Supplementary material:

Legend of Figures:

Figure S1: Forest plot of studies showing prevalence of SIBO in patients with FD, stratified according to the type of breath test. Overall, the prevalence of SIBO in FD utilizing breath tests is 32.7 (95%CI 21.6-46.1), p=0.012), (I_2=86.26, p=0.0001). SIBO prevalence in FD patients utilizing GBT is 17.2(95% CI 8.6-31.6), (I_2=0, p=0.651) and that utilizing LBT is 53.4(95% CI 33.9-71.9), (I_2=85.35, p=0.001).

Figure S2: Forest plot of studies showing prevalence of SIBO in patients with FD and controls, including only high-quality studies (OR=2.8 (95%CI 0.8-10.0), p=0.122), (I^2=20.38, p=0.285). All high-quality studies utilized GBT for SIBO diagnosis.

Figure S3(A): Search strategy for MEDLINE.

Figure S3(B): Search strategy for EMBASE.

Legend of Tables:

Table S1: Assessment of risk factors for SIBO in FD patients in the studies included in the systematic review and meta-analysis.

Table S2: Assessment of cut off criteria for diagnosing SIBO in FD patients and controls.

Table S3(A): Newcastle-Ottawa scale for assessment of quality of Case control studies included in the Systematic review and meta-analysis.

Table S3(B): Joanna Briggs Institute (JBI) Critical Appraisal Tools for assessment of quality of prevalence studies and the case group of the case-control studies included in the systematic review and meta-analysis.

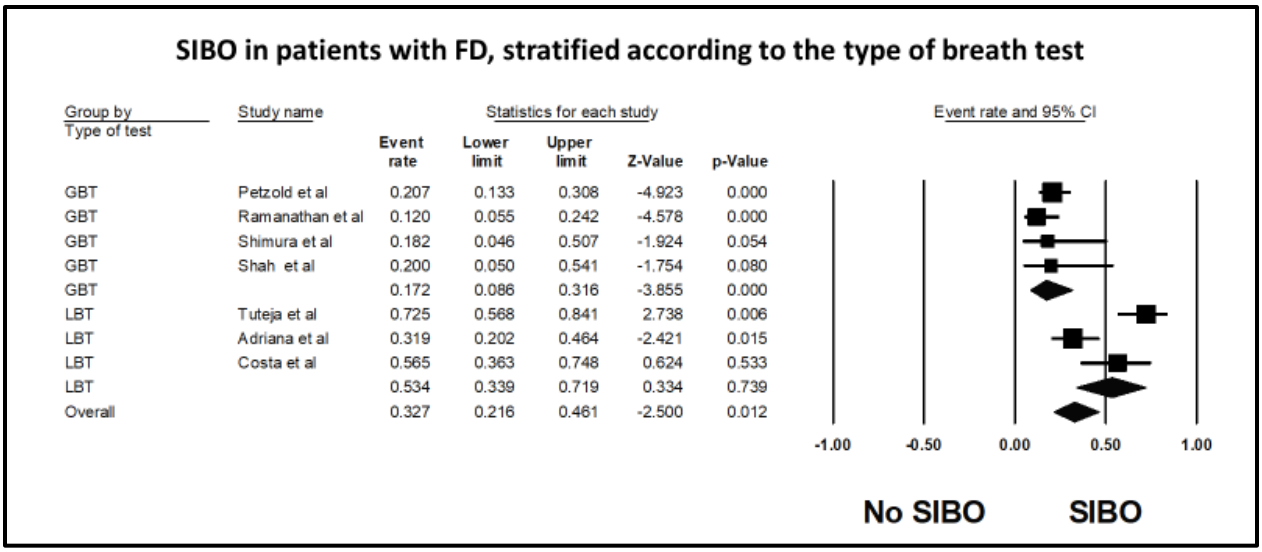

Figure S1: Forest plot of studies showing prevalence of SIBO in patients with FD, stratified according to the type of breath test. Overall, the prevalence of SIBO in FD utilizing breath tests is 32.7 (95%CI 21.6-46.1), p=0.012), (I^2=86.26, p=0.0001). SIBO prevalence in FD patients utilizing GBT is 17.2(95% CI 8.6-31.6), (I_2=0, p=0.656) and that utilizing LBT is 53.4(95% CI 33.9-71.9), (I_2=85.35, p=0.001).

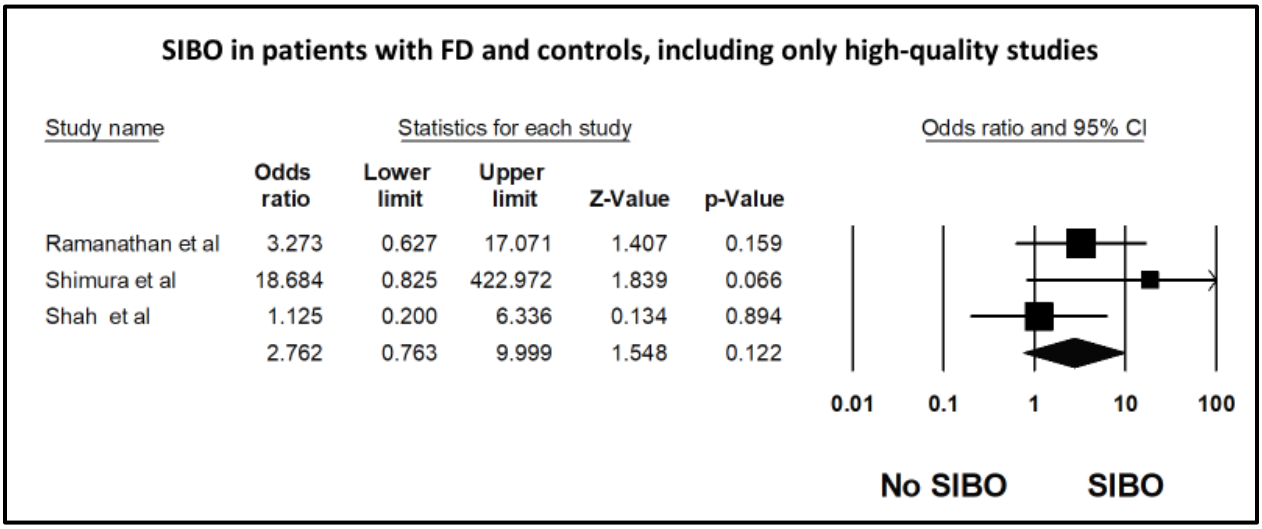

Figure S2: Forest plot of studies showing prevalence of SIBO in patients with FD and controls, including only high-quality studies (OR=2.8 (95%CI 0.8-10.0), p=0.122), (I^2=20.38, p=0.285).

Figure S3(A): Database search strategy MEDLINE(PubMed)
1. functional dyspepsia[tw] OR functional gastrointestinal disorder[tw] OR non-ulcer dyspepsia 2. Dyspepsia [MeSH Terms] 3. #1 OR #2 4. breath test[tw] OR small intestinal bacterial overgrowth[tw] OR SIBO[tw] OR small bowel bacterial overgrowth[tw] OR bacterial overgrowth[tw] OR gastric microbiome[tw] OR gut microbiome[tw] OR gut flora overgrowth[tw] OR intestinal flora overgrowth[tw] 5. breath tests [MeSH Terms] OR intestine, small [MeSH Terms] OR gastrointestinal microbiome [MeSH Terms] 6. #4 OR #5 7. #3 AND #6 **Limit:** 20yrs *Text Word [tw] = search in following fields, title, abstract, MeSH headings and subheadings, author supplied keywords, substances.*

Figure S3(A): Search strategy for MEDLINE.

Figure S3(B): Database search strategy EMBASE
1. 'functional dyspepsia': ti,ab OR 'functional gastrointestinal disorder':ti,ab 2. 'Dyspepsia'/exp 3. #1 OR #2 4. 'breath test':ti,ab OR 'small intestinal bacterial overgrowth':ti,ab OR 'SIBO':ti,ab OR 'small bowel bacterial overgrowth':ti,ab OR 'bacterial overgrowth':ti,ab OR 'gastric microbiome':ti,ab OR 'gut microbiome':ti,ab OR 'gut flora overgrowth':ti,ab OR 'intestinal flora overgrowth':ti,ab 5. 'breath analysis'/de OR 'hydrogen breath test'/exp OR 'single breath nitrogen test'/exp OR 'small intestine'/de OR 'intestine flora'/de 6. #4 OR #5 7. #3 OR #6 **Limit:** 20yrs *Article title: ti, abstract: ab, index term: de, drug trade name: tn, exploded index term /exp.*

Figure S3(B): Search strategy for EMBASE.

Table S1: Assessment of risk factors for SIBO in FD patients in the studies included in the systematic review and meta-analysis.

No	Author	Prior antibiotic use	Concurrent PPI use	Treatment with antibiotic	Duration of treatment	Treatment efficacy	Prior surgery
1	Petzold et al[1]	None within 1 week	NA	NA	NA	NA	NA
2	Tuteja et al[2]	NA	NA	NA	NA	NA	NA
3	Adriana et al[3]	None within prior 2 weeks	NA	NA	NA	NA	NA
4	Ramanathan et al[4]	None	None	Rifaximin 1200 mg once daily	10 days	Improvement in symptoms Normalization of GBT 4 weeks after completion of treatment.	None
5	Shimura et al[5]	None within prior 4 weeks	12/23 were on PPI	Levofloxacin 500 mg once daily	7 days.	Improvement in symptoms Normalization of GBT at the end of treatment. No adverse events were reported.	None (except appendicectomy)
6	Costa et al[6]	NA	Yes	NA	NA	NA	NA
7	Shah et al[7]	NA	3/10 were on PPI	NA	NA	NA	No

FD: functional dyspepsia; SIBO: small intestinal bacterial overgrowth; GBT: glucose breath test; NA: not applicable.

Table S2: Assessment of cut off criteria for diagnosing SIBO in FD patients and controls.

No	Author	Mode of diagnosis of SIBO	Type of breath collection devices	Dose of substrate	Cut off criteria for SIBO diagnosis
1	Petzold et al[1]	GBT	NA	50g glucose	Hydrogen rise of > 20 ppm from the baseline.
2	Tuteja et al[2]	LBT	"AlveoSampler" (Quintron Instrument Co. Inc., Milwaukee, WI, USA)	10g lactulose	Hydrogen rise of ≥20 ppm during the first 90 mins. Dual hydrogen peaks (12 ppm increase over baseline with a decrease of ≥5 ppm before 2nd peak). Positive for methane if any concentration of methane during the test was >1 ppm.
3	Adriana et al[3]	LBT	NA	10g lactulose	No clear cut off for SIBO diagnosis.
4	Ramanathan et al[4]	GBT	Gastro+ Gastrolyzer (Bedfont, Scientific, Kent, UK).	100g glucose	Hydrogen rise >12 ppm above the baseline value.
5	Shimura et al[5]	GBT	(Gastro+ Gastrolyzer, Bedfront Scientific, Kent, UK).	50g glucose	Baseline hydrogen value >10 ppm and the subtracted peak value above the baseline at ≥10 ppm within 60 or >120 mins after glucose ingestion.
6	Costa et al[6]	LBT	"AlveoSampler" (Quintron Instrument Co. Inc., Milwaukee, WI, USA)	15 mL lactulose	Fasting hydrogen peak >20 parts per million(ppm) or two peaks >10 ppm sustained until 60 minutes after ingestion of lactulose.
7	Shah et al[7]	GBT	Breathtracker digital microlyser (Quintron Instrument Company Inc., Milwaukee, WI, USA).	75g glucose	Rise in $CH_4 \geq 10$ppm and/ or in $H_2 \geq 20$ppm above baseline.

FD: functional dyspepsia; SIBO: small intestinal bacterial overgrowth; GBT: glucose breath test; LBT: lactulose breath test; ppm: parts per million; NA: not applicable.

Table S3(A): Newcastle-Ottawa scale for assessment of quality of Case control studies included in the systematic review and meta-analysis.

	Ramanathan et al[4]	Shimura et al[5]	Costa et al[6]	Shah et al[7]
SELECTION				
Is the case definition adequate?	*	*	-	*
Representativeness of the cases	*	*	*	*
Selection of Controls	*	*	*	-
Definition of Controls	*	*	-	*
COMPARIBILITY	*			
Study controls for single factor	*	*	-	*
Study controls for additional factors	*	*	-	*
EXPOSURE				
Ascertainment of exposure (presence of SIBO)	*	*	*	*
Same method of ascertainment for cases and controls	*	*	*	*
Non-Response rate	*	*	*	-
Overall Quality Score (Maximum = 9)	**9**	**9**	**5**	**7**
Reason for exclusion			**a & b**	

*each asterisk represents if individual criterion within the subsection was fulfilled.

a) Criteria for cases or controls insufficiently defined.

b) Controls include could include patients with unexplained gastrointestinal symptoms. Thus, the study lacks appropriate control group.

Ramanathan et al: 50 consecutive patients attending gastroenterology outpatient's clinic, newly diagnosed with FD (according to Rome III) were prospectively recruited. Well defined exclusion criteria. FD patients were further subclassified into FD-subtypes. 50 healthy, asymptomatic individuals attending the master health check-up OPD, not on a PPI and/or antibiotics were selected. All participants underwent GHBT within 2 days of recruitment.

Shimura et al: 28 patients with refractory FD (Rome III), defined as the condition, which was failed initial treatment, including prokinetics, acid inhibitory drugs, antidepressants for at least 4 weeks. FD patients were further subclassified into FD-subtypes. Well defined exclusion criteria. 35 control subjects (healthy volunteers) with no gastrointestinal symptoms were recruited. All participants fulfilled the exclusion criteria. Abdominal symptoms in all enrolled patients were assessed using the locally developed validated symptom questionnaire (Izumo scale) prior to the hydrogen breath test.

Costa et al: 23 patients with one or more dyspeptic symptoms (Rome III) and 11 controls (without dyspeptic symptoms) were recruited in this study. Structural lesions excluded in patients. Symptoms were assessed with a questionnaire, based on Rome III criteria. Authors state that they difficulties to recruit asymptomatic controls.

Shah et al: 10 consecutive patients attending gastroenterology outpatient's clinic, diagnosed with FD (according to Rome IV) were prospectively recruited. Well defined exclusion criteria. FD patients were further subclassified into FD-subtypes. Control group included 44 patients referred for investigation of IDA or positive faecal occult blood test (negative findings on endoscopy) and without gastrointestinal symptoms. All participants underwent GBT and symptoms were recorded utilizing a standardized validated questionnaire.

Table S3(B): Joanna Briggs Institute (JBI) Critical Appraisal Tools for assessment of quality of prevalence studies and the case groups of the case-control studies included in the systematic review and meta-analysis.

	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Risk of bias
Shimura et al[5]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NA	Low
Costa et al[6]	No	Yes	No	Yes	Yes	Yes	Yes	Yes	NA	Moderate
Ramanathan et al[4]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Low
Adriana et al[3]	No	Unknown	No	No	Unclear	Yes	Yes	Unclear	NA	High
Petzold et al[1]	Yes	No	Yes	No	No	Unclear	Unclear	No	NA	High
Tuteja et al[2]	No	No	Yes	Yes	Yes	Yes	No	Yes	NA	High
Shah et al[7]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NA	Low

NA; not applicable.

References:

1. Petzold G, Amanzada A, Gress TM, Ellenrieder V, Neesse A, Kunsch S. High Prevalence of Pathological Hydrogen Breath Tests in Patients with Functional Dyspepsia. Digestion 2019;100:186-91.
2. Tuteja AK, Talley NJ, Stoddard GJ, Samore MH, Verne GN. Risk factors for upper and lower functional gastrointestinal disorders in Persian Gulf War Veterans during and post-deployment. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society 2019;31:e13533.
3. Adriana B AB, Matthew D, Angela A, Doming T and Miguel PJ. Gastric Fermentation in Functional Dyspepsia. Gastroenterology & Hepatology International Journal 2019;4.
4. Ramanathan S, Karunakaran P, Mohamed KS, et al. A study on the role of small intestinal bacterial overgrowth in patients with functional dyspepsia. International Archives of Integrated Medicine 2017;4:88.
5. Shimura S, Ishimura N, Mikami H, et al. Small Intestinal Bacterial Overgrowth in Patients with Refractory Functional Gastrointestinal Disorders. Journal of neurogastroenterology and motility 2016;22:60-8.
6. Costa MB, Azeredo IL, Jr., Marciano RD, Caldeira LM, Bafutto M. Evaluation of small intestine bacterial overgrowth in patients with functional dyspepsia through H2 breath test. Arquivos de gastroenterologia 2012;49:279-83.
7. Shah A, Talley NJ, Koloski N, et al. Duodenal bacterial load as determined by quantitative polymerase chain reaction in asymptomatic controls, functional gastrointestinal disorders and inflammatory bowel disease. Alimentary pharmacology & therapeutics 2020;52:155-67.