caused GI sx, but also systemic sx like hives or wheezing
• More often in infants, can outgrow

Lactose Intolerance: history & physical

Symptoms
- Abd pain, bloating, diarrhea, borborygmi, nausea
- Onset w/in 3 hr of consuming lactose-containing products

Exam
- Nonspecific
  - Usually not helpful

Red Flags: bloody diarrhea, wt loss, fever, loss of appetite, signs of obstruction or perforation

Lactose Intolerance: Accuracy of history

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>39%</td>
<td>90%</td>
<td>3.90</td>
<td>0.680</td>
</tr>
<tr>
<td>Borborygmi</td>
<td>65%</td>
<td>75%</td>
<td>2.60</td>
<td>0.470</td>
</tr>
<tr>
<td>Bloating</td>
<td>70%</td>
<td>69%</td>
<td>2.30</td>
<td>0.430</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>55%</td>
<td>72%</td>
<td>2.00</td>
<td>0.630</td>
</tr>
<tr>
<td>Nausea</td>
<td>41%</td>
<td>71%</td>
<td>1.40</td>
<td>0.830</td>
</tr>
</tbody>
</table>

Lactose Intolerance: diagnostic tests

• Hydrogen breath test
  - Fasting pt consumes lactose load; serially measure H2 excretion over 3 hr
  - Noninvasive, cost ~$125

• Lactose tolerance test
  - Measure serial blood glucose following lactose load
  - Fecal pH
    - Decreases b/c formation of fatty acids r/t CHO malabsorption
  - Not used b/c high rates false positives and negatives
  - Duodenal biopsy, measure lactase levels
  - LCT gene
    - CC genotype 100% correlation with +breath test; CT intermediate, and TT = lactase persistent

Lactose Intolerance: diagnostic tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath test*</td>
<td>89%</td>
<td>90%</td>
<td>5.9</td>
<td>0.14</td>
</tr>
<tr>
<td>Lactose tolerance test*</td>
<td>94%</td>
<td>90%</td>
<td>9.4</td>
<td>0.67</td>
</tr>
<tr>
<td>Genetic test**</td>
<td>89%</td>
<td>98%</td>
<td>22</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*Aliment Pharmacol Ther 2012; 35:429; LOE 1
**Aliment Pharmacol Ther 2008; 27: 265; LOE 4
LI: Treatment

- Lactose-free or reduced diet
  - Variable quantities of lactose tolerated; typically 1 cup milk OK
  - Beware ‘hidden’ sources of lactose
    - Powdered sauces, cheese flavored salty snacks
    - Some medications!

- Addition of lactase
  - Lactaid tablets
  - Lactase drops

- Addition of probiotics not effective
  - Though some people with LI tolerate yogurt, kefir

Ann Intern Med 2010; 152(12):797-803. LOE 3a

Lactose intolerance: bottomline

- Suspect LI if abd pain, diarrhea, gas, bloating following lactose consumption

- Diagnosis can often be made clinically
  - Food & symptom diary
  - Elimination diet→resolution of sx
  - If questionable, breath test suffices for dx

- Treatment is lactose reduced/free diet
  - Remember diary does not equate w/ lactose

Irritable Bowel Syndrome

- What is it?
  - Disorder that causes abdominal pain and change in stooling pattern; “functional” vs structural
  - No clear etiology; generally dx of ruling out other causes
    - Manning Criteria 1995—empirical assessment of sx clusters

- Prevalence in US 10-15%
  - Female:Male 2:1; White:Black 1:1
  - NCHA 2013 2.8%

IBS: symptoms → diagnosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Looser stools at onset of pain</td>
<td>58</td>
<td>73</td>
<td>2.1</td>
<td>0.6</td>
</tr>
<tr>
<td>More frequent stools at onset of pain</td>
<td>53</td>
<td>72</td>
<td>1.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Pain relieved by defecations</td>
<td>60</td>
<td>66</td>
<td>1.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Visible abd distension</td>
<td>39</td>
<td>77</td>
<td>1.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Feeling incomplete evacuation</td>
<td>74</td>
<td>45</td>
<td>1.4</td>
<td>0.6</td>
</tr>
<tr>
<td>3 or 4 Manning Criteria</td>
<td>63</td>
<td>85</td>
<td>4.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

BMJ 1978; 2:653. LOE 4

Diagnostic criteria

Rome III, 2006

- Recurrent abd pain &/or discomfort at least 3d/month x 3 months with 2 or more of the following:
  - Improvement with defecation
  - Onset assoc w/ change in frequency of stool
  - Onset assoc w/ change in form of stool

- Two flavors:
  - Constipation dominant
  - Diarrhea dominant
IBS: history & physical

Symptoms: Rome III
- Incr sx w/ stress & anxiety
- 2/3 IBS pts have concomitant psych dx
  - Weight loss
  - Dysphagia
  - No malignancy
  - Age>50 at sx onset
- Possibility of mild tenderness
- Guaiac neg

Exam
- NORMAL!
- Biopsing
- Guarding/rebound
- Anemia

IBS: diagnostic tests

- Diagnosis of exclusion: ruling out, not ruling in

<table>
<thead>
<tr>
<th>Bowel sx → organic dx (NOT IBS!)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>50</td>
<td>81</td>
<td>2.6</td>
<td>0.6</td>
</tr>
<tr>
<td>ESR&gt;10</td>
<td>58</td>
<td>72</td>
<td>2.1</td>
<td>0.6</td>
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</table>

Bowel sx → organic dx (NOT IBS!)

IBS referral?

- Acceptable to make diagnosis clinically
- Need not refer all students to GI for colonoscopy to formally dx IBS
- College students LOW risk population for organic conditions
  - Prevalence of inflammatory bowel disease in 26yo’s 0.33%
  - Crohns 2/10^6 → Ulcerative colitis 12/10^6
  - Malignancy rates even lower

BMJ 1998; 316:1058
LOE 2

IBS treatments: Prescriptions

- Antidepressants
  - TCA & SSRIs: pain improvement
  - NNT = 5

- Anti-spasmodics
  - Dicyclomine (Bentyl) & Hyoscymine (Levsin)
  - NNT = 5

Treatment for IBS flavors

IBS-D
- Alosetron (lotronex)
  - 5-HT3 receptor antagonist; strict Rx reg, reserved for those who fail tx

IBS-C
- Tegaserod (zelnorm)
  - 5-HT4 receptor agonist
  - Modest benefit but pulled from market 2007 b/c CV adv effects; available via restricted use only

Quiz time: which supplement works best?
And the winner is…

<table>
<thead>
<tr>
<th>Treatment</th>
<th># studies</th>
<th># patients</th>
<th>RR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber**</td>
<td>12</td>
<td>591</td>
<td>0.87</td>
<td>11</td>
</tr>
<tr>
<td>Antispasmodics**</td>
<td>22</td>
<td>1778</td>
<td>0.68</td>
<td>5</td>
</tr>
<tr>
<td>Probiotics*</td>
<td>10</td>
<td>918</td>
<td>0.71</td>
<td>4</td>
</tr>
<tr>
<td>Peppermint oil**</td>
<td>4</td>
<td>392</td>
<td>0.43</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Rx: 2 tabs twice a day!

*Gut 2010; 59: 325
**BMJ 2008; 337:a2313

IBS: Nonpharm/supplemental tx

- CBT—Small benefit noted in summary studies
- Exercise—single RCT demo’s benefit
- Accupuncture, Hypnotherapy—inconclusive
- Chinese medicine—slight benefit but poor quality studies