

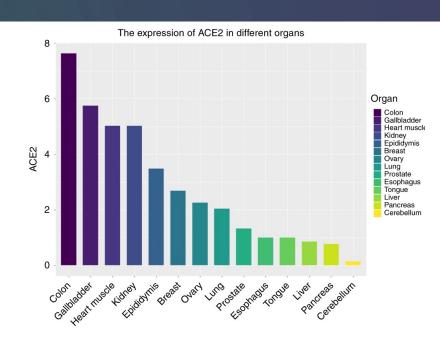


Disclosures

- Bausch Health
 - Speaker, Research Grant
- Gemelli Biotech
 - Equity
- Alnylam
 - Honorarium

Gut microbiome and COVID-19

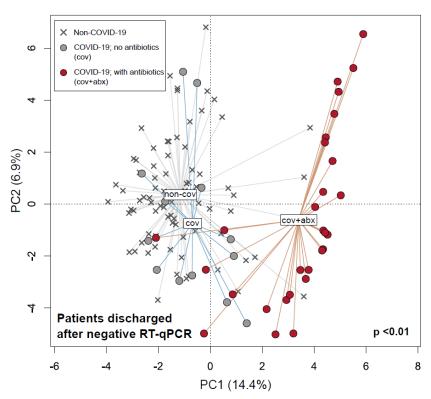
- SARS-COV-2 entry receptors (ACE-2) are heavily expressed in the GI tract
- Shedding of virus in stool is common and can outlast respiratory shedding
- Exact fecal—oral transmission route is not yet established!



Guo M et al. Nature Rev. 2021 Xu H et al. International Journal of Oral Science. 2020

Gut microbiome and COVID-19

- COVID-19 patients commonly have GI symptoms (diarrhea, N/V,...)
- Gut microbiome is significantly altered in COVID-19 pts
- Microbiome changes may persist beyond recovery



Yeoh et al. Gut. 2021

The gut microbiome of COVID-19 recovered patients returns to uninfected status in a minority-dominated United States cohort



Rachel C. Newsome¹, Josee Gauthier¹, Maria C. Hernandez¹, George E. Abraham², Tanya O. Robinson², Haley B. Williams², Meredith Sloan², Anna Owings², Hannah Laird², Taylor Christian², Yilianys Pride², Kenneth J. Wilson², Mohammad Hasan,² Adam Parker², Michal Senitko², Sarah C. Glover², Raad Z. Gharaibeh¹, and Christian Jobin¹

¹University of Florida College of Medicine, Gainesville, FL, ²University of Mississippi Medical Center, Jackson, MS

- Prospectively collected stool via rectal swab from:
 - 50 COVID-19 pts in ICU
 - 9 recovered COVID-19 pts
 - 34 non-COVID pulmonary inpatients

	(COVID	COVII	D recovered	Non-COVID		
	Number	Percent or SD	Number	Percent or SD	Number	Percent or SD	
Number of participants	50	100%	9	100%	34	100%	
Age, mean years	62.3	13.4	46.7	16.1	55.0	15.8	
Sex: Male	28	56%	4	44%	14	41%	
Sex: Female	22	44%	5	56%	20	59%	
Race, Caucasian	11	22%	4	44%	14	41%	
Race, Black	35	70%	4	44%	20	59%	
Race, Hispanic	1	2%	1	11%	0	0%	
Race, Choctaw	3	6%	0	0%	0	0%	
BMI, mean	33.6	9.8	31.5	7.6	26.6	7.9	

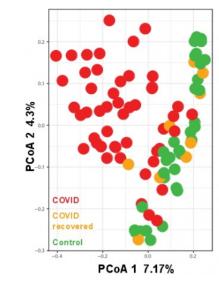
The gut microbiome of COVID-19 recovered patients returns to uninfected status in a minority-dominated United States cohort

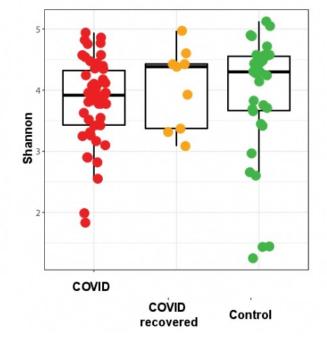


Rachel C. Newsome¹, Josee Gauthier¹, Maria C. Hernandez¹, George E. Abraham², Tanya O. Robinson², Haley B. Williams², Meredith Sloan², Anna Owings², Hannah Laird², Taylor Christian², Yilianys Pride², Kenneth J. Wilson², Mohammad Hasan,² Adam Parker², Michal Senitko², Sarah C. Glover². Raad Z. Gharaibeh¹, and Christian Jobin¹

¹University of Florida College of Medicine, Gainesville, FL, ²University of Mississippi Medical Center, Jackson, MS

- COVID pts have different gut microbiome composition than covid recovered and controls
- COVID-recovered pts showed similar diversity as hospitalized non-covid pts
- COVID patients showed higher relative abundance of Campylobacter and Klebsiella





Gut microbiome and COVID-19

- Somewhat discordant with data from Hong Kong, stool microbiome appears to recover in COVID pts in the US!
- Promising but larger studies with longer follow-up are needed
- GI symptoms in "long COVID" patients are yet to be fully defined

Demographic and clinical factors associated with severe abdominal bloating in FGIDs: Gardiner CP, Sing P, Ballou S, Hassan R, Yu V, Lembo A, Nee J, Iturrino J

- Bloating is seen in 16% of the general population and up to 70% of FGIDs
- Complex and multifactorial pathophysiology



Demographic and clinical factors associated with severe abdominal bloating in FGIDs Gardiner CP, Sing P, Ballou S, Hassan R, Yu V, Lembo A, Nee J, Iturrino J

- 612 (78% female, age 44±16.5) consecutive new patients were recruited from a single center.
- Rome IV criteria used for diagnosis of FGID
- PAGISYM was used for assessment of bloating severity for two weeks prior to recruitment

Demographic and clinical factors associated with severe abdominal bloating Gardiner CP, Sing P, Ballou S, Hassan R, Yu V, Lembo A, Nee J, Iturrino J

- Bloating severity was mild, moderate and severe in 38%, 35% and 27%, respectively
- Multivariate analysis showed bloating severity is associated with
 - Younger age
 - Presence of functional dyspepsia
 - Presence of functional constipation
 - Abdominal pain severity and somatization score
- Severity of anxiety, depression and sleep disturbance were not associated with bloating severity

Bloating is associated with many organic diseases

- Commonly missed DDx of bloating:
 - Anatomical (enterocele, hypermobile Ehlers-Danlos syndrome)
 - Motility (Pseudoobstruction, gastroparesis, rapid gastric emptying, intraabdominal adhesions/bands)
 - Microbiome (SIBO, Small intestinal fungal overgrowth, probiotics, post-FMT)
 - Miscellaneous (POTS, mast cell activation syndrome)

PREVENTING HEMORRHOIDS AND FISSURES OF PREGNANCY: RESULTS OF THE RANDOMIZED CONTROLLED TRIAL

- T. Poskus¹, Z. Sabonyte Balsaitiene¹, M. Smigelskaite¹, G. Barkauskaite¹, E. Jasiunas², M. Jakubauskas¹, L. Jakubauskiene¹, K. Strupas¹, G. Drasutiene¹.
- l Vilniaus universitetas, Vilnius, Vilnius, Lithuania; 2 Vilniaus Universiteto ligonines Santariskiu klinikos, Vilnius, Lithuania
 - Incidence of hemorrhoids during pregnancy is 15-40%
 - Pathophysiology: Increased circulating blood volume, increased intraabdominal pressure, relaxation of venous smooth muscles by progesterone, and constipation

Hemorrhoids in pregnancy

- Aim: To assess effectiveness of dietary and behavior recommendations for prevention of hemorrhoids during pregnancy
- Single-blind Multicenter trial: During the first trimester 260 women were randomized 1:1 to dietary/behavior recommendations or standard care
- Endpoint: Reduction in postpartum rate of hemorrhoids

Dietary/behavior recommendations

Dietary:

- Consume at least 1.5 liters of fluid
- Consume a tablespoon of bran and 2-5 prunes daily
- Consume ~300g of fruits and 500g vegetables and 30g nuts

Behavior

- Exercise 30-60 minutes daily
- Spend less than 3 minutes on the commode
- Washing after bowel movements

Results

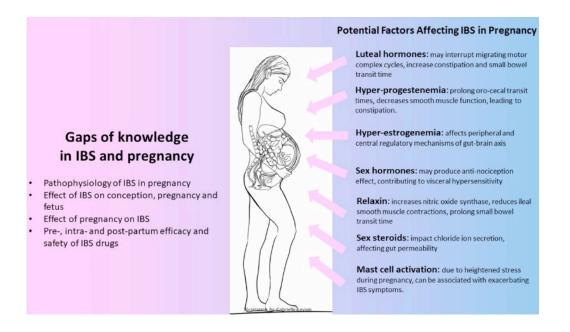
- Hemorrhoids were seen in 40.8% of control group as compared to 15.4% in the intervention group (p <0.01)
- There was no difference in maternofetal outcomes

Irritable Bowel Syndrome in Pregnancy

Sarvee Moosavi, MD1, Mark Pimentel, MD2,3,4, Melissa S. Wong, MD5 and Ali Rezaie, MD, MSc2,3,4

Am J Gastroenterol 2021;116:480-490. https://doi.org/10.14309/ajg.000000000001124

 Review on management of IBS-D, IBS-C and IBS-M in pregnancy



Gut microbiome samples - does stool represent right?

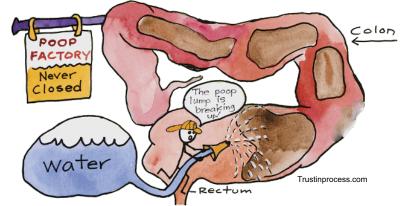
Orly Levitan¹, Dawn B. Burleson¹, Peter McCaffrey², Lanying Ma², Ayin Vala², David A. Johnson³

 1 Hygieacare Inc., Norfolk, VA, USA 2 VastBiome, San Carlos, CA, USA 3 Eastern VA Medical School, Norfolk VA, USA

- High volume colonic irrigation or "Colonic" has been considered for:
 - Alternative therapy for constipation
 - Preparation for colonoscopy

Parekh et al. J Clin Gastro Hep 2018 Harish K et al. J Gastrointest Dig Syst 2016

 Several other techniques/devices widely available in California with unfounded claims of "detoxification"



Gut microbiome samples - does stool represent right?

Orly Levitan¹, Dawn B. Burleson¹, Peter McCaffrey², Lanying Ma², Ayin Vala², David A. Johnson³

¹Hygieacare Inc., Norfolk, VA, USA ²VastBiome, San Carlos, CA, USA ³Eastern VA Medical School, Norfolk VA, USA

- 20 subjects underwent high volume colonic irrigation before colonoscopy
- Stool samples were collected prior to irrigation
- Three serial stool samples were collected during colonic for metagenomic sequencing





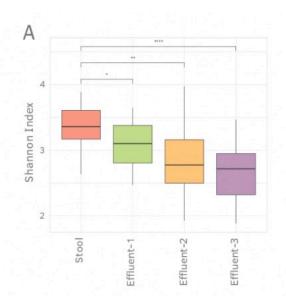
Gut microbiome samples - does stool represent right?

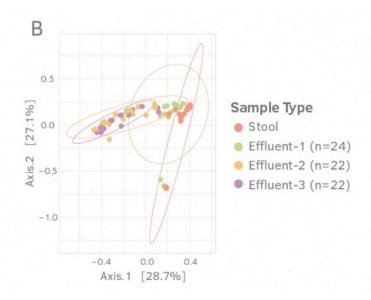
Orly Levitan¹, Dawn B. Burleson¹, Peter McCaffrey², Lanying Ma², Ayin Vala², David A. Johnson³

Hygieacare Inc., Norfolk, VA, USA ²VastBjome, San Carlos, CA, USA ³Eastern VA Medical School, Norfolk VA, USA

There was drastic difference in microbiome alpha diversity of each sample

There was drastic difference in microbiome beta diversity



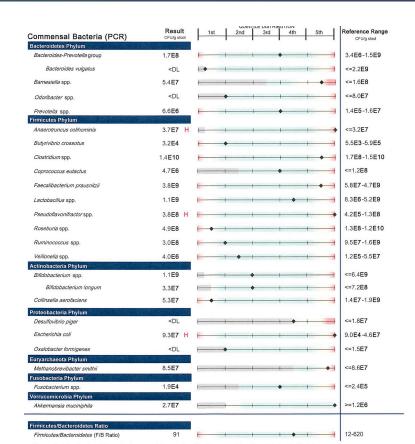


Conclusion

 Unclear each sample represents which part of the colon, but the study highlights that stool is an unreliable medium for global assessment of microbiome

Stool microbiome testing not ready for clinical use

	Reference Range	IBS	IBD	Metabolic Syndrome	Chronic Fatigue	Auto- immune	Type 2 Diabetes	High Blood Pressure	Mood Disorders
Bacteroidetes Phylum									
Bacteroides-Prevotella group		1	1	1	†	1	1	1	1
Bacteroides vulgatus		1			1	1		1	1
Barnesiella spp.									
Odoribacter spp.									
Prevotella spp.		1		^	1	1	,	1	1
Firmicutes Phylum									
Anaerotruncus colihominis	н	1	1	1	†	1	1	1	1
Butyrivibrio crossotus	1	•							
Clostridium spp.									
Coprococcus eutactus		1		,	↑	1		1	1
Faecalibacterium prausnitzii		1				1			1
Lactobacillus spp.									
Pseudoflavonifractor spp.	н	1	1	1	↑	1	1	1	1
Roseburia spp.	T		+						
Ruminococcus spp.		₹↑	+	+	+	*↑	₹↑	*↑	*↑
Veillonella spp.		1	1	1	1	1	1		1
Actinobacteria Phylum									
Bifidobacterium spp.									
Bifidobacterium longum									
Collinsella aerofaciens		*↑	•↑	+	*↑	*↑	₹↑	*↑	₹↑
Proteobacteria Phylum									
Desulfovibrio piger									1
Escherichia coli	н	1	1	^	^	1	1	1	1
Oxalobacter formigenes	1	1		1	1				1
Euryarchaeota Phylum									
Methanobrevibacter smithii		1				↑			1
Fusobacteria Phylum									
Fusobacterium spp.		1	1	1	1	1	1	1	1
Verrucomicrobia Phylum									
Akkermansia muciniphila		1	1	1	+	1	1	1	+



Stool microbiome testing not ready for clinical use

- Stool microbiome testing has multiple limitations
 - Extremely wide range of "Normal" stool microbiome
 - Extremely wide range of stool microbiome in disease
 - Daily variability of stool microbiome
 - Variability of stool microbiome even within one BM
 - Normal ≠ Healthy
- Microbiome field moving to mucosal and small bowel microbiome