Liver and lower GI update

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Objectives

- Describe relevant primary care research updates in hepatology
- Explain new research regarding the management of irritable bowel syndrome
- Discuss updates in lower gastrointestinal disease management

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Roadmap of this talk

- Update on MASH/NAFLD
- Guideline updates
- IBS deep dive

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1. Resmetirom in NASH with Liver Fibrosis

- 966 adults with biopsy-confirmed NASH and liver fibrosis randomized to:
  - Resmetirom 80 mg daily
  - Resmetirom 100 mg daily
  - Placebo
- Followed for 52 weeks
- Primary outcomes
  - NASH resolution (≥2-point reduction in NAFLD activity score, no fibrosis worsening)
  - ≥1-stage fibrosis improvement (no worsening of NAFLD activity score)

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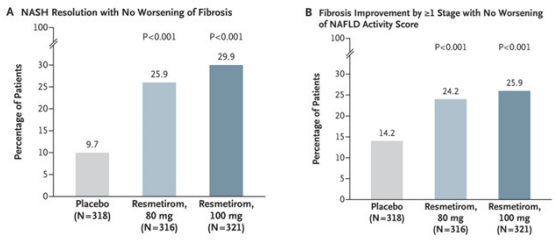
1. Resmetirom in NASH with Liver Fibrosis



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1. Resmetirom in NASH with Liver Fibrosis

- Diarrhea and nausea more common with resmetirom
- Serious adverse events: similar across groups
  - 10.9% (80 mg), 12.7% (100 mg), 11.5% (placebo)
- Both resmetirom doses increased NASH resolution and fibrosis with an acceptable safety profile
- Cost: $4000/month cash

Harrison SA, Bedossa P, Guy CD, Schattenberg JM, Loomba R, Taub R, Labriola D, Moussa SE, Neff GW, Rinella ME, Anstee QM. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. New England Journal of Medicine. 2024 Feb 8;390(6):497-509.

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1a. Dapagliflozin for MASH

- 154 adults with metabolic dysfunction-associated steatohepatitis (MASH)
  - 45% with diabetes
- Randomized to dapagliflozin 10 mg daily or matched placebo
- Followed for 48 weeks
- Primary outcome: MASH improvement ((≥2-point reduction in MASH activity score or a MASH score <3) without worsening of fibrosis

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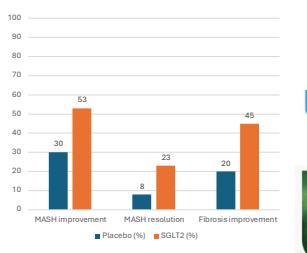
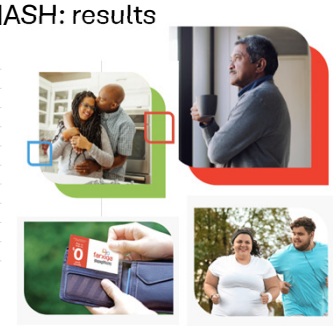
1a. Dapagliflozin for MASH: results



P<0.01 for each comparison



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2. Management of Patients With Acute Lower Gastrointestinal Bleeding: An Updated ACG Guideline

- Developed using GRADE framework
- Applies to adults with hemodynamically stable LGIB
- Multidisciplinary panel; systematic evidence review
- Graded recommendations by strength and certainty of evidence
- Emphasis on shared decision-making and individualized care

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Recommendation Summary	SOR	Quality of Evidence
Recommend against antifibrinolytic agents (e.g., tranexamic acid).	Strong	Moderate
Recommend colonoscopy for most hospitalized LGIB patients.	Strong	Low
Patients with extravasation on CT angiography should be promptly referred for transcatheter arteriography/embolization. Colonoscopy may be considered in specialized centers.	Strong	Moderate
For hospitalized LGIB requiring colonoscopy, non-emergent inpatient colonoscopy is recommended. Urgent (<24 hours) colonoscopy does not improve outcomes.	Strong	Moderate
Treat diverticular stigmata of hemorrhage with through-the-scope clips, band ligation, or coagulation.	Strong	Moderate
Discontinue non-aspirin NSAIDs.	Strong	Low
Re-evaluate risks/benefits of non-aspirin antiplatelets in a multidisciplinary setting.	Strong	Low
Suggest discontinuing aspirin for primary prevention.	Conditional	Low
Suggest continuing aspirin for secondary prevention (established CVD).	Conditional	Low

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Recommendation Summary	SOR	Quality of Evidence
Recommend resuming anticoagulation after LGIB cessation to decrease thromboembolism and mortality risks.	Strong	Moderate
Use risk stratification tools (e.g., Oakland score) to identify low-risk patients for early discharge and outpatient evaluation.	Conditional	Low
Use restrictive RBC transfusion strategy (threshold 7 g/dL) in hemodynamically stable patients.	Conditional	Low
Reversal suggested for life-threatening LGIB with substantially elevated INR. 4-factor PCC preferred over FFP.	Conditional	Very Low
Xa reversal ((idarucizumab, andexanet alfa) suggested for life-threatening LGIB unresponsive to initial resuscitation and drug cessation.	Conditional	Very Low
Colonoscopy may not be needed if bleeding has stopped and high-quality colonoscopy within 12 months shows diverticulosis without neoplasia.	Conditional	Very Low
CT angiography suggested as initial test for ongoing hemodynamically	Conditional	Low

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3. Ultrasound and CRP for diagnosing acute diverticulitis in primary care

- Meta-analysis of 17 studies (15 prospective, 2 retrospective)
- Focused on tests feasible in primary care
  - No studies conducted in primary care settings
- Limited and inconsistent data on signs and symptoms
- Evaluated WBC, CRP, and ultrasound

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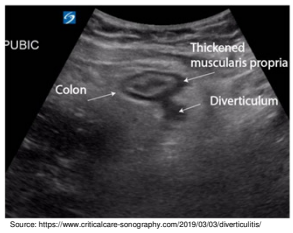
3. Ultrasound and CRP for diagnosing acute diverticulitis in primary care

- **WBC >10**
  - LR+: 1.6
  - LR–: 0.56
- **CRP >10 mg/L**
  - Sensitivity: 93% (95% CI 87–96)
  - LR–: 0.17
- **Ultrasound (radiology or point-of-care)**
  - Sensitivity: 92%
  - Specificity: 94%
  - LR+: 15.3
  - LR–: 0.08



Source: https://www.criticalcare-sonography.com/2019/03/03/diverticulitis/

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4. IBS and antibiotics

- Case-control study
- 29,000 patients with IBS and 135,000 matched controls
- Rate of antibiotic rx higher in IBS group in the 1 year prior to diagnosis for IBS group (74.9%) compared with controls (57.8%)
  - OR 2.21 (95%CI 2.14-2.28)
- Persisted after adjustment for demographics, healthcare use, and other comorbidities
- Rate increased more with >3 courses of abx
  - OR 3.36 (95%CI 3.24-3.49)

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5. British IBS guidelines for primary care

- Developed by a multidisciplinary panel:
  – Gastroenterologists, primary care physicians, dietitians, psychologists, patient representatives
- Based on systematic review and critical appraisal of evidence
- Used GRADE framework to assess evidence quality and recommendation strength
- Addressed diagnostic criteria, investigations, and treatment in both primary and secondary care
- Emphasized practical, symptom-based approach suitable for real-world settings

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5. British IBS Guidelines

- Confirms definition of IBS as ≥6 months of abdominal pain/discomfort with altered bowel habits, no alarm features
- Initial primary care tests can include
  - CBC, CRP or ESR, celiac serology
- If <45 years with diarrhea include fecal calprotectin to rule out IBD
- Colonoscopy only if alarm signs, risk for microscopic colitis, or per national CRC screening guidelines
- Consider bile acid diarrhea if nocturnal diarrhea or history of cholecystectomy
- Do **not** routinely test for:
  – Pancreatic insufficiency
  – SIBO
  – Carbohydrate intolerance

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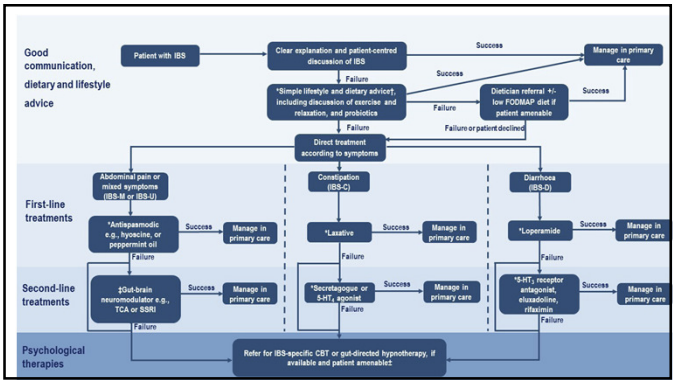

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British IBS Guidelines

- First-line
  - Regular exercise
  - Gradual soluble fiber (psyllium); avoid insoluble fiber
  - Consider probiotics (no specific strain/dose recommended)
  - Symptom-targeted options
  - Loperamide for diarrhea
  - Antispasmodics or peppermint oil for global symptoms/pain
  - PEG for constipation
  - FODMAP diet
- Second-line
  - Tricyclic antidepressants
  - SSRIs
  - Consider GI eval before offering treatments like 5-HT_3 or 5-HT_4 agents or secretogogues (linoclotide, lubiprostone, etc)

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6. FODMAPs diet or oral spasmolytic for IBS

- Pragmatic RCT
- Enrolled ~310 patients
- Randomized to low FODMAPS diet via app (100+ recipes, guided reintroduction) or otilonium bromide 40 mg TID
  - Oral spasmolytic similar to dicyclomine
- Followed for 8 weeks
- Primary outcome: ≥50-point improvement on 500-point IBS Severity Symptom Scale

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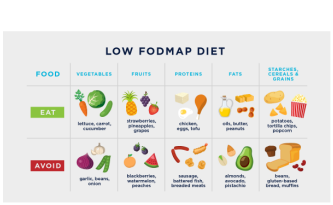
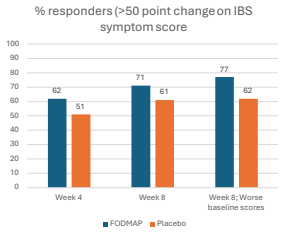
6. FODMAPs diet or oral spasmolytic for IBS





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7. Low FODMAP diet most likely to improve symptoms for patients with irritable bowel syndrome

- Network meta-analysis
- 13 studies, 940 patients with IBS
- FODMAP or British Diatetic Association diet
- Literature was thin and some risk of bias due to methods but FODMAP better at improving outcomes than patient's usual diet or the BDA diet

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8. Amitriptyline for IBS

- Randomized controlled trial done in primary care in UK
- 500 adults with at least moderate IBS with persistent symptoms after first line treatments
  - 80% IBS-d, 84% with normal depression scores at baseline
  - Diet, lifestyle, antispasmodics, laxatives/antidiarrheals
- Randomized to amitryptiline 10 mg QHS or placebo
- Followed for 6 months
- Primary outcome was score on IBS symptom score and % of patients answering "yes" to the question *Have you had adequate relief of your IBS symptoms?*

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8. Amitriptyline for IBS

- % of patients reporting adequate relief of IBS sx for at least 50% of weeks:
  - Amitryptiline: 40%
  - Placebo: 30%
- % reporting considerable or complete relief of IBS sx
  - Amitryptiline: 36%
  - Placebo: 23%
- Between-group difference in IBS SSS: -27 (-46.0 to -7.1), favors active
- Discontinued treatment
  - Amitryptiline: 20%
  - Placebo: 26%

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9. Enterosgel for IBS-D

- Randomized controlled trial
- 440 adults (16+) with IBS-D randomized
- Escalating dose enterosgel, target 30 g TID
  - Polymethylsiloxane polyhydrate, a pharmacologically inactive intenstinal absorbant
- Matched placebo
- Followed for 8 weeks with an 8 week open-label period following

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9. Enterosgel for IBS-D

- Relief of symptoms (30% decrease in abd pain and 50% decrease in diarrhea)
  - Gel: 37.4%
  - Placebo: 24.3%
  - NNT 8
- Relief of symptoms reported as adequate by patient
  - Gel: 69%
  - Placebo: 45%

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9. Esterosgel

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10. Probiotics for IBS

- Meta-analysis of RCTs
- 82 studies, 10,000+ patients
- Various types of probiotics, formulations, doses, and applications
- Probiotics > placebo for most outcomes studied including
  - Global symptom score
  - Abdominal pain
- Various probiotics found to be effective
  - Combination> individual
- Global symptoms were better with combination probiotics in 20 trials, but none of the individual components was better than placebo

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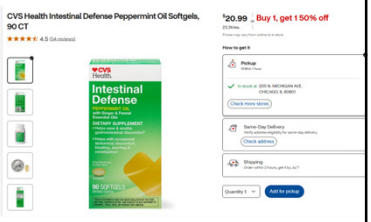
11. Peppermint oil for IBS

- Systematic review and meta-analysis
- 10 RCTs, 1030 participants
- Adults with IBS randomized
  - Peppermint oil in delayed-release capsules
  - Placebo
- Response rate better in peppermint oil: 45.7% vs 27.7% (NNT: 4)
- Adverse effect rate higher in peppermint oil: GERD, dyspepsia (NNTH: 7)



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12. Hypnosis for IBS

- Randomized controlled trial (unblinded)
- 119 patients with IBS who had failed usual care
- Randomized to
  - Group "gut directed" hypnotherapy
  - Individual "gut directed" hypnotherapy
- Followed for 12 weeks
- Primary outcome was at least a 50 point drop IBS symptom score

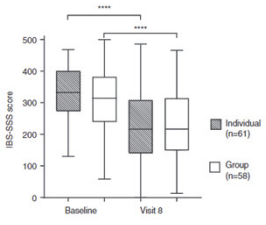

FIGURE 3 Severity of gastrointestinal symptoms before (baseline) and after (visit 8) hypnotherapy treatment assessed with the IBS severity scoring system (IBS-SSS) (median, IQR). ****p<0.0001

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13. CBT or hypnosis for children with functional abdominal pain

- Systematic review and meta-analysis
- 33 trials, 2600 children with functional abdominal pain
- CBT, educational support, hypnotherapies, guided imagery, relaxation
- Comparisons included no intervention or other therapies
- Follow up ranged from 5 days to 4 months
- Mixed quality overall with generally high risk of bias
- Found to be effective
  - CBT: NNT 5
  - Hypnotherapy: NNT 3
- Not apparently effective
  - Yoga
  - Journal keeping
  - Biofeedback
  - OMT
- Small trials, possible publication bias

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14. Placebo for children with functional abdominal pain or IBS

- Randomized controlled cross-over trial
- 30 children ages 8-18 with IBS or functional abdominal pain and pain on VAS of at least 25mm
- Randomized to
  - Symptom diary plus rescue analgesic (control)
  - Daily unblinded placebo with placebo information
- Followed for 3 weeks then crossed to other group

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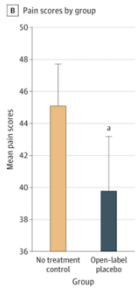
14. Placebo for children with functional abdominal pain or IBS

- Pain scores
  - Baseline VAS: 45
  - VAS during control: 45.0
  - VAS during placebo: 39.9
- Use of rescue meds
  - Control: 53%
  - Placebo: 6.7%
- Placebo response was better in patients who expected that it might work



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Bottom lines

- Watch for new meds to treat MASLD
- POCUS plus CRP if you have it assess for diverticulitis, but a history and physical exam and CT will probably still be what most of us fall back on
- Antibiotics are associated with IBS. Some kinds of probiotics may help with symptoms.
- A low-FODMAPs diet can be helpful for IBS, as can some kinds of CAM therapies like hypnosis.

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Thank you!

- Questions?

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