Appendix 1: Rome criteria[44]

Rome I	Rome II	Rome III	Rome IV
At least 3 months of continuous or recurrent abdominal pain or discomfort relieved with defecation *and* disturbed defecation (2 or more features):	At least 12 weeks or more, which need not be consecutive, in the preceding 12 months, of abdominal discomfort or pain with at least 2/3 features:	Recurrent abdominal pain or discomfort at least 3 months days/months in the last 3 months, with onset 6 months prior to diagnosis, associated with two or more of the following criteria:	Recurrent abdominal pain or discomfort at least 1 day/week in the last 3 months with onset 6 months prior to diagnosis associated with two or more of the following criteria:
1. Altered stool frequency	1. Relieved by defecation	1. Improvement with defecation	1. Related to defecation
2. Altered stool form (hard or loose/watery)	2. Onset associated with a change in frequency of stool	2. Onset associated with a change in frequency of stool	2. Associated with a change in frequency of stool
3. Altered stool passage (straining or urgency, feeling of incomplete evacuation)	3. Onset associated with a change in form (appearance) of stool	3. Onset associated with a change in form (appearance) of stool	3. Associated with a change in form (appearance) of stool
4. Passing of mucus			
Note: the original Rome classification was first published in 1990 and has since been modified with each iteration to develop the subsequent classifications with Rome II, III and IV.			

Appendix 2: National Health Institute Quality Assessment Tool[11]

Criteria	**Yes**	**No**	**Other (CD, NR, NA)**
1. Was the study described as randomized, a randomized trial, a randomized clinical trial or an RCT?	(1)		
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	**(1)**		
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	(1)		
4. Were study participants and providers blinded to treatment group assignment?	(2)		
5. Were the people assessing the outcomes blinded to the participants' groups assignments?	(1)		
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	(2)		
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	(2)		
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	(2)		
9. Was there high adherence to the intervention protocols for each treatment group?	(1)		
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	(1)		
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	(1)		
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the	(2)		

main outcome between groups with a least 80% power?			
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	(1)		
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	(2)		
	(20)		

Quality rating: good (≥16), fair (11-15), or poor (≤11)

Appendix 3. Characteristics and quality assessment of excluded articles ordered by publication date

Author, year of publication, country	**Population and sample size**	**Intervention**	**Quality assessment**
Anastasi et al., 2009, United States[38]	Male and female patients with IBS. **n=29**	Acupuncture and moxibustion (Acu/Moxa) Sham/placebo	POOR - High overall drop-out (21%) - Small sample size (n=29)
Spiller et al., 2008, United Kingdom[39]	Male and female non-D, non-C IBS patients according to Rome II n=168	Renzapide 1mg Renzapide 2mg Renzapide 4mg Placebo	POOR - High overall drop-out (30%) - Differential drop-out >15%
Lackner et al., 2007, United States[40]	Male and female IBS patients according to Rome II **n=147**	Cognitive behavioral therapy Psychoeducation Waiting list control	POOR - Not blinded - Control group was on waiting list: bias risk was high
Nakai et al., 2004, Canada[41]	Male and female non-C IBS patients according to Rome I **n=11**	Alosetron 1mg placebo	POOR - Small sample size - Not enough statistical power
Parisi et al. , 2002, Italy[42]	Male and female patients with IBS according to Rome I **n=188**	Fiber (30 g/day of wheat bran) Partially hydrolyzed guar gum (PHGG) (5 g/day)	POOR - Study not blinded nor placebo controlled. - Crossover between groups was allowed.