

Adherence with low FODMAPs diet in Irritable Bowel Syndrome: are eating disorders the missing link?

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Abstract

Objectives: The low FODMAPs diet has emerged as an option for the treatment of irritable bowel syndrome (IBS). One major challenge of this diet is that it is very restrictive, and compliance is usually low. Preliminary findings suggest an association between eating disorder (ED) and the risk of developing IBS. The primary aim of the study is to assess the correlation between compliance to low FODMAPs diet and risk of eating disorder behaviours among an irritable bowel syndrome cohort.

Methods: We report a single centre study in the IBS patient population at University College London Hospital (UCLH). 233 patients (186 female) who commenced a low FODMAPs group programme for IBS (Rome III or IV). Self-reported diet adherence at the end of the 6-week programme was measured. At baseline, participants completed the SCOFF questionnaire (a validated 5-item screening tool for EDs), the validated HADS questionnaire and the validated IBS-symptom severity score (IBS-SSS).

Results: The SCOFF questionnaire identified 54 (23%) patients at an increased risk of ED behaviour. Overall, 95 (41%) participants were diet-adherent at 6 weeks, with significantly greater adherence in identified ED individuals (57%). The highest adherence rate (51%) was in the IBS-D subtype and the lowest rate (10%) in IBS-C. There was no significant relationship between IBS symptom severity and either adherence or ED severity.

Conclusion: In our IBS patient cohort greater adherence to a low FODMAPs diet is associated with eating disorder behaviour. The implications of our study are for clinicians to have a high index of suspicion of EDs in IBS patients, but also that low FODMAPs dietary advice to the general IBS population should be couched alongside psychological support.

Keywords: Irritable bowel syndrome, SCOFF, FODMAP, IBS-SSS, HADS

Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder with a United Kingdom (UK) prevalence estimated at 10-20% according to the criteria used to define IBS[1-3]. One meta-analysis showed a pooled estimate of international IBS prevalence of 11.2% (95% confidence interval [CI] 9.8–12.8), with variation by geographic region; the lowest occurring in South Asia (7.0%) and the highest in South America (21.0%) [X]. Rome IV criteria allow classification into IBS subtypes based on stool frequency and consistency – hence IBS with constipation (IBS – C), diarrhoea (IBS – D), mixed stool pattern (IBS – M) and unclassifiable (IBS – U) [4].

IBS is a heterogeneous condition with a mixed aetiology [5]. A psychological dimension to the aetiology of IBS is also proposed and there is frequent comorbidity with anxiety and affective disorder [6]. In addition negative self-esteem and aberrant coping mechanisms [7], somatization tendency [8] and eating disorder (ED) behaviour have been described. Studies have shown that ED behaviour can increase the likelihood of IBS diagnosis [9] and IBS is prevalent in patients with bulimia nervosa [10].

Consequently, management of IBS requires a multi-modal approach including medications, patient education and lifestyle change. Of particular interest in recent times has been to reduce fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs). Collectively

these are short chain carbohydrates which are not well absorbed in the small intestines and hence transit into the large intestine. This leads to an osmotic effect and coupled to the fermentation can enhance the symptoms of IBS [11]. Reducing the intake of these food components have been shown to reduce the symptom severity of IBS and it has been suggested as a first line therapy [12-15].

Clinically the aim of a low FODMAP diet is to globally restrict all FODMAPs from the diet for approximately 4-8 weeks to establish if there is any reduction of IBS symptoms. If there is a symptomatic improvement, then FODMAPs are slowly reintroduced, individually, while closely monitoring symptoms. The long-term aim is to allow a nutritionally robust diet with effective symptom control [16]. However even this short term global restriction can be very challenging because of how widespread these carbohydrates are in a normal diet [14].

The effectiveness of a diet must always be balanced against the risk of inadequate nutrient intake and in the case of the low FODMAP diet, some studies have suggested that long term adherence is associated with lower carbohydrate and energy intake [13,17,18 W Y]. Therefore, strict long-term adherence the low FODMAP diet can pose risk to health. This effect is particularly relevant to the subgroup of IBS who are at risk of ED. The main aim of our study is to investigate the association between high compliance with a low FODMAPs diet and eating disorders trait.

Methods

This was a prospective single centre study which was carried out at University College London Hospital (UCLH) on patients who attended the IBS clinic. A total of 233 patients were enrolled into the study, 186 females with a mean age of 38 years (range 20-70). All patients who were refractory to conservative therapy (low-fibre diet, anti-spasmodics, anti-diarrhoeal) were referred to the low FODMAP diet service. All patients were assessed to exclude gastrointestinal organic diseases. Patients with previous bowel surgery, bile acid diarrhoea (positive SeHCAT study), positive celiac serology (Anti Transglutaminase Antibodies) or faecal Calprotectin >50 micrograms/gram – all were excluded. All patients signed informed consents. The study was undertaken as part of the prospective data collection and audit of the dietary service in our institution.

All patients completed the standard instruments used in the service including the SCOFF questionnaire, the Hospital anxiety and Depression Scale (HADS) and the IBS-symptom severity score (IBS-SSS). At the baseline and routine follow-up visits after six weeks, symptom outcome (subjective and IBS-SSS based) and adherence were assessed by semi-structured interview, and the data recorded on the previously printed questionnaires. Adherence was defined as complying with the low FODMAP diet for more than 75% of total food intake.

QUESTIONNAIRES:

The SCOFF questionnaire was developed in 1999 by John Morgan at Leeds Partnerships NHS Foundation trust and is now a widely used screening tool which helps detect patients with eating disorder behaviour. The questionnaire has been shown to have a sensitivity of 84.6% and a specificity of 89.6% in the primary care setting (19) and reports a false positive

rate of 12.5%; which is thought to be an acceptable trade off to the high sensitivity (20). It consists of the following questions:

1. Do you make yourself Sick because you feel uncomfortably full?
2. Do you worry you have lost Control over how much you eat?
3. Have you recently lost more than One stone in a 3-month period?
4. Do you believe yourself to be Fat when others say you are too thin?
5. Would you say that Food dominates your life?

Each positive response to these questions give a score of 1 and a score of 2 or greater indicates an increased risk of eating disorder behaviour (19).

The Hospital Anxiety and Depression Scale (HADS) is a validated screening tool to assess levels of anxiety (HAD-A) and depression (HAD-D) in hospital patients(21). It consists of 14 questions which can be answered on a 4-point scale. A score of 0-7 is considered normal, 8-10 is borderline and 11-21 is considered abnormal and likely to represent a underlying depressive or anxiety disorder (22). HADS has been used previously in IBS to screen for anxiety and depression (23) and to explore the link between these conditions (24).

The irritable bowel syndrome severity scoring system (IBS-SSS) was validated in 1997 to help monitor progress of IBS and to group patients according to severity in mild moderate and severe; to allow research and tailor treatments. A score of less than 75 is considered normal and the maximum score is 500 (25).

Results

A total of 233 patients were enrolled with long history of IBS symptoms mean 13 years, mean age is 38 years old, 79.8% was female. Using the Roma IV criteria subjects were classified in four subtypes: % IBS-D, % IBS-C, % IBS-M, % IBS-U. The demographics of each group are shown in table 1.

Table1:

	n	mean age [range ±SD]	symptom duration [range ±SD]	<u>Sex (f %)</u>
IBS-D	140	37.8 (21-68 ±)	12.4 (0.5-19 ±)	<u>49.4</u>
IBS-C	19	35.5 (25-69 ±)	14.5 (1-23 ±)	<u>7.3</u>
IBS-M	15	38.8 (20-66 ±)	10.8 (4-13 ±)	<u>3.0</u>
IBS-U	59	40.0 (23-70 ±)	15.6 (3-20 ±)	<u>20.2</u>
Total	233	38.2 (20-70 ±)	13.3 (0.5-23 ±)	<u>79.8</u>

At baseline no difference of IBS-SSS was detected in the various IBS subgroups.

	Mean baseline IBS-SSS [±SD] (range)	Mean IBS-SSS at 6 weeks* [±SD] (range)
IBS -D	286 [± 97]# (n=140) (138-404)	258 [±94] (n=133) (144-380)
IBS- C	239 [±80] (n=19) (169-355)	276 [±86] (n=19) (186-370)
IBS-M	270 [± 86] (n=15) (188-382)	247 [±77] (n=14) (187-361)
IBS-U	297 [±90]# (n=59) (179-396)	260 [±89] (n=56) (153-389)
Total	284 [±89] (n=233) (138-404)	259 [±87] (n=222) (144-389)

We found no significant relationship between IBS-SSS and either adherence or eating disorder behaviour

At baseline the SCOFF questionnaire identified 54 (23%) IBS patients at an increased risk of eating disorder behaviour in the cohort (table 2). The most common positive response was to 'would you say food dominates your life' and the least common was to 'do you believe to be fat when others say you are too thin'.

Table 2 shows SCOFF outcomes with adherence rates

	adherent	non-adherent
1. Do you make yourself <u>S</u> ick because you feel uncomfortably full?	15	3
2. "Do you worry you have lost <u>C</u> ontrol over how much you eat?	28	38
3. Have you recently lost more than <u>O</u> ne stone in a 3-month period?	31	24
4. Do you believe yourself to be <u>F</u> at when others say you are too thin?	9	1
5. Would you say that <u>F</u> ood dominates your life?	38	45
0 SCOFF replies (n=119)	46	73
1 SCOFF reply (n=60)	18	42
2 SCOFF replies (n=16)	8	8
3 SCOFF replies (n=19)	10	9
4 SCOFF replies (n=12)	8	4
5 SCOFF replies (n=7)	5	2

	baseline SCOFF[±SD] (range)	SCOFF at 3 months* [±SD] (range)
SCOFF = 0 (n=119)	275 [± 93] (138-389)	239 [±87] (n=115)# (144-342)
SCOFF =1 (n=60)	287 [±87] (145-404)	266 [±91] (n=55)# (156-381)
SCOFF >2 (n=54)	301 [± 86] (203-402)	296 [±86] (n=52) (198-389)
Total	284 [±89] (n=233) (138-404)	259 [±87] (n=222) (144-389)

In the whole cohort, 95 (41%) participants were adherent to the low FODMAPs diet at the six weeks follow up appointment. The highest adherence was seen in the IBS-D group with a rate of 51%. The lowest adherence rate was seen in the IBS-C group with a rate of 10% (albeit that this was a small sub-group). Table 3 shows the adherence rates based on IBS subtype. There was significantly higher adherence (57%) in the patients who tested positive

in the SCOFF questionnaire.

There were significant differences in adherence in the different subclasses of IBS.

Table 3: Diet adherence, IBS-SSS, HAD score in different IBS subtypes.

	diet adherence at 6 weeks (%)	baseline IBS-SSS (range)	baseline HAD-A		baseline HAD-D	
			mean (range)	n score >10 (%)	mean (range)	n score >10 (%)
IBS-D	51%	286 (138-404)	7.6 (4-18)	32%	5.9 (3-19)	18%
IBS-C	10%	239 (169-355)	6.8 (3-16)	16%	6.7 (4-18)	32%
IBS-M	40%	270 (188-382)	6.7 (4-16)	20%	6.3 (3-17)	27%
IBS-U	27%	297 (179-396)	7.1 (3-19)	31%	5.7 (4-18)	24%
Total	41%	284 (138-404)	7.4 (3-19)	30%	5.9 (3-19)	21%

In the whole cohort, 30% of patients scored positively (i.e. >10) in the HAD-A questionnaire and 21% scored positively (i.e. >10) in the HAD-D. Higher HAD-A scores were seen in the IBS-D and IBS-U subgroups whereas higher HAD-D scores were seen in the IBS-C and IBS-M subgroups. There was a positive correlation between HAD-A score and SCOFF questionnaire ($p=0.01$) and also between HAD-D score and SCOFF questionnaire ($p=0.03$).

Discussion

Eating disorders are a group of similar conditions where one can develop a negative outlook on their eating habits, body image and weight. This can lead patients to adopt unhealthy behaviours such as dietary restriction, excessive exercise or bulimia [26]. These underlying beliefs about themselves help drive the disorder and often can lead to severe malnourishment states. It has been estimated that in the UK, between 2012-2013, there were 725,000 admissions to hospital due to eating disorder behaviour [26]. It is estimated that currently approximately 1.25 million people in the UK are affected with a form of eating disorder [27].

There are some groups who are more at risk of developing eating disorder behaviour, such as females are at increased risk and this finding has been replicated outside the UK as well [28–30]. In addition to this, although it is widely thought that teenage girls are at the most risk, eating disorders are known affect people of all ages [31]. Previous studies have shown that eating disorders are prevalent in the student population and it is thought that factors such as high stress levels, high academic expectations, competition and social isolation can increase this risk [29, 32, 33]. This study is the first publication to identify the prevalence of eating disorder traits in a cohort of IBS patients. With approximately one out of four patients in a tertiary care IBS service having abnormal SCOFF scores, it is important that clinicians keep in mind the possibility of anorexia and bulimia as co-morbidities which may influence patient care.

Eating disorder behaviour can often present in a comorbid nature with other psychological illnesses such as anxiety based personality disorders (obsessive compulsive disorder) and borderline personality disorder [34,35]. Depression and anxiety are also strongly linked to

eating disorder behaviour [6,36] and thought to play a role in its progression [37]. A study by Winstead et al [38] highlighted that eating disorder behaviour has strong associations with physiological abnormalities also. They carried out a cohort study and found that patients with eating disorders were significantly more likely to present with a gastrointestinal complaint before seeking treatment for the eating disorder itself. The symptoms that these patients presented with had a huge degree of overlap with functional gastrointestinal disorders such as IBS and the authors proposed that screening should be implemented with patients who present in this manner [39], these findings are crucial since they address a potential relationship between IBS and ED.

In our cohort, there was a relationship between anxiety and depression, as measured by the HADS questionnaire, to adherence to the low FODMAP diet. Several studies have used the HADS to show the link between anxiety and depression with functional abdominal pain [40]. Other studies have shown that anxiety is a strong indicator of severity of symptoms [41] and quality of life in patients with IBS [42].

From our data it can be seen that greater adherence to a low FODMAP diet is associated with the symptoms associated with eating disorder behaviour, as measured by the SCOFF questionnaire. Of all the patients who tested positive for eating disorder behaviour, there was an adherence rate of 57.4% compared to 35.8% in those who tested negative for eating disorder behaviour. This is a 60% difference between the two groups.

In a study by Geary et al [43], a low FODMAP diet was used to treat inflammatory bowel disease and they found an adherence rate of up to 70% in their study population. Shephard et al [44] found that adherence was 77% when a low fructose diet was used to treat IBS and Maagaard et al [45] found that in long term a third of their functional gastrointestinal patient population remained adherent to a low FODMAP diet. Although there are variations between studies, partly due to variations on what defines adherence and variations among patient's

populations, all these studies found that the diet helps control the symptoms of IBS, and adherence was higher among IBS patients, compared to other patient's groups, like IBD patients. Therefore, although associated with greater effect, strict adherence with a low FODMAP diet should raise the suspicion of a possible underlying eating disorder.

Adherence is also related to the subtype of IBS. The highest rate of adherence in the IBS-D group could be explained by the fact that FODMAPs are poorly absorbed in the gut and hence reducing this leads to less fermentation. As a result, the symptoms associated with IBS-D would be improved and this would motivate participants to adhere more to the diet. The converse could be true for the IBS-C subtype, where the symptoms could have been worsened and hence lead the participants to be less adherent.

This study has limitations in that it relies on the patients' self-reported adherence to the diet as reported to a dietitian. To reduce the chance of misreporting, a more formal dietary diary could have been undertaken. In addition a more frequent follow-up study could provide better understanding of the reasons for adherence or lack thereof. It would also be interesting to see how sustained the adherence is in the identified eating disorder group with an increased dieting period. Furthermore, this study did not have a control group which made it difficult to assess the baseline adherence to the low FODMAPs diet.

In conclusion, this study shows that higher level of adherence to the low FODMAPs diet is associated with eating disorder behaviour among patients with IBS. This has clinical implications in that one should have a high index of suspicion of EDs in IBS patients highly adherent to low FODMAPs diet.

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References

1. Sood R, Law GR, Ford AC. Diagnosis of IBS: symptoms, symptom-based criteria, biomarkers or “psychomarkers”. *Nat Rev Gastroenterol Hepatol*. 2014;11:683–691.
2. Sperber AD, Dumitrascu , Fukudo S, Gerson C , Ghoshal UC, Gwee KA, et al. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. *Gut*.2017 ;66:1075–1082.
3. NICE. Irritable bowel syndrome in adults: diagnosis and management. Clinical guideline [CG61].
4. Chang L. Updates to the Rome Criteria for Irritable Bowel Syndrome. *Gastroenterol Hepatol (N Y) [Internet]*. 2017;13:304–306. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5479345/>
5. El-Salhy M. Recent developments in the pathophysiology of irritable bowel syndrome. *World J Gastroenterol*. 2015;21:7621–7636. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491952/>
6. Fond G, Loundou A, Hamdani N, Boukouaci W, Dargel A, Oliveira J, et al. Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. *Eur Arch Psychiatry Clin Neurosci*. 2014;264:651–660.
7. Grodzinsky E, Walter S, Viktorsson L, Carlsson AK, Jones MP, Faresjo A. More negative self-esteem and inferior coping strategies among patients diagnosed with IBS compared with patients without IBS-a case-control study in primary care. *BMC Fam Pract*. 2015;16:6.
8. Folks DG. The interface of psychiatry and irritable bowel syndrome. *Curr Psychiatry Rep*.2003;6:210–215.

9. Perkins SJ, Keville S, Schmidt U, Chalder T. Eating disorders and irritable bowel syndrome: is there a link? *J Psychosom Res.* 2015;59:57–64.
10. Dejong H, Perkins S, Grover M, Schmidt,U. The prevalence of irritable bowel syndrome in outpatients with bulimia nervosa. *Int J Eat Disord.* 2011;44:661–664.
11. Mullin GE, Shepherd SJ, Chander RB, Ireton-Jones C, Matarese LE. Irritable bowel syndrome: contemporary nutrition management strategies. *JPEN J Parenter Enteral Nutr.* 2014;38(7):781–799.
12. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology.* 2014;146:67–75.e5.
13. Bohn L, Storsrud S, Liljebo T, Collin L, Lindfors P , Tornblom, et al. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology.* 2015;149:1399–1407.e2.
14. Mansueto P, Seidita A, D’Alcamo A, Carroccio A. Role of FODMAPs in Patients With Irritable Bowel Syndrome. *Nutr Clin Pract.* 2015;30:665–682.
15. Staudacher HM, Lomer MC, Farquharson FM, Louis P, Fava F, Franciosi E, et al. A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial. *Gastroenterology.* 2017;153:936–947.
16. Staudacher HM, Whelan K. The low FODMAP diet: recent advances in understanding its mechanisms and efficacy in IBS. *Gut.* 2014 1;66:1517 LP-1527. Available from: <http://gut.bmj.com/content/66/8/1517.abstract>
17. Staudacher HM, Lomer MC, Anderson JL, Barrett JS, Muir JG, Irving PM, et al. Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome. *J Nutr.* 2012 1;142:1510–1518.

18. Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D. *Am J Gastroenterol.* 2016;111:1824-1832.
19. Hill LS, Reid F, Morgan JF, Lacey JH. SCOFF, the development of an eating disorder screening questionnaire. *Int J Eat Disord.* 2010;43:344–351.
20. Morgan JF, Reid F, Lacey JH. The SCOFF questionnaire: assessment of a new screening tool for eating disorders. *BMJ.* 1999;319:1467–1478.
21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1999;67:361–370.
22. Snaith RP. 2003 The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes [Internet]. Aug 1;1:29.* Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC183845/>
23. Sugaya, N., Nomura, S., & Shimada, H. 2012 Relationship between cognitive factors and anxiety in individuals with irritable bowel syndrome. *Int J Behav Med.* Sep;19(3):308–15.
24. Hartono, J.L., Mahadeva, S., & Goh, K-L. 2012 Anxiety and depression in various functional gastrointestinal disorders: do differences exist? *J Dig Dis.* May;13(5):252–7.
25. Francis, C.Y., Morris, J., Whorwell, P.J. 1997 The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther.* Apr;11(2):395–402.
26. NICE. Eating disorders: recognition and treatment [Internet]. NICE guideline [NG69]. 2017 [cited 2018 Feb 19]. Available from:
<https://www.nice.org.uk/guidance/ng69/chapter/Context>
27. Statistics for Journalists [Internet]. Beat - Eating Disorders. 2017. Available from:
<https://www.beateatingdisorders.org.uk/media-centre/eating-disorder-statistics>
28. Garcia, F.D., Grigioni, S., Chelali, S., Meyrignac, G., Thibaut, F., & Dechelotte, P. 2010 Validation of the French version of SCOFF questionnaire for screening of eating disorders among adults. *World J Biol Psychiatry.* Oct 1;11(7):888–93. Available from:

<https://doi.org/10.3109/15622975.2010.483251>

29. Memon, A.A., Adil, S.E-R., Siddiqui, E.U., Naeem, S.S., Ali, S.A., & Mehmood, K. 2012 Eating disorders in medical students of Karachi, Pakistan-a cross-sectional study. *BMC Res Notes* . Feb;5(1):84. Available from: <https://doi.org/10.1186/1756-0500-5-84>
30. Nakai, Y., Nin, K., & Noma, S. 2014 Eating disorder symptoms among Japanese female students in 1982, 1992 and 2002. *Psychiatry Res*. Sep;219(1):151–6.
31. Cooper, R. 2013 Could your patient have an eating disorder? *Nurs Womens Health*.;17(4):317–24.
32. Tavoracci, M.P., Ladner, J., Grigioni, S., Richard, L., Villet, H., & Dechelotte, P. 2013 Prevalence and association of perceived stress, substance use and behavioral addictions: a cross-sectional study among university students in France, 2009–2011. *BMC Public Health*.;13(1):724. Available from: <https://doi.org/10.1186/1471-2458-13-724>
33. Hefner, J., & Eisenberg, D. 2009 Social support and mental health among college students. *Am J Orthopsychiatry*. Oct;79(4):491–9.
34. Gabriel, C., & Waller, G. 2014 Personality disorder cognitions in the eating disorders. *J Nerv Ment Dis*. Feb;202(2):172–6.
35. Becker, D.F., & Grilo, C.M. 2015 Comorbidity of mood and substance use disorders in patients with binge-eating disorder: Associations with personality disorder and eating disorder pathology. *J Psychosom Res*. Aug;79(2):159–64.
36. Fursland, A., & Watson, H.J. 2014 Eating disorders: a hidden phenomenon in outpatient mental health? *Int J Eat Disord*. May;47(4):422–5.
37. Hughes, E.K., Goldschmidt, A.B., Labuschagne, Z., Loeb, K.L., Sawyer, S.M., & Le Grange, D. 2013 Eating disorders with and without comorbid depression and anxiety: similarities and differences in a clinical sample of children and adolescents. *Eur Eat Disord Rev*. Sep;21(5):386–94.
38. Winstead, N.S., & Willard, S.G. 2006 Gastrointestinal complaints in patients with

- eating disorders. *J Clin Gastroenterol. Sep;40(8):678–82.*
39. Wang, X., Luscombe, G.M., Boyd, C., Kellow, J., & Abraham, S. 2014 Functional gastrointestinal disorders in eating disorder patients: Altered distribution and predictors using ROME III compared to ROME II criteria. *World J Gastroenterol [Internet]. Nov 21;20(43):16293–9.* Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4239520/>
 40. Walter, S.A., Jones, M.P., Talley, N.J., Kjellstrom, L., Nyhlin, H., Andreasson, A.N., & Agréus, L. 2013 Abdominal pain is associated with anxiety and depression scores in a sample of the general adult population with no signs of organic gastrointestinal disease. *Neurogastroenterol Motil. Sep;25(9):741-e576.*
 41. Thijssen, A.Y., Jonkers, D.M.A.E., Leue, C., Van der Veek, P.P.J., Vidakovic-Vukic, M., van Rood, Y.R., Clemens, C.H., & Masclée, A.A. 2010 Dysfunctional cognitions, anxiety and depression in irritable bowel syndrome. *J Clin Gastroenterol.;44(10):e236-41.*
 42. Jerndal, P., Ringstrom, G., Agerforz, P., Karpefors, M., Akkermans, L.M., Bayati, A., & Simrén, M. 2010 Gastrointestinal-specific anxiety: an important factor for severity of GI symptoms and quality of life in IBS. *Neurogastroenterol Motil. Jun;22(6):646-e179.*
 43. Gearry, R.B., Irving, P.M., Barrett, J.S., Nathan, D.M., Shepherd, S.J., & Gibson, P.R. 2009 Reduction of dietary poorly absorbed short-chain carbohydrates (FODMAPs) improves abdominal symptoms in patients with inflammatory bowel disease—a pilot study. *J Crohns Colitis. Feb;3(1):8–14.*
 44. Shepherd, S.J., & Gibson, P.R. 2006 Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. *J Am Diet Assoc. Oct;106(10):1631–9.*
 45. Maagaard, L., Ankersen, D. V., Vegh, Z., Burisch, J., Jensen, L., Pedersen, N., & Munkholm, P. 2016 Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. *World J Gastroenterol. Apr;22(15):4009–19.*

- X.Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol.* 2012;10(7):712–721. e4
- W. Staudacher HM & Whelan K (2017) The low FODMAP diet: recent advances in understanding its mechanisms and efficacy in irritable bowel syndrome. *Gut* 66, 1517–1527.
- Y. Catassi G, Lionetti E, Gatti S *et al.* (2017) The low FODMAP diet: many questions for a catchy acronym. *Nutrients* 9, 292