Using FoodMarble's Handheld Breath Testers (Aire) in SIBO. **A Game Changer?**

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FoodMarble Aire*

Validation studies and clinical applications

FoodMarble, Aire, and Aire2 are Trademarked etc. by FoodMarble (registered in Ireland with the number 574999)
QuinTron is Trademarked etc. as well

Conflict of Interest Statement

- I have no conflicts of interest to report
- I use the Aire and Aire2 in practice but receive no payments, honoraria, etc. of any kind from FoodMarble.
- I have deferred all referral fees for any purchases made by any of my clients or patients.
- I simply find the devices useful and wish to share my experience.

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- This presentation is not meant to replace medical advice. It is meant to provide some educational information. It cannot treat, prevent, or diagnose disease. Please, for your health, consult with a qualified medical professional for all medical matters.
- I attempt to provide education around the FoodMarble handheld Aire devices as well as SIBO and sugar malabsorption. However please be aware that research is constantly changing and only you and your medical provider can decide what is appropriate for your care and what is worth implementing.
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Who Am I?

Teacher with a focus on:

- Evidence-evaluation
- Critical review of the medical literature
- Evidence-based medicine

NATIONAL UNIVERSITY OF Natural Medicine

AIHM ACADEMY OF INTEGRATIVE HEALTH & MEDICINE

Dr. Journal Club

Researcher with a focus on:

- SIBO
- IBS
- Evidence-based medicine

GastroANP
Gastroenterology Association of Naturopathic Physicians

THE GOLDENBERG GI CENTER, LLC

Clinician with a focus on:

- SIBO, IBS, IBD & GERD
- Past President of the Gastroenterology Association of Naturopathic Physicians

What is the Aire?

- Handheld gas sensor/s linked to an app on your phone
- “Fermentation Scores” are presented
  - Note this is NOT linear in Aire2
- Clinicians can see the actual ppm
- Aire measures H2
- Aire2 measures H2 and CH4
- Plans for H2S in the future (“currently under development and should be available through a software update by the end of 2022”)
- Does not measure CO2

What is FoodMarble?

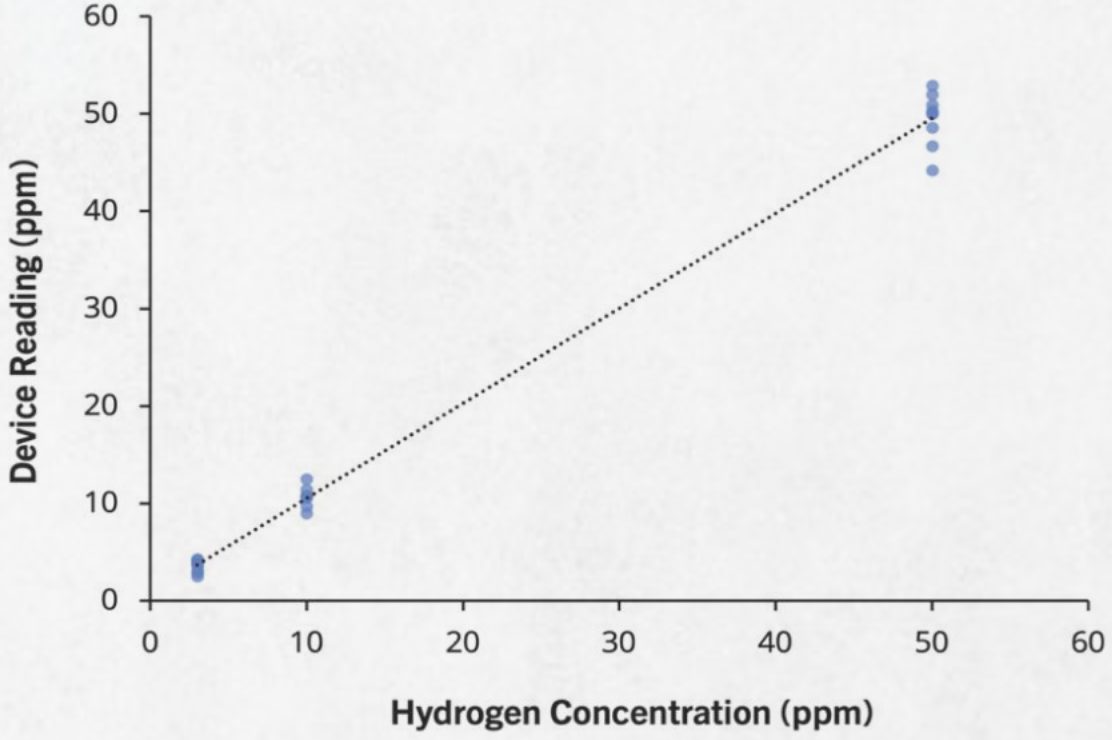
- Amazing story of a PhD engineer with a girlfriend (now wife) struggling with IBS.
- Six years and 6 million dollars in funding later the company has 25 employees and has sold over 30,000 Aire devices

Validation Studies

--Note most of these are industry sponsored/authored--

Technical Performance

- MEDRXIV paper. In peer review now.
- Barahona et al 2022
- Accredited testing and calibration laboratory
- QuinTron vs. Aire
- Tested certified ppm H2 gases of 3ppm, 10ppm, and 50ppm.
- 3 Aires tested 3 times on 3 non-consecutive days
- Overall mean absolute error 1.2 ppm



Comparison to QuinTron in Healthy Participants (Orocecal time)

- Shortt et al 2019 Poster
- N=14 healthy adults
- Each participant compared two Aire devices to QuinTron Device
- Lactulose (10g); 3-hour test
- Breath tests q5min switch between the 3 devices x 3 hours
- Malabsorption defined as >/= to 20 ppm increase in H2 over baseline (so really just measuring orocecal time?)
- Of 14 one had baseline H2 over 15 so excluded

RESULTS:

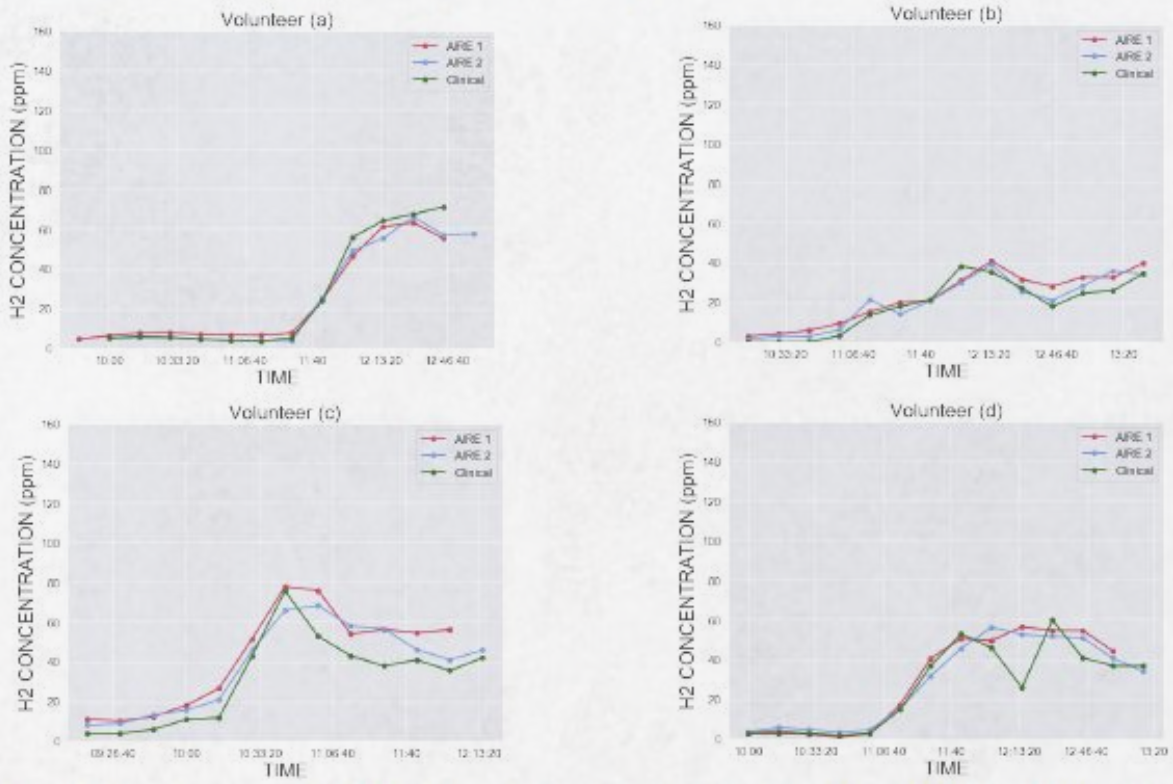
- One did not have a 20+ rise within 3 hours (slow transit)
- Of the 13 included, all had congruence within 10 min – hitting the 20 point rise all lined up with both Aire and the QuinTron

(1) There was diagnostic agreement in all cases

- One volunteer was excluded due to a high H_2 baseline, leaving 13 volunteers for the final analysis;
- One volunteer did not display malabsorption (<20ppm rise in breath H_2) with the 3 hour testing period;
- 12 volunteers displayed malabsorption (>20ppm rise in breath H_2) with the 3 hour testing period.

	True	False
Positive	12	0
Negative	1	0

(3) Comparison of interpolated H_2 concentrations



Link between fiber, gas, and symptoms

Mo1958

UTILITY OF A CONSUMER-FRIENDLY PORTABLE HYDROGEN BREATH ANALYSER DEVICE FOR MONITORING COLONIC FERMENTATION AND SENSATION IN RESPONSE TO SUPPLEMENTAL FIBER

Claire Shortt, Niall McGovern, Eoghan Lafferty, Pankaj J. Pasricha

BACKGROUND: Fermentation of soluble fibers by fecal microbiota is vital for colonic health and leads to production of hydrogen (H2) and other volatiles. On the other hand, excessive or aberrant fermentation is associated with gastrointestinal distress. There are currently no practical methods for monitoring fermentation in the gut. To address this need, we developed a handheld breathalyzer device linked to a smartphone (AIRE, FoodMarble, Dublin, Ireland) and validated its utility to measure breath H2 and associated symptoms in response to supplemental fiber. **METHOD:** We studied 20 subjects (15 healthy, 5 IBS) in a double-blind, randomized, crossover design (1-week baseline, 2-weeks 1st fiber, 2-week wash-out, 2-weeks 2nd fiber, 1-week washout) using 2 different prebiotics a galacto-oligosaccharide (GOS) and a wheat dextrin (WD) fiber. 6-9 breath measurements were made daily along with scoring bloating, flatulence and abdominal pain, on a 0-10 scale. Data was analysed using 2-way ANOVA and Pearson's correlation and linear regression as appropriate. **RESULTS:** Interim results show that for the group as a whole, both prebiotic fibers produced a highly significant change in breath H2 compared to baseline, for both week 1 and 2 (Figure 1). After discontinuation of the prebiotic, H2 values returned to baseline. There were no statistically significant differences between the H2 levels in weeks 1 and 2 for the two prebiotics. However, there was large inter-subject variability in the individual responses. We next examined patient-reported sensation which was mild and comparable in both groups, with no overall change in either prebiotic group, compared to baseline period (GOS versus WD; "pain"= 0.7 vs. 0.65; bloating = 1.45 vs. 1.41; flatulence = 1.27 vs. 1.07, P= NS for all). Nevertheless, there were significant correlations between breath H2 and "pain" (r=0.18; P=0.02), bloating (r=0.31; p <0.0001) and flatulence (r=0.49; p <0.0001). **CONCLUSION:** This study demonstrates the ability of a portable device/app to continually monitor breath H2 levels along with subjective symptoms, detecting the expected increase in colonic fermentation by supplemental fiber before returning to baseline after discontinuation. Results of fecal microbial analysis are awaited but the preliminary results suggest that the device may enable the consumer to monitor the activity of their own microbiota in response to fiber or fermentable foods (such as FODMAPs) and potentially titrate the quantity in an objective, quantifiable and personalized manner. The correlation analysis also suggests that colonic fermentation can be sensed by consumers, even at subclinical levels. While further studies are needed, this device may enable more accurate detection of symptoms in a number of patient populations including IBS and small intestinal bacterial overgrowth.

"There were significant correlations between breath H2 and "pain" (r=0.18, p=0.02), bloating (r=0.31, p<0.0001), and flatulence (r=0.49, p<0.0001)."

- Study: Crossover RCT design
- Population: N=20 (15 healthy, 5 IBS)
- Intervention: GOS, wheat dextrin
- Control: Crossover w/ washouts
- Outcomes: Symptoms and ppm H2

Shortt et al 2020 (DDW poster)

Comparison to QuinTron in suspected SIBO Participants

- MEDRXIV paper. In peer review now.
- Barahona et al 2022
- 36 pts suspected of SIBO
- LBT done with QuinTron and Aire
- Diagnostic agreement 31/36=86%

Table 1. LHBT comparison of AIRE and mail-in kit (n=36). LHBT positive ≥ 20 ppm rise in H_2. LHBT negative ≤ 20 ppm rise in H_2.

	LHBT Positive	LHBT Negative
AIRE	12	24
Mail-in kit	9	27

Table 2. Mean baseline, overall and peak breath H_2 ppm for AIRE devices and mail-in kits (n=36).

	AIRE	Mail-in kit
Baseline H_2 ppm (mean ± SD)	8.5 ± 7.4	5.4 ± 6.5
Overall H_2 ppm (mean ± SD)	18.6 ± 24.9	15.2 ± 23.3
Peak H_2 ppm (mean ± SD)	39.2 ± 32.8	33.9 ± 34.6

Comparison to QuinTron in Suspected SIBO Participants

Some Take Homes

- It appears the mail ones are running lower which may be due to gas leakage in the bags over time
- In general looks similar but if anything more positives with Aire
- Of the 3 ‘extra’ positive cases with Aire, two responded to abx treatment, one result pending. (Barahona 2021)

Comparison to QuinTron in Participants with Suspected Lactose Malabsorption

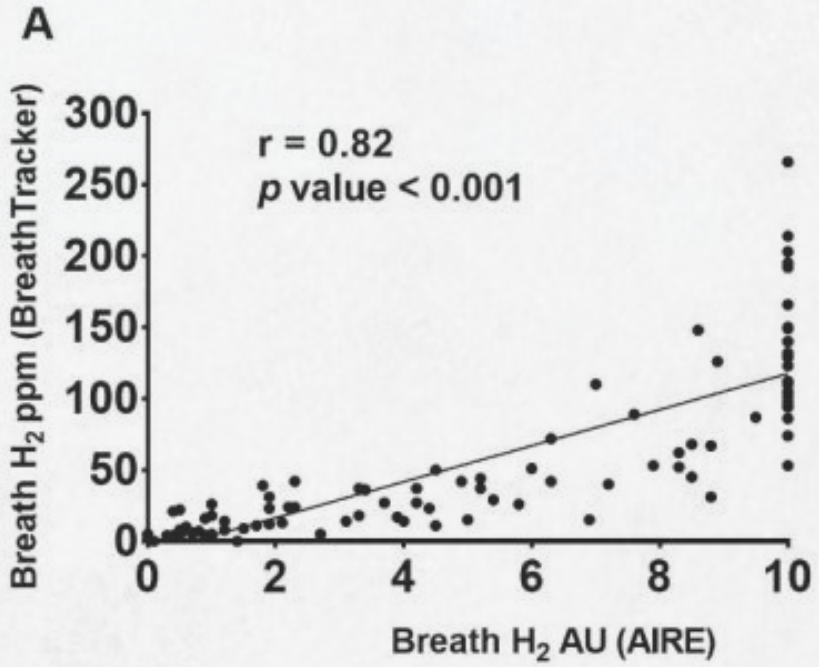
- Shrestha 2019
- 75% of world population has limited expression of beta-lactase - a proportion of which will experience adverse GI sx from lactose when the amount ingested exceeds the enzymatic capacity of the residual intestinal lactase activity.
- According to Aire paper a positive is a rise of **25 ppm with 50 g lactose** at any time
- According to Dynamed a positive is a rise of **20 ppm with 25 g lactose** within 3 hours
- SIBO can cause false positive (or have both)

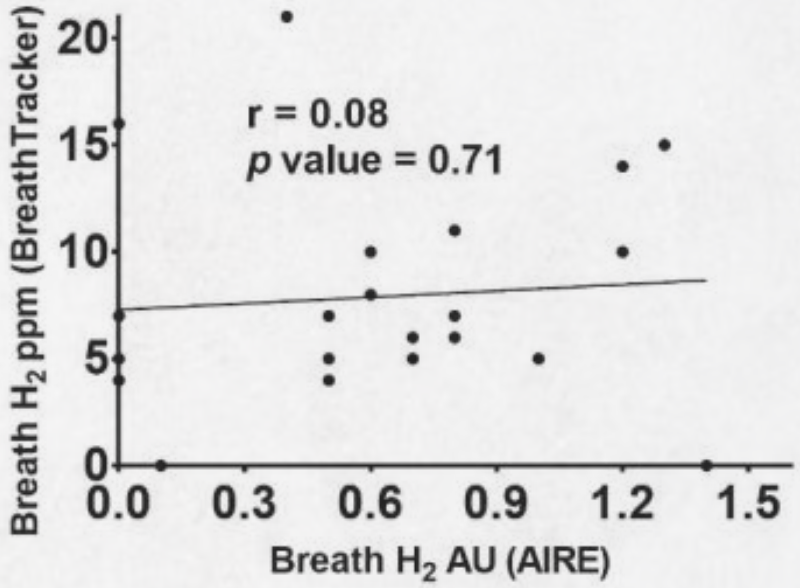
- 19 healthy participants (12 self reported dairy intolerant (cohort 1); 7 only females avoiding dairy (cohort 2))
- Cohort 1: 50g lactose measure for 5 hours
- Cohort 2: 650 ml milk (32g lactose) measure for 4 hours
- AIRE versus QuinTron (Aire used the arbitrary units (AU))

Results

- Strong correlation with lactose (r=0.82; P<0.001) and milk ingestion (r=0.90; p<0.001)
- Baseline and maximum levels don't line up very well. But overall very correlated
- I am a bit curious about the AU conversion messing with the extremes. Perhaps if you had the true ppm there would be better correlation there too. But perhaps be wary at extreme values
- They calculated 3 AU as equivalent to 25ppm. Of the 12 suspected LI individuals, there was baseline data for ten. Nine tested pos for LM with Quintron and all ten did with AIRE

"lactose intolerance study was unknown to us, found out when published"





Aire2 validation studies

- In process according to the company

Important Notes

- Fermentation scores are not in linear relationship to ppm
- Need to have clinician dashboard to see ppm
- Will need Rx for lactulose
- Hard to get multiple packets of fructose/lactose for SIBO testing. Company says may make them more available in the future.
- Calibration (how is it calibrated? Degrades over time?) *FoodMarble: "Each unit is uniquely calibrated using gas standards and then sensor drift over time is managed remotely using a machine learning approach"*
- Correction factor not needed
- Need minimum of 15 min between tests (issue for sequential testing)

Clinical applications

- Food and symptoms exploration
  - ’Matt Method’
- Lactose/Fructose malabsorption testing
- Formal SIBO testing
- Spot testing to track progress
- AUC analysis

Food and symptom exploration

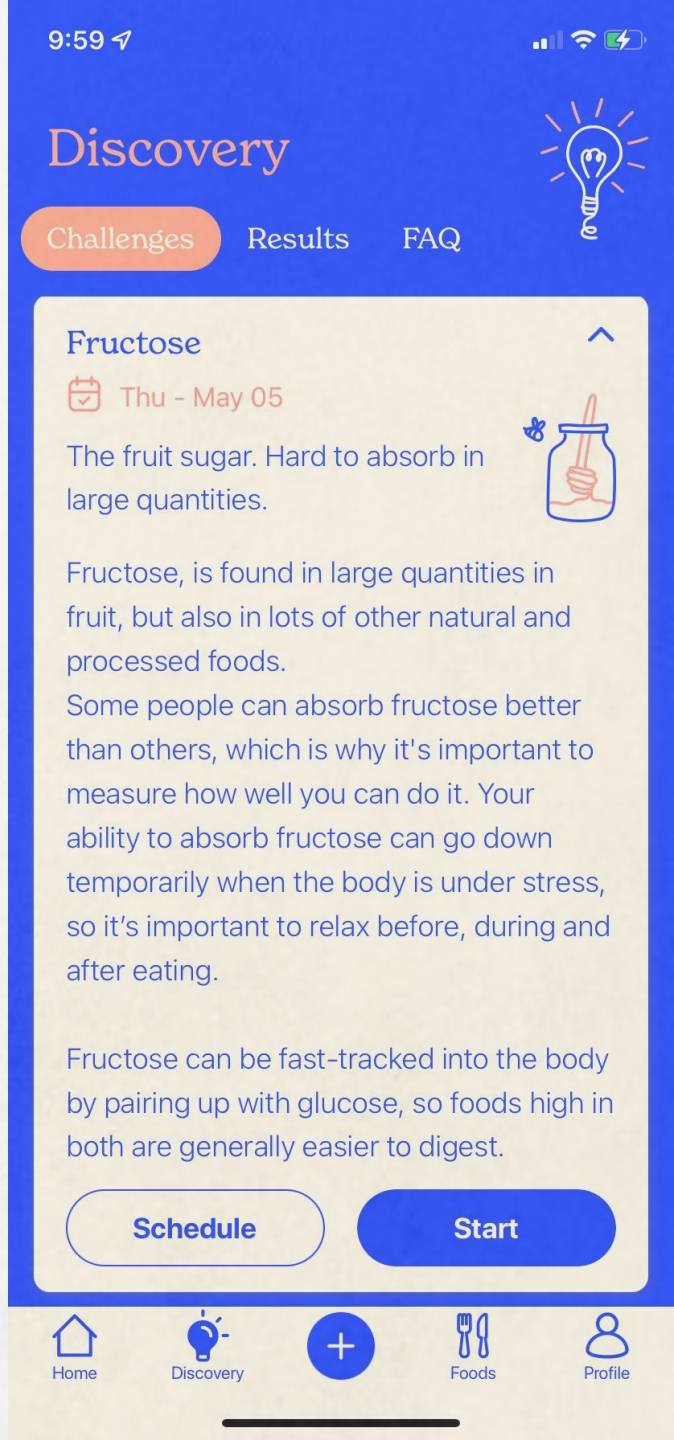
- Can track F scores with various foods and look for association between symptoms and gas levels.
- Recall that gas may be from fermentation anywhere along the GI track (i.e. from dinner last night)
- Foodmarble's 'Food Intolerance Kit'
- 'Matt Method': Intermittent fasting 16 hours. Breakfast with challenge of known Ok foods plus one new variable. Test for up to 3 hours. Then eat as you will through the rest of the day. With each new tested variable add this to green food list or red food list and continue testing new variable each am for breakfast until you have a good sense of ok foods and foods to avoid.

Lactose/Fructose Malabsorption Testing

- Can do formal lactose/fructose malabsorption testing
- Lactose 25g, fructose 25g (mixed with or followed by one cup of water) (NA Consensus, Rezaie 2017)
- Note that the ‘challenge pack’ has 25g of fructose and lactose
- Recall that malabsorption is not the same as intolerance. It needs to cause symptoms to be intolerance
- Fructose and lactose breath testing should be performed for at least 3 hours (NA Consensus, Rezaie 2017)
- The presence of bacterial overgrowth should be ruled out before performing lactose or fructose breath testing (NA Consensus, Rezaie 2017)

Formal SIBO Testing

- Recall: Barahona et al 2021
- No validation study yet for the methane sensor
- Nothing for H2S SIBO yet
- Can get Rx for lactulose (10g in 15 ml solution) or 75g glucose OTC (proximal SIBO only?)
- Can even use the fructose packet in the ‘challenge kit’ (false positive with fructose intolerance?)
- Follow the identical instructions for a mail order test. The app’s “challenge” function is excellent and gives step by step guidance.

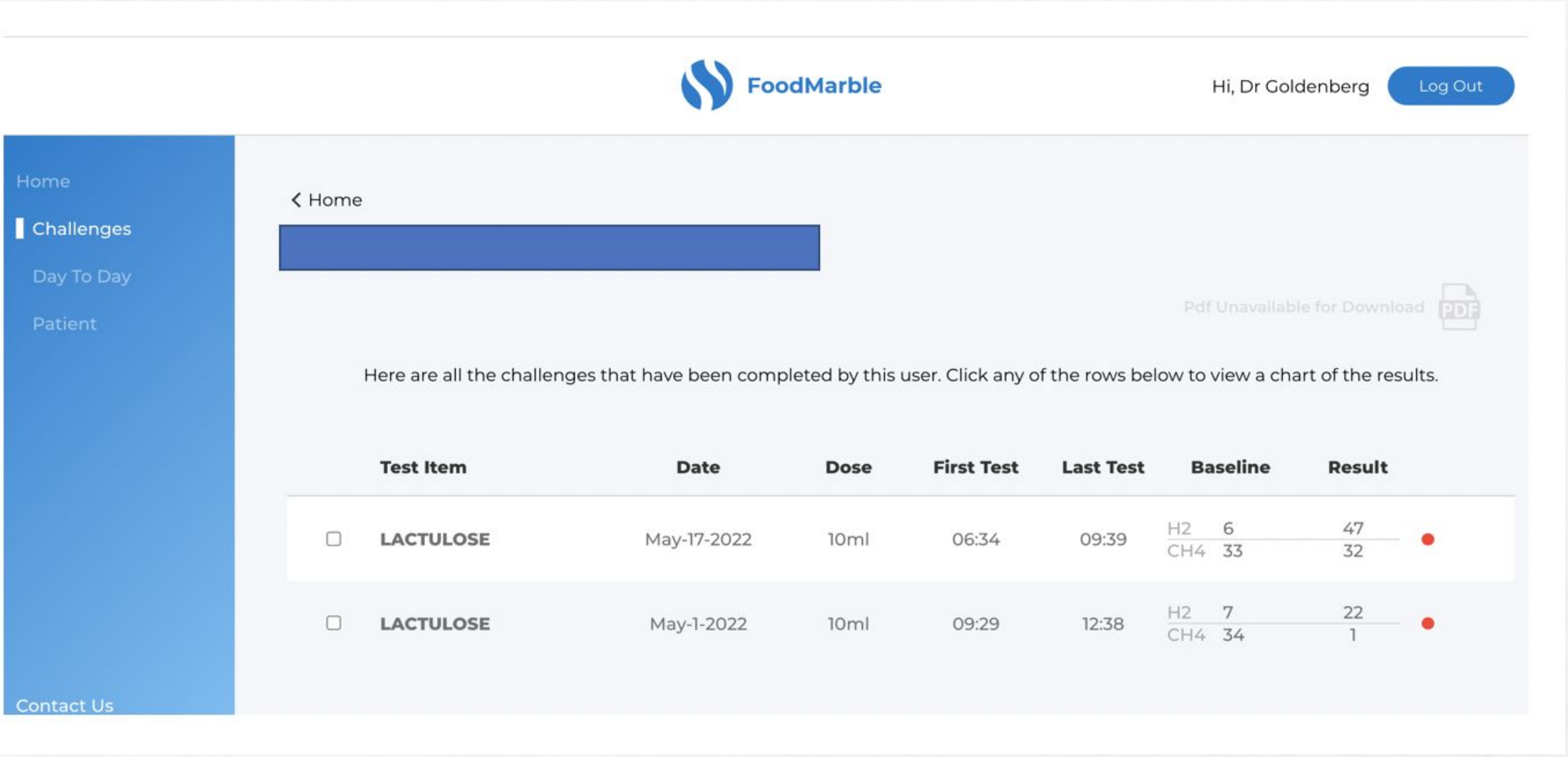


Formal SIBO Testing

Spot Testing to Track Progress

- In a patient with high SIBO levels I will start an intervention and then ask them to do a spot test once a week.
- I ask them to pick the same day of the week each time eat the same dinner the night before and breakfast and test using the breakfast as the challenge.
- I would like to see a steady decrease in gasses each week and if it starts plateauing we would do a formal challenge (SIBO test) to confirm.
- This is useful clinically in theory and easier on patients than doing a bunch of challenges.

Clinician Dashboard



Clinician Dashboard

Home

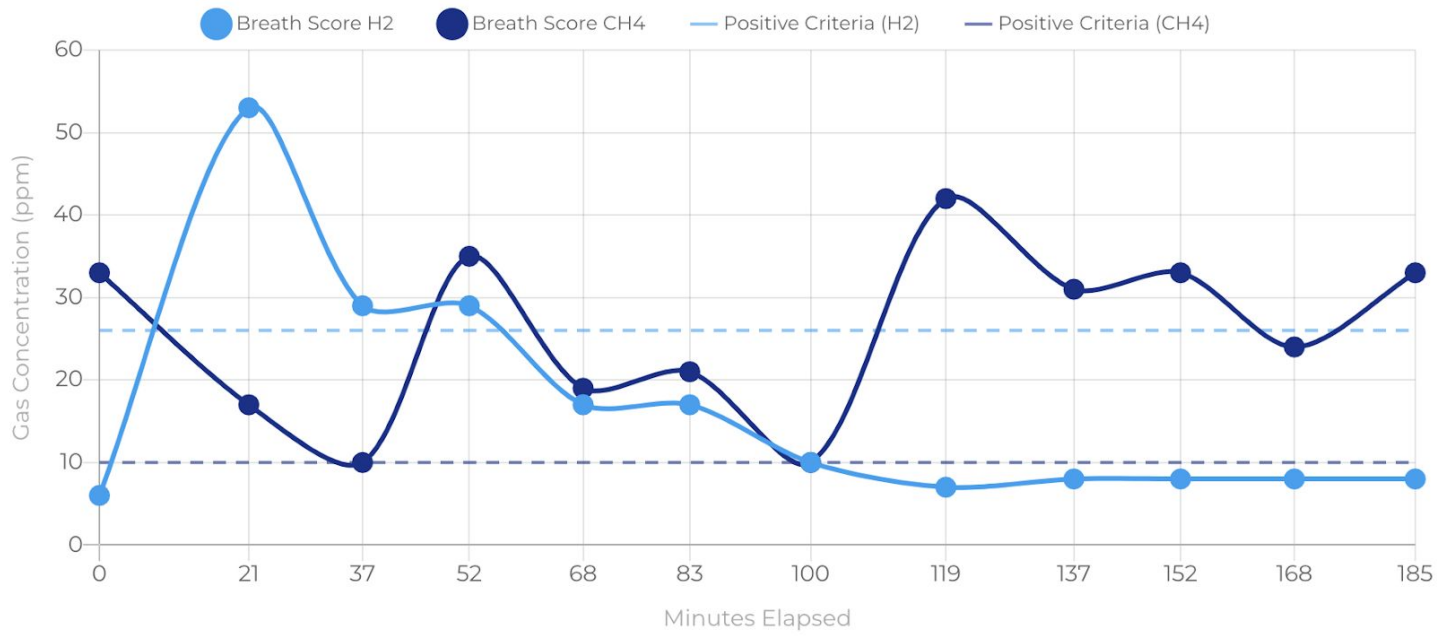
Challenges

Day To Day

Patient

Contact Us

	Test Item	Date	Dose	First Test	Last Test	Baseline	Result
☑	**LACTULOSE**	May-17-2022	10ml	06:34	09:39	H2 6 CH4 33	47 32



Download Challenge Report

FoodMarble

Patient

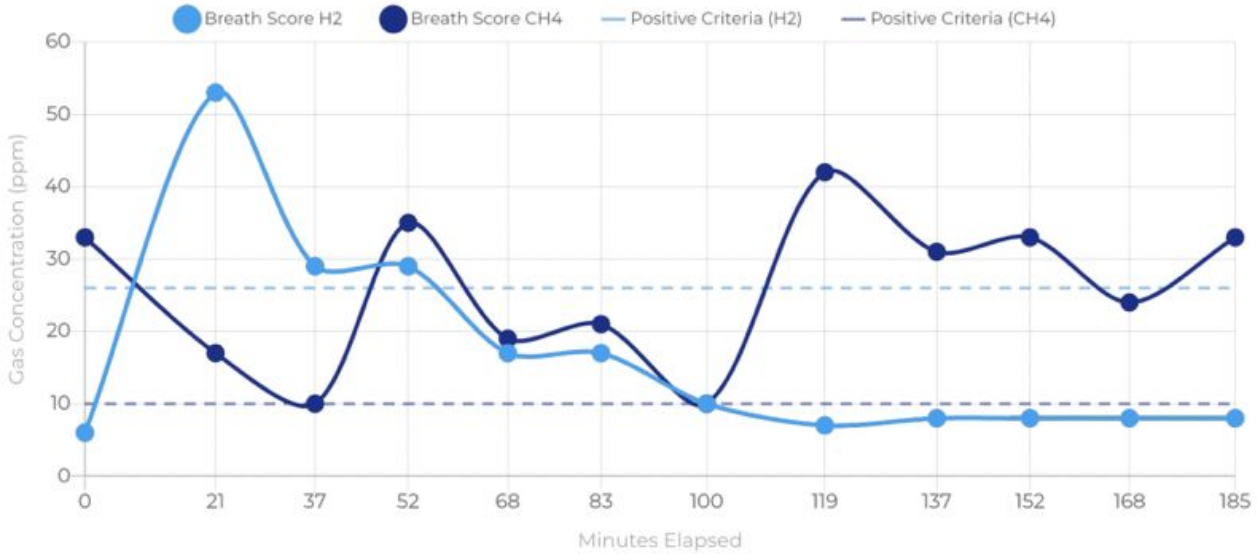
[redacted]

Clinician

Name: Dr Goldenberg

Email: drg@goldenberggicenter.com

Lactulose Challenge Result (05/17/2022)



Breath no.	base	1	2	3	4	5	6	7	8	9	10	11
Time, mins	0	21	37	52	68	83	101	119	137	153	168	185
H2, ppm	6	53	29	29	17	17	10	7	8	8	8	8
CH4, ppm	33	17	10	35	19	21	10	42	31	33	24	33
Gurgling			5.5	5.5	5.5	5.5	5.5	5.5	5.5	5.5	5.5	

Results

Hydrogen

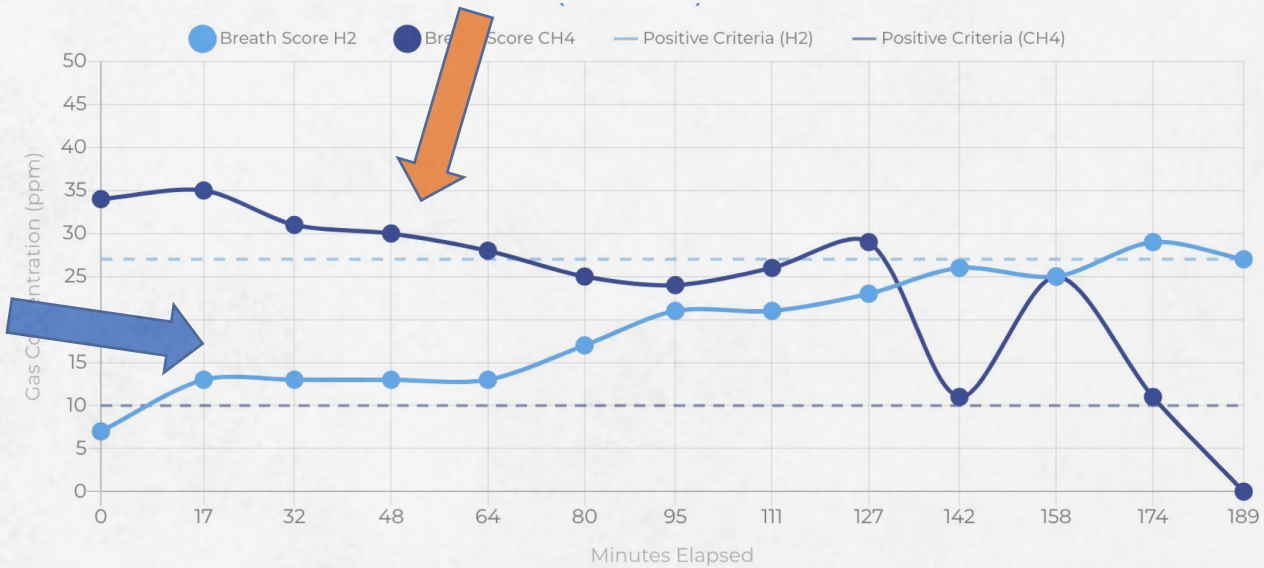
Baseline: 6 ppm (LOW) **Rise in 90 min:** 47 ppm (HIGH) **Peak in 90 min:** 53 ppm after 21 min

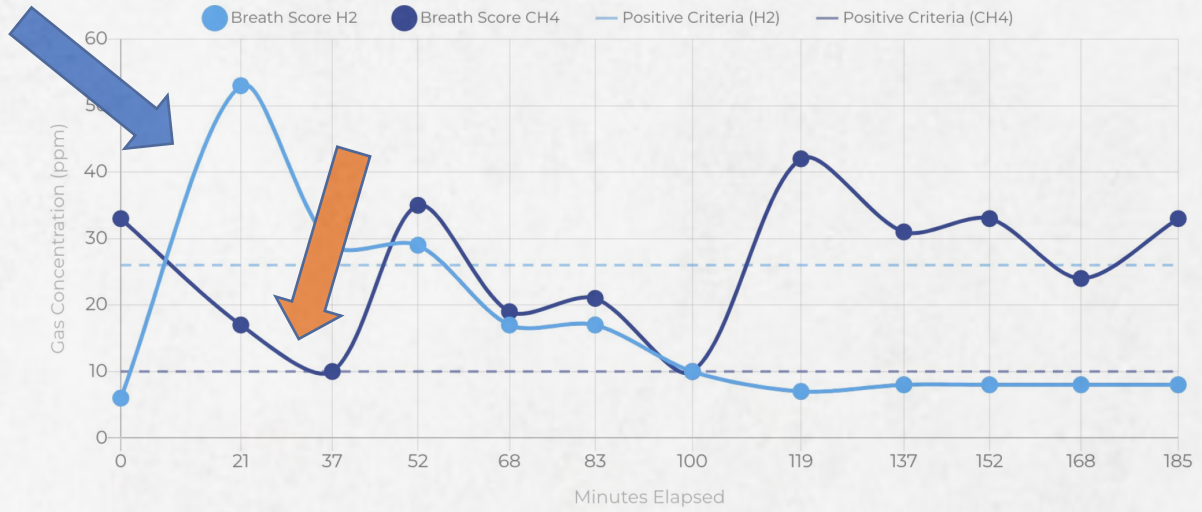
Methane

Baseline: 33 ppm (HIGH) **Rise in 90 min:** 2 ppm (HIGH) **Peak in 90 min:** 35 ppm after 52 min

AUC Analysis

- New feature in the works for clinician dashboard
- Case example. Pre/Post testing (lactulose) for a rifaximin intervention
- Hydrogen worse? Methane better? Overall improvement or worsening? Bail or stay the course?





AUC Analysis

- What was at first a confusing gas response is now clearer -> overall drop of 20ppm H2 equivalent. A positive gas response.
- Don’t bail!

Hours	AUC H2 ppm.hrs	AUC CH4 ppm.hrs	AUC H2 eq.hrs	AUC H2	AUC CH4	AUC H2 eq
0.00						
0.29	2.87	9.89	42.41			
0.54	3.36	8.53	37.47			
0.81	3.42	8.03	35.55			
1.07	3.37	7.51	33.43	12.19	31.81	139.45
1.34	4.05	7.15	32.66			
1.60	4.93	6.36	30.37			
1.86	5.43	6.46	31.29			
2.12	5.76	7.19	34.53			
2.38	6.34	5.17	27.03			
2.63	6.59	4.65	25.19			
2.90	7.18	4.79	26.32			
3.16	7.35	1.44	13.12	15.06	13.67	69.73

Hours	AUC H2 ppm.hrs	AUC CH4 ppm.hrs	AUC H2 eq.hrs	AUC H2	AUC CH4	AUC H2 eq
0.00						
0.35	10.44	8.84	45.81			
0.61	10.66	3.51	24.70			
0.87	7.50	5.82	30.76			
1.13	5.95	6.99	33.90	30.54	22.24	119.51
1.39	4.40	5.18	25.10			
1.68	3.86	4.43	21.60			
1.99	2.63	8.04	34.80			
2.28	2.23	10.85	45.63			
2.54	2.08	8.32	35.37			
2.80	2.07	7.38	31.58			
3.09	2.31	8.23	35.23	6.34	16.97	74.21

Important

- Fermentation scores **DO NOT** equal ppm!
- Nor are they in a linear relationship especially in Aire2
- High levels (>25ppm) in either gas can throw the overall “F” score
- For example, in trying to track the impact of oral methanogens on a patient with a high baseline methane (Erdrich 2021) a patient recorded a 6 before and then a 2 after chlorhexidine mouthwash for her methane ‘Fermentation score’ (out of 10). This looked like oral methanogens were dramatically impacting results, but when I checked the ppm, they were actually 31 ppm and 31 ppm both times! NO CHANGE and we could stick with future testing without mouthwash.
- FoodMarble is aware of this issue and is planning to change their calculations for Fermentation Scores

Pros

- Relatively cheap device that can be used hundreds of times allows for real life H2 and CH4 testing
- In small congruence testing Aire appears to perform similarly to Mail-ordered tests in healthy, SIBO suspected, and lactose intolerance suspected populations
- Allows for cheap and timely repeat testing, which is essential to good SIBO care in my opinion.
- Good for a ‘have it at the ready if you get nervous’ purpose for those in remission
- Clinician dashboard is excellent
- New features rolling out
- A small startup company but extremely responsive
- The company is clearly dedicated to a research focused approach

Cons

- **SO MUCH DATA.** Hard for some patients to tell the forest from the trees
- Can’t do H2S
- Patients/clients can’t see ppm
- It appears that (all?) the studies were industry sponsored although perhaps not all from FoodMarble.
- Can we trust the CH4 data? Validation studies are still pending

So... Game Changer?

- **I think so!**
- Bearing in mind all the caveats mentioned previously, this technology allows for cheap and timely repeat testing which has lowered the barriers to ideal SIBO monitoring in my practice.
- However, formal research on these devices is minimal and there are significant gaps particularly with the Aire2. So while I have embraced this technology I remain vigilant in terms of potential findings from future research or issues with clinical interpretation.

Questions & FoodMarble's Answers

Clinician Dashboard

- "Yes, the clinical dashboard is out of beta but we are always adding new features to improve the clinician experience and data interpretation abilities. The dashboard is free of charge for clinicians... We don't ask for people to submit their credentials. We do ask for a profile or company page so we can get a sense of them."
- We have recently created FoodMarble Classroom which provides guidance on data interpretation and has been particularly helpful for those new to breath testing.
- We also are creating a platform called FoodMarble Connect which is a database of clinicians who are already set up with FoodMarble. We have over 30k users and many of these are working without a clinician. However, very frequently we get asked to recommend a clinician to help them. Interested clinicians can sign up and we will make this database available to all of our existing and future users.

Questions & FoodMarble's Answers

Will end-users (customers/clients) be able to see ppm at any point or will you stick to fermentation scores?

- The direct-to-consumer device, AIRE, is designated a wellness device by the FDA, which basically means the device can be used for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.
- MedAIRE is listed as a medical device with the FDA, which is considered a tool to aid the clinician in the diagnosis of carbohydrate malabsorption or SIBO. We are currently getting advice on this from legal counsel, however, we hope to show ppm values to patients (and possibly consumers), if allowed by the FDA. It's a grey area!
- In the meantime, we also plan to split the Fermentation Score, to show one relating to each gas. This should help users track how each gas is changing over time.

Questions & FoodMarble's Answers

Loving the AUC approach and can use the excel you sent me. You mentioned this might be rolled out on the clinician dashboard.

- As mentioned above, we will offer a report to help assess changes and response to treatment. AUC seems like a useful measure to include.
- We are also adding medication tracking to the app, which will be helpful when tracking response to treatments over time.

Questions & FoodMarble's Answers

How does calibration work for Aire?

- The devices are calibrated in the factory upon manufacture and are remotely monitored when in use. If any sensor drift is identified, it can be automatically adjusted using a machine learning approach that has been developed over the last six years.

Questions & FoodMarble's Answers

Correction factors based on CO2 levels. Am I correct in understanding that you don't need to do this because the device measures after a certain number of seconds of blowing ensuring the measurements are indeed from alveolar air?

- A high-quality end-tidal breath sample is required for a reliable breath test result. In the case of AIRE, the user is instructed to hold their breath for three seconds before exhaling in order to promote adequate gas exchange in the lungs. Upon exhalation, the user is instructed to breathe slowly into the mouthpiece for five seconds. The sensor in the AIRE device performs optimally with a steady flow of breath and once the patient starts to exhale, readings are recorded continuously throughout the five seconds. The proprietary algorithm selects the end-tidal breath sample and is recorded in ppm. If a patient stops breathing before five seconds have been reached, they will be asked to retake the breath sample one minute later.

Questions & FoodMarble's Answers

What is MedAire versus Aire?

- MedAIRE (H2 only) and MedAIRE2 (H2 and CH4) are FDA-listed devices. There are minor differences between these and the direct-to-consumer devices. The key difference is that if a clinician wants to submit reimbursement, they must use a medical device. The colour of the device, packaging, and inner materials differ slightly (attached to the email). The Healthcare app only works with users who are linked to a dashboard account as a patient, whereas the direct-to-consumer app can work with consumers and patients. If a user is working with a doctor (linked to the dashboard as a patient), the app will provide access to SIBO tests (glucose and lactulose), and will not share test results with the patient, only the doctor. The pricing also differs slightly between the two and depends on volume.

Citations

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