
2026
ACG'S OBESITY AND METABOLIC DISORDERS SCHOOL &
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Participating in the Webinar



Moderator:
Turki AlAmeel, MBBS

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them.
Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.

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Week 37 – Thursday, September 10, 2026
"Functional" GI Conditions in the Older Adult: DGBIs and Beyond
Faculty: Xiao Jing (Iris) Wang, MD, FAC
Moderator: Swapna Gayam, MD, FACG
At Noon and 8pm Eastern





Week 38 – Thursday, September 17, 2026
ACG Clinical Guideline Update: Preventive Care in Inflammatory Bowel Disease
Faculty: Francis A. Farraye, MD, MSc, MACG
Moderator: Sunanda V. Kane, MD, MSPH, MACG
At Noon and 8pm Eastern

Visit **gi.org/ACGVGR** to Register

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Advances in the Diagnosis and Management of SIBO
Mark Pimentel, MD, FACG
Professor of Medicine, Cedars-Sinai
Execute Director, MAST Program
Los Angeles, California
MAST
MEDICALLY ASSOCIATED SCIENCE AND TECHNOLOGY

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Causes of SIBO

Table 4. Conditions associated with small intestinal bacterial overgrowth

Category	Specific condition
Mechanical causes	Small bowel tumor Volvulus Intussusception Postsurgical causes
Systemic disease	Diabetes Scleroderma Amyloidosis
Motility	IBS Pseudo-obstruction Visceral myopathies Mitochondrial diseases
Medications	Opiates Potent antisecretory agents
Malabsorptive conditions	Pancreatic insufficiency Cirrhosis (altered bile acid composition) Other malabsorptive conditions
Immune-related	Human immunodeficiency virus Combined variable immunodeficiency IgA deficiency
Other	Aging (the elderly) Small bowel diverticulosis

IBS, irritable bowel syndrome; IgA, immunoglobulin A.

OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY | ACG

Pimentel, et al. Am J Gastroenterol 2020

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Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-025-09170-0

INVITED COMMENTARY

Biomarkers in Patients with IBS: Continue the Grail Quest or Give It a Rest?

Mauricio Jin[1] · Xiao Jing Wang[2]

Received: 20 May 2025 / Accepted: 5 June 2025
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Keywords Enterochromaffin cells · Post-infectious IBS · CdtB · Vinculin · Rome IV criteria · Chromogranin a cell density

FULL TEXT ARTICLE

Biomarkers in Irritable Bowel Syndrome

Article in Press: Corrected Proof

Michelle Guan MD and Lin Chang MD
Gastroenterology Clinics of North America, Copyright © 2025 Elsevier Inc.

Irritable bowel syndrome (IBS) is currently diagnosed based on symptoms and limited diagnostic testing, highlighting the need for noninvasive biomarkers and personalized therapies. Emerging blood-based biomarkers such as cytolethal distending toxin B and antivinculin antibodies, DNA methylation profiles, and intestinal permeability measures, along with stool-based microbiome and metabolite markers, show promise in distinguishing IBS, and its bowel habit subtypes, from other gastrointestinal disorders with overlapping symptoms. Additionally, stool-based biomarkers and breath tests may also predict response to interventions, like the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet, and rifaximin, supporting more personalized treatment strategies.

Gastroenterology Clinics of North America

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Review

Mechanisms and pathophysiology leading to development of small intestinal microbial dysbiosis

John A Damianos, Xiao Jing Wang, Michael Camilleri

Small intestinal microbial dysbiosis (SIMD) describes clinical syndromes attributed to overabundance of microbes within the small intestine. Usually attributed to bacteria (but also less commonly to archaea and fungi), SIMD arises as a secondary condition, when there is disruption of one or more key physiological mechanisms. We provide a comprehensive review of the current understanding of SIMD pathophysiology. We highlight the key physiological factors including gastric acid, pancreatic enzymes, bile acids, small intestinal dysmotility and obstruction, colonic motility, and intestinal mucosal immunity. We then describe the disease states associated with failure of these mechanisms, providing SIMD prevalence estimates for each. Finally, we address some of the controversies regarding SIMD including testing modalities, significance of intestinal methanogen overgrowth, and the role of SIMD in irritable bowel syndrome.

Lancet Gastroenterol Hepatol 2026

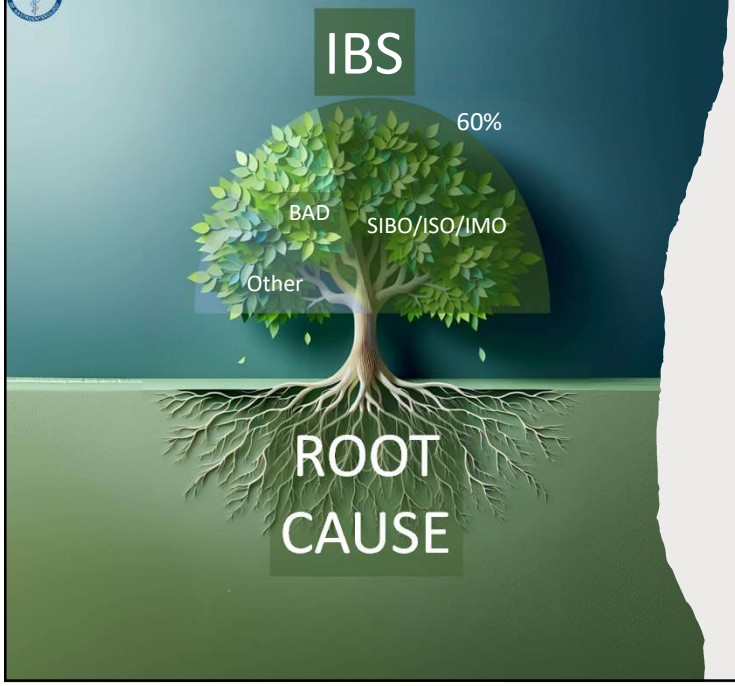
Published Online January 14, 2026

https://doi.org/10.1016/S2468-1253(25)00295-X

Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA

(J A Damianos MD, X J Wang MD, M Camilleri MD DSc)

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Roots of IBS

- Bile acid diarrhea – but what is the root cause of this?
- SIBO/ISO/IMO – Root cause identified

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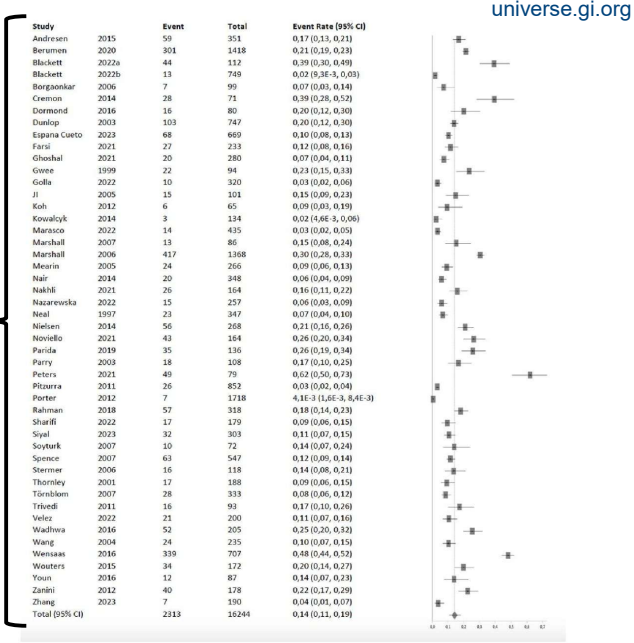
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Acute Gastroenteritis Causes IBS

49 Outbreaks Studied

Pooled prevalence = 14.5% (CI=11.2-18.1)
That's 1 in every 6.9 infections!



Study		Event	Total	Event Rate (95% CI)
Andresen	2015	59	351	0,17 (0,13, 0,21)
Berumen	2020	301	1418	0,21 (0,19, 0,23)
Blackett	2022a	44	112	0,39 (0,30, 0,49)
Blackett	2022b	13	749	0,02 (9,3E-3, 0,03)
Borgaonkar	2006	7	99	0,07 (0,03, 0,14)
Cremon	2014	28	71	0,39 (0,28, 0,52)
Dormond	2016	16	80	0,20 (0,12, 0,30)
Dunlop	2003	103	747	0,20 (0,12, 0,30)
Espana Cueto	2023	68	669	0,10 (0,08, 0,13)
Farsi	2021	27	233	0,12 (0,08, 0,16)
Ghoshal	2021	20	280	0,07 (0,04, 0,11)
Gwee	1999	22	94	0,23 (0,15, 0,33)
Golla	2022	10	320	0,03 (0,02, 0,06)
JI	2005	15	101	0,15 (0,09, 0,23)
Koh	2012	6	65	0,09 (0,03, 0,19)
Kowalcyk	2014	3	134	0,02 (4,6E-3, 0,06)
Marasco	2022	14	435	0,03 (0,02, 0,05)
Marshall	2007	13	86	0,15 (0,08, 0,24)
Marshall	2006	417	1368	0,30 (0,28, 0,33)
Mearin	2005	24	266	0,09 (0,06, 0,13)
Nair	2014	20	348	0,06 (0,04, 0,09)
Nakhli	2021	26	164	0,16 (0,11, 0,22)
Nazarewska	2022	15	257	0,06 (0,03, 0,09)
Neal	1997	23	347	0,07 (0,04, 0,10)
Nielsen	2014	56	268	0,21 (0,16, 0,26)
Noviello	2021	43	164	0,26 (0,20, 0,34)
Parida	2019	35	136	0,26 (0,19, 0,34)
Parry	2003	18	108	0,17 (0,10, 0,25)
Peters	2021	49	79	0,62 (0,50, 0,73)
Pitzurra	2011	26	852	0,03 (0,02, 0,04)
Porter	2012	7	1718	4,1E-3 (1,6E-3, 8,4E-3)
Rahman	2018	57	318	0,18 (0,14, 0,23)
Sharifi	2022	17	179	0,09 (0,06, 0,15)
Siyal	2023	32	303	0,11 (0,07, 0,15)
Soyturk	2007	10	72	0,14 (0,07, 0,24)
Spence	2007	63	547	0,12 (0,09, 0,14)
Stermer	2006	16	118	0,14 (0,08, 0,21)
Thornley	2001	17	188	0,09 (0,06, 0,15)
Törnblom	2007	28	333	0,08 (0,06, 0,12)
Trivedi	2011	16	93	0,17 (0,10, 0,26)
Velez	2022	21	200	0,11 (0,07, 0,16)
Wadhwa	2016	52	205	0,25 (0,20, 0,32)
Wang	2004	24	235	0,10 (0,07, 0,15)
Wensaas	2016	339	707	0,48 (0,44, 0,52)
Wouters	2015	34	172	0,20 (0,14, 0,27)
Youn	2016	12	87	0,14 (0,07, 0,23)
Zanini	2012	40	178	0,22 (0,17, 0,29)
Zhang	2023	7	190	0,04 (0,01, 0,07)
Total (95% CI)		2313	16244	0,14 (0,11, 0,19)

Porcari, et al. Gut 2024.

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Molecular Mimicry

- "Molecular mimicry is one of the leading mechanisms by which infectious or chemical agents may induce autoimmunity."
- "Molecular mimicry is a process that occurs when the immune system mistakes a foreign substance for a part of the body."

Causes of Post-infection IBS



Shigella
Salmonella
Campylobacter
E. coli

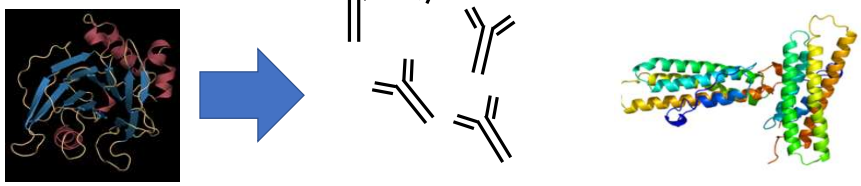
Cytolethal Distending Toxin B (CdtB)

Rojas, et al. J Autoimmun 2018

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Molecular Mimicry/Autoimmunity



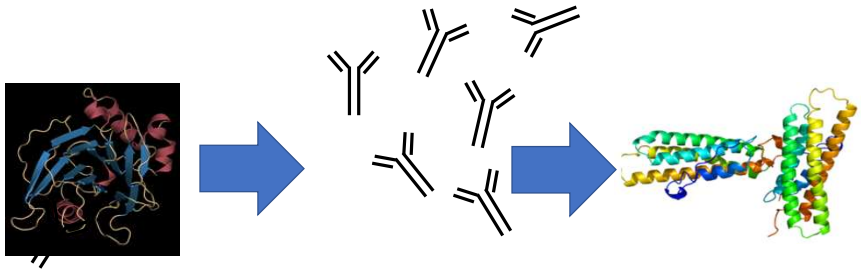
Cytolethal Distending Toxin B

Human Vinculin

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Molecular Mimicry/Autoimmunity



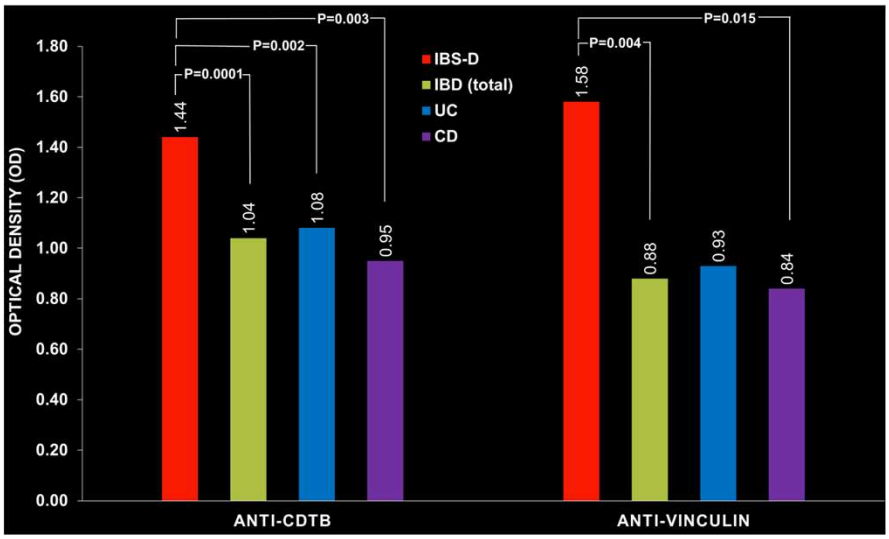
Cytolethal Distending Toxin B

Human Vinculin

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Generation 2 Blood Test for Diagnosing IBS-D



Morales, et al. Dig Dis Sci 2019

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Generation 2 test dynamics

Anti-CdtB	Anti-vinculin	Post-Test Probability of IBS
+	-	89%
-	+	88%
+	+	98%

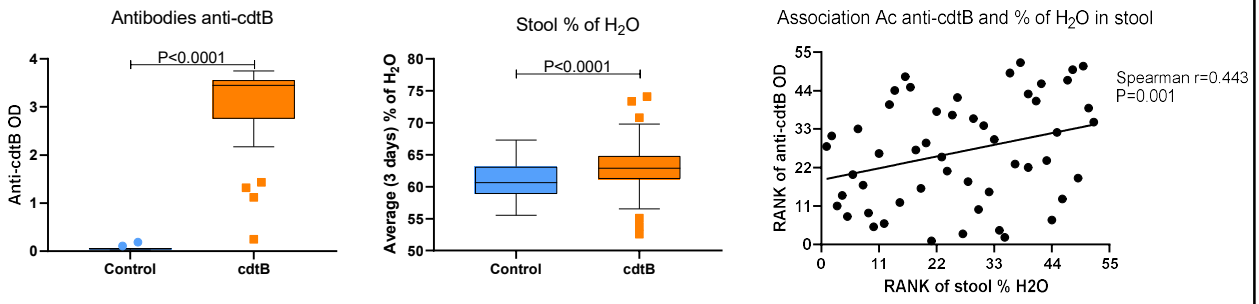
	Sensitivity	Specificity	PPV	NPV	LR+	The old Assay
Anti-CdtB	43%	93.5%	95.6	33.7	6.3	5.2
Anti-vinculin	52%	90.9%	96.3	29.4	5.3	2.0
And/or	56%					

Morales, et al. Dig Dis Sci 2019

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Rats get IBS-D phenotype after CdtB injection

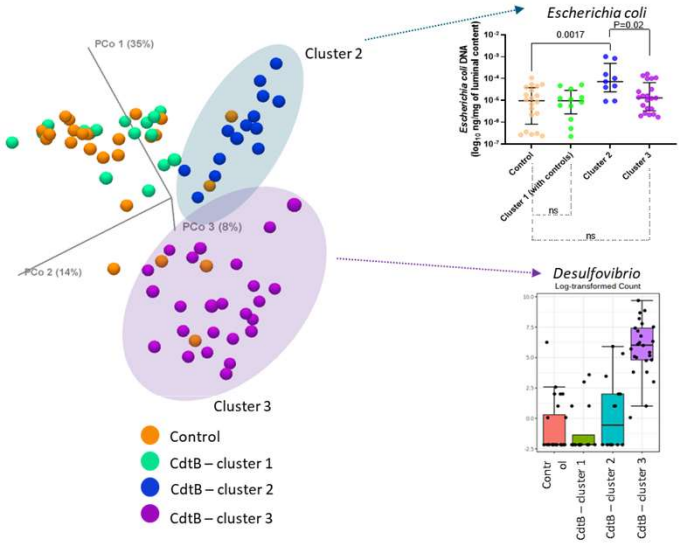


Leite, et al Gut Microbes, 2024.

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Animal Model of Post-Infectious IBS-D: 3 Microtypes



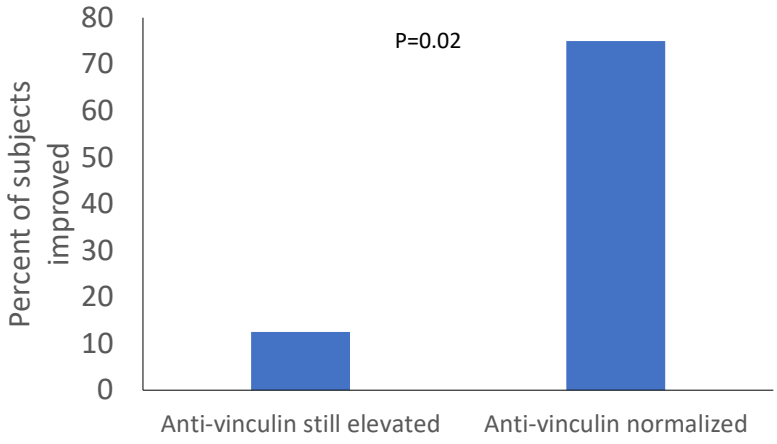
Hydrogen cluster

Hydrogen sulfide cluster

Leite, et al. Gut Microbes, 2024.

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Anti-vinculin antibodies and IBS Symptoms



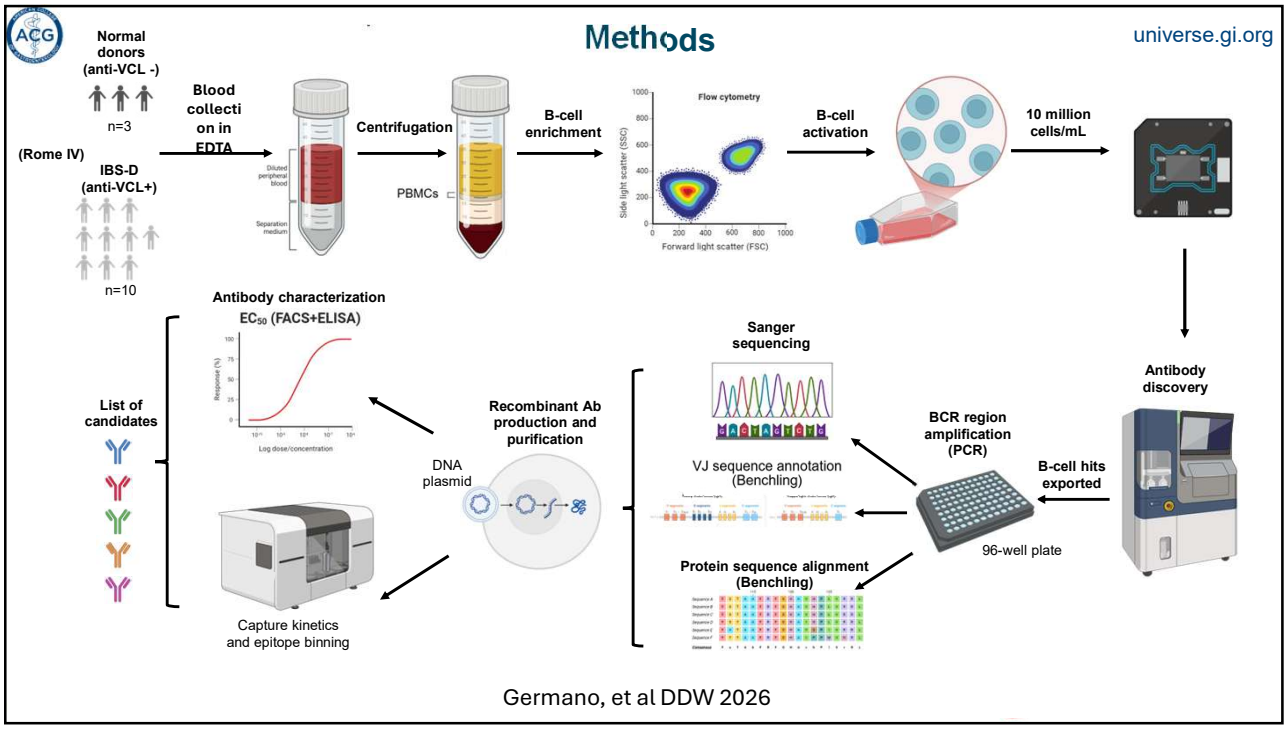
-spontaneous
-IVIG
-Plasmapheresis

Sharabi, et al. Dig Dis Sci 2025

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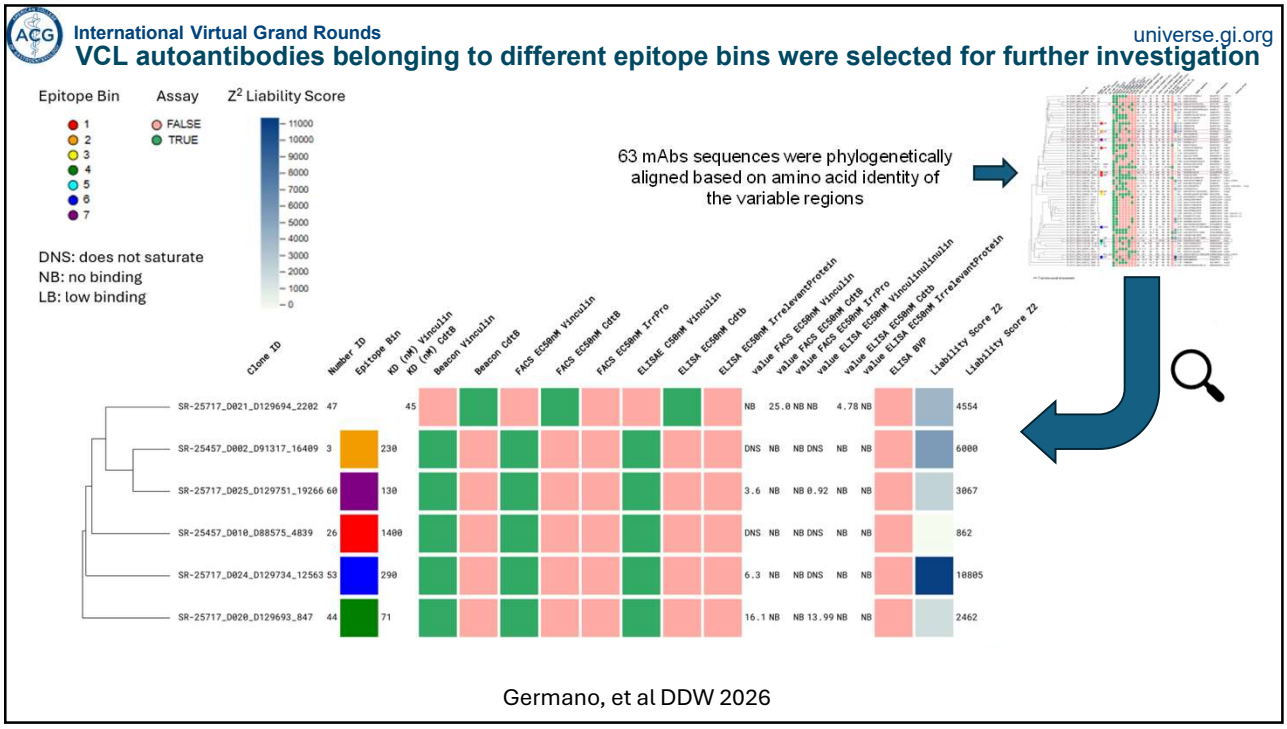
Vinculin Antibody Drug Development Update – DDW 2026

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Germano, et al DDW 2026

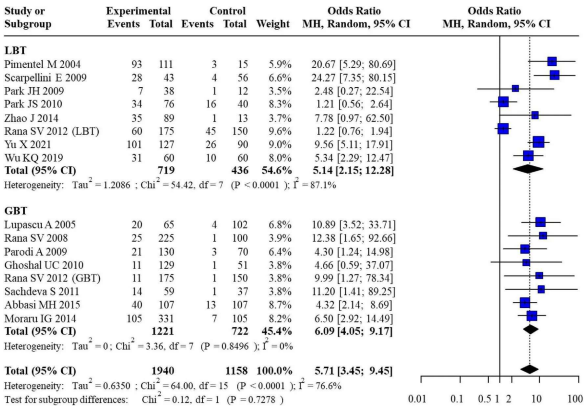
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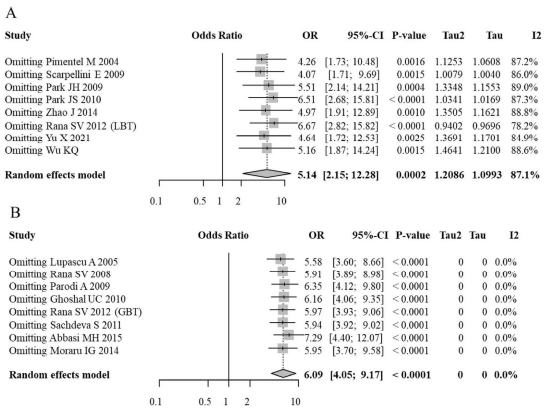
Germano, et al DDW 2026

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New meta-analysis



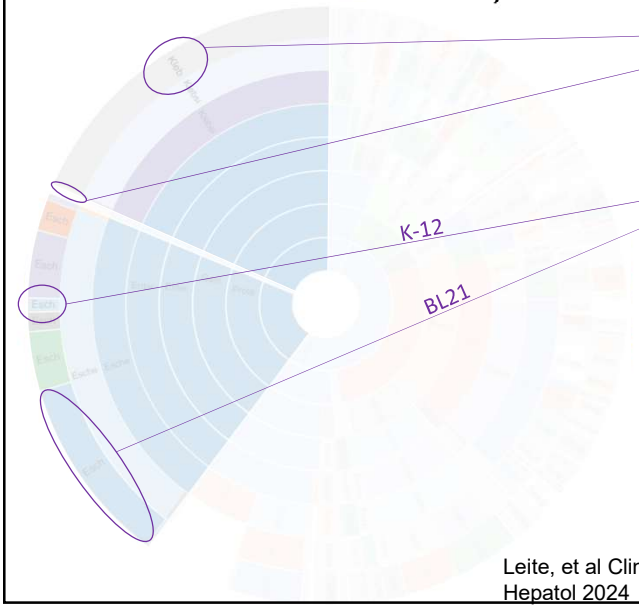
"Leave one out" analysis



Lu, et al. Front Microbiol March 2026

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SIBO is characterized by *Klebsiella* and *Escherichia coli*



- *Klebsiella pneumoniae* (~18% of the whole microbiome)
- *Klebsiella aerogenes* (less than 1% of the whole microbiome)

- *Escherichia coli* (~28% of the whole microbiome)
  - total of 8 potential strains were detected
  - 2 strains with more genomic similarities to the common strains BL21 and K-12 were more abundant in SIBO and associated with GI symptoms

Bacterial species/strains	SIBO vs. Non-SIBO (Log_2 fold change)	Adj-P-value
Klebsiella pneumoniae	22.39	< 0.0001
Klebsiella aerogenes	12.93	< 0.0001

Leite, et al Clinical Gastro Hepatol 2024

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Overgrowth of *Escherichia coli* and *Klebsiella* spp. in the small bowel is associated with enrichment of sugar degradation pathways and biogenic amines metabolism

	Detected pathway	SIBO vs. non-SIBO fold change	Adj. P-value
H_2 production	Glucose degradation	63.07	< 0.0001
	Galactose degradation	1.84	< 0.0001
	Mixed acid fermentation	1.22	< 0.0001

Leite, et al. Clin Gastroenterol Hepatol 2023

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Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus

Rezaie, et al. Am J Gastroenterol, 2018

Ali Rezaie, MD, MSc, FRCP(C)[1], Michelle Buresi, MD[2], Anthony Lembo, MD[3], Henry Lin, MD[4], Richard McCallum, MD[5], Satish Rao, MD[6], Max Schmulson, MD[7], Miguel Valdovinos, MD[8], Salam Zakko, MD[9], Mark Pimentel, MD, FRCP(C)[1] and on behalf of The North American Consensus group on hydrogen and methane-based breath testing

European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition consensus

Hammer, et al. United Europ Gastroenterol J, 2021

Heinz F. Hammer[1] | Mark R. Fox[2,3] | Jutta Keller[4] | Silvia Salvatore[5] | Guido Basilisco[6] | Johann Hammer[7] | Loris Lopetuso[8,9] | Marc Benninga[10] | Osvaldo Borrelli[11] | Dan Dumitrascu[12] | Bruno Hauser[13] | Laszlo Herszenyi[14] | Radislav Nakov[15] | Daniel Pohl[3] | Nikhil Thapar[11,16] | Marc Sonyi[1,17] | European H_2-CH_4-breath test group

Asian-Pacific consensus on small intestinal bacterial overgrowth in gastrointestinal disorders: An initiative of the Indian Neurogastroenterology and Motility Association

Ghoshal, et al. Ind J Gastroenterol, 2022

Uday C. Ghoshal[1] · Sanjeev Sachdeva[2] · Ujjala Ghoshal[3] · Asha Misra[1] · Amarender Singh Puri[2] · Nitesh Pratap[4] · Ayesha Shah[5] · M. Masudur Rahman[6] · Kok Ann Gwee[7,8] · Victoria P Y Tan[9] · Tahmeed Ahmed[10] · Yeong Yeh Lee[11,12] · B S Ramakrishna[13] · Rupjyoti Talukdar[14] · S V Rana[15] · Saroj K Sinha[16] · Minhu Chen[17] · Nayoung Kim[18] · Gerald Holtmann[5]

DIAGNOSIS AND TREATMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH: AN OFFICIAL POSITION PAPER FROM THE BRAZILIAN FEDERATION OF GASTROENTEROLOGY

Diagnóstico e tratamento do supercrescimento bacteriano no intestino delgado: um posicionamento oficial da Federação Brasileira de Gastroenterologia



1. Mostly agree about criteria for SIBO
2. Mostly agree about dosing for substrates
3. Mostly agree that SIBO and IBS are interrelated

GUIDELINES

Annals of Gastroenterology (2026) **39**, 383-389

A national consensus guideline on the performance and interpretation of hydrogen- and methane-based breath tests for carbohydrate malabsorption, small intestinal bacterial overgrowth, and intestinal methanogen overgrowth

Tsachi Tsadok Perets[a,b], Tamar Thurm[c,d], Meirav Ben-Yehoyada[c,d], Liat Deutsch[c,d], Yishai Ron[c,d], Ronnie Baruch[c,d], Eva Niv[e], Tiberiu Hershcovici[f], Orit Picard[g,d], Tal Engel[h,d], Tsili Zangen[h,d], Sigal Frishman[i], Ram Dickman[a,d]

REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

GUÍAS Y CONSENSOS

Consenso argentino sobre la utilidad clínica de las pruebas de aire espirado y manejo del sobrecrecimiento microbiano intestinal en pacientes con trastornos de la interacción intestino-cerebro

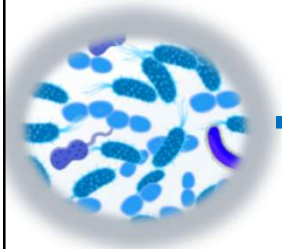
L.O. Soifer[a,*], M.V. Contreras[b], F. Man[c] y A. González-Flórez[d]

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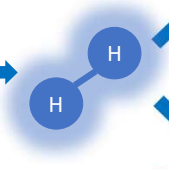
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There are 3 Main Gases that must be Measured

Hydrogen Producers

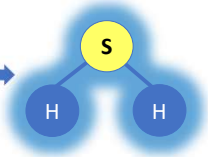


Typical SIBO H_2 is *E. coli* and *Klebsiella*[1] from inside the small intestine



Hydrogen Sulfide Producers

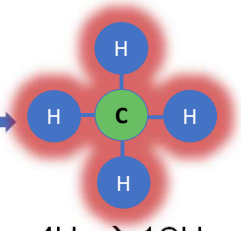
Many H_2S producers



$5H_2 \rightarrow 1H_2S$

Methane Producers

Methanogens such as *M. smithii*[2] found in colon and small bowel[3]



$4H_2 \rightarrow 1CH_4$

Phenotype

-Diarrhea
-Pain
-Urgency

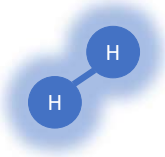
-Constipation
-Discomfort
-Bloating

[1]Leite, et al. PlosOne 2019.
[2]Kunkel, et al. Dig Dis Sci 2011.
[3]Villanueva, et al. DDW 2022.

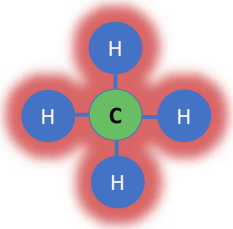
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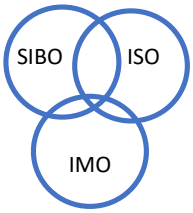
Three Gas Microtypes

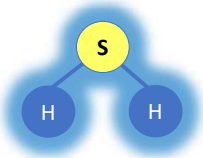


Small Intestinal Bacterial Overgrowth (SIBO)



Intestinal Methanogen Overgrowth (IMO)



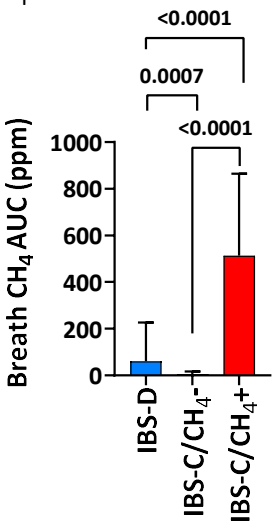


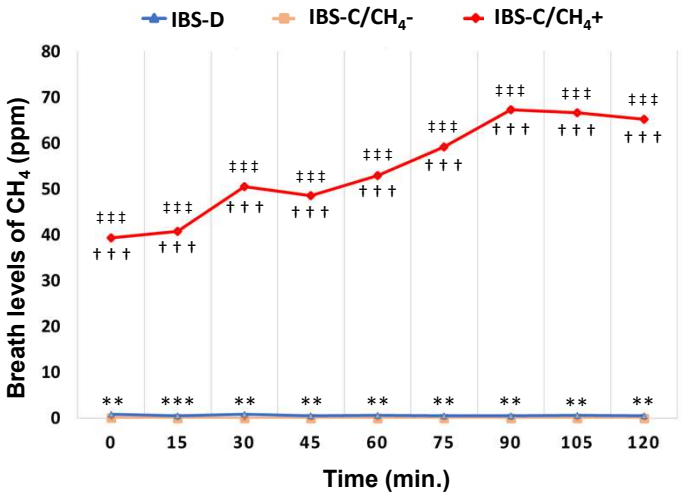
Intestinal Sulfide Overproduction (ISO)

28

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CH_4 Levels Are Not Elevated In IBS-D Subjects





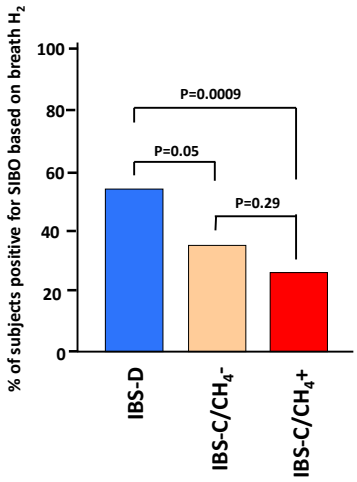
**P < 0.01; ***P < 0.001 IBS-D vs IBS-C/CH_4-
†††P < 0.001 IBS-D vs IBS-C/CH_4+
‡‡‡P < 0.001 IBS-C/CH_4- vs IBS-C/CH_4+

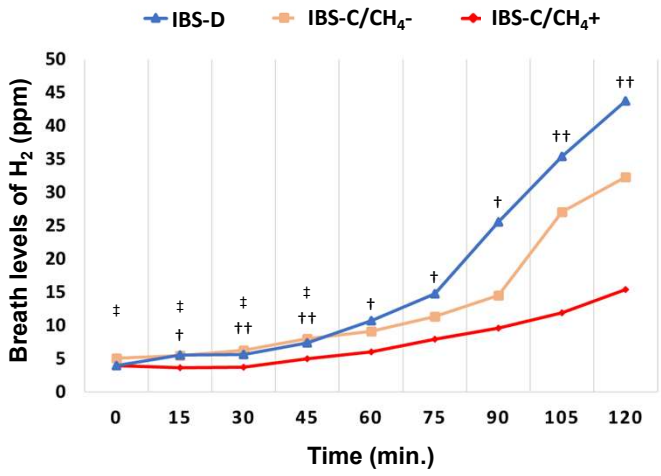
Villanueva, et al. Am J Gastroenterol, 2022

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H_2 Levels Are Elevated In IBS-D Subjects





SIBO: ≥ 20ppm rise in H_2 from baseline

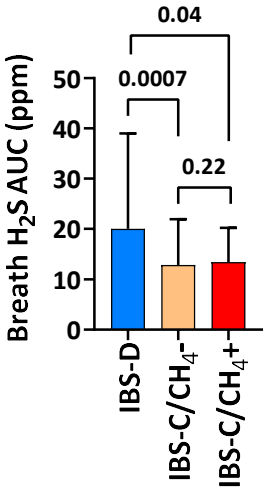
†P < 0.05; ††P < 0.01 IBS-D vs IBS-C/CH_4+
‡P < 0.05 IBS-C/CH_4- vs IBS-C/CH_4+

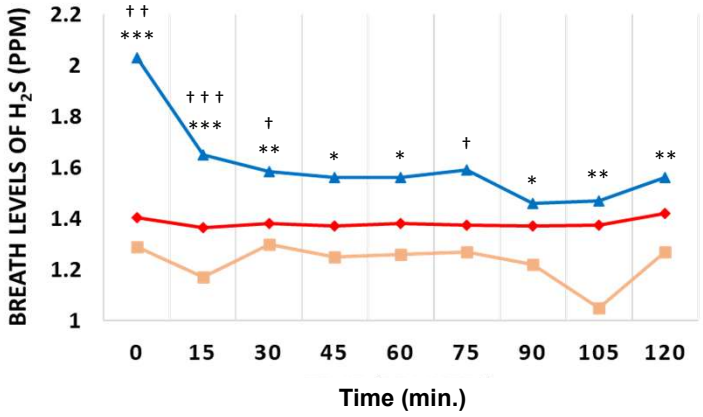
Villanueva, et al. Am J Gastroenterol, 2022

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H_2S Levels Are Elevated In IBS-D Subjects





*P < 0.05; **P < 0.01; ***P < 0.001 IBS-D vs IBS-C/CH_4-
†P < 0.05; ††P < 0.01; †††P < 0.001 IBS-D vs IBS-C/CH_4+

Villanueva, et al. Am J Gastroenterol, 2022

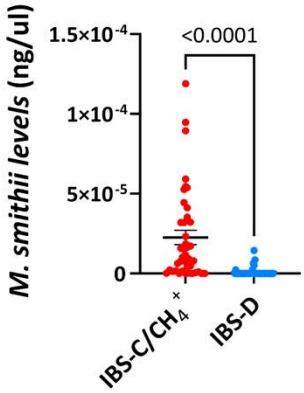
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Methanogens in IBS-C vs IBS-D

IBS-C subjects had higher abundance of family Methanobacteriaceae and species *Methanobrevibacter smithii*

Methanobrevibacter smithii positively correlated with breath CH_4 and negatively correlated with H_2



Breath test time point (minutes)	Absolute load of *M. smithii* (qPCR)			
	Methane levels		Hydrogen levels	
	R	P-value	R	P-value
0	0.410	0.003	-0.047	0.750
15	0.478	0.001	0.073	0.621
30	0.480	<0.0001	0.045	0.759
45	0.533	<0.0001	0.100	0.494
60	0.540	<0.0001	-0.019	0.897
75	0.564	<0.0001	-0.179	0.217
90	0.545	<0.0001	-0.265	0.065
105	0.560	<0.0001	-0.375	0.008
120	0.492	<0.0001	-0.332	0.020

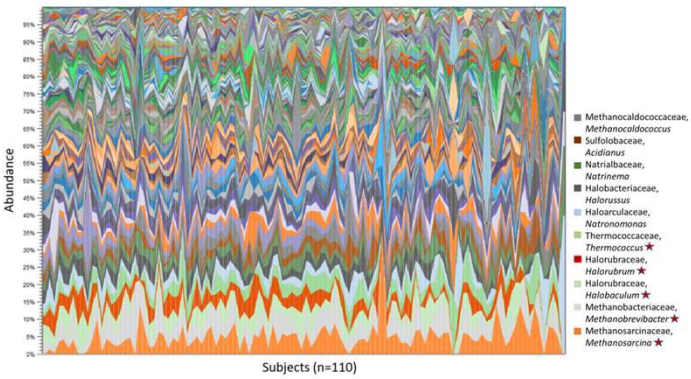
All subjects pooled (n=81)

Villanueva, et al. Am J Gastroenterol, 2022

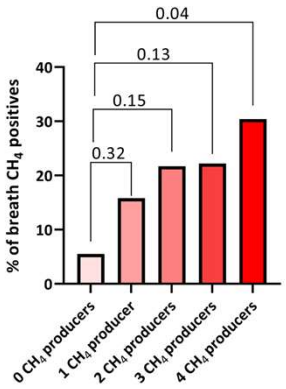
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Methane on Breath Test Reflects the Small Bowel



The Archaeome in the small intestine



Breath Methane and Methanogens

N=110 subjects with small bowel aspirate and shotgun sequencing
Of the 110 subject, 22 had IMO based on single baseline breath test

Villanueva-Milan, et al. Dig Dis Sci 2024

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Methanogens in small bowel and CH_4 on Breath

	Archaeal species	Prevalence (n=110)	Correlation with methane		Correlation with *M. smithii*		Methane production
			R	P value	R	P value	
1	***Methanothermococcus okinawensis***	40%	0.319	0.001	0.282	0.003	Uses H_2 and CO_2 as sole sources of energy and carbon. Formate can be used as an alternative source
2	***Halomicroarcula sp. SHR3***	55.45%	0.291	0.002	0.194	0.042	Not enough information
3	***Halarchaeum* sp. CBA1220**	63.64%	0.277	0.003	No	No	Contains enzymes for methane metabolism
4	***Thermococcus argininiproducens***	29.09%	0.226	0.017	0.277	0.003	Contains enzymes for methane metabolism
5	***Methanobrevibacter smithii***	**63.64%**	**0.221**	**0.02**	**N/A**	**N/A**	**Uses H_2 and CO_2 as sole sources of energy and carbon. Formate can be used as an alternative source**
6	***Candidatus Nitrosotenuis cloacae***	36.36%	0.209	0.028	0.379	<0.0001	Contains enzymes for methane metabolism
7	***Halobacterium litoreum***	57.27%	0.209	0.028	0.312	0.025	Contains enzymes for methane metabolism
8	***Desulfurococcus mucosus***	27.27%	0.19	0.046	No	No	Contains enzymes for methane metabolism
9	***Halobaculum rubrum***	61.82%	0.188	0.049	No	No	Contains enzymes for methane metabolism

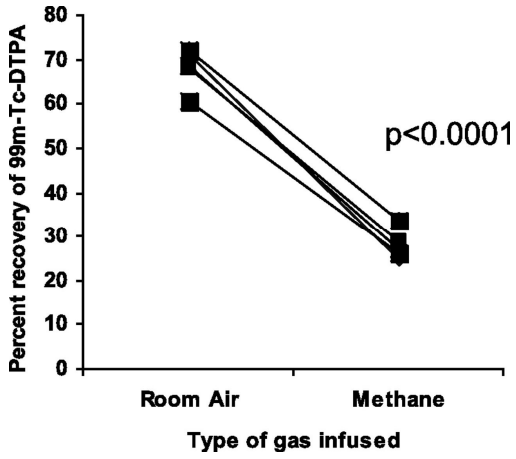
Villanueva-Milan, et al. Dig Dis Sci 2024

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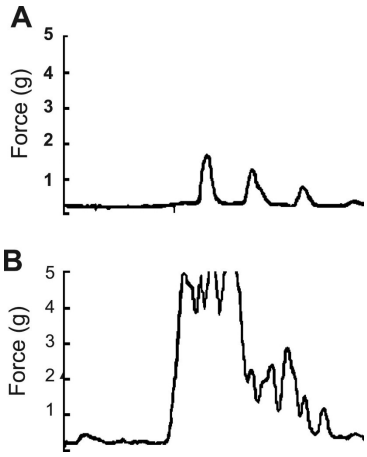
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Methane and Gut Physiology

Small bowel transit time in animals
-Room air or methane infused in gut



Peristaltic reflex intensity after brush stroke



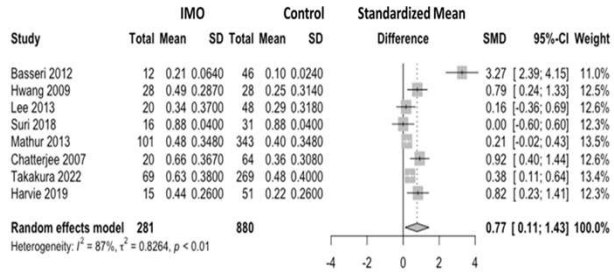
Pimentel, et al. Am J Phsyiol 2006

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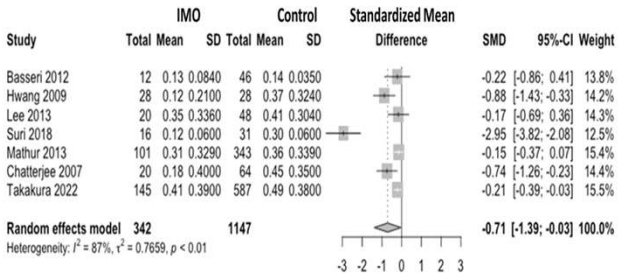
Intestinal Methanogen Overgrowth (IMO) Meta-analysis of CH_4 and Symptoms

A)



MORE CONSTIPATION WITH CH_4

B)



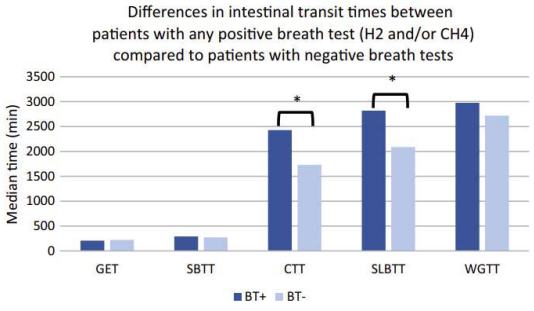
LESS DIARRHEA WITH CH_4

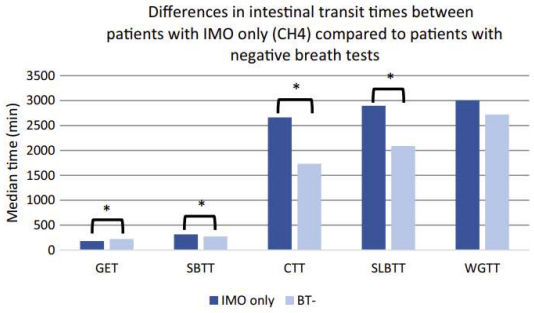
Mehravar, et al. Clin Gastroenterol Hepatol 2024

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IMO and Small bowel/Colonic transit





Wireless capsule in SIBO/IMO and non BT-ve groups

Talamantes, et al. Dig Dis Sci 2024

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Duodenal H_2S producers were associated with H_2S on Breath

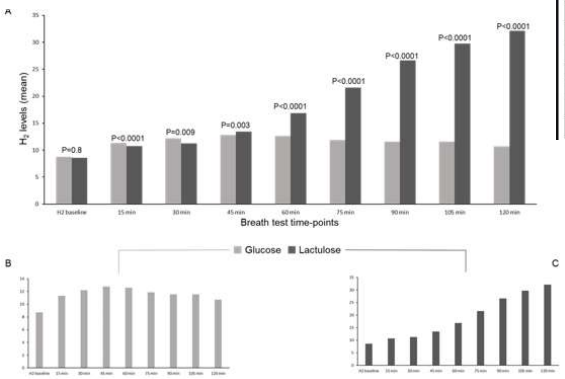
	Bacterial H_2S producers	Prevalence	R	P value
1	*Proteus mirabilis*	77.98%	0.313	0.001
2	*Desulfobulbus oralis*	71.6%	0.194	0.043
3	*Desulfovibrio desulfuricans*	64.2%	0.210	0.028
4	*Desulfuromonas sp.* DDH964	56.9%	0.242	0.011
5	*Desulfosarcina widdelii*	55%	0.243	0.011
6	*Desulfurispirillum indicum*	53.2%	0.229	0.017
7	*Desulfobulbus oligotrophicus*	51.4%	0.202	0.035
8	*Desulfoluna limicola*	41.3%	0.189	0.049



Villanueva-Milan, et al. Dig Dis Sci 2024

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Glucose vs Lactulose



	Glucose	Lactulose	
	Count (%)	Count (%)	P-value*
No-SIBO/No-IMO/No-ISO2.0	707 (62.5%)	800 (42.7%)	
SIBO only	82 (7.3%)	505 (27%)	<0.0001
IMO only	222 (19.6%)	272 (14.5%)	0.44
ISO 2.0 only	60 (5.3%)	89 (4.8%)	0.12
SIBO/IMO (no ISO 2.0)	19 (1.7%)	100 (5.3%)	<0.0001
SIBO/ISO 2.0 (no IMO)	12 (1.1%)	53 (2.8%)	<0.0001
IMO/ISO 2.0 (no SIBO)	26 (2.3%)	40 (2.1%)	0.23
SIBO/IMO/ISO 2.0	3 (0.3%)	14 (0.7%)	0.02

1. Glucose misses people who might benefit
2. Glucose works well for H_2S and CH_4

Pimentel, et al. J Clin Gastroenterol 2026 (epub)

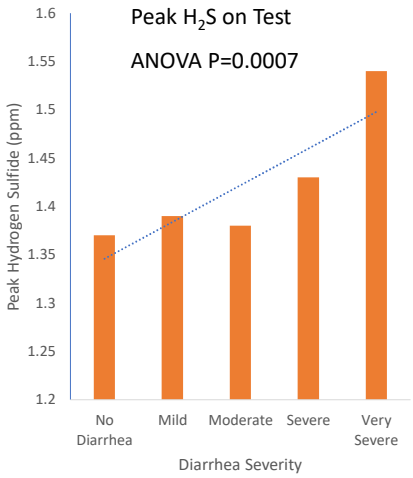
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Real World Study – H_2S and Diarrhea/Urgency

DIARRHEA SEVERITY

Peak H_2S on Test

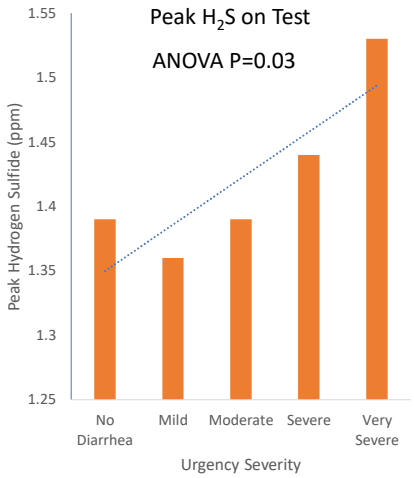
ANOVA P=0.0007



URGENCY SEVERITY

Peak H_2S on Test

ANOVA P=0.03



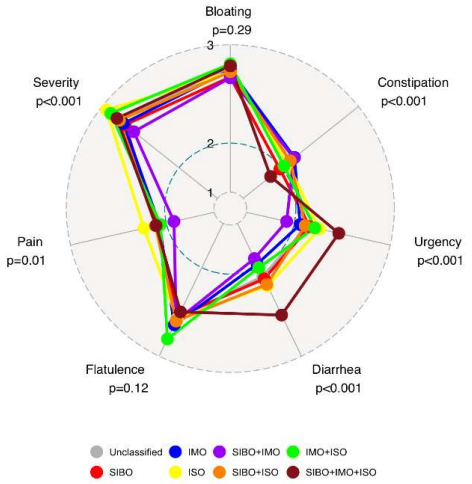
Range of H2S=0.44-4.55

Note:
No correlation with bloating or abdominal pain severity

Pimentel, et al. J Clin Gastroenterol 2026 (epub)

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H_2S≥2ppm presence or absence is the most important determinant of symptoms



Elevated H_2S

- -Diarrhea dominates
- -More severe diarrhea
- -More severe pain
- -More severe urgency

Normal H_2S Positive CH_4

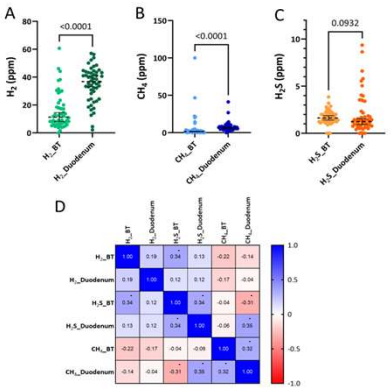
- -Constipation dominates

Only H_2 – milder diarrhea

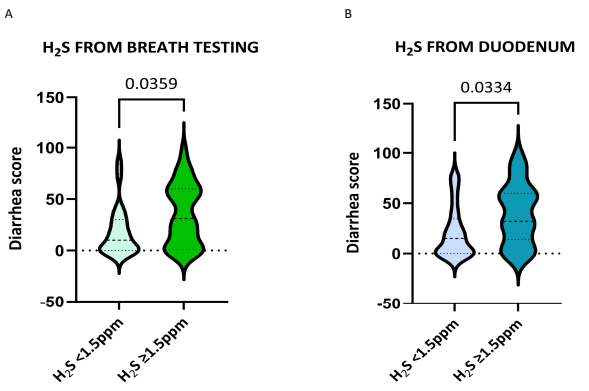
Pimentel, et al. J Clin Gastroenterol 2026 (epub)

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Breath H_2S and CH_4 = Duodenal gas production



H_2S (breath or duodenum) = more severe diarrhea scores



Villanueva-Millan, et al. DDW 2026

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What H_2S does to you….

Functional Change	Finding	Function/Impact
Mitochondrial	↑TXN2	Cells high in TXN2 are more resistant to redox changes
Redox	↓CTH	Reduction in the key enzyme responsible for endogenous H_2S production
	↓SLC7A11	Low levels would produce a pro-oxidative state in the cell
	↑SOD1	Encourages H_2O_2 production (oxidative) Interacts with aquaporin 9 to secrete H_2O_2 Counteracts H_2S
Gut Motor Function	↑HTR3e receptor	Serotonin receptor for sensation
	↓Piezo 2	Detects luminal distension and affects serotonin release and HTR3e function. Increases gut water content.
	↑Serotonin	Binds to HTR3e and other receptors controlling peristalsis and visceral sensation
Aquaporins	↓aquaporin 6	Ion transport
	↑aquaporin 7	Glycerol absorption
	↓aquaporin 9	Reduction in hydrogen peroxide absorption by cells
Defensins	↑DefensinB1	Antimicrobial peptide that is highly sensitive to redox. Highly active when reduced.
Neuroendocrine	↑SST	Expect an increase in somatostatin which affects gut motility

Germano, et al. mSystems 2026

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Conclusion

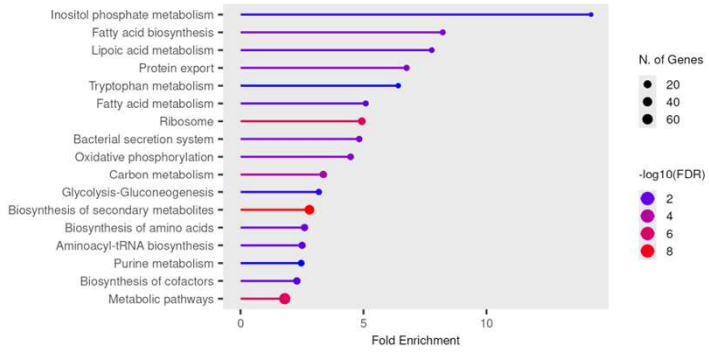
ISO in humans		H_2S-producers gavaged animals	*E. coli* BL21
✓	Δ Mitochondrial pathways	✓	
✓	Δ Response to oxidative stress	✓	
✓	Δ Transcription/splicing pathways	✓	
✓	Δ Immune response pathways	✓	✓
✓	Δ Fluid homeostasis	✓	✓
✓	Δ Nociception	✓	
✓	Δ Motility	✓	

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Metatranscriptomics profile of the duodenal microbiome in SIBO positive by culture vs not



>200 pathways up or downregulated

Pathways associated with H_2 production are upregulated

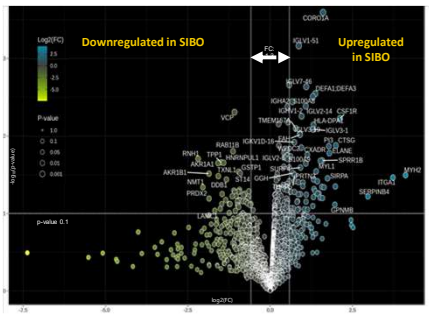
Germano, et al. DDW 2026

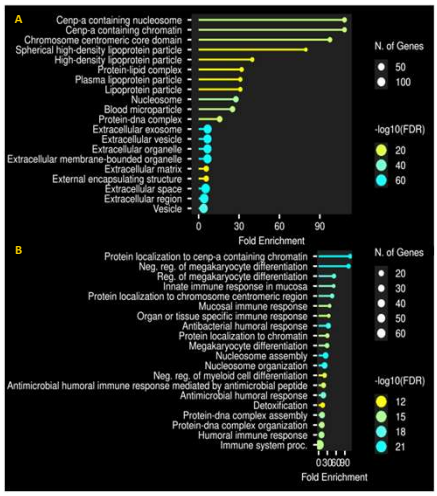
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Proteomics profile of SIBO





-Neutrophil activation

-Defensins

-Increased luminal Immunoglobulins

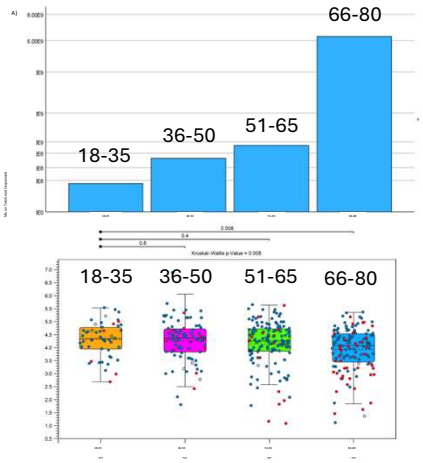
Hendricks, et al. DDW 2026

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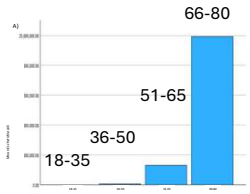
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SIBO increases with age (absolute abundance assessment)

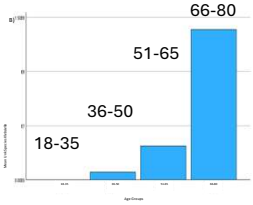
Total bacterial load by age



E. coli levels in duodenum by age



Klebsiella levels in duodenum by age



ALSO…

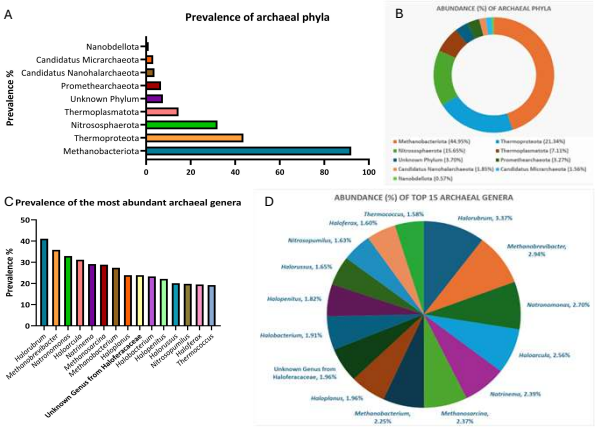
More *E. coli* (H_2 producer) and more *Fusobacterium* (H_2S producer) meant greater diarrhea in the elderly

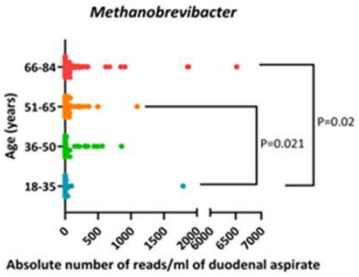
Leite, et al. DDW 2026

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Methanogens are in the small intestine AND Older age also means more methanogens

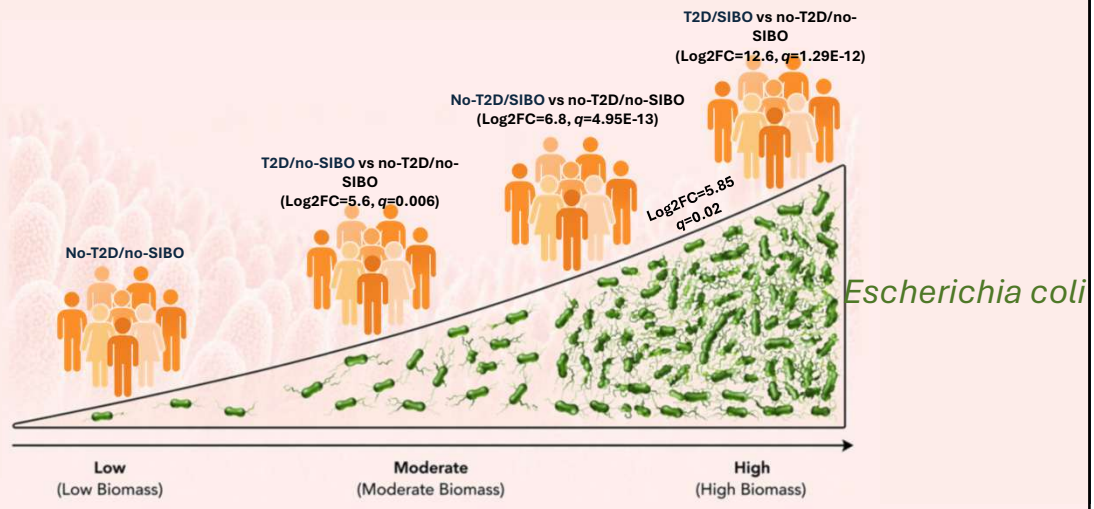




Villanueva-Millan, et al. DDW 2026

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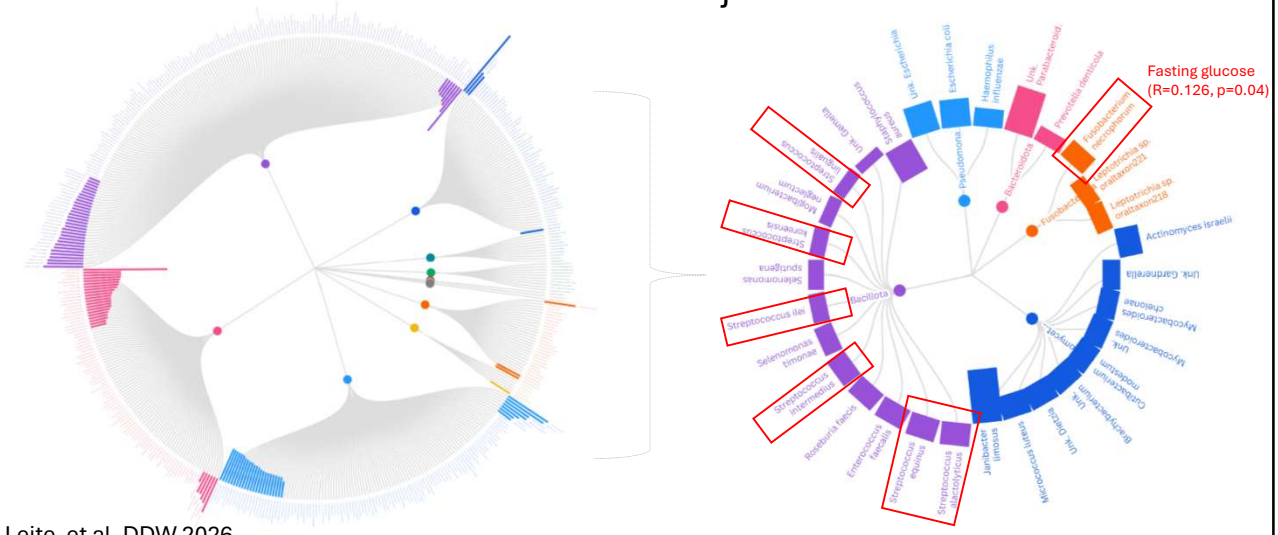
Duodenal *Escherichia coli* absolute abundance is substantially associated with T2D and SIBO co-positivity



Leite, et al. DDW 2026

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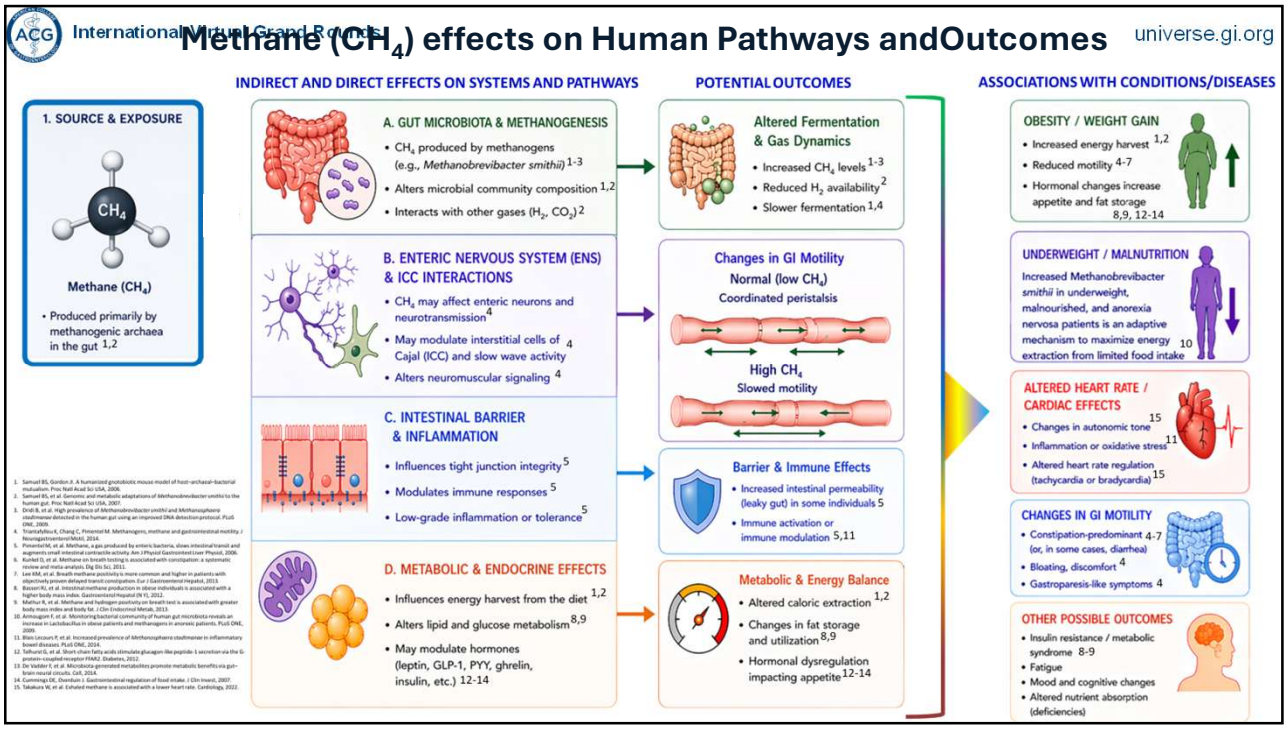
Several *Streptococcus* species and *Fusobacterium necrophorum* are enriched in the small bowel of subjects with T2D



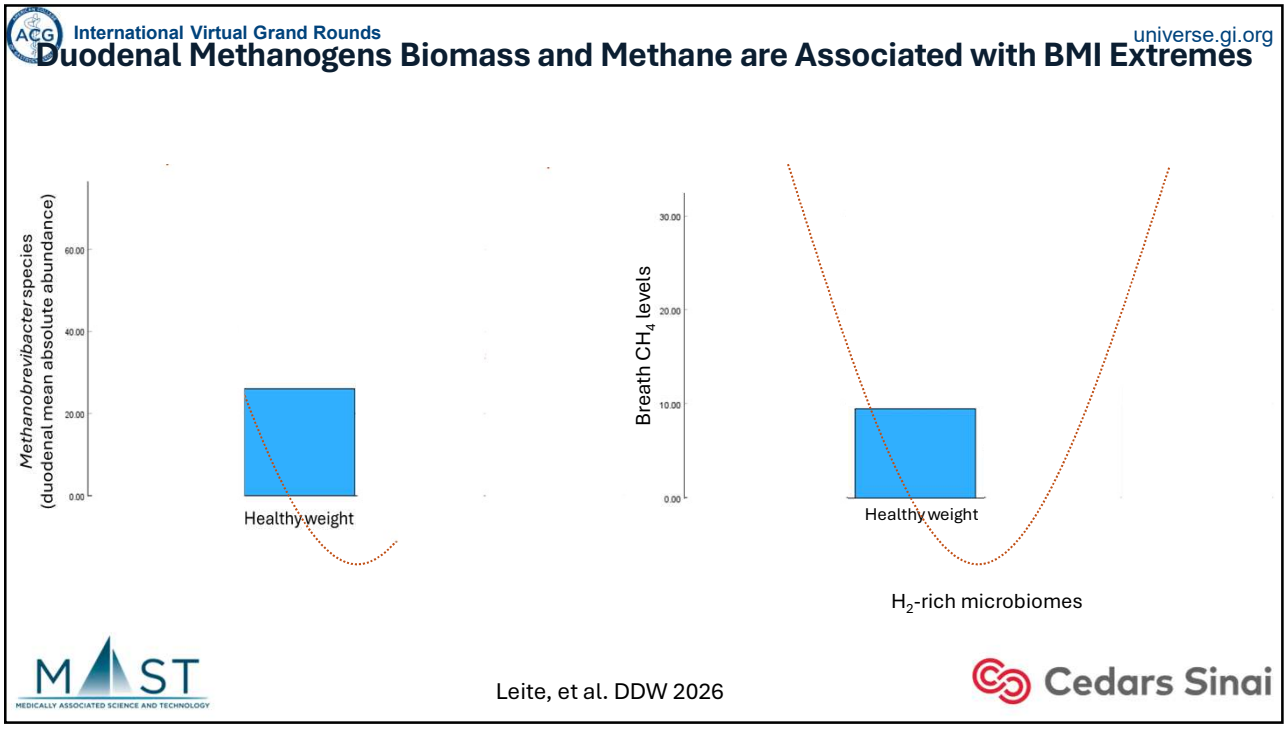
Leite, et al. DDW 2026

*Results were corrected for age, BMI, and SIBO

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Methane (CH_4) effects on Human Pathways andOutcomes
universe.gi.org
INDIRECT AND DIRECT EFFECTS ON SYSTEMS AND PATHWAYS
POTENTIAL OUTCOMES
ASSOCIATIONS WITH CONDITIONS/DISEASES
1. SOURCE & EXPOSURE
Methane (CH_4)
• Produced primarily by methanogenic archaea in the gut 1,2
A. GUT MICROBIOTA & METHANOGENESIS
• CH_4 produced by methanogens (e.g., Methanobrevibacter smithii) 1-3
• Alters microbial community composition 1,2
• Interacts with other gases (H_2, CO_2) 2
B. ENTERIC NERVOUS SYSTEM (ENS) & ICC INTERACTIONS
• CH_4 may affect enteric neurons and neurotransmission 4
• May modulate interstitial cells of Cajal (ICC) and slow wave activity 4
• Alters neuromuscular signaling 4
C. INTESTINAL BARRIER & INFLAMMATION
• Influences tight junction integrity 5
• Modulates immune responses 5
• Low-grade inflammation or tolerance 5
D. METABOLIC & ENDOCRINE EFFECTS
• Influences energy harvest from the diet 1,2
• Alters lipid and glucose metabolism 8,9
• May modulate hormones (leptin, GLP-1, PYY, ghrelin, insulin, etc.) 12-14
Altered Fermentation & Gas Dynamics
• Increased CH_4 levels 1-3
• Reduced H_2 availability 2
• Slower fermentation 1,4
Changes in GI Motility
Normal (low CH_4)
Coordinated peristalsis
High CH_4
Slowed motility
Barrier & Immune Effects
• Increased intestinal permeability (leaky gut) in some individuals 5
• Immune activation or immune modulation 5,11
Metabolic & Energy Balance
• Altered caloric extraction 1,2
• Changes in fat storage and utilization 8,9
• Hormonal dysregulation impacting appetite 12-14
OBESITY / WEIGHT GAIN
• Increased energy harvest 1,2
• Reduced motility 4-7
• Hormonal changes increase appetite and fat storage 8,9, 12-14
UNDERWEIGHT / MALNUTRITION
Increased Methanobrevibacter smithii in underweight, malnourished, and anorexia nervosa patients is an adaptive mechanism to maximize energy extraction from limited food intake 10
ALTERED HEART RATE / CARDIAC EFFECTS
• Changes in autonomic tone 15
• Inflammation or oxidative stress 11
• Altered heart rate regulation (tachycardia or bradycardia) 15
CHANGES IN GI MOTILITY
• Constipation-predominant 4-7 (or, in some cases, diarrhea)
• Bloating, discomfort 4
• Gastroparesis-like symptoms 4
OTHER POSSIBLE OUTCOMES
• Insulin resistance / metabolic syndrome 8-9
• Fatigue
• Mood and cognitive changes
• Altered nutrient absorption (deficiencies)

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International Virtual Grand Rounds
universe.gi.org
Duodenal Methanogens Biomass and Methane are Associated with BMI Extremes
Methanobrevibacter species (duodenal mean absolute abundance)
60.00
40.00
20.00
0.00
Healthy weight
Breath CH_4 levels
30.00
20.00
10.00
0.00
Healthy weight
H_2-rich microbiomes
MAST
MEDICALLY ASSOCIATED SCIENCE AND TECHNOLOGY
Leite, et al. DDW 2026
Cedars Sinai

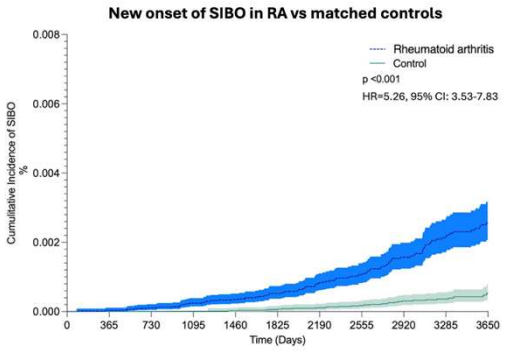
52

SIBO in Rheumatoid Arthritis

REIMAGINE population characteristics

Variable	RA group	Non-RA group	P-Value
N	77	987	—
Age (yrs)*	62.9 ± 13.4	55.7 ± 15.5	<0.001
Female (%)	76.6%	53.7%	<0.001
BMI (kg/m^2)*	28.5 ± 8.3	26.0 ± 6.2	0.013
SIBO positive (n)	22	171	0.0034

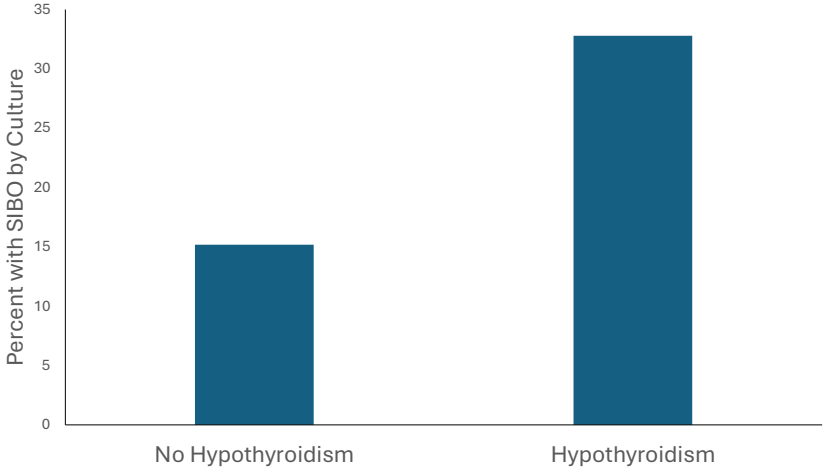
*Continuous variables are represented as mean ± SD



Bustos, et al. DDW 2026

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SIBO and Hypothyroidism



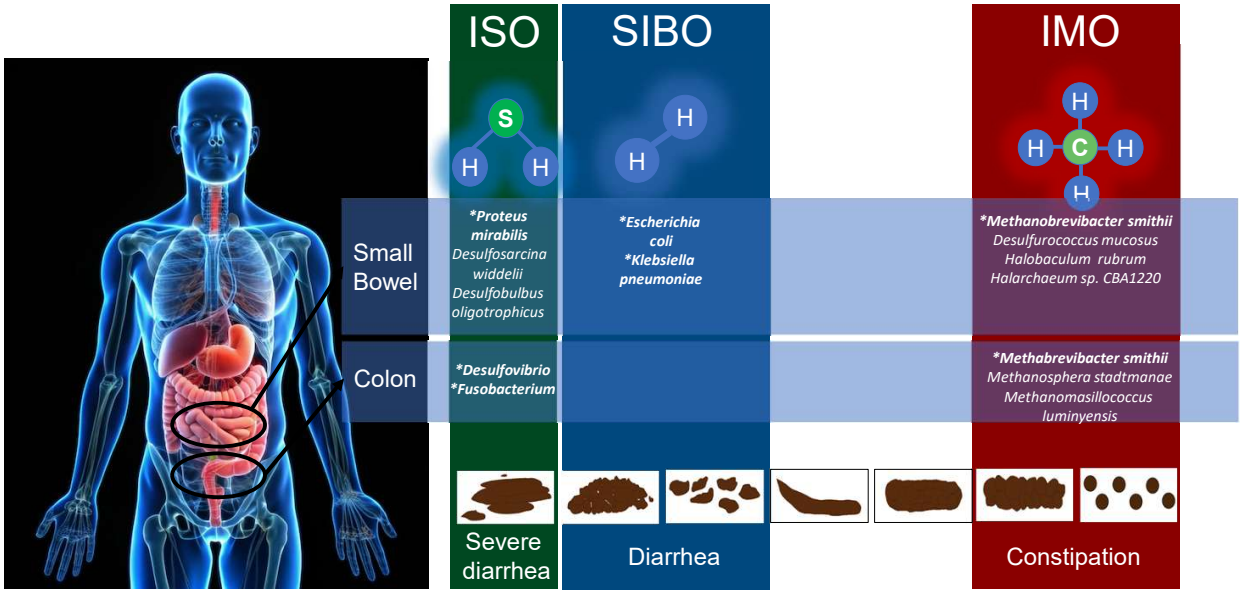
Wei, et al. J Clin Endocrinol Metab 2025

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IBS DISEASE MICROTYPES



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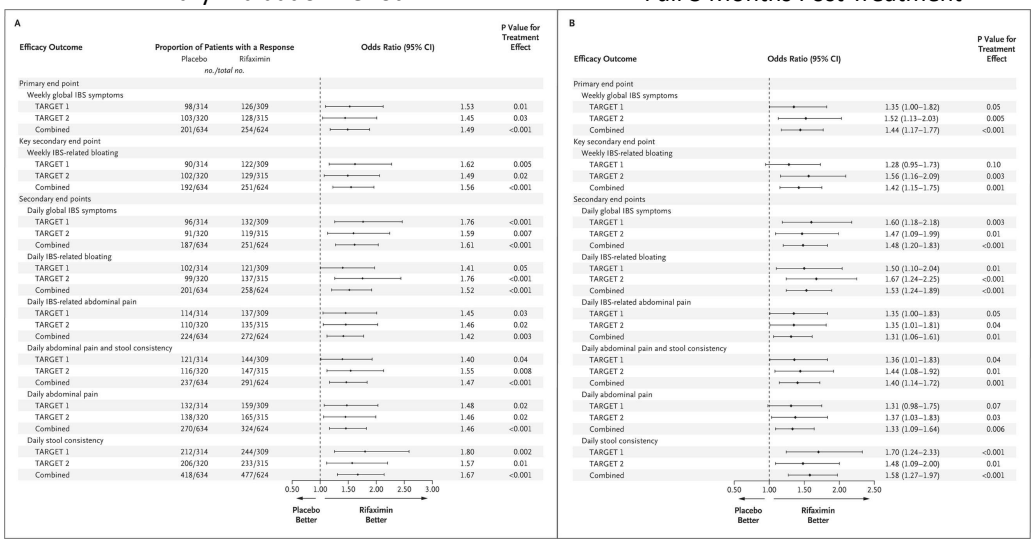
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Rifaximin Benefits in IBS

Primary Evaluation Period

Full 3 Months Post Treatment



A

Efficacy Outcome	Proportion of Patients with a Response: Placebo (no./total no.)	Proportion of Patients with a Response: Rifaximin (no./total no.)	Odds Ratio (95% CI)	P Value for Treatment Effect
Primary end point				
Weekly global IBS symptoms				
TARGET 1	98/314	126/309	1.53	0.01
TARGET 2	103/320	128/315	1.45	0.03
Combined	201/634	254/624	1.49	<0.001
Key secondary end point				
Weekly IBS-related bloating				
TARGET 1	90/314	122/309	1.62	0.005
TARGET 2	102/320	129/315	1.49	0.02
Combined	192/634	251/624	1.56	<0.001
Secondary end points				
Daily global IBS symptoms				
TARGET 1	96/314	132/309	1.76	<0.001
TARGET 2	91/320	119/315	1.59	0.007
Combined	187/634	251/624	1.61	<0.001
Daily IBS-related bloating				
TARGET 1	102/314	121/309	1.41	0.05
TARGET 2	99/320	137/315	1.76	<0.001
Combined	201/634	258/624	1.52	<0.001
Daily IBS-related abdominal pain				
TARGET 1	114/314	137/309	1.45	0.03
TARGET 2	110/320	135/315	1.46	0.02
Combined	224/634	272/624	1.42	0.003
Daily abdominal pain and stool consistency				
TARGET 1	121/314	144/309	1.40	0.04
TARGET 2	116/320	147/315	1.55	0.008
Combined	237/634	291/624	1.47	<0.001
Daily abdominal pain				
TARGET 1	132/314	159/309	1.48	0.02
TARGET 2	138/320	165/315	1.46	0.02
Combined	270/634	324/624	1.46	<0.001
Daily stool consistency				
TARGET 1	212/314	244/309	1.80	0.002
TARGET 2	206/320	233/315	1.57	0.01
Combined	418/634	477/624	1.67	<0.001

0.50 1.00 1.50 2.00 2.50 3.00

Placebo Better — Rifaximin Better

B

Efficacy Outcome	Odds Ratio (95% CI)	P Value for Treatment Effect
Primary end point		
Weekly global IBS symptoms		
TARGET 1	1.35 (1.00–1.82)	0.05
TARGET 2	1.52 (1.13–2.03)	0.005
Combined	1.44 (1.17–1.77)	<0.001
Key secondary end point		
Weekly IBS-related bloating		
TARGET 1	1.28 (0.95–1.73)	0.10
TARGET 2	1.56 (1.16–2.09)	0.003
Combined	1.42 (1.15–1.75)	0.001
Secondary end points		
Daily global IBS symptoms		
TARGET 1	1.60 (1.18–2.18)	0.003
TARGET 2	1.47 (1.09–1.99)	0.01
Combined	1.48 (1.20–1.83)	<0.001
Daily IBS-related bloating		
TARGET 1	1.50 (1.10–2.04)	0.01
TARGET 2	1.67 (1.24–2.25)	<0.001
Combined	1.53 (1.24–1.89)	<0.001
Daily IBS-related abdominal pain		
TARGET 1	1.35 (1.00–1.83)	0.05
TARGET 2	1.35 (1.01–1.81)	0.04
Combined	1.31 (1.06–1.61)	0.01
Daily abdominal pain and stool consistency		
TARGET 1	1.36 (1.01–1.83)	0.04
TARGET 2	1.44 (1.08–1.92)	0.01
Combined	1.40 (1.14–1.72)	0.001
Daily abdominal pain		
TARGET 1	1.31 (0.98–1.75)	0.07
TARGET 2	1.37 (1.03–1.83)	0.03
Combined	1.33 (1.09–1.64)	0.006
Daily stool consistency		
TARGET 1	1.70 (1.24–2.33)	<0.001
TARGET 2	1.48 (1.09–2.00)	0.01
Combined	1.58 (1.27–1.97)	<0.001

0.50 1.00 1.50 2.00 2.50

Placebo Better — Rifaximin Better

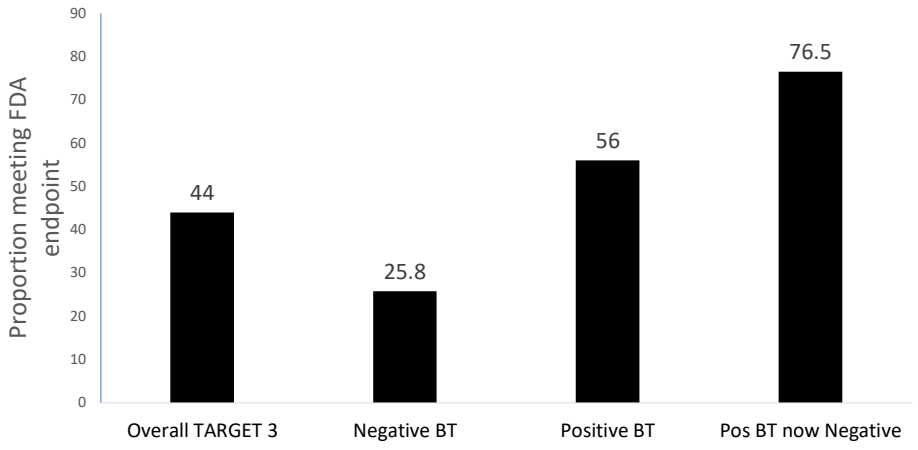
Pimentel, et al. N Engl J Med 2011

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Breath Testing Predicts Rifaximin Response



Rezaie, et al., Am J Gastroenterol 2019

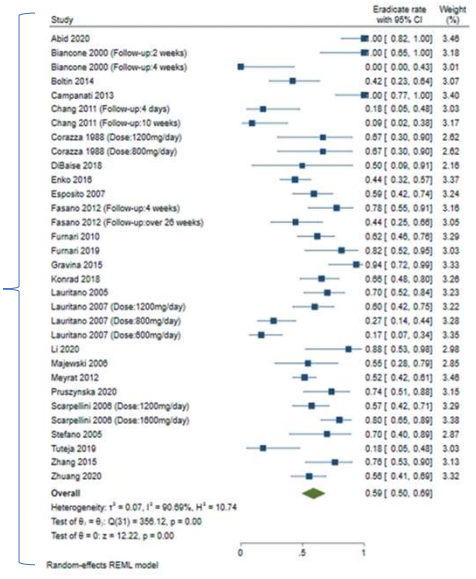
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Meta-analysis of Rifaximin for SIBO

32 Studies



Wang, et al. Expert Rev Gastroenterol Hepatol 2021

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SIBO Predicts Response to Antibiotics in IBS

Author(s) and year	SIBO Event	SIBO Nonevent	Control Event	Control Nonevent	Weight (%)	Relative ratio [95% CI]
Pimentel, 2003	25	21	6	3	16.35%	1.37 [0.52, 3.64]
Ghoshal, 2016	7	12	18	3	12.82%	4.42 [1.47, 13.31]
Rezaie, 2019	25	37	23	8	39.14%	2.31 [1.23, 4.35]
Zhuang, 2020	27	18	25	8	31.69%	1.65 [0.82, 3.33]
RE model for all studies (Q = 3.03, df = 3, P = 0.390; I^2 = 0.01%, τ^2 = 0.00)					100.00%	2.07 [1.40, 3.08]

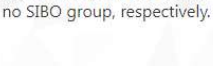


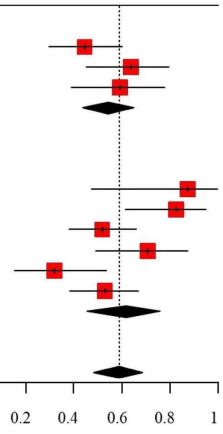
Fig. 3. Forrest plot of studies comparing the efficacy of antibiotics in irritable bowel syndrome (IBS) patients with or without small intestinal bacterial overgrowth (SIBO). The pooled response rate was 51.2% vs 23.4% in the SIBO and no SIBO group, respectively. Relative risk (95% CI) for improvement was 2.07 (1.40-3.08), P = 0.0003. Heterogeneity was I^2 = 0.01%, P = 0.300.

Takakura, et al. J Neurogastroenterol Motil 2024

59

Newest meta-analysis on rifaximin in IBS with SIBO

Study or Subgroup	Events	Total	GLMM, Random, 95% CI
600-800mg/d			
Zhuang X 2020	20	45	0.44 [0.30; 0.60]
Scarpellini E 2013	21	33	0.64 [0.45; 0.80]
von Muhlenbrock C 2025	16	27	0.59 [0.39; 0.78]
Total (95% CI)		**105**	**0.55 [0.44; 0.65]**
Heterogeneity: Tau^2 = 0.0186 ; Chi^2 = 3.15, df = 2 (P = 0.2071); I^2 = 36.5%			
>=1200 mg/d			
Moraru IG 2013	7	8	0.88 [0.47; 1.00]
Cuoco L 2006	19	23	0.83 [0.61; 0.95]
Peralta S 2009	28	54	0.52 [0.38; 0.66]
Parodi A 2009	17	24	0.71 [0.49; 0.87]
García-Cedillo MF 2025	8	25	0.32 [0.15; 0.54]
Barkin JA 2019	28	53	0.53 [0.39; 0.67]
Total (95% CI)		**187**	**0.62 [0.45; 0.76]**
Heterogeneity: Tau^2 = 0.4599 ; Chi^2 = 16.32, df = 5 (P = 0.0060); I^2 = 69.4%			
Total (95% CI)		**292**	**0.59 [0.48; 0.68]**
Heterogeneity: Tau^2 = 0.2374 ; Chi^2 = 19.54, df = 8 (P = 0.0122); I^2 = 59.1%			
Test for subgroup differences: Chi^2 = 0.54, df = 1 (P = 0.4612)			

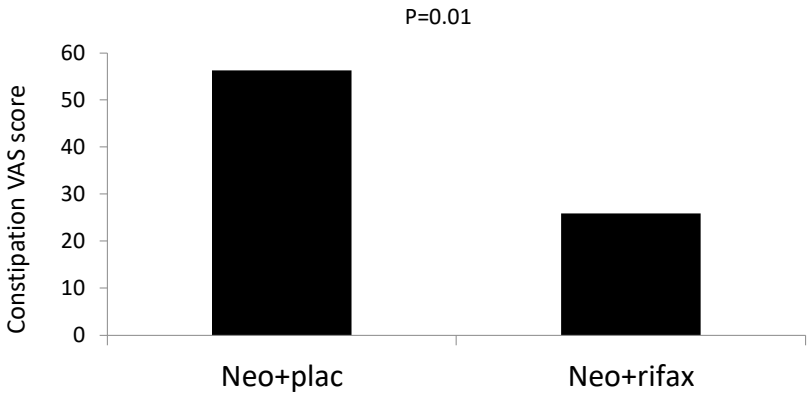


Again meets the 60% rule

Lu, et al Front Microbiol March 2026

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Methane Positive C-IBS
Double Blind Placebo Controlled Trial



Pimentel, et al. Dig Dis Sci, 2014.

61

Bismuth Effective for Hydrogen Sulfide

GASTROENTEROLOGY 1998;114:923–929

Bismuth Subsalicylate Markedly Decreases Hydrogen Sulfide Release in the Human Colon

FABRIZIS L. SUAREZ, JULIE K. FURNE, JOHN SPRINGFIELD, and MICHAEL D. LEVITT
Research Department, Minneapolis Veterans Affairs Medical Center, Minneapolis, Minnesota

Background & Aims: Hydrogen sulfide is one of the main malodorous compounds in human flatus. This toxic gas also has been implicated in the pathogenesis of ulcerative colitis. Therefore, a treatment that reduces colonic H_2S levels could be clinically useful in the treatment of flatus odor and of ulcerative colitis. In this study the ability of bismuth subsalicylate, a compound that binds H_2S, to reduce H_2S release in the colon, was tested. *Methods:* Homogenates made from human and rat feces were incubated with and without bismuth subsalicylate, and gas production was measured. Fecal samples from 10 healthy subjects were analyzed before and after ingestion of bismuth subsalicylate (524 mg four times a day) for 3–7 days. *Results:* Fecal homogenates showed a dose-dependent relationship between the concentration of bismuth subsalicylate and H_2S release. Treatment of subjects with bismuth subsalicylate produced a >95% reduction in fecal H_2S release. *Conclusions:* The ability of bismuth subsalicylate to dramatically reduce H_2S could provide a clinically useful means of controlling fecal and/or flatus odor and of decreasing the putative injurious effects of H_2S on the colonic mucosa.

containing compounds to the colon could also limit H_2S production. However, a variety of endogenous compounds (e.g., mucin and taurocholic acid) as well as dietary substances (e.g., amino acids and sulfate) serve as sources of sulfur for the colonic bacteria,[7] and it seems unlikely that delivery of sulfur to the colon can be drastically reduced.

A simple approach to reducing H_2S release in the colon would be the administration of a compound that binds H_2S. In the test tube, bismuth reacts with sulfide to form very insoluble bismuth sulfide. In the present report, we carried out a series of experiments in rats and humans to determine whether bismuth subsalicylate (BSS) decreases the fecal release of H_2S.

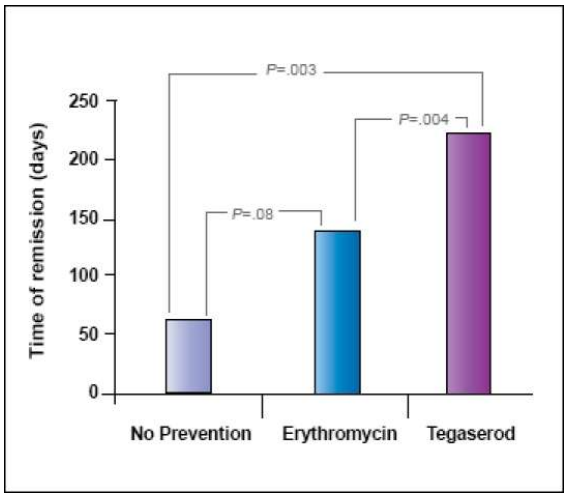
Materials and Methods

In Vitro Studies

The ability of BSS to bind the three major sulfur gases present in human flatus[8] was studied by incubating 1 mL of a 1:10 dilution of BSS (4.84 μmol of bismuth) in the form of Pepto-Bismol (Procter & Gamble, Cincinnati, OH) in buffer (0.1 mol/L sodium phosphate, pH 7.0) with 20 mL of N_2

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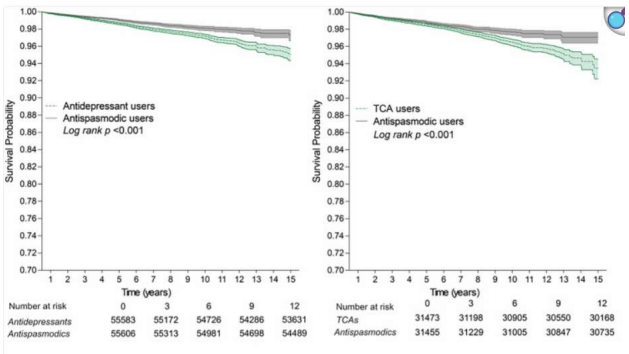
Prokinetics prevent relapse of SIBO



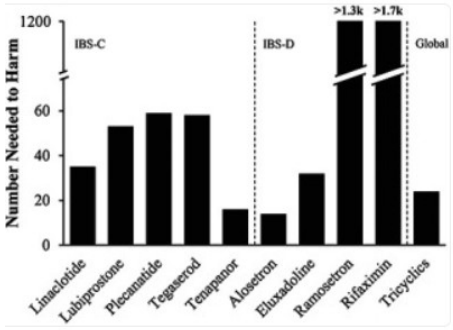
Pimentel, et al. Gastroenterol Hepatol 2009

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Antidepressants and IBS



Mehravar, et al. Commun Med 2026



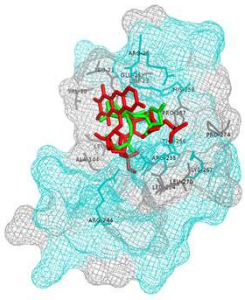
Busam, et al. Am J Gastroenterology 2025

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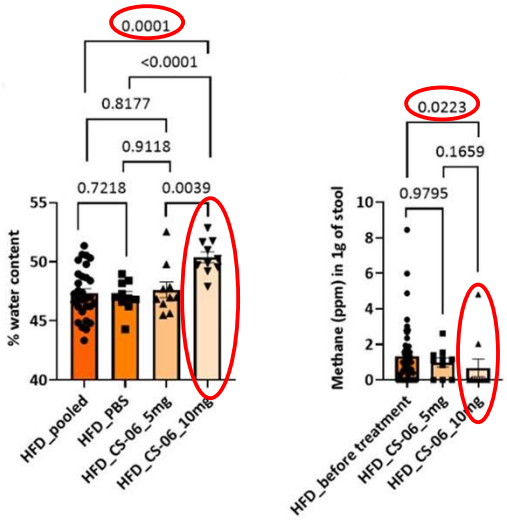
FUTURE THERAPIES

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CS-06 Reduces Methane and Constipation *in vivo*



Blocks the binding site for the methylenetetrahydromethanopterin (mtd) enzyme

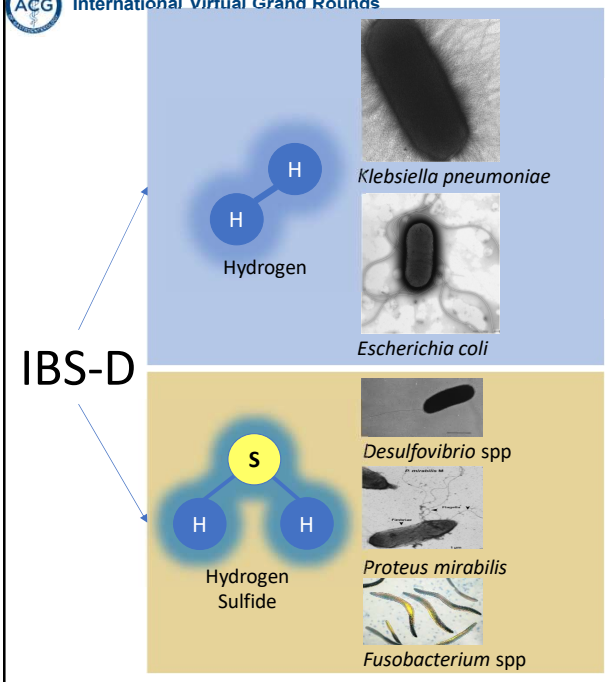


Villanueva-Millan, et al DDW 2025 Su2010

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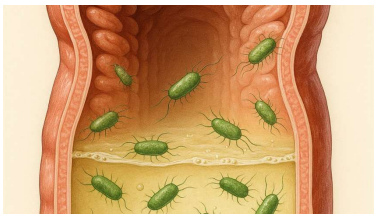


Many of the main taxa associated with IBS-D partially reside in the mucous of small intestine

Table 1 Differential abundance of the top six phyla in DA-DTT versus DA-U

Taxonomy	DA-DTT ($n = 43$) versus DA-U ($n = 112$)				
	Average Relative abundance % DA-DTT[a]	Average Relative abundance % DA-U[a]	Fold Change (calculated from the GLM)[b]	*P*-value	FDR *P*-value
Firmicutes	49.3	62.25	1.05	0.65	0.70
Proteobacteria	28.97	14.8	6.22	**1.4E-7**	**7.71E-7**
Actinobacteria	8.91	12.02	−1.23	0.21	0.42
Fusobacteria	5.36	3.93	1.96	**0.01**	**0.03**
Bacteroidetes	6.16	4.63	2.19	**0.01**	**0.03**
TM7	1.17	1.86	−1.34	0.32	0.48

P-value< 0.05 and FDR *P*-value< 0.05 are shown in bold. [a]The relative abundances were calculated from the original counts (number of sequences in the OTU table). [b]Fold changes were calculated from the GLM, which corrects for differences in library size between the samples and the effects of confounding factors. It is therefore not possible to derive these fold changes from the original counts (number of sequences in the OTU table) by simple algebraic calculations



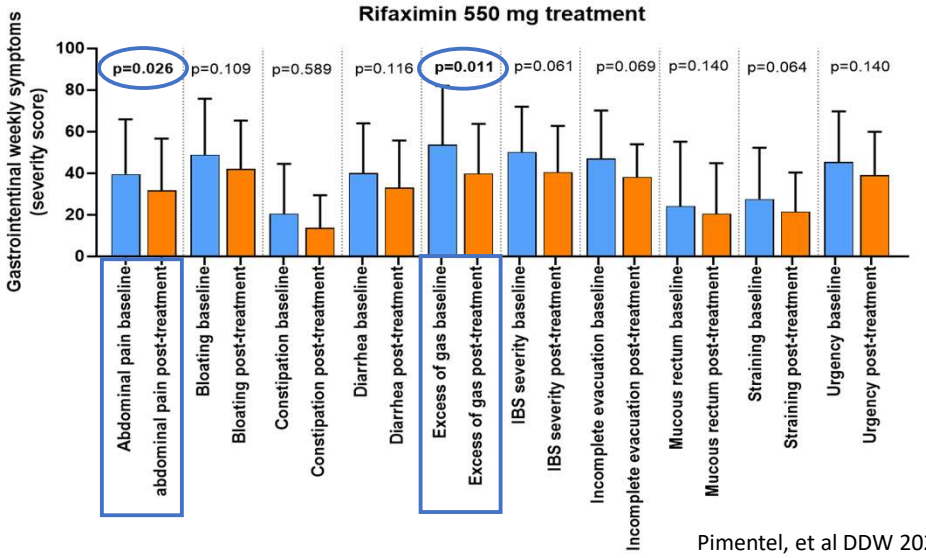
Fernandez-Delgado, et al. Ann Microbiol 2015
Struv, et al. Infect Immunity 2008
Jorgensen, et al. Stand Genom Sci 2018
Leite, et al. BMC Microbiol 2019
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Within group changes (Rifaximin 550mg)

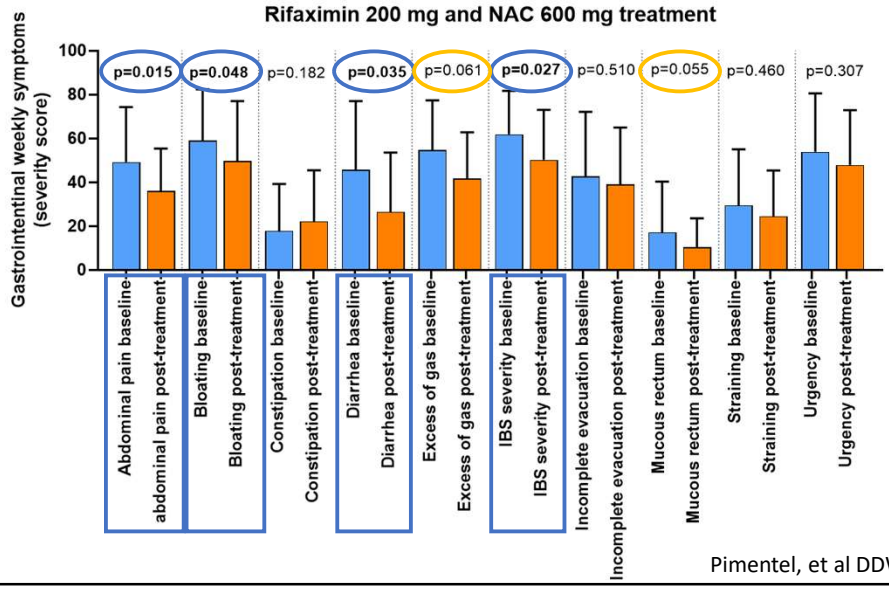


Pimentel, et al DDW 2025

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Within group changes (Rifaximin + NAC)

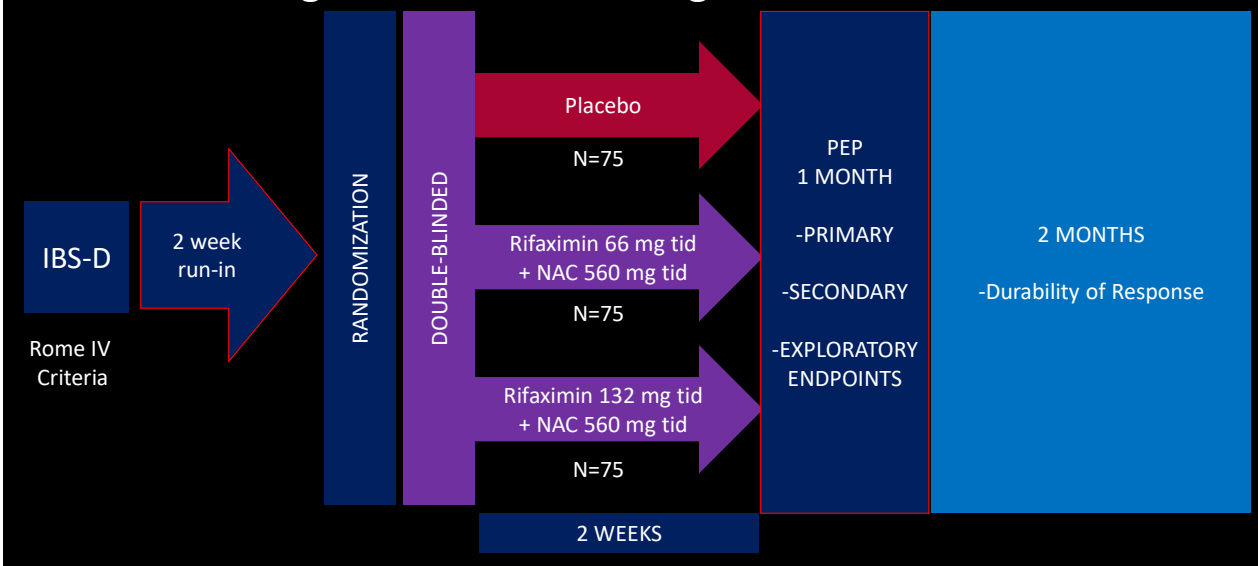


Pimentel, et al DDW 2025

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Phase IIB Registered Trial has begun



NAC = N-acetylcysteine

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Indian Journal of Gastroenterology (March–April 2023) 42(2):249–273
https://doi.org/10.1007/s12664-022-01333-5

CONSENSUS

Indian consensus statements on irritable bowel syndrome in adults: A guideline by the Indian Neurogastroenterology and Motility Association and jointly supported by the Indian Society of Gastroenterology

Uday C. Ghoshal[1] · Sanjeev Sachdeva[2] · Nitesh Pratap[3] · Arun Karyampudi[4] · Uzma Mustafa[1] · Philip Abraham[5] · Chetan B. Bhatt[6] · Karmabir Chakravartty[7] · Sujit Chaudhuri[8] · Omesh Goyal[9] · Govind K. Makharia[10] · Manas Kumar Panigrahi[11] · Prasanta Kumar Parida[12] · Sudhanshu Patwari[13] · Rajesh Sainani[14] · Shine Sadasivan[15] · M. Srinivas[16] · Rajesh Upadhyay[17] · Jayanthi Venkataraman[18]

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Statement 5: Patients with IBS, particularly those with diarrhea-predominant IBS (IBS-D), are more likely to have SIBO and gut dysbiosis

Voting summary: Accepted completely: (72.22%), accepted with minor reservation: (27.78%).
Level of evidence: II-1
Grade of recommendation: A

Statement 6: Excessive methane production slows gut transit and is associated with constipation-predominant IBS (IBS-C)

Voting summary: Accepted completely: (77.78%), accepted with minor reservation: (22.22%).
Level of evidence: I
Grade of recommendation: B

Statement 7: Gastrointestinal infection with varied pathogens may result in post-infection IBS (PI-IBS)

Voting summary: Accepted completely: (100%).
Level of evidence: II-1
Grade of recommendation: A

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Conclusions

1. IBS is a disease and Autoimmunity with SIBO are common
2. A blood test can diagnose and risk-stratify IBS-D
3. Three gas breath testing is the most validated breath test in history
4. H_2S may be the most important gas in how it affects you
5. New therapies are coming soon for SIBO, ISO, and IMO
6. SIBO is being found more commonly
7. SIBO has a dramatic effect on the host

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Questions



Mark Pimentel, MD, FACG



Turki AlAmeel, MBBS, FRCPC, FACP

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