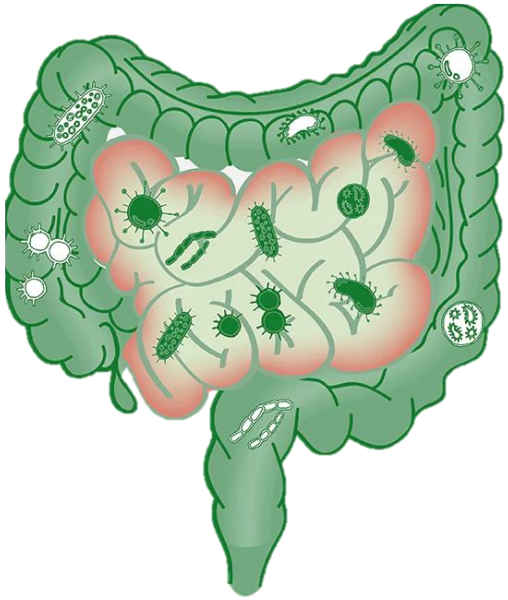
SIBO and Nutrition Interventions



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SIBO Basics

SIBO Definition

- Clinical syndrome of GI symptoms caused by the presence of excessive numbers of bacteria within the small intestine (based on aspirate/culture):
  - >/= 10^5 CFU/ml proximal jejunum
  - >/= 10^3 CFU/ml duodenal aspirates

- 2 Types – Hydrogen and Hydrogen Sulfide
  - Methane predominant SIBO became Intestinal Methanogen Overgrowth (IMO) in 2022

Saad & Chey. Clin Gastro and Hepatol 2014
Rezaie et al. Am J Gastroenterol 2017
Pimentel et al. Am J Gastroenterol 2020

SIBO Prevalence

	Reports prevalence of SIBO
Normal populations	
Healthy study controls	0–20%
Dysmotility/gut wall injury	
Celiac disease	9–67%
Connective tissue diseases	43–55%
Crohn's disease	25–88%
Diabetes mellitus	8–44%
Hypothyroidism	54%
Nonspecific dysmotility	76%
Radiation enteropathy	26%
Ulcerative colitis	81%
Miscellaneous	
Chronic fatigue syndrome	81%
Chronic pancreatitis	34–92%
Drug-induced inhibition of acid secretion	26–75%
End-stage renal failure	36%
Fibromyalgia	93%
Irritable bowel syndrome	4–78%
Immunodeficiency syndromes	30–50%
Liver cirrhosis	17–36%
Obesity	17–41%
Parenteral nutrition	70%
Rosacea	46%

	Reports prevalence of SIBO
Neuromuscular diseases	
Muscular dystrophy	65%
Parkinson's disease	54%
Surgery	
Abdominal surgery	82%
Bilateral truncal vagotomy	93%
Gastrectomy	63–78%
Ileocaecal valve resection	32%
Roux-en-Y reconstruction	86%

True prevalence of SIBO unknown

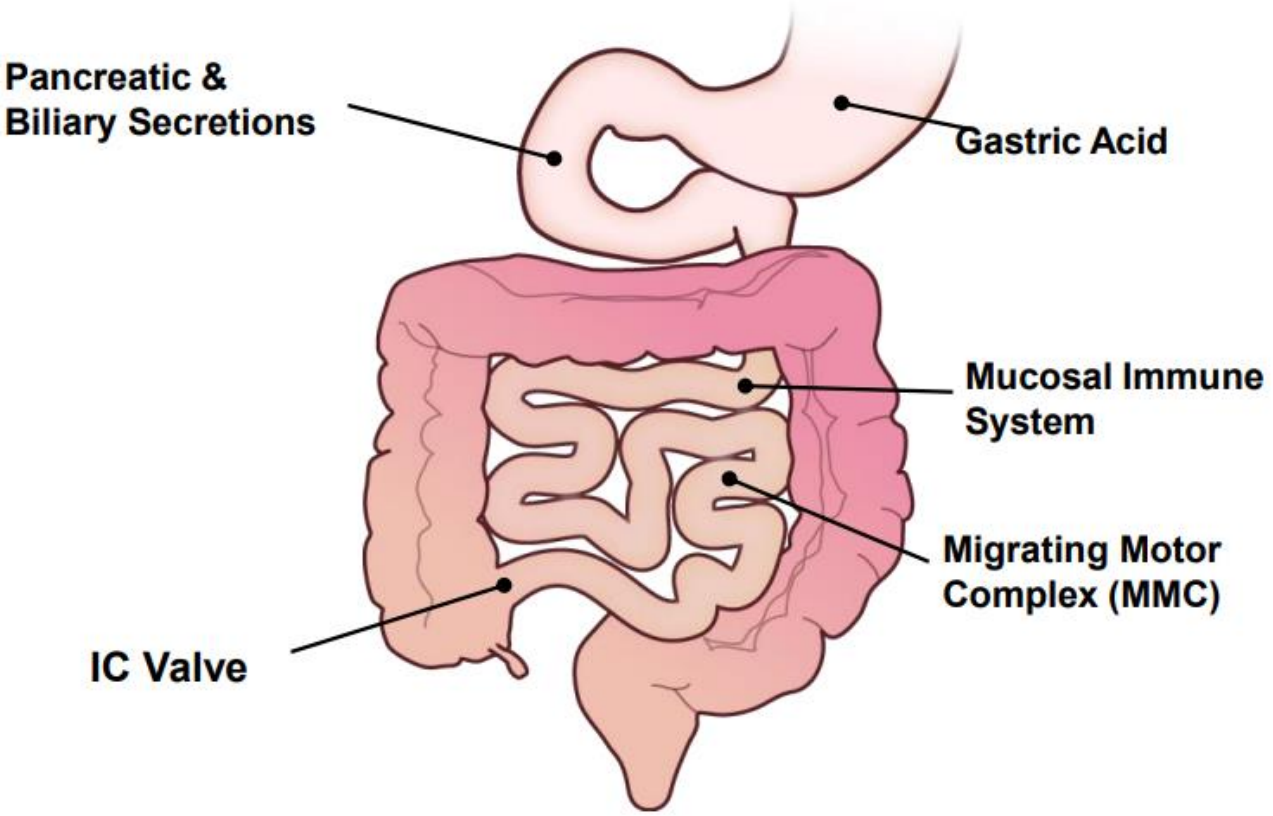
Grace et al. Aliment Pharmacol Ther 2013

SIBO Risk Factors

Structural Abnormalities	Motility Disturbances	Biochemical Disturbances
Post-operative adhesions	Chronic intestinal pseudo-obstruction	Hypochlorhydria (atrophic gastritis, pernicious anemia)
Small bowel diverticula	Connective tissue disorders (scleroderma, Parkinson's, Sjogren's)	Chronic Pancreatitis
Small bowel strictures	Diabetes mellitus (poorly controlled)	Common variable immunodeficiency
Blind intestinal loops	Medications (opiates, anticholinergics)	
Ileocecal valve dysfunction or ileocolonic resection		
Small bowel surgical resection		

Ahuja A, Nitin K. Ahuja NK. Practical Gastroenterology. 2018
Quigley et al. Gastroenterology 2020

Protection Against SIBO



O'Hara AM, Shanahan F. EMBO Rep. 2006;7:688-693; Kloetzer et al. Gastroenterol 2007;132 (suppl 2):A461 Roland et al. Dig Dis Sci 2017;62:3525–3535; Ginnebaugh et al. GI Cl NA 2020;49:571

Pathophysiological Effects of SIBO

Mucosal Injury	Competition for Luminal Nutrients	Bacterial Metabolism
Epithelial damage, loss of brush border enzymes, inflammatory responses	Consumption of dietary protein, vitamin B12, thiamine, nicotinamide	Fermentation of dietary carbohydrates, bile acid deconjugation, synthesis of vitamin K, folate, D-lactic acid, alcohol, acetaldehyde
Maldigestion, enteropathy, systemic inflammatory responses, bacterial translocation	Macro / micronutrient deficiencies, weight loss	Bloating, flatulence, diarrhea, clinical symptoms associated with bacterial metabolites

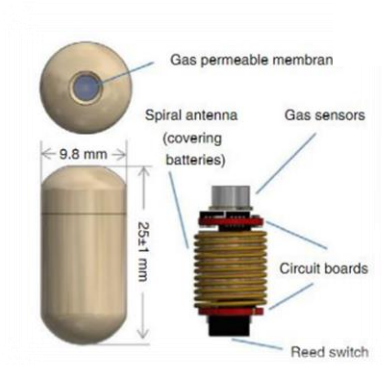
Slide Courtesy Andrea Shin MD, /UCLA

Diagnosing SIBO

- EGD Aspirate and Culture
- Breath Testing

Future Options

- Portable / at home breathing devices
- Gas capturing/sensing capsules



Quigley et al. Gastroenterology 2020;159:1526–1532

Diagnosing: Aspirate/Culture

Pros

- Performed at time of endoscopy
- Direct assessment for SIBO
- Allows identification of potential organism and antibiotic sensitivity

Cons

- Cost
- Invasive
- Time consuming
- Contamination risk
- Culturing difficulties
- Potential for missing distal SIBO

Saad RJ, Chey WD. Clin Gastroenterol Hepatol. 2014

Diagnosing SIBO: Breath Testing

ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth, 2020:

Table 1. Summary and strength of GRADED recommendations for SIBO

Diagnosis of SIBO
1. We suggest the use of breath testing (glucose hydrogen or lactulose hydrogen) for the diagnosis of SIBO in patients with IBS (conditional recommendation, very low level of evidence).
2. We suggest using glucose hydrogen or lactulose hydrogen breath tests for the diagnosis of SIBO in symptomatic patients with suspected motility disorders (conditional recommendation, very low level of evidence).
3. We suggest testing for SIBO using glucose hydrogen or lactulose hydrogen breath tests in symptomatic patients (abdominal pain, gas, bloating, and/or diarrhea) with previous luminal abdominal surgery (conditional recommendation, very low level of evidence).
Other conditions associated with SIBO
4. We suggest against the use of breath testing for the diagnosis of SIBO in asymptomatic patients on PPIs (conditional recommendation, very low level of evidence).
5. We suggest testing for methane using glucose or lactulose breath tests to diagnose the overgrowth of methane-producing organisms (IMO) in symptomatic patients with constipation (conditional recommendation, very low level of evidence).

Pimentel, Mark MD, FRCP(C), FACG et al. ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. 2020.

Diagnosing SIBO: Breath Testing

Substrate	Dose	Abnormal Rise in H_2	Abnormal Rise in CH_4	Sensitivity / Specificity
Lactulose	10 grams	>20 ppm (90 minutes)	>10 ppm (90 minutes)	42% / 71%
Glucose	50-75 grams	>12-20 ppm (90 minutes)	>10 ppm (90 minutes)	55% / 83%

Recent studies performing glucose or lactulose breath testing and scintigraphy found that 65-85% of positive breath tests were falsely positive for SIBO.

Chey, W. personal communication, 2019
able adapted from Rezaie, et al. 2017
Saad RJ, Chey WD. Clin Gastroenterol Hepatol. 2014

Diagnosing SIBO: Breath Testing

Before the test:

- Avoid antibiotics for 4 weeks
- Avoid promotility agents & laxatives for 1 week

Day before test:

- Avoid fermentable carbohydrates
- Fast for 8–12 hours

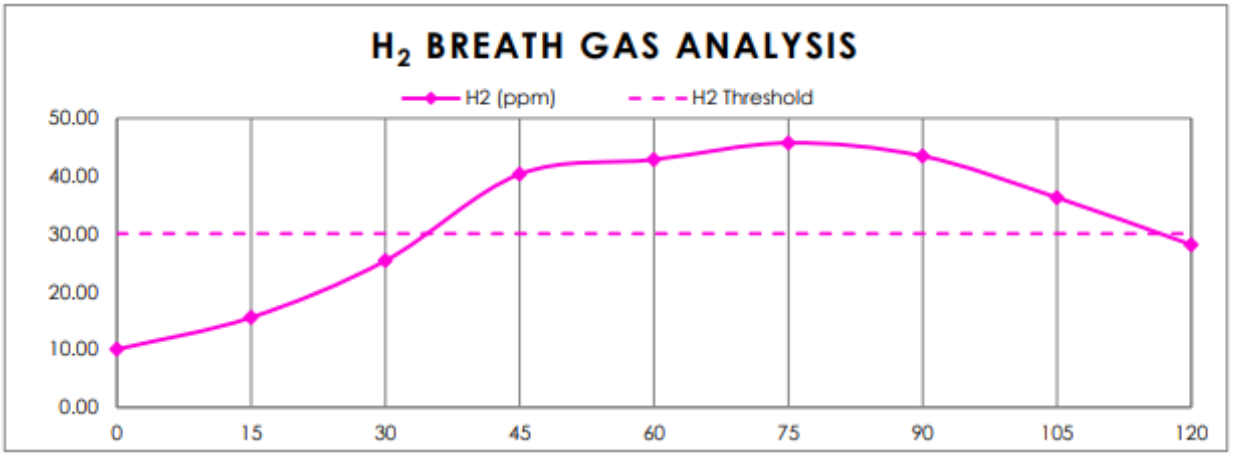
During the breath test:

- Avoid smoking & minimize physical exertion

Pimentel et al. Am J Gastroenterol 2020

Diagnosing SIBO: Breath Testing

ELEVATED HYDROGEN: SIBO

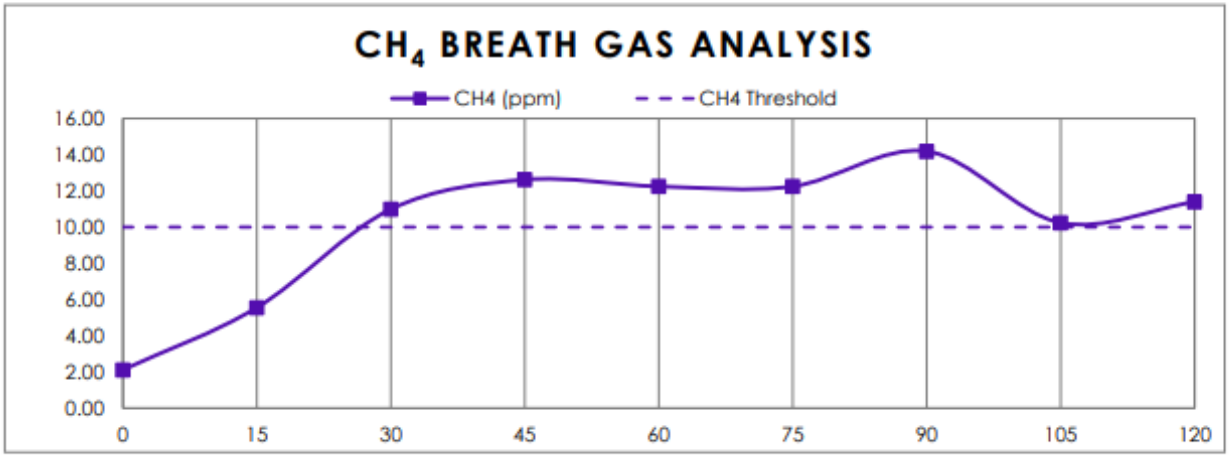


An increase in hydrogen concentrations **of ≥20 ppm** from the baseline within 90 minutes is recommended to be diagnostic of **small intestinal bacterial overgrowth (SIBO)**.[6, 16]

Slide Image Courtesy William Chey MD

Diagnosing SIBO: Breath Testing

ELEVATED METHANE: IMO

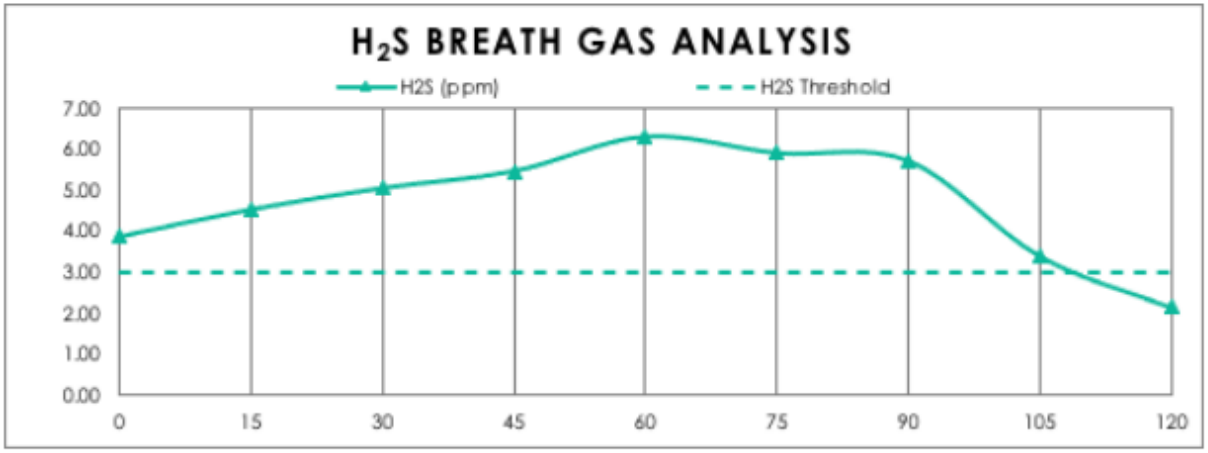


The presence of methane levels **≥10 ppm** is diagnostic of **intestinal methanogenic overgrowth (IMO).**[6, 16]

Slide Image Courtesy William Chey MD

Diagnosing SIBO: Breath Testing

ELEVATED HYDROGEN SULFIDE



The presence of hydrogen sulfide levels **≥3ppm** is indicative of **excess hydrogen sulfide** and is associated with **chronic diarrhea**[14] **or diarrhea-predominant irritable bowel syndrome (IBS-D)**[17] with a **specificity of 90%**, compared to healthy subjects.[17]

Slide Image Courtesy William Chey MD

Treating SIBO: Medications

Antibiotic	Recommended dose	Efficacy
Nonabsorbable antibiotic		
Rifaximin	550 mg t.i.d.	61%–78%
Systemic antibiotic		
Amoxicillin-clavulanic acid	875 mg b.i.d.	50%
Ciprofloxacin	500 mg b.i.d.	43%–100%
Doxycycline	100 mg q.d. to b.i.d.	[a]
Metronidazole	250 mg t.i.d.	43%–87%
Neomycin	500 mg b.i.d.	33%–55%
Norfloxacin	400 mg q.d.	30%–100%
Tetracycline	250 mg q.i.d.	87.5%
Trimethoprim-sulfamethoxazole	160 mg/800 mg b.i.d.	95%

Most of the studies are small and methodologically flawed.
Lack of a gold standard for diagnosis presents problems
Most treat to negative BT result but others to symptom relief
Largest amount of data with rifaximin

Pimentel et al. Am J Gastroenterol 2020;115:165-78

SIBO Nutrition Advice:
This Lecture in Context

1 Year Ago

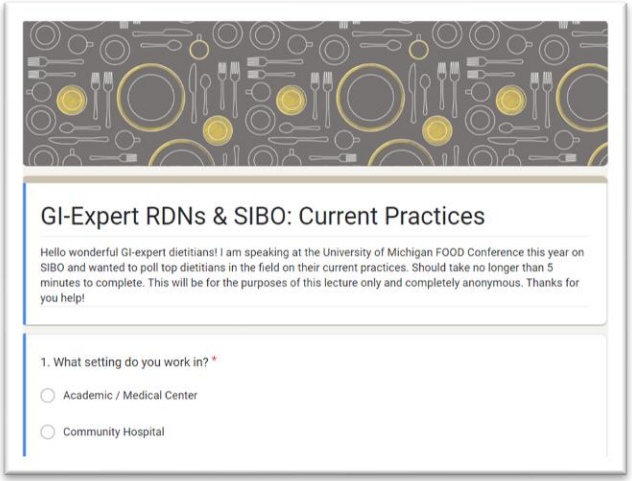
FOOD

THE MAIN COURSE

TO DIGESTIVE HEALTH

Current Practices?

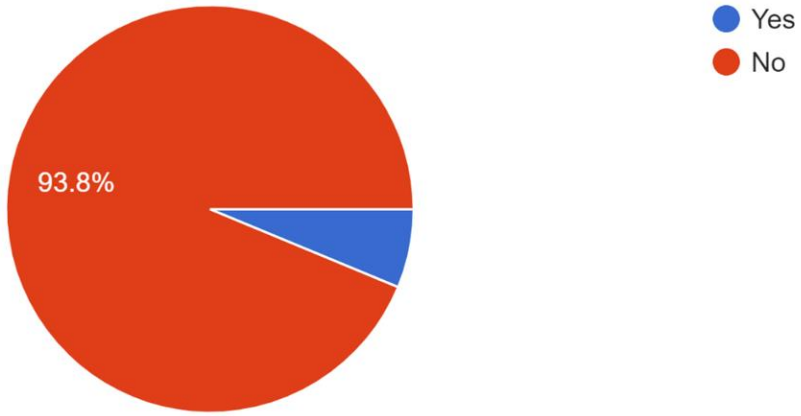
- Informal survey sent to 55 dietitians in May 2023 after DDW
  - All dietitians are recognized experts in GI Nutrition (DIGID Leadership)
  - 26 questions related to SIBO with regard to:
    - Diet
    - Supplements
    - Current evidence
    - Current practices
  - 34 (62%) dietitians responded



Informal RDN Survey

10. Do you believe there is standardized evidence-based nutrition advice at this time for working with SIBO patients?

32 responses



SIBO Guidelines

CLINICAL GUIDELINES

ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth

Mark Pimentel, MD, FRCP(C), FACG[1], Richard J. Saad, MD, FACG[2], Millie D. Long, MD, MPH, FACG (GRADE Methodologist)[3] and Satish S. C. Rao, MD, PhD, FRCP, FACG[4]

Gastroenterology 2020;159:1526–1532

CLINICAL PRACTICE GUIDELINES

AGA Clinical Practice Update on Small Intestinal Bacterial Overgrowth: Expert Review

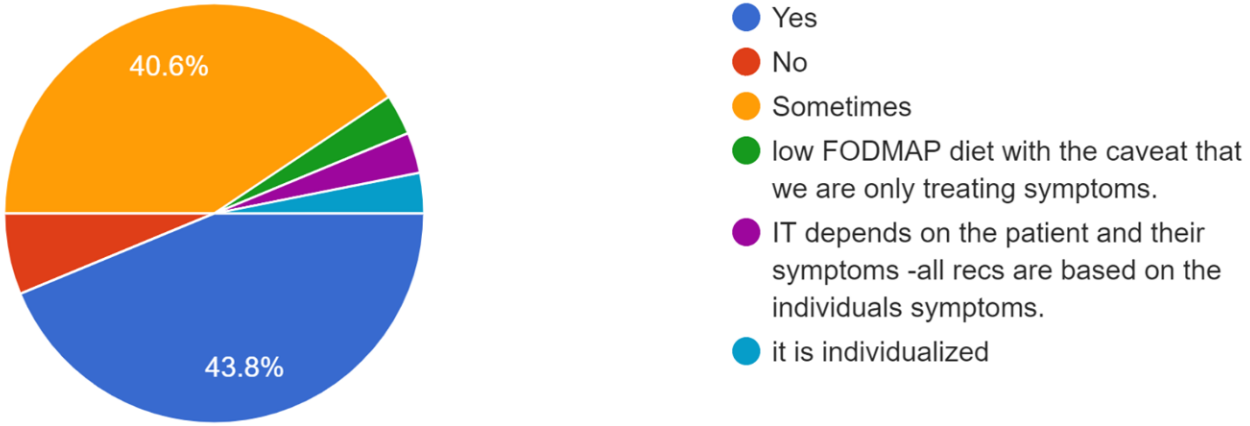
Eamonn M. M. Quigley,[1] Joseph A. Murray,[2] and Mark Pimentel[3]

SIBO Nutrition:
The Evidence for Diet

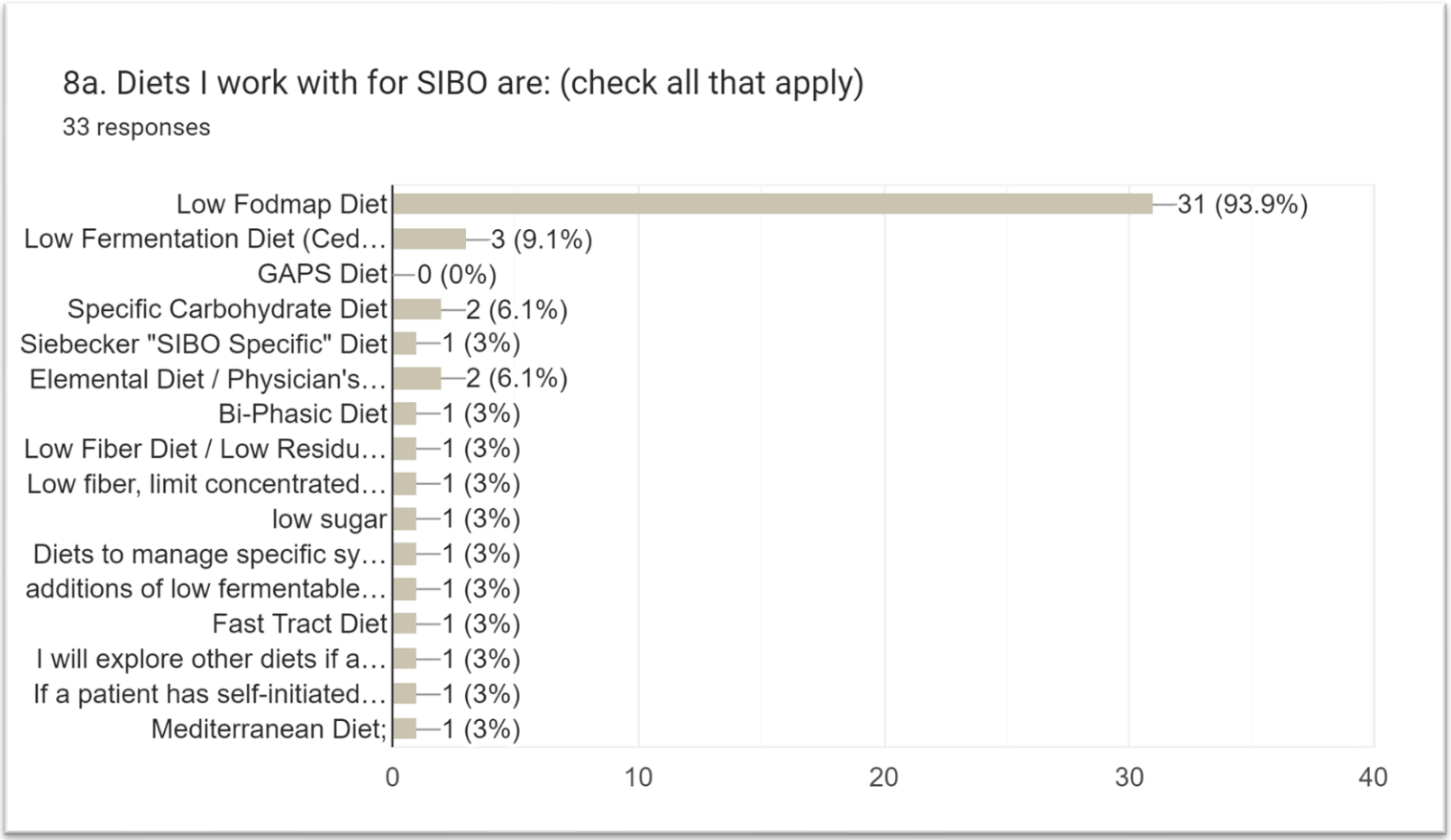
Informal RDN Survey - DIET

8. Do you recommend specific dietary interventions when working with SIBO?

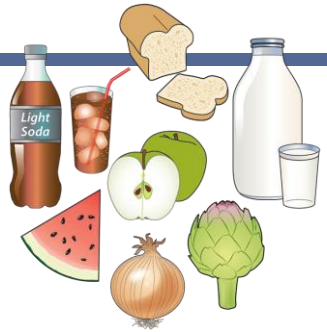
32 responses



Informal RDN Survey - DIET



Low FODMAP Diet

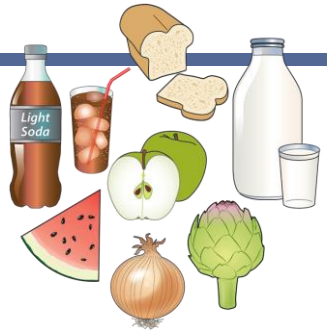


Acronym for specific sugars that ferment in the gut and contribute to GI symptoms

- **F** – fermentable
- **O** – oligosaccharides (Fructans and GOS)
- **D** – disaccharides (Lactose)
- **M** – monosaccharides (excess Fructose)
- **A –** and
- **P** – polyols (sorbitol, mannitol, maltitol, xylitol, isomalt)

Wielgosz-Grochowska JP, Domanski N, Drywień ME. Nutrients. 2022
McIntosh K, et al. Gut. 2017
Patcharatrakul T, et al. Nutrients. 2019

Low FODMAP Diet

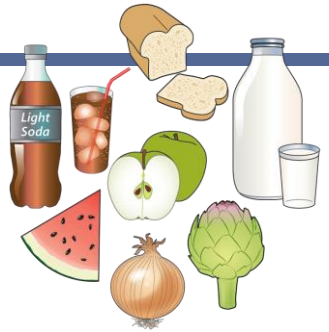


Theory for Low Fodmap Diet (LFD) in SIBO

- Evidence shows can reduce symptoms of gas, bloating, abdominal pain
- Some FODMAPs = prebiotics and affect the gut microbiome
- According to Pimentel Lab (Cedars Sinai Medical Center)
  - Carbohydrate digestion with SIBO is much higher than healthy control
  - 60% of IBS-D cases are SIBO
    - Low FODMAP Diet is first-line dietary treatment for IBS-D

Wielgosz-Grochowska JP, Domanski N, Drywień ME. Nutrients. 2022
McIntosh K, et al. Gut. 2017
Patcharatrakul T, et al. Nutrients. 2019

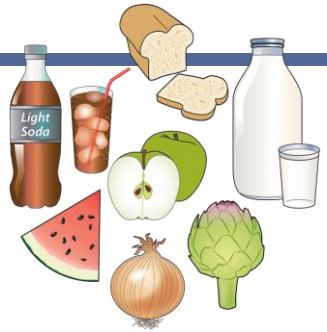
Low FODMAP Diet



- NO studies at this time have evaluated the effect of the low fodmap diet (LFD) directly on treating or managing SIBO
- 12 studies = potential connection between changes in microbiome and LFD
- ***End result:***
  - Contradictory evidence for increasing or decreasing different species of bacteria in the gut
  - Low FODMAP diet can significantly increase hydrogen-sulfide-producing species (may be involved in H2S-SIBO?)
  - 2 studies focused on measuring exhaled gases in breath tests
    - Slight to significant decrease in hydrogen production in LFD group

Wielgosz-Grochowska JP, Domanski N, Drywień ME. Nutrients. 2022
McIntosh K, et al. Gut. 2017
Patcharatrakul T, et al. Nutrients. 2019

Low FODMAP Diet



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- ***End result:***
  - Con pecies of bacteria in the g
  - Lo ulfide-producing species (
  - 2 studies foc g d gase reath tests
    - Slight to significant decrease in hydrogen production in LFD group

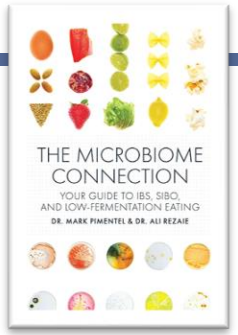
END POINT

No evidence for using low fodmap diet to treat SIBO

Low-FODMAP diet might improve symptoms of SIBO related to carbohydrate fermentation or IBS-related symptoms

Wielgosz-Grochowska JP, Domanski N, Drywień ME. Nutrients. 2022
McIntosh K, et al. Gut. 2017
Patcharatrakul T, et al. Nutrients. 2019

Low Fermentation Diet



Background

- Created in the early 2000s by Pimentel Lab at Cedars Sinai Medical Center
- Premise:
  - *Current scientific knowledge of gut microbiome*
  - *Interaction of human body's microbiome with food*
  - *Pathophysiology of IBS / SIBO*
  - *Restrict high carbohydrate foods, foods that cannot be digested*
- Low-Fermentation Eating has 2 essential rules:
  1. *Restrict products that contain high levels of carbohydrates or ingredients in food that humans can't digest, and therefore are digested by bacteria*
  2. *Space meals 4-5 hours apart*

The Microbiome Connection: Your Guide to IBS, SIBO, and Low-Fermentation Eating, Dr. Mark Pimentel and Dr. Ali Rezaie, 2022

Low Fermentation Diet

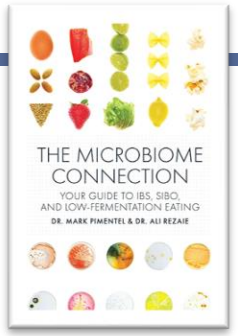
	Include	Exclude
Vegetables	Side salad, onions, garlic, peppers, tomatoes, cucumber, zucchini, squash, eggplant, peas, mushrooms	Cabbage, brussels sprouts, broccoli, cauliflower, leafy greens, big salad
Fruits	All others	Small amounts of apple, pears, banana only
Grains / starches	Rice, potato, sweet potato, white bread, rice krispies, white pasta, cream of wheat/rice	Whole grain bread, multigrain bread, oatmeal
Dairy	Lactose free	Yogurt, butter
Plant protein	Nuts	Beans, legumes
Sweeteners	Cane sugar	Artificial sweeteners (except aspartame)
Other		Gum
Dessert	Wheat-based cookies and cakes made with cane sugar	***Not in alignment with Fodmap***

Reminder: Fiber Basics

- *Fiber Considerations*
  - Solubility
  - Viscosity
  - Effect on microbiome
    - *Creation of metabolites (SCFA)*
  - pH changes of stool
  - Fermentability
    - *Extent and rate to which a fiber can be broken down*
    - *Fibers can be readily fermentable to minimally fermentable*
    - *The rate of fermentation plays a key role in symptom development*

Eswaran, S. ,Muir, J., Chey, W., American Journal of Gastroenterology 2013
https://www.monashfodmap.com/blog/more-fodmaps-fermentable-fibers-ibs/#:~:text=Fermentability%20describes%20the%20rate%20and,acids%20(2%2C%204).

Low Fermentation Diet

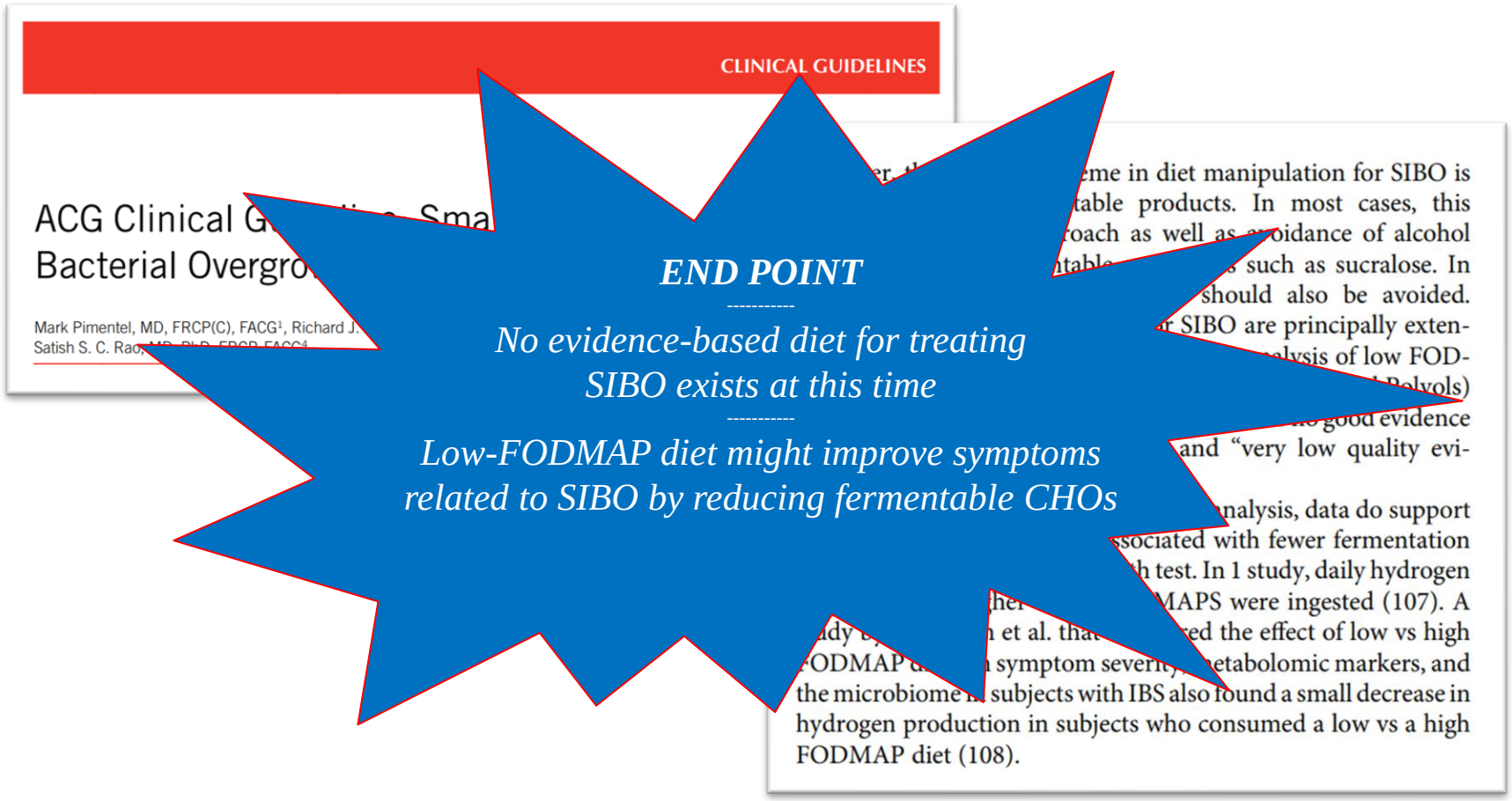


- Low fermentation diet assumptions
  - *All fiber is fermentable*
  - *White is better*
    - White refined flour can be high in fructan / GOS = gas / bloating / discomfort
  - *Vegetables that are "fruits or roots" are GI friendly*
    - Short-chain carbohydrates can be culprits for fermentation, not just fiber
    - Ex: garlic and onion are "roots" so safe but contain fructan / GOS

- <u>NO</u> studies at this time have evaluated the effect of the low fermentation diet directly on treating SIBO or symptoms related to SIBO

Eswaran, S. ,Muir, J., Chey, W., American Journal of Gastroenterology 2013
The Microbiome Connection: Your Guide to IBS, SIBO, and Low-Fermentation Eating, Dr. Mark Pimentel and Dr. Ali Rezaie, 2022

Diet in SIBO

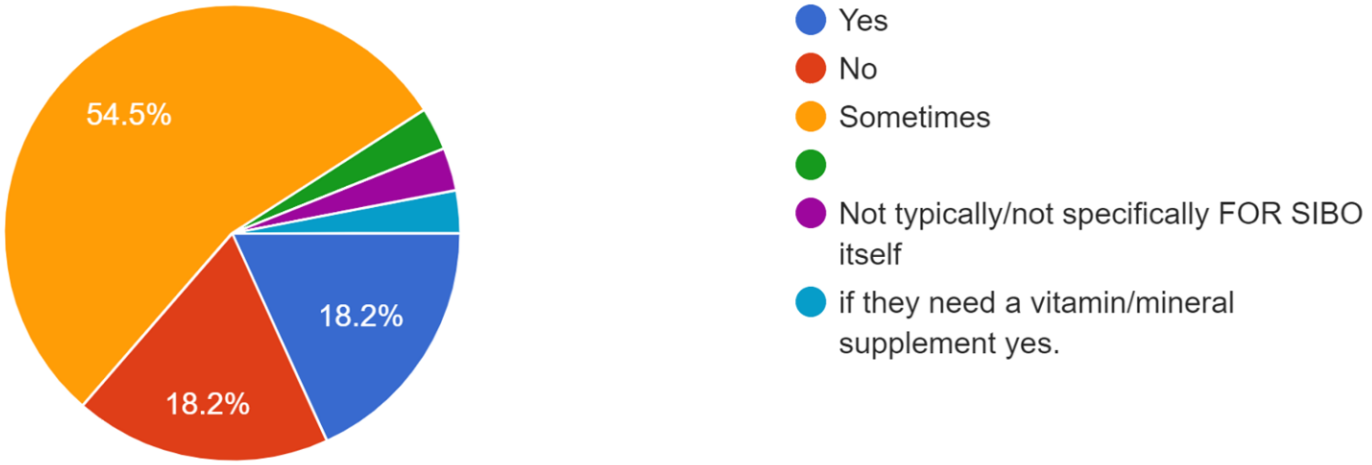

CLINICAL GUIDELINES
ACG Clinical G
Bacterial Overgro
Mark Pimentel, MD, FRCP(C), FACG[1], Richard J.
Satish S. C. Rao
me in diet manipulation for SIBO is
table products. In most cases, this
oach as well as
such as sucralose. In
should also be avoided.
SIBO are principally exten-
alysis of low FOD-
Polyols)
good evidence
and "very low quality evi-
nalysis, data do support
sociated with fewer fermentation
h test. In 1 study, daily hydrogen
MAPS were ingested (107). A
et al. that
ed the effect of low vs high
ODMAP
symptom severity
etabolomic markers, and
the microbiome
subjects with IBS also found a small decrease in
hydrogen production in subjects who consumed a low vs a high
FODMAP diet (108).
END POINT
No evidence-based diet for treating SIBO exists at this time
Low-FODMAP diet might improve symptoms related to SIBO by reducing fermentable CHOs

SIBO Nutrition:
The Evidence for Supplements

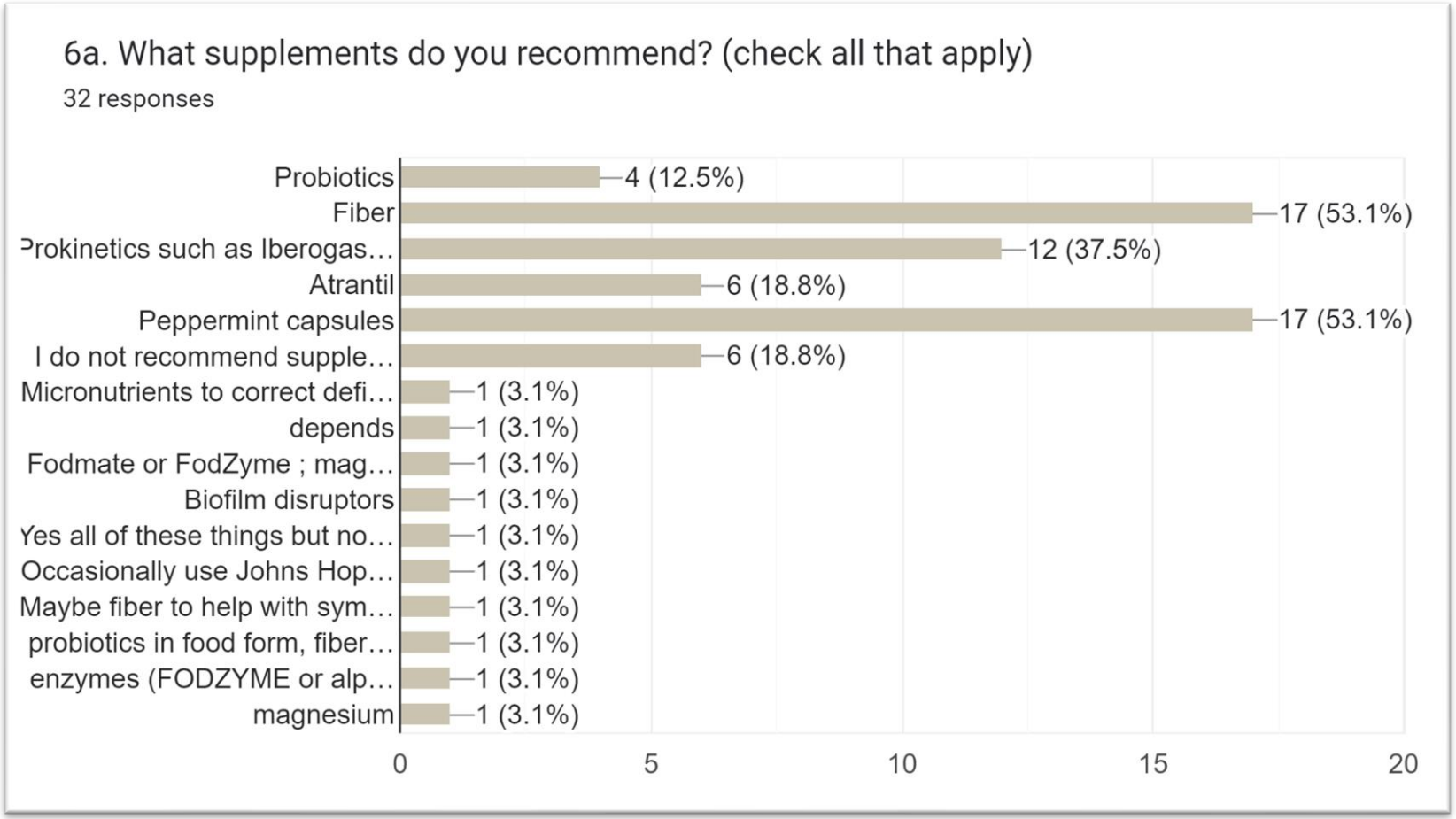
Informal RDN Survey - SUPPS

6. Do you recommend dietary specific supplements for patients with SIBO?

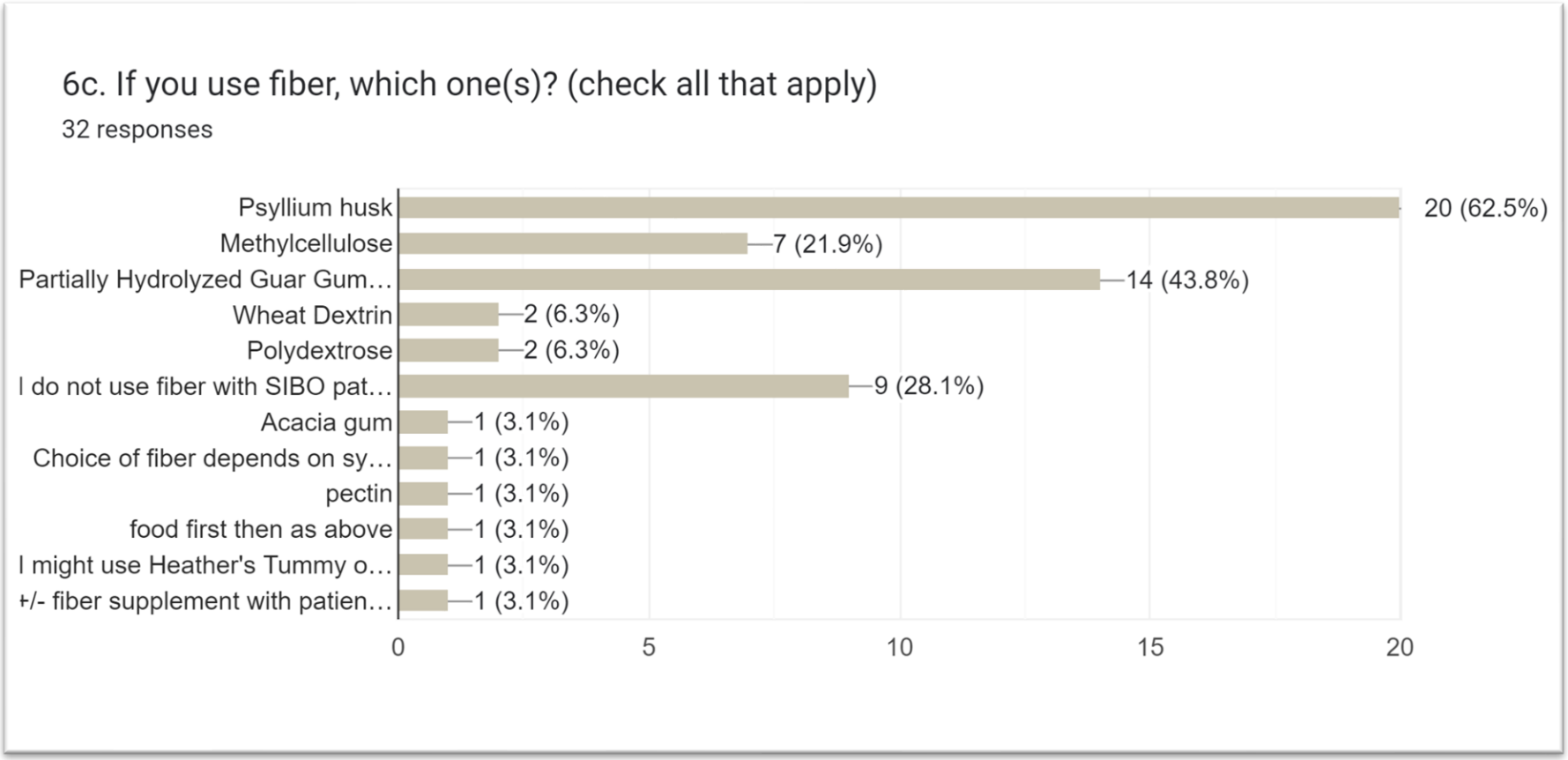
33 responses



Informal RDN Survey - SUPPS

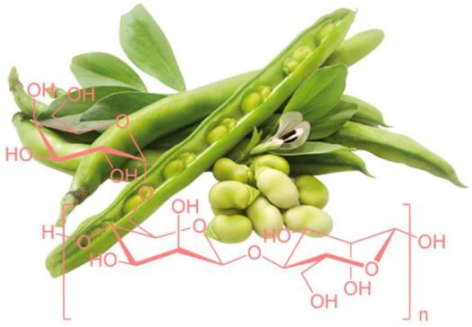


Informal RDN Survey - FIBER



Fiber - PHGG

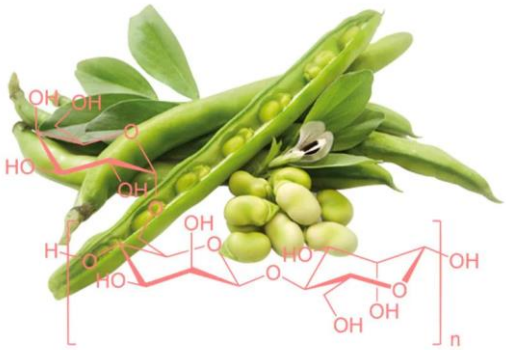
- Guar gum (guaran) = galactomannan polysaccharide extracted from guar beans that has thickening and stabilizing properties
- Partially hydrolyzed guar gum (PHGG) and treating SIBO
  - 1 study in 2010
  - 77 patients with H-SIBO by 50 g-glucose breath test
  - Randomized
    - *37 patients = Rifaximin 1200 mg/day*
    - *40 patients = Rifaximin 1200 mg/day plus PHGG 5 g/day for 10 days*
  - Symptom questionnaire and glucose breath test completed at baseline and 1 month after completion of ABX



Furnari M, et al. Aliment Pharmacol Ther. 2010

Fiber - PHGG

- **Results:**
  - Eradication rate of SIBO:
    - 62.1% = rifaximin group
    - 87.1% = rifaximin + PHGG group
  - Clinical improvement in Eradicated Cases:
    - 86.9% = rifaximin group
    - 91.1% = rifaximin + PHGG
- **Limitations / Considerations:**
  - Single Study
  - Not standard dose for ABX treatment
  - Not standard length for ABX treatment
  - NAC guidelines recommend 75 grams glucose for GBT
  - No follow up after the study (recurrence rates?)
  - Clinical improvements not statistically significant



Furnari M, et al. Aliment Pharmacol Ther. 2010

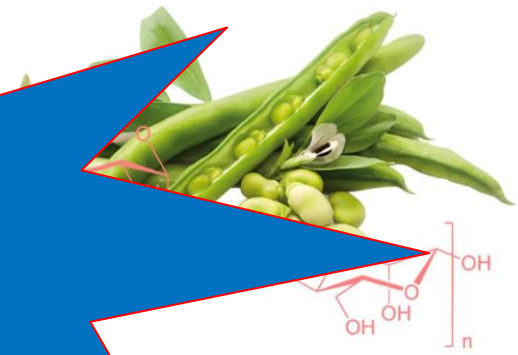
Fiber - PHGG

- **Results:**
  - Eradication rate of S
    - 62.1% = rifaxim
    - 8
  - Clinical i
    - 86.9%
- **Limitati**
  - Single
  - Not st
  - N
  - NAC guide
  - No follow u
  - Clinical imp

END POINT

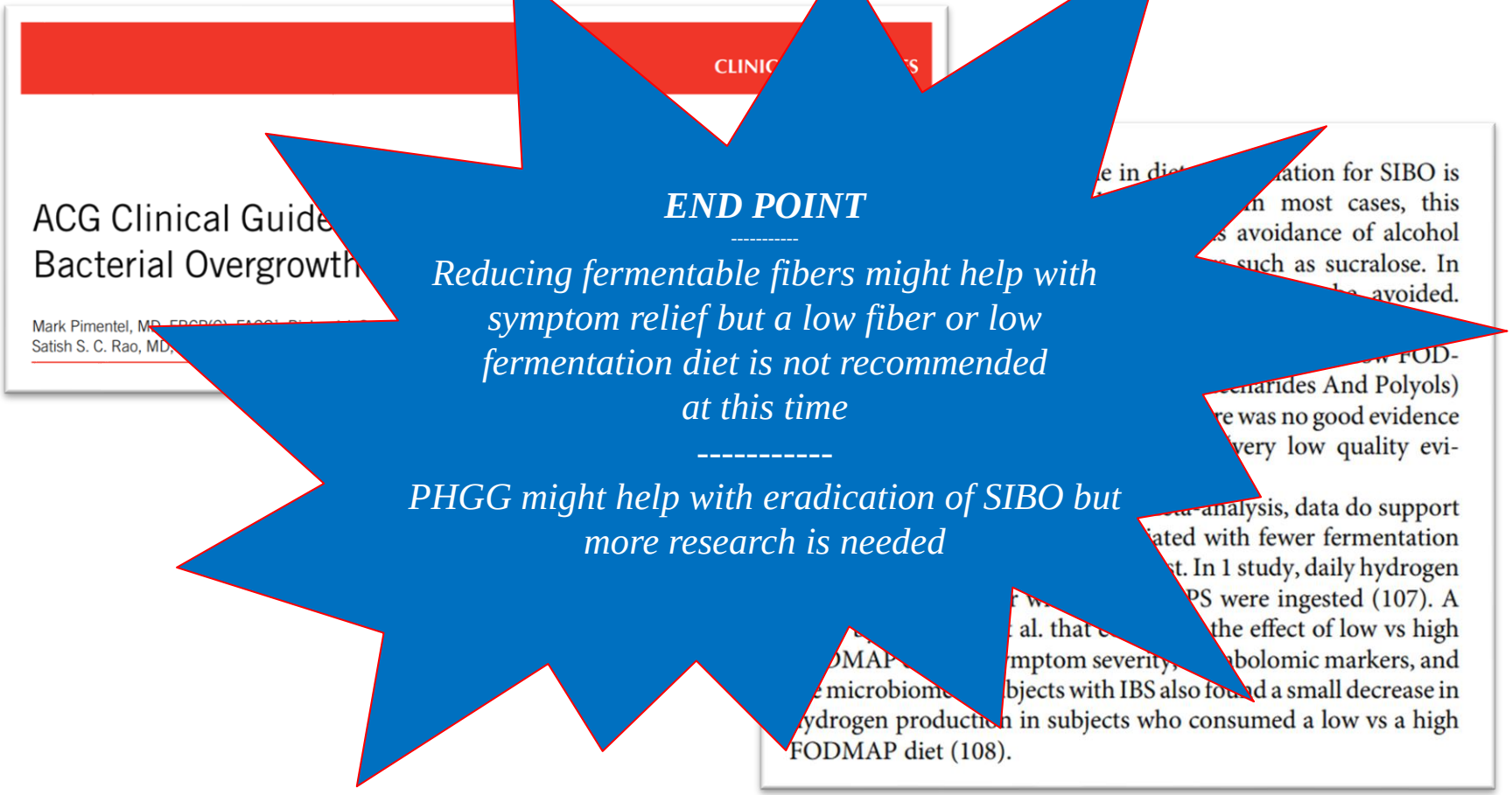
Poor evidence for using PHGG to treat SIBO

May improve eradication rates in H-SIBO, however does not improve symptoms over ABX alone



Furnari M, et al. Aliment Pharmacol Ther. 2010

Fiber in SIBO



END POINT

Reducing fermentable fibers might help with symptom relief but a low fiber or low fermentation diet is not recommended at this time

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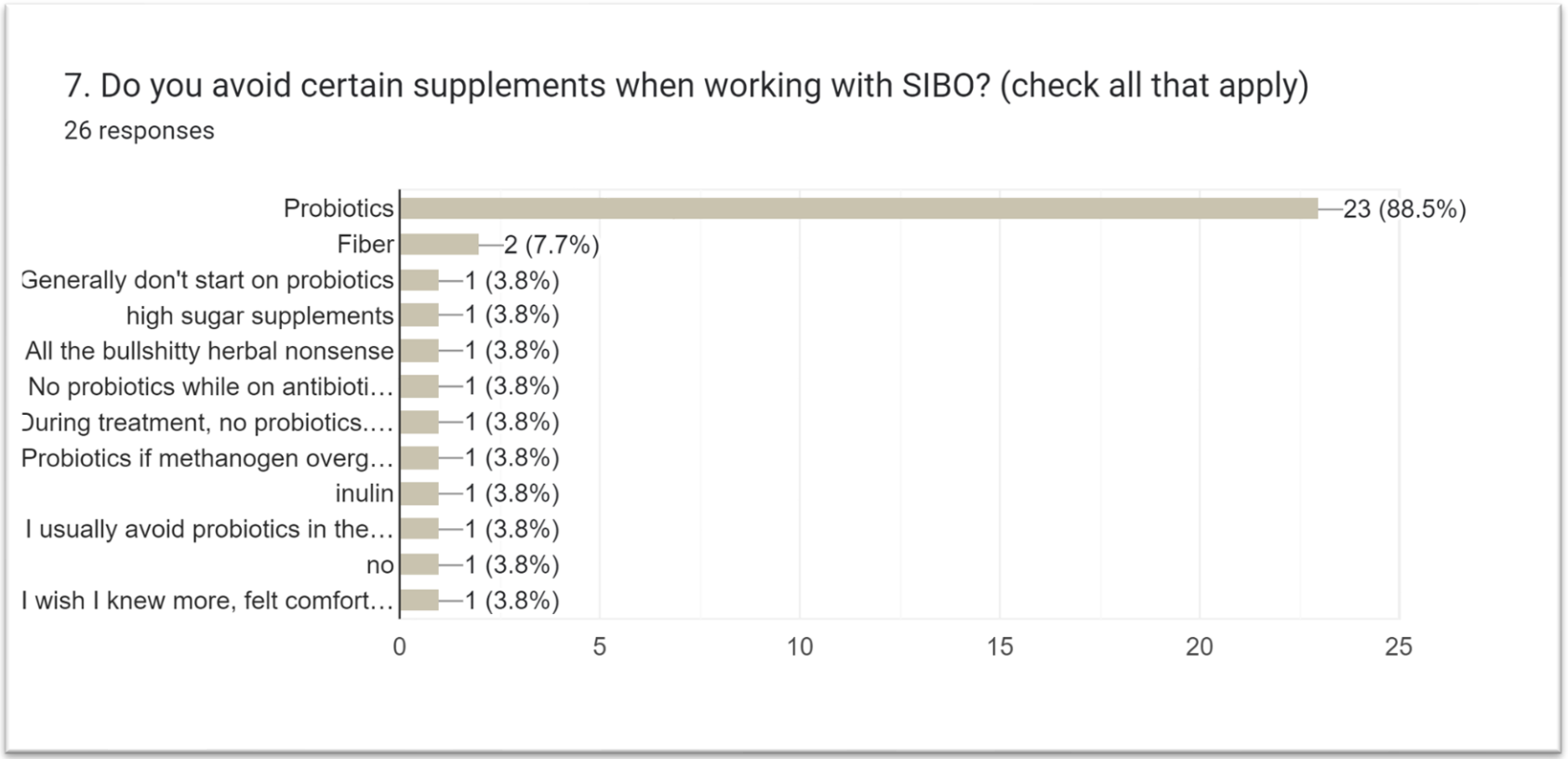
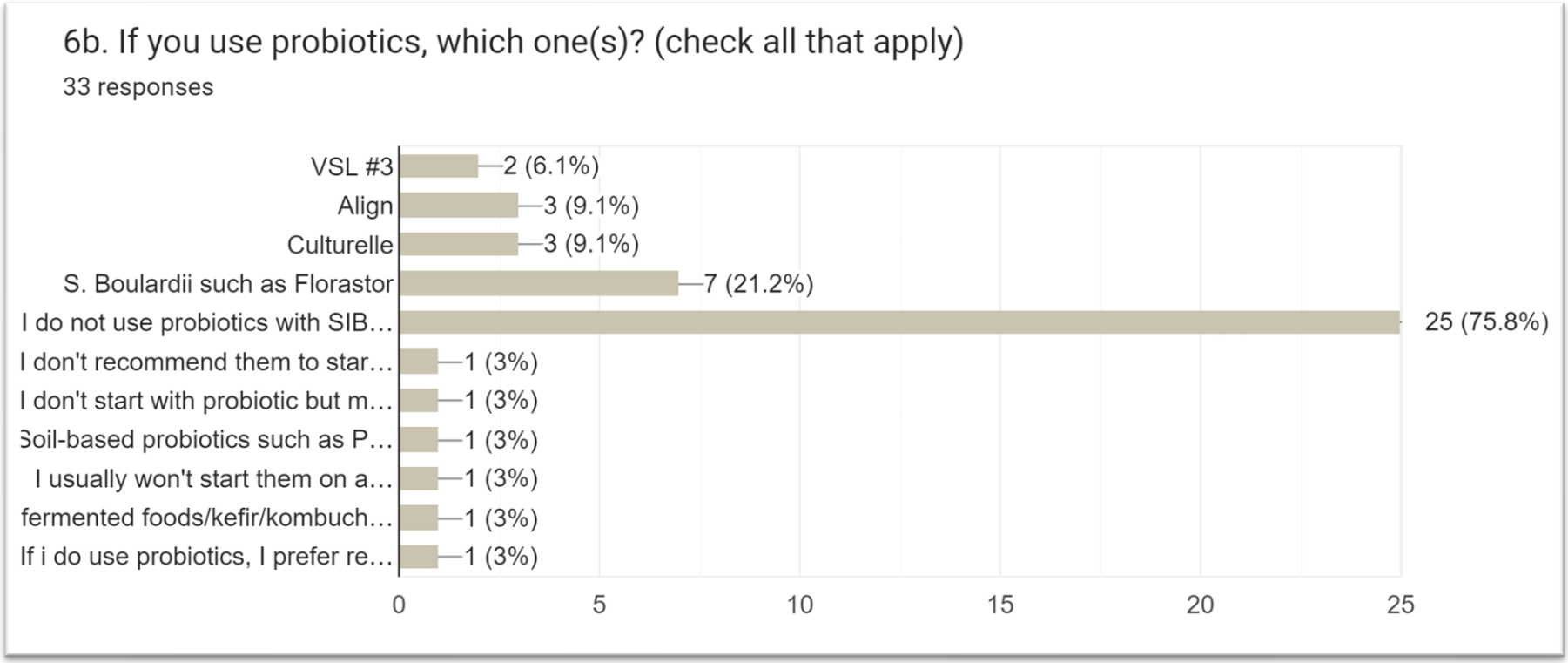
PHGG might help with eradication of SIBO but more research is needed

https://fg.bmj.com/content/flgastro/13/1/25.full.pdf

Informal RDN Survey - PROBIOTICS



Informal RDN Survey - PROBIOTICS



Probiotics

- 1 comprehensive meta-analysis and systematic review explored probiotic in SIBO
  - 14 full-text articles + 8 abstracts were included
  - Patients on probiotics showed an insignificant trend toward low SIBO incidence
  - Probiotics group showed a significantly higher SIBO decontamination rate than the non-probiotic group - 62.8%
  - Conclusion by authors:
    - *"the present findings indicated that probiotics supplementation could effectively decontaminate SIBO, decrease H2 concentration, and relieve abdominal pain, but were ineffective in preventing SIBO."*
- **Limitations**
  - Many included papers focused on poly-probiotics and did not give strain types
  - Mostly small studies of poor quality

Zhong C, et al. J Clin Gastroenterol. 2017

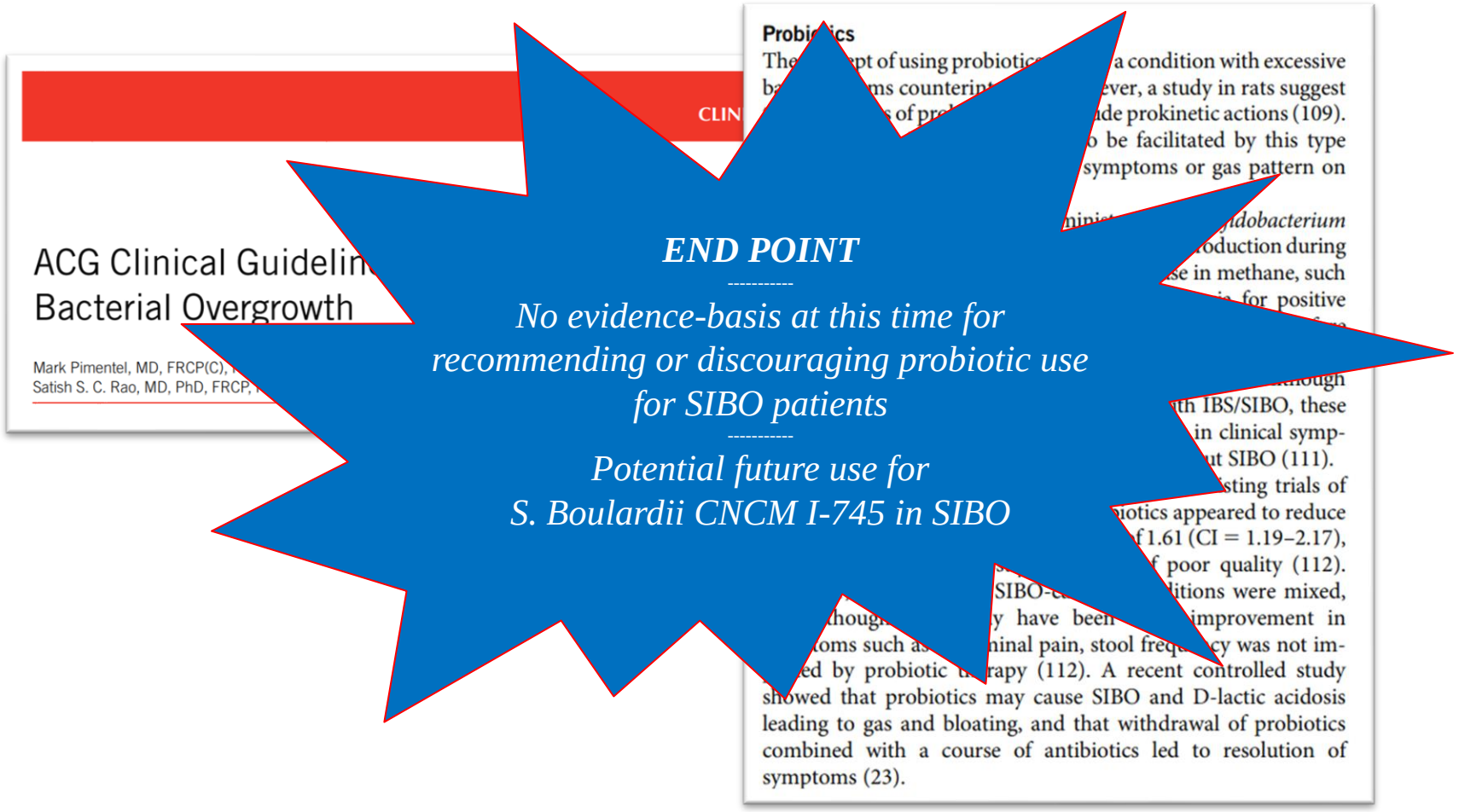
Probiotics - S. Boulardii

(CNCM I-745)

- *García-Collinot G, et al. Dig Dis Sci. 2020*
  - **S. boulardii (CNCM I-745)** H-SIBO scleroderma significantly higher eradication rates and decline in exhaled hydrogen compared to metronidazole therapy alone
- *Fernández, B. et al. Dig Dis. 2023*
  - **S. boulardii (CNCM I-745)** + dietary advice reduced SIBO and improved symptoms
- *Bustos Fernández LM, Man F, Lasa JS. Dig Dis. 2023*
  - **S. boulardii (CNCM I-745)** + dietary advice or dietary advice alone
  - Probiotic + diet group = lower LHBT at end of study (not statistically significant)
  - Reduced the incidence of diarrhea compared to dietary advice alone
- *Efremova, J Clin Med. 2024*
  - **S. boulardii (CNCM I-745)** H-SIBO decompensated cirrhosis
  - SIBO was absent in 80% of patients in the probiotic group compared to 23% of patients in the placebo group; reduced ascites and hepatic encephalopathy

Zhong C, et al. J Clin Gastroenterol. 2017
Bustos Fernández LM, Man F, Lasa JS. Dig Dis. 2023
García-Collinot G, et al. Dig Dis Sci. 2020
Bustos Fernández LM, Man F, Lasa JS. Dig Dis. 2023

Probiotics in SIBO



END POINT

No evidence-basis at this time for recommending or discouraging probiotic use for SIBO patients

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Potential future use for S. Boulardii CNCM I-745 in SIBO

Herbals - Atrantil

Botanical Component	Information about Botanical	Active Compounds	Theorized Effect
Quebracho	Hardwood variety from Central and South America	Tannins	• Free radical scavengers • Bind hydrogen and fiber • Disrupt biofilm
Horse Chestnut	Chestnut or conker tree	Saponins	• Free radical scavengers • Bind hydrogen • Reduce methane emissions • Promote intestinal motility
Peppermint	Wild mentha balsamea extract	Menthol	• Antispasmodic • Modulates nerves in enteric nervous system • Antibacterial effect

https://atrantil.com/ingredients/

Herbals - Atrantil

- *Brown, K. et al.. Journal of Gastroenterology and Hepatology, 2015*
  - 16 IBS-C patients
  - 2 weeks on treatment; single-site, double-blind, randomized, placebo-controlled
  - Patients qualified to participate only after failing to find relief from at least four other therapies (fiber supplements, laxatives, stimulants, prosecretory agents and probiotics)
  - 80% of patients found relief of bloating, constipation and abdominal discomfort

- *Brown K, et al. World J Gastrointest Pharmacol Ther. 2016*
  - 24 IBS-C patients from 1 community practice (of the inventor)
  - 2+ weeks on treatment; Double-Blind Study
  - Overall response rate = 88%
  - Significant reduction in abdominal pain, bloating, and constipation

Brown K, et al. World J Gastrointest Pharmacol Ther. 2016
Brown, K. et al.. Journal of Gastroenterology and Hepatology, 2015

Herbals - Atrantil

- **Clinical Trial in IMO**
  - Assess Atrantil as a treatment for IMO
  - Northwestern University Feinberg School of Medicine Study
  - 39 participants
  - All participants received 4 week supply of Atrantil (2 capsules TID)
  - Results:
    - Abdominal pain, gas and bloating = significant improvement
    - Constipation improved but not statistically significant
    - 56% had adequate response
    - No change in GBT

https://clinicaltrials.gov/ct2/show/NCT04755673
https://atrantil.com/clinical-trials/

Herbals - Atrantil

- **Clinical Trial in IMO**
  - Asses Atrantil as a t
  - Northwe
  - 39 particip
  - A
  - Result
    -
    - G
    - 56% h
    - No ch ge in GBT

END POINT

No evidence-basis for either recommending or discouraging Atrantil use for treating SIBO or IMO at this time

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Might help with symptoms of pain and bloating related to IBS-C

https://clinicaltrials.gov/ct2/show/NCT04755673
https://atrantil.com/clinical-trials/

Herbals – OTC Mixed Formulas

- 1 study in 2014
  - 104 patients
  - Either given 200mg TID Rifaximin or 2 capsules of 2 sets of 2 commercially available herbal preparations for 4 weeks
  - Rifaximin non-responders were then prescribed either the herbal protocol or triple antibiotics for 4 additional weeks
  - 37 patients received herbal therapy
    - 46% had a negative follow-up LHBT compared to 34% of rifaximin users
    - 31.8% rifaximin non-responders were offered herbal rescue therapy
      - 57.1% had a negative LHBT after completing rescue herbal therapy
      - 10 non-responders were offered triple antibiotics with 6 responding (60%)

Chedid V, et al. Glob Adv Health Med. 2014

Herbals – OTC Mixed Formulas

- 1 study in 2014
  - 104 patients
  - Either … commercially available
  - Rifaximin … or triple
  - 37 …
    - … rifaximin users
    - … rescue therapy
    - … rescue herbal therapy
    - … offered … ble antibiotics with 6 responding (60%)

END POINT

Poor evidence to use mixed OTC herbals to treat SIBO

Limitations

1) non-standardized dose of ABX; 2) non-standard length for ABX use; 3) lacks statistical significance; 4) never replicated

Chedid V, et al. Glob Adv Health Med. 2014

Herbals – OTC Mixed Formulas

- New Study 2024
  - 179 patients followed for 3 months
    - 56 H-SIBO
    - 123 IMO
  - 2 Phases
    - Phase 1 – Cleansing (4 weeks)
      - H-SIBO – Low Fodmap diet +
        - Rifaximin 600mg for 10 days
        - Oleocaps 2 + Berberine for 20 days
      - IMO – Low Fodmap diet +
        - Rifaximin 600mg + neomycin 500mg + S. Boulardii for 10 days
        - Oleocaps 2 + Wormwood for 20 days

Redondo-Cuevas, et al. Nutrients 2024

Herbals – OTC Mixed Formulas

- New Study 2024
  - Phase 2 – Mucosal Recover (6 weeks)
    - H-SIBO – Low Fodmap diet +
      - Probiotic Bifidobacterium longum ES1
      - L-glutamine 10 grams
      - PHGG 5 grams
    - IMO – Low Fodmap diet +
      - Probiotic Bifidobacterium longum ES1
      - L-glutamine 10 grams
  - Results
    - No significant difference between controls and interventions for exhaled gas
    - IMO group had improvement in symptoms

Redondo-Cuevas, et al. Nutrients 2024

Herbals – OTC Mixed Formulas

- New Study 2024
  - Ph… Mucos…
    - …
    - …
  - Results
    - No …ant …ence …een con…s and interventions for exhaled gas
    - IM… group had improvement in symptoms

END POINT

Poor evidence to use mixed OTC herbals to treat SIBO

Redondo-Cuevas, et al. Nutrients 2024

Herbals - Berberine

- Berberine and rifaximin effects for small intestinal bacterial overgrowth (BRIEF-SIBO)
  - Single-center, open-label, double-arm randomized controlled trial
  - 180 patients will be recruited and allocated to:
    - Intervention group (berberine)
    - Control group (rifaximin)
  - Outcomes
    - The primary outcome is a negative breath test
    - The secondary outcomes include abdominal symptom relief and alteration in gut microbiota

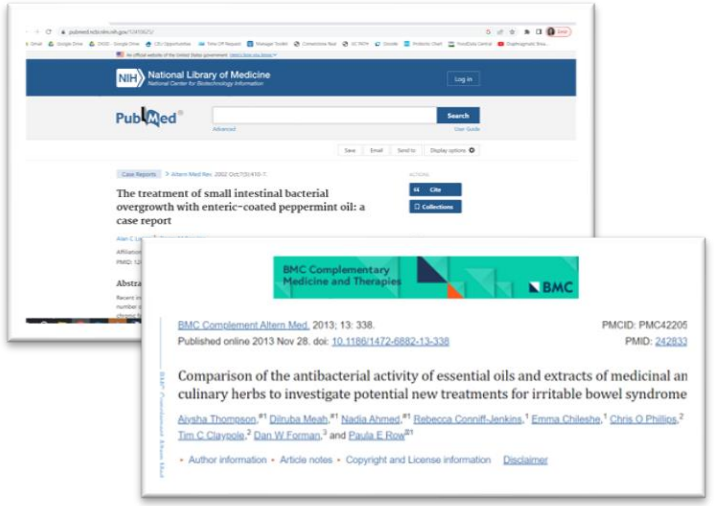
STAY TUNED!

Guo H, et al. Front Pharmacol. 2023

Herbals - Peppermint

Theory for Peppermint in SIBO

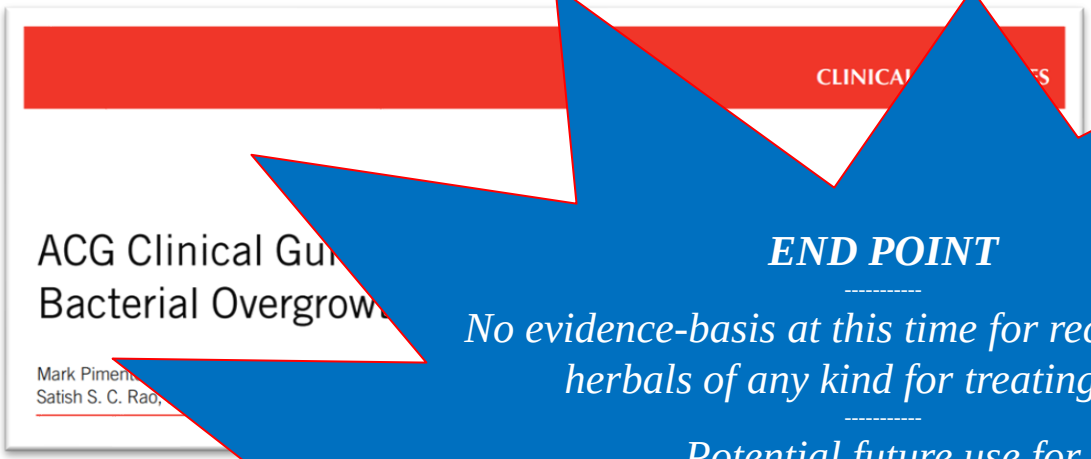
- Smooth muscle calcium channel antagonist
- Normalization of orocecal transit time
- Carminative effects
- Serotonergic (5HT3) antagonism



- NO studies at this time have evaluated the effect of peppermint on treating or managing symptoms of SIBO
  - One case in 2002 showed marked subjective improvement in IBS-like symptoms and significant reductions in hydrogen production
- May be beneficial for symptom reduction of gas, bloating, abdominal pain

Logan AC, Beaulne TM. Altern Med Rev. 2002

Herbals in SIBO



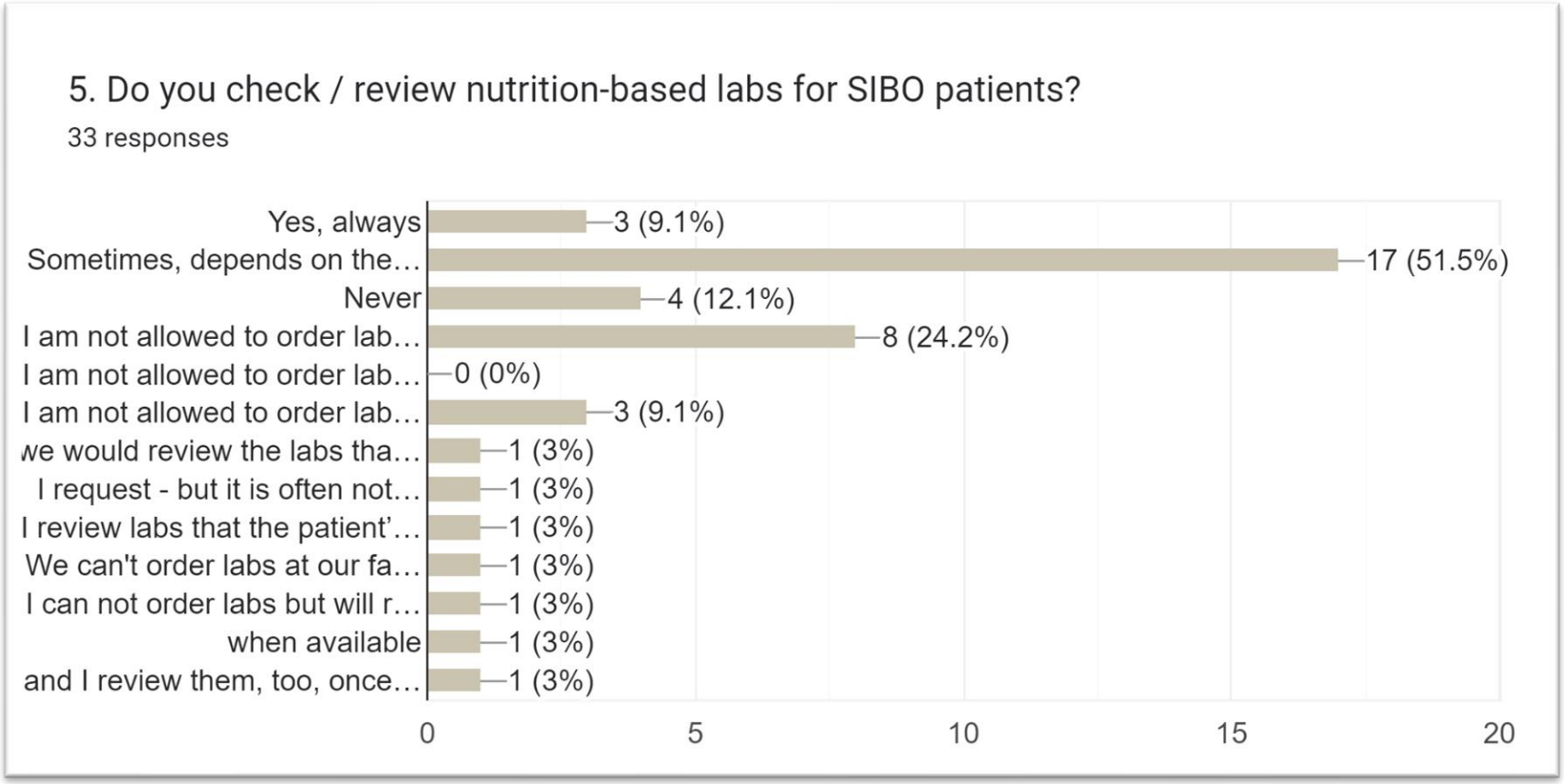
END POINT

No evidence-basis at this time for recommending herbals of any kind for treating SIBO

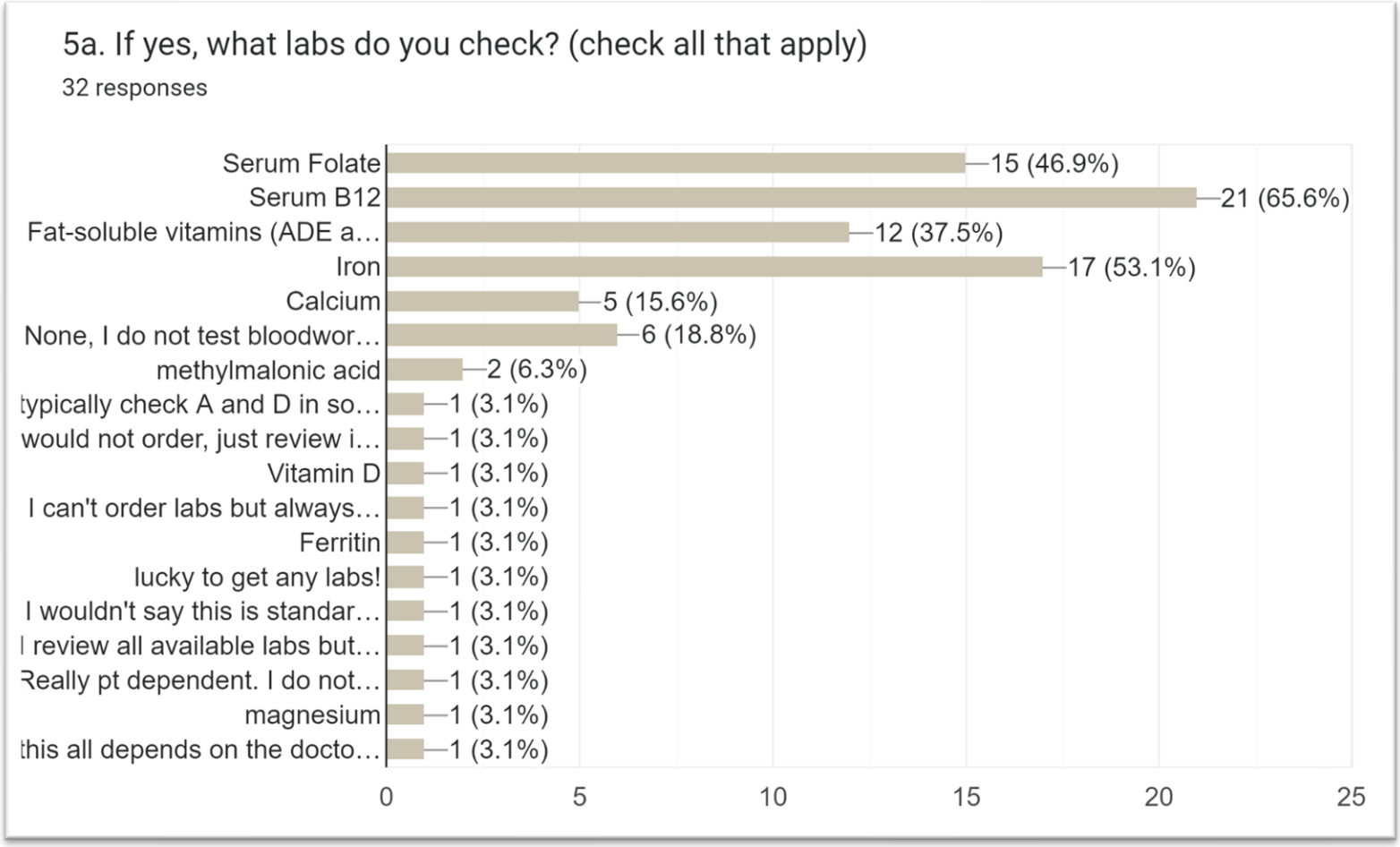
Potential future use for
Atrantil in IMO to reduce symptoms of bloating, gas and discomfort; Peppermint to help with symptoms related to IBS

SIBO Nutrition:
(Some of) the Gaps

Informal RDN Survey – Vits/Mins



Informal RDN Survey – Vits/Mins



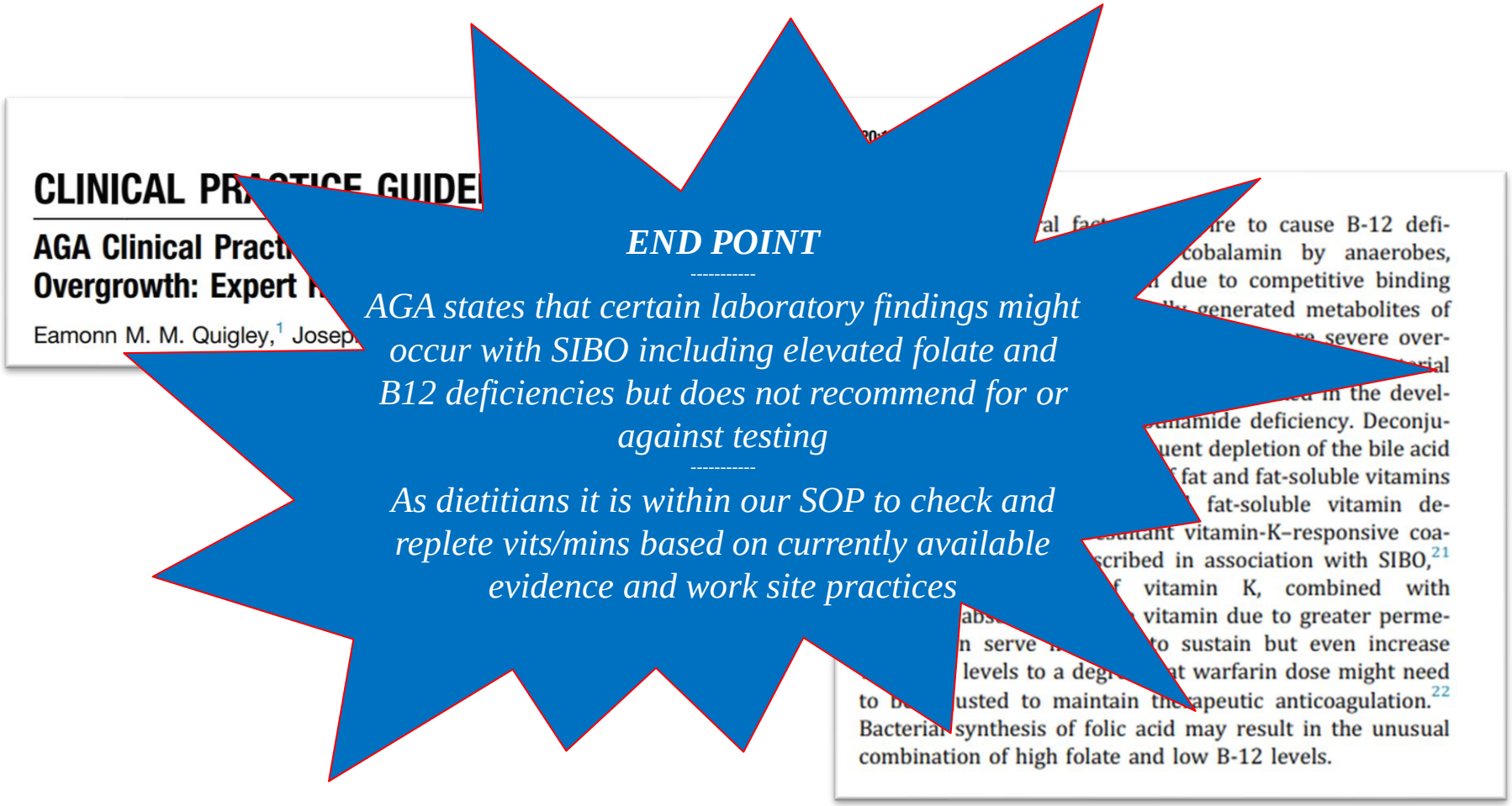
Vits / Mins in SIBO

Table 3. Pathophysiology of Symptoms and Clinical Findings in SIBO

Process	Mechanisms of action	Clinical consequences
Mucosal injury induced by bacteria and/or their toxins or products	1. Loss of brush-border enzymes	1. Carbohydrate maldigestion
	2. Injury to the epithelial barrier leading to enhanced intestinal permeability	2. Protein-losing enteropathy; bacterial translocation and portal and systemic endotoxemia
	3. Inflammatory response generating inflammatory cytokines	3. Liver injury and inflammation, systemic inflammatory responses
Luminal competition with host for nutrients	1. Consumption of dietary protein	1. Hypoproteinemia, edema
	2. Consumption of vitamin B_{12}	2. B_{12} deficiency, megaloblastic anemia, neurologic symptoms
	3. Consumption of thiamine	3. Thiamine deficiency
	4. Consumption of nicotinamide	4. Nicotinamide deficiency
Bacterial metabolism	1. Fermentation of unabsorbed carbohydrates	1. Bloating, distension, flatulence
	2. Deconjugation of primary bile acids	2. Diarrhea due to effects of deconjugated bile acids in the colon; depletion of the bile acid pool leading to fat and fat-soluble vitamin malabsorption
	3. Synthesis of vitamin K	3. Interference with anticoagulant activity
	4. Synthesis of folate	4. High serum folate levels
	5. Synthesis of D-lactic acid	5. D-lactic acidosis
	6. Synthesis of alcohol	6. Liver injury
	7. Synthesis of acetaldehyde	7. Liver injury

Bushyhead D, Quigley EMM. Gastroenterology. 2022

Vits / Mins in SIBO



END POINT

AGA states that certain laboratory findings might occur with SIBO including elevated folate and B12 deficiencies but does not recommend for or against testing

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As dietitians it is within our SOP to check and replete vits/mins based on currently available evidence and work site practices

Informal RDN Survey – Meal Spacing

12. Do you recommend patients avoid snacking and/or place 3-5 hours between meals?

33 responses

Meal Spacing in SIBO

Theory for Meal Spacing in SIBO

- Housekeeping waves (cleaning, migrating motor complex/MMC)
  - Begins about 90 minutes after a meal
  - Ends with the start of the next meal
  - Consists of 4 phases
    - Total time is roughly 90-230 minutes

- *Pimentel et al Dig Dis Sci 2002*
  - Inspired by a paper from 1977 that looked at MMC's and bacterial overgrowth
  - Less or no cleaning waves in 4 hours of fasting for IBS with SIBO patients
  - 50% of IBS patients with SIBO had no MMC

Pimentel et al, Dig Dis Scie, 2022
Vantrappen et al J Clin Invest 1977
Deloose E, Janssen P, Depoortere I, Tack J. Nat Rev Gastroenterol Hepatol. 2012
The Microbiome Connection: Your Guide to IBS, SIBO, and Low-Fermentation Eating, Dr. Mark Pimentel and Dr. Ali Rezaie, 2022

Meal Spacing in SIBO

Theory for Meal Spacing [illegible]IBO

- Housekeeping waves (cl[illegible]igr[illegible]MMC)
  - Begins [illegible]
  - Ends with t[illegible]
  - C[illegible]
    - To[illegible]
- *Pimentel*
  - Inspired b[illegible]M[illegible]bacterial overgrowth
  - Less or no c[illegible]g wa[illegible]4 h[illegible]of fas[illegible]for IBS wi[illegible]SIBO patients
  - 50% of IBS patients with SIBO had no MMC

END POINT

1-2 study directly on MMC and SIBO; begs the question "if already not working, does meal spacing change anything?"

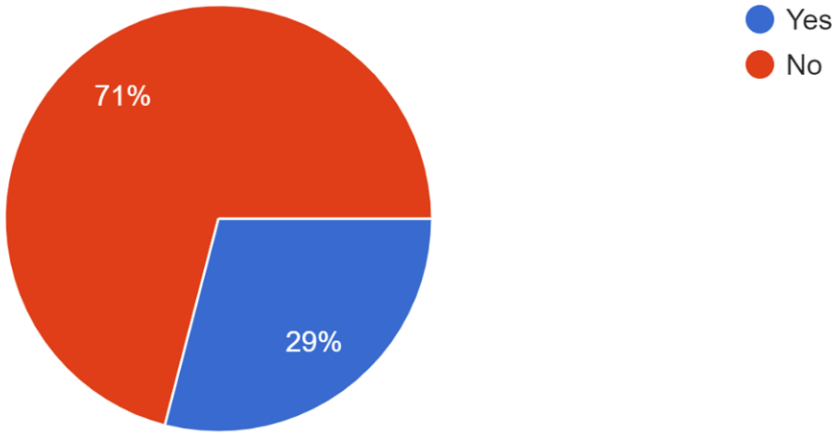
Reasonable but not evidence-based to encourage meal spacing (or to avoid all day grazing) for patients with SIBO

Pimentel et al, Dig Dis Scie, 2022
Vantrappen et al J Clin Invest 1977
Deloose E, Janssen P, Depoortere I, Tack J. Nat Rev Gastroenterol Hepatol. 2012
The Microbiome Connection: Your Guide to IBS, SIBO, and Low-Fermentation Eating, Dr. Mark Pimentel and Dr. Ali Rezaie, 2022

Informal RDN Survey – H2S / IMO

9. Do you recommend different dietary advice for Hydrogen SIBO (H-SIBO) vs Intestinal Methanogen Overgrowth (IMO) vs Hydrogen Sulfide SIBO (H2S-SIBO)?

31 responses



H2S-SIBO?

- What we know about H2S?
  - *There are many bacteria that produce hydrogen sulfide gas; most common are Fusobacterium and Desulfovibrio*
  - *Most common symptoms are diarrhea, pain and urgency*
- What we do not know about H2S?
  - *Best practices for Diagnosing (only one test validated for all 3 gases)*
  - *Best practices for Medication treatment (limited evidence for bismuth + rifaximin)*
- Diet Therapy to improve H2S?
  - *Suggestions have included:*
    - *Low or reduced sulfur diet – no evidence to substantiate at this time*
    - *Avoid low fodmap diet – again, no evidence to substantiate at this time*

Villanueva-Millan, et al. Am J Gastro 2022
Suarez et al. Gastro 1998
Wielgosz-Grochowska JP, et al. Nutrients. 2022

IMO?

- What we know about IMO
  - *More than 30% of SIBO patients colonized with archaea*
  - *Archaea in the small bowel and colon (hence not called SIBO)*
  - *Main methanogen is Methanobrevibacter Smithii*
  - *M. Smithii consumes hydrogen and produces methane (1C + H4 = CH4)*
  - *Most common symptom is constipation; bloating and discomfort can also occur*
  - *Absence of B12 deficiency*
- What we do not know about IMO
  - *What causes it – constipation (chicken egg scenario)*
  - *Best practices for Medication – 1 study on neomycin + rifaximin; statins failed testing so far*
- Diet Therapy to improve IMO
  - *Focuses on resolving constipation at this time*

Informal RDN Survey

"I am very concerned about diet recommendations leading to increased disordered eating and health anxiety. I think it is important to discuss the evidence/lack of evidence for various diet interventions and the possible risks of undergoing these interventions (i.e. lack of symptom improvement, increased food fear, social isolation, financial expense, conditioned food intolerances, disordered eating). My goal is to respect patient autonomy by assisting them in making an informed decision"

Informal RDN Survey

"The amount of craziness for SIBO management out there is really frustrating as a dietitian. I see colleagues suggesting herbal protocols based off teachings from 'gurus' etc. It drives me crazy and I feel that its not ethical that dietitians are appearing to diagnose SIBO themselves due to available access to the tests and then treating with herbal protocols with no basis. It looks bad on the profession and more importantly I believe it puts patients at risk of harm. Looking forward to hear your talk on this Nancee!"

Thank You!

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