

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Clinical guideline

CG61: Irritable bowel syndrome in adults: Diagnosis and management of irritable bowel syndrome in primary care

Publication date

February 2008

Previous review dates

3 year review: June 2011 (no update)

CG61 was previously reviewed for update in 2011 when the review recommendation was that the guideline should not be considered for an update. Through the 2011 review new evidence was identified focusing on the role of antidepressants, biofeedback and relaxation therapy in the management of irritable bowel syndrome (IBS) symptoms. It was concluded that this new evidence may warrant further investigation but was not sufficient to recommend a standard update of the guideline. These areas were therefore considered to form part of the pilot for the rapid update programme and the IBS guideline was signed-off by Guidance Executive as a rapid update topic in June 2013. As these areas of the guideline have been scheduled to undergo a rapid update they were not considered through the 6 year surveillance review.

Surveillance report for GE

November 2013

Key findings

			Potential impact on guidance	
			Yes	No
Evidence identified from literature search			✓	
Feedback from Guideline Development Group			✓	
Anti-discrimination and equalities considerations				✓
No update	Rapid update	Standard update	Transfer to static list	Change review cycle
	✓			

Surveillance recommendation

GE is asked to consider the proposal to update the guideline as a rapid update (using Guideline Updates standing committee). GE are asked to note that this 'yes to update' proposal will not be consulted on.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Surveillance review of CG61: Irritable bowel syndrome in adults: Diagnosis and management of irritable bowel syndrome in primary care

Recommendation for Guidance Executive

Background information

Guideline issue date: 2008

3 year review: 2011 (no update)

6 year review: 2013

NCC: National Clinical Guidelines Centre (formally National Collaborating Centre for Nursing and Supportive Care)

Main conclusions from previous surveillance review

1. CG61 was previously reviewed for update in 2011 when the review recommendation was that the guideline should not be considered for an update. Through the 2011 review new evidence was identified focusing on the role of antidepressants, biofeedback and relaxation therapy in the management of irritable bowel syndrome (IBS) symptoms. It was concluded that this new evidence may warrant further investigation but was not sufficient to recommend a standard update of the guideline. These areas were therefore considered to form part of the pilot for the rapid update programme and the IBS guideline was signed-off by Guidance Executive as a rapid update topic in June 2013. As these areas of the guideline have been scheduled to undergo a rapid update they were not considered through the 6 year surveillance review.

Six year surveillance review

2. A literature search for systematic reviews was carried out between November 2010 (the end of the search period for the last review) and September 2013 and relevant abstracts were assessed. Clinical feedback on the guideline was obtained from three members of the GDG through a questionnaire.

3. New evidence that may impact on recommendations was identified relating to 3 clinical areas within the guideline:

Clinical area 1: Diagnosis of IBS – recommendations 1.1.2.1/1.1.2.2		
Q: What is the clinical utility of diagnostic tests to exclude alternative diagnoses in people meeting the diagnostic criteria for IBS?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence identified from literature search</u> The evidence identified at the 3 year surveillance review was considered unlikely to impact the guideline recommendations.^{1,2}</p> <p>Through a systematic review search conducted for the 6 year surveillance review, two studies were identified which highlighted the potential benefit of newer diagnostic methods, such as stool-form examination, faecal inflammatory markers and serum biomarkers as adjunctive tools to aid in diagnosis of IBS.^{3,4} CG61 did not cover these diagnostic methods however, since the guideline has been published, NICE has published guidance on diagnosis of gastrointestinal conditions such as IBS using noninvasive methods:</p> <ul style="list-style-type: none"> • Tauroselcholic acid – DG7: SeHCAT (Tauroselcholic [75Selenium] acid) for the investigation of bile acid malabsorption (BAM) and measurement of bile acid pool 	<p>Feedback from the GDG highlighted that using faecal calprotectin for the assessment of inflammation in the gut may be useful as a negative test would indicate that patients do not have inflammation and IBS is a likely diagnosis. This could mean that many patients do not need the reassurance from having a negative colonoscopy.</p>	<p>The guideline should cross-refer, at the earliest opportunity, to new diagnostic guidance (DG7 and DG11) that was previously not mentioned in the guideline.</p>

<p>loss, Nov 2012</p> <ul style="list-style-type: none"> • Faecal calprotectin – DG11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel, Oct 2013 <p>CG61 should cross-refer to these diagnostic guidelines.</p> <p>One additional systematic review identified at the 6 year surveillance review found that the odds of breath test positivity among IBS patients was significantly greater than that among healthy controls.⁵ However, the details about the breath test used, such as type of test and diagnostic accuracy outcomes were not reported in the abstract therefore it is not possible to determine whether this review would impact on the guideline recommendations.</p>		
<p>Clinical area 2: Diet and lifestyle (exclusion diets) – recommendation 1.2.1.8</p>		
<p>Q: Do exclusion diets improve IBS or related symptoms?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence identified from literature search</u> Two studies were identified at the 3 year surveillance review (2011) which indicated a potential improvement in IBS symptoms among people who followed the FODMAP diet (involves restricting fermentable oligo-di-monosaccharides and polyols).^{6,7} No evidence was identified through the 6 year literature search for this clinical area.</p>	<p>Four studies focusing on the FODMAP approach were highlighted by GDG members at the 3 year surveillance review conducted in 2011.⁸⁻¹¹ Furthermore, two trials were highlighted by the GDG at the 6 year surveillance review which indicated improved symptom response in patients with IBS when following a diet restricted in fermentable carbohydrates.^{12,13} These</p>	<p>Since the guideline was published the evidence base relating to the potential benefit of restricting fermentable oligo-di-monosaccharides and polyols (FODMAP) as a diet intervention in IBS has grown (6 studies identified at 3 year surveillance review plus 2 studies identified at 6 year surveillance review). This intervention should be considered for inclusion in the guideline as it may enable a more specific recommendation about exclusion diets to</p>

	studies were not identified through the literature search conducted for the surveillance review as this was limited to systematic reviews.	be made.
Clinical area 3: Pharmacological interventions for IBS (linaclotide and lubiprostone) – recommendation 1.2.2.2		
Q: Are laxatives effective in the management of IBS?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence identified from literature search</u> The evidence identified at the 3 year surveillance review was considered consistent with the guideline recommendations.¹⁴⁻²¹</p> <p>Through an assessment of abstracts from a high-level systematic review search conducted for the 6 year surveillance, evidence was identified on new drug treatments for IBS with constipation. Eight reviews of linaclotide (a guanylate cyclase-C receptor agonist) were identified which indicated that linaclotide may be an effective treatment for IBS with constipation (IBS-C).²²⁻²⁹ Furthermore, five reviews were identified which indicated that lubiprostone may be a beneficial treatment for IBS.^{26,28,30-32} Lastly, one review reported the efficacy and safety of laxatives for IBS indicating that these treatments are beneficial.³³</p>	<p>Feedback from the GDG indicated that a new drug for IBS, linaclotide, has recently been licensed in the UK for symptomatic treatment of moderate to severe IBS-C in adults and should be included in an update of the guideline.</p>	<p>Since the guideline was published, linaclotide and lubiprostone have been licensed in the UK for symptomatic treatment of IBS with constipation, and chronic idiopathic constipation plus associated symptoms in adults respectively. There is now a body of literature indicating that linaclotide and lubiprostone may be of benefit for management of IBS-C symptoms and therefore these drugs should be considered for inclusion in the guideline as this may enable a more specific recommendation on laxative treatment to be made.</p> <p>Linaclotide for IBS was non-prioritised in the Technology Appraisal (TA) topic selection process as the Topic Selection Consultant Clinical Advisor's view was that this would be better dealt with in context of a review of the IBS guideline. A TA on lubiprostone for chronic constipation is currently in development and expected to publish Oct 2014. However, CG61 stated in the methodology that studies reporting patients with single symptoms, such as chronic constipation / diarrhoea in isolation should not be included. As</p>

		such, the TA is unlikely to be directly relevant to the population covered in CG61.
--	--	---

Ongoing research

4. None identified.

Anti-discrimination and equalities considerations

5. None identified.

Implications for other NICE programmes

6. Three areas of the guideline have already been scheduled to undergo a rapid update (the role of antidepressants, biofeedback and relaxation therapy in the management of IBS symptoms) and are scheduled to be presented to the Rapid Updates Committee in April 2014.
7. A Quality Standard for IBS has been scheduled into the 2015/16 workplan with a provisional start date still to be agreed.

Conclusion

8. Through the review of CG61 new evidence which may potentially impact guideline recommendations was identified in the following areas:
 - a. The role of exclusion diets (specifically the FODMAP diet which involves restricting fermentable oligo-di-monosaccharides and polyols) in improving IBS or related symptoms
 - b. Pharmacological interventions for IBS (inclusion of linaclotide and lubiprostone within the laxatives section of the guideline)
9. The guideline should cross-refer to new diagnostic guidance (DG7 and DG11) that was previously not mentioned in the guideline.
10. For all other areas of the guideline no evidence was identified which would impact on recommendations.

Surveillance recommendation

11. GE is asked to consider the proposal to update the guideline as a rapid update (using Guideline Updates standing committee). GE are asked to note that this 'yes to update' proposal will not be consulted on.

Mark Baker – Centre Director
Sarah Willett – Associate Director
Emma McFarlane – Technical Analyst

Centre for Clinical Practice
November 2013

References

1. Ford AC, Spiegel BMR, Talley NJ et al. (2009) Small Intestinal Bacterial Overgrowth in Irritable Bowel Syndrome: Systematic Review and Meta-analysis. *Clinical Gastroenterology and Hepatology* 7:1279-1286.
2. Shah ED, Basseri RJ, Chong K et al. (2010) Abnormal breath testing in IBS: a meta-analysis. *Digestive Diseases & Sciences* 55:2441-2449.
3. Burbige EJ. (2010) Irritable bowel syndrome: Diagnostic approaches in clinical practice. *Clinical and experimental gastroenterology* 3:127-137.
4. Halpert AD. (2010) Importance of early diagnosis in patients with irritable bowel syndrome. *Postgraduate Medicine* 122:102-111.
5. Shah ED, Basseri RJ, Chong K et al. (2010) Breath testing appears to discriminate IBS from healthy controls: A systematic review and meta-analysis. *Gastroenterology* 138:S378-S379.
6. Ong DK, Mitchell SB, Barrett JS et al. (2010) Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. *Journal of Gastroenterology & Hepatology* 25:1366-1373.
7. Shepherd SJ, Parker FC, Muir JG et al. (2008) Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clinical Gastroenterology & Hepatology* 6:765-771.
8. Barrett JS and Gibson PR. (2007) Clinical ramifications of malabsorption of fructose and other short chain carbohydrates. *Practice Gastroenterology* 53:51-65.
9. Barrett JS, Gearry RB, Muir JG et al. (2010) Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. *Aliment.Pharmacol.Ther.* 31:874-882.
10. Gibson PR and Shepherd SJ. (2010) Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. *J Gastroenterol.Hepatol.* 25:252-258.
11. Staudacher HM, Whelan K, Irving PM et al. (2010) Symptom response to a low FODMAP (Fermentable Oligo-, Di-, Mono-saccharides and Polyols) diet compared to standard dietary advice in patients with irritable bowel syndrome. *Journal of Human Nutrition and Diet* 23:462-463.
12. Staudacher HM, Whelan K, Irving PM et al. (2011) Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. *J Hum.Nutr Diet.* 24:487-495.
13. Staudacher HM, Lomer MC, Anderson JL et al. (2012) Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. *J Nutr* 142:1510-1518.
14. Andresen V, Montori VM, Keller J et al. (2008) Effects of 5-Hydroxytryptamine (Serotonin) Type 3 Antagonists on Symptom Relief and Constipation in Nonconstipated Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Clinical Gastroenterology and Hepatology* 6:545-555.

15. Chey WD, Par#x00E9, P et al. (2008) Tegaserod for female patients suffering from IBS with mixed bowel habits or constipation: a randomized controlled trial. *American Journal of Gastroenterology* 103:1217-1225.
16. Drossman DA, Danilewitz M, Naesdal J et al. (2008) Randomized, double-blind, placebo-controlled trial of the 5-HT_{1A} receptor antagonist AZD7371 tartrate monohydrate (robalzotan tartrate monohydrate) in patients with irritable bowel syndrome. *American Journal of Gastroenterology* 103:2562-2569.
17. Drossman DA, Chey WD, Johanson JF et al. (2009) Clinical trial: Lubiprostone in patients with constipation-associated irritable bowel syndrome - Results of two randomized, placebo-controlled studies. *Alimentary Pharmacology and Therapeutics* 29:329-341.
18. Ford AC, Brandt LJ, Young C et al. (2009) Efficacy of 5-HT₃ antagonists and 5-HT₄ agonists in irritable bowel syndrome: Systematic review and meta-analysis. *American Journal of Gastroenterology* 104:1831-1843.
19. George AM, Meyers NL, and Hickling RI. (2008) Clinical trial: renzapride therapy for constipation-predominant irritable bowel syndrome--multicentre, randomized, placebo-controlled, double-blind study in primary healthcare setting. *Alimentary pharmacology & therapeutics* 27:830-837.
20. Lembo AJ, Cremonini F, Meyers N et al. (2010) Clinical trial: renzapride treatment of women with irritable bowel syndrome and constipation - a double-blind, randomized, placebo-controlled, study. *Alimentary pharmacology & therapeutics* 31:979-990.
21. Spiller RC, Meyers NL, and Hickling RI. (2008) Identification of patients with non-d, non-C irritable bowel syndrome and treatment with renzapride: an exploratory, multicenter, randomized, double-blind, placebo-controlled clinical trial. *Digestive Diseases & Sciences* 53:3191-3200.
22. Ahmad D, Esmadi M, Firwana B et al. (2013) Effect of linaclotide in the treatment of irritable bowel syndrome and chronic constipation: A meta-analysis. *Gastroenterology* 144:S215.
23. Johnston JM, Shiff SJ, and Quigley EMM. (2013) A review of the clinical efficacy of linaclotide in irritable bowel syndrome with constipation. *Current medical research and opinion* 29:149-160.
24. Lee N and Wald A. (2011) The pharmacokinetics, pharmacodynamics, clinical efficacy, safety and tolerability of linaclotide. *Expert opinion on drug metabolism & toxicology* 7:651-659.
25. Lee N and Wald A. (2012) Linaclotide: evidence for its potential use in irritable bowel syndrome and chronic constipation. *Core evidence* 7:39-47.
26. Mozaffari S, Nikfar S, and Abdollahi M. (2013) Metabolic and toxicological considerations for the latest drugs used to treat irritable bowel syndrome. *Expert opinion on drug metabolism & toxicology* 9:403-421.
27. Sayuk GS. (2012) Editorial: Linaclotide: Promising IBS-C efficacy in an era of provisional study endpoints. *American Journal of Gastroenterology* 107:1726-1729.
28. Shah ED, Chong K, and Pimentel M. (2012) Evaluation of treatment-associated harm for irritable bowel syndrome with constipation. *Gastroenterology* 142:S580.

29. Videlock EJ, Cheng V, and Cremonini F. (2013) Effects of Linaclotide in Patients With Irritable Bowel Syndrome With Constipation or Chronic Constipation: A Meta-analysis. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association* 11:1084-1092.
30. Joswick TR, Woldegeorgis F, and Ueno R. (2012) Patient response to lubiprostone for the treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C). *Gastroenterology* 142:S449.
31. Shah E, Kim S, Chong K et al. (2012) Evaluation of harm in the pharmacotherapy of irritable bowel syndrome. *The American journal of medicine* 125:381-393.
32. Trinkley KE and Nahata MC. (2011) Treatment of irritable bowel syndrome. *Journal of clinical pharmacy and therapeutics* 36:275-282.
33. Muller-Lissner S. (2013) Pharmacokinetic and pharmacodynamic considerations for the current chronic constipation treatments. *Expert Opinion on Drug Metabolism and Toxicology* 9:391-401.

Appendix 1 Decision matrix

Surveillance and identification of triggers for updating CG61. The table below provides summaries of the evidence for key questions for which studies were identified.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
What is the clinical utility and diagnostic accuracy of different diagnostic criteria for people with IBS?			
Two studies were identified through a high-level RCT search which advised that symptom criteria for diagnosis IBS (such as Manning, Kruis and Rome) should be validated in primary care populations. These studies were judged as not likely to impact on guideline recommendations.	Yes	No: One systematic review was identified which examined the validation and utilisation of IBS criteria concluding that the Manning criteria had been validated in more studies compared with the Rome criteria (I, II and III) and Kruis. This new evidence is unlikely to impact on the current guideline recommendations as the diagnostic criteria recommended by the GDG is based to a degree on the Manning and the ROME III criteria.	New evidence is unlikely to impact on guideline recommendations.
What is the clinical utility of diagnostic tests to exclude alternative diagnoses in people meeting the diagnostic criteria for IBS?			
Two studies identified through a high-level RCT search reported that breath test findings support a role for abnormal intestinal bacterial distribution in IBS. However, at this surveillance point the role of testing for small intestine bacteria overgrowth in individuals with suspected IBS was unclear.	Yes	No: One systematic review found that the odds of breath test positivity among IBS patients was significantly greater than that among healthy controls. However, the details about the breath test used, such as type of test and diagnostic accuracy outcomes were not reported in the abstract therefore it is not possible to determine whether this review would impact on the guideline recommendations. Lastly, two systematic reviews highlighted	The guideline should cross-refer, at the earliest opportunity, to new diagnostic guidance (DG7 and DG11) that was previously not mentioned in the guideline.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
		<p>potential benefit of newer diagnostic methods, such as stool-form examination, faecal inflammatory markers and serum biomarkers as adjunctive tools to aid in diagnosis of IBS. CG61 did not cover these diagnostic methods however, since the guideline has been published, NICE has published guidance on diagnosis of gastrointestinal conditions such as IBS using noninvasive methods:</p> <ul style="list-style-type: none"> • Faecal calprotectin – DG11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel, Oct 2013 • Tauroselcholic acid – DG7: SeHCAT (Tauroselcholic [75Selenium] acid) for the investigation of bile acid malabsorption (BAM) and measurement of bile acid pool loss, Nov 2012 <p>CG61 should cross-refer to these diagnostic guidelines.</p>	
What is the cost-effectiveness of tests to identify alternative diagnoses in patients meeting the diagnostic criteria for IBS who do not have any “red-flag” symptoms?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
What associations are there between diet and IBS? What dietary interventions improve symptoms / quality of life?			
One RCT identified through a high-	Yes	No: The conclusions reported in a systematic	New evidence is consistent with guideline

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
level RCT search reported that a diet of specially processed cereals (SPC) known to induce anti-secretory factor (ASF) production improved QoL in IBS patients. At this review point this was considered insufficient new evidence to impact on the guideline recommendations.		review support the current guidance which states that diet and nutrition should be assessed for people with IBS and general diet advice should be given. The guideline also recommends that if diet continues to be considered a major factor in a person's symptoms and they are following general lifestyle/dietary advice, they should be referred to a dietician for advice and treatment, including single food avoidance and exclusion diets.	recommendations.
Does Aloe Vera have a role in managing symptoms?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
What associations are there between physical activity and IBS? Does physical activity improve IBS or related symptoms?			
One study was identified through a high-level RCT search which indicated that exercise may be an effective intervention for symptom management in patients with IBS. The results of the study supported guideline recommendations.	Yes	No	No relevant evidence identified.
Does fibre improve IBS or related symptoms?			
One systematic review was identified through a high-level RCT search which indicated that fibre was more effective than placebo in the treatment of IBS. It was concluded at this review point that	Yes	No: The identified new evidence on fibre is conflicting particularly since the included studies evaluated different types of fibre: soluble (psyllium); bran and unknown type of fibre (fibre supplements). Two reviews found no benefit of	New evidence is consistent with guideline recommendations.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
the results of the study were considered unlikely to impact on guideline recommendations.		bran on IBS which supports the current guideline recommendation which states that people with IBS should be discouraged from eating insoluble fibre such as bran. Furthermore, one review found some benefit of psyllium supplementation (soluble fibre) for IBS which does not contradict the guideline which currently recommends that if an increase in dietary fibre is advised, it should be soluble fibre such as ispaghula powder or foods high in soluble fibre (for example, oats).	
Do probiotics and prebiotics improve IBS or related symptoms?			
Through a focused search 20 relevant studies were identified, 17 of which found a beneficial effect of probiotics. It was concluded at this review point that the results of the study were considered unlikely to impact on guideline recommendations.	Yes	No: The evidence reviewed in the guideline indicated that some probiotics are effective in people with IBS, but others are not, whilst the effect is dose and strain dependent. The evidence identified for the 6 year surveillance review is consistent with this conclusion. At the time of guideline publication the GDG agreed there was insufficient evidence to make a recommendation on prebiotics. No evidence on prebiotics was identified through this 6 year surveillance review.	New evidence is consistent with guideline recommendations.
Do exclusion diets improve IBS or related symptoms?			
Through a focused search 2 studies on the FODMAP diet for IBS were identified. The aim of this diet is to	No	Yes: Two studies were highlighted by the GDG which indicated improved symptom response in patients with IBS when following a diet restricted	There is a body of literature indicating that restricting fermentable oligo-di-monosaccharides and polyols (FODMAP

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
exclude fermentable oligo-di-monosaccharides and polyols such as fructose, lactose, fructans, galactans and polyols. The results of both studies indicated a potential improvement in symptoms in people with IBS. Furthermore, 5 additional studies focusing on the FODMAP approach were highlighted by a GDG member.		<p>in fermentable carbohydrates. Since the guideline was published the evidence base relating to the potential benefit of restricting fermentable oligo-di-monosaccharides and polyols (FODMAP) as a diet intervention in IBS has grown. As this intervention may potentially be of benefit in people with IBS it warrants investigation in the guideline.</p> <ul style="list-style-type: none"> • Staudacher HM, Whelan K, Irving PM et al. (2011) Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. <i>J Hum.Nutr Diet.</i> 24:487-495. • Staudacher HM, Lomer MC, Anderson JL et al. (2012) Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. <i>J Nutr</i> 142:1510-1518. 	diet) may be of benefit for management of IBS symptoms and therefore should be considered for inclusion in CG61.
Are antispasmodics effective in managing IBS symptoms?			
Through a focused search 6 studies on antispasmodics were identified which suggested that generally these agents are well tolerated and have some efficacy in people with IBS. It was concluded that this evidence was consistent with the guideline recommendations.	Yes	No: The identified new evidence (5 systematic reviews) generally indicated a benefit of antispasmodics in managing IBS. This new evidence supports the current guideline recommendation which states that healthcare professionals should consider prescribing antispasmodic agents for people with IBS.	New evidence is consistent with guideline recommendations.
Are laxatives effective in the management of IBS?			
Through a high-level RCT search 9 studies on laxatives were identified which suggested that these agents are	No	Yes: 8 reviews of linaclotide plus clinical feedback from the GDG indicated that linaclotide may be an effective treatment for IBS with constipation (IBS-	Since the guideline was published, linaclotide and lubiprostone have been licensed in the UK for symptomatic

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
<p>have some efficacy in people with IBS and adverse events are rare. It was concluded that this evidence was consistent with the guideline recommendations.</p> <p>In addition, evidence was identified for new drugs not currently covered by the guideline. One RCT conducted in patients with IBS with constipation (IBS-C) indicated a beneficial effect of linaclotide. In addition, a systematic review and an RCT reported that lubiprostone may be a reasonable alternative for use in patients with IBS-C. As these drugs were not licensed for use in the UK in 2011 and the evidence base was small this was not considered sufficient evidence to warrant inclusion of these drug in the guideline at this time.</p>		<p>C). Initial intelligence gathering and feedback from the GDG highlighted that linaclotide was licensed in the UK in 2012 for symptomatic treatment of moderate to severe IBS-C in adults. Linaclotide for IBS was B listed (non-prioritised) in the Technology Appraisal (TA) topic selection process as the Topic Selection Consultant Clinical Advisor's view was that this would be better dealt with in context of a review of the IBS guideline. Linaclotide was covered in an Evidence Summary: New Medicine published by the Medicines Prescribing Centre in April 2013 however, as this is a summary of key trials it does not constitute guidance and provides no recommendations on use. A TA on lubiprostone for chronic constipation is currently in development and expected to publish Oct 2014. However, CG61 stated in the methodology that studies reporting patients with single symptoms, such as chronic constipation / diarrhoea in isolation should not usually be included. As such, the TA is unlikely to be directly relevant to CG61.</p> <ul style="list-style-type: none"> • <i>Ahmad D, Esmadi M, Firwana B et al. (2013) Effect of linaclotide in the treatment of irritable bowel syndrome and chronic constipation: A meta-analysis. Gastroenterology 144:S215.</i> • <i>Johnston JM, Shiff SJ, and Quigley EMM. (2013) A review of the clinical efficacy of linaclotide in irritable bowel syndrome with constipation. Current medical</i> 	<p>treatment of IBS and chronic idiopathic constipation and associated symptoms in adults respectively. There is now a body of literature indicating that linaclotide and lubiprostone may be of benefit for management of IBS-C symptoms and therefore these drugs should be considered for inclusion in the guideline.</p>

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
		<p><i>research and opinion 29:149-160.</i></p> <ul style="list-style-type: none"> • <i>Lee N and Wald A. (2011) The pharmacokinetics, pharmacodynamics, clinical efficacy, safety and tolerability of linaclotide. Expert opinion on drug metabolism & toxicology 7:651-659.</i> • <i>Lee N and Wald A. (2012) Linaclotide: evidence for its potential use in irritable bowel syndrome and chronic constipation. Core evidence 7:39-47.</i> • <i>Mozaffari S, Nikfar S, and Abdollahi M. (2013) Metabolic and toxicological considerations for the latest drugs used to treat irritable bowel syndrome. Expert opinion on drug metabolism & toxicology 9:403-421.</i> • <i>Videloock EJ, Cheng V, and Cremonini F. (2013) Effects of Linaclotide in Patients With Irritable Bowel Syndrome With Constipation or Chronic Constipation: A Meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 11:1084-1092.</i> • <i>Shah ED, Chong K, and Pimentel M. (2012) Evaluation of treatment-associated harm for irritable bowel syndrome with constipation. Gastroenterology 142:S580.</i> • <i>Sayuk GS. (2012) Editorial: Linaclotide: Promising IBS-C efficacy in an era of provisional study endpoints. American Journal of Gastroenterology 107:1726-1729.</i> <p>Five systematic reviews were identified which indicated that lubiprostone may be a beneficial treatment for IBS.</p> <ul style="list-style-type: none"> • <i>Mozaffari S, Nikfar S, and Abdollahi M. (2013) Metabolic and toxicological considerations for the latest drugs used to treat irritable bowel syndrome. Expert opinion on drug metabolism & toxicology 9:403-421.</i> • <i>Shah ED, Chong K, and Pimentel M. (2012) Evaluation of</i> 	

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
		<p><i>treatment-associated harm for irritable bowel syndrome with constipation. Gastroenterology 142:S580.</i></p> <ul style="list-style-type: none"> • <i>Joswick TR, Woldegeorgis F, and Ueno R. (2012) Patient response to lubiprostone for the treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C). Gastroenterology 142:S449.</i> • <i>Shah E, Kim S, Chong K et al. (2012) Evaluation of harm in the pharmacotherapy of irritable bowel syndrome. The American journal of medicine 125:381-393.</i> • <i>Trinkley KE and Nahata MC. (2011) Treatment of irritable bowel syndrome. Journal of clinical pharmacy and therapeutics 36:275-282.</i> <p>Lastly, one systematic review reported the efficacy and safety of laxatives for IBS indicating that these treatments are beneficial.</p>	
Are anti-motility agents effective in symptom control in IBS?			
No relevant evidence identified – question does not need to be updated.	Yes	No: One systematic review found a benefit of loperamide for IBS. This review supports the guideline recommendation which states that loperamide should be the first choice of antimotility agent for diarrhoea in people with IBS.	New evidence is consistent with guideline recommendations.
Do antidepressants have a role in the management of IBS symptoms?			
12 RCTs and 4 meta-analyses were identified in the previous review (2011). It was concluded that the identified new evidence was inconclusive and may warrant further investigation. As such, it was recommended that this review	Question not reviewed	Question not reviewed	Review question scheduled for rapid update

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
question be updated using the rapid update process.			
What is the cost effectiveness of pharmacological interventions as long-term maintenance therapy for IBS?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
Does CBT have a role in managing symptoms?			
Through a high-level RCT search 2 studies on CBT concluded that this intervention improves symptoms in people with IBS. This evidence was considered consistent with the guideline recommendations.	Yes	No: One systematic review was identified which suggested that CBT based interventions may be promising in improving IBS symptoms. This new evidence is unlikely to change the direction of the current guideline recommendation which states that referral for psychological interventions CBT, hypnotherapy and/or psychological therapy) should be considered for people with IBS who do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (described as refractory IBS).	New evidence is consistent with guideline recommendations.
Does psychotherapy have a role in managing symptoms?			
One study was identified through a high-level RCT search which concluded that psychotherapy for interpersonal problems may play a role in improving health status of patients with chronic painful IBS. This evidence was considered consistent with the guideline recommendations.	Yes	No: The identified new evidence for psychotherapy in IBS was generally supportive (2 systematic reviews found positive effects of psychotherapy for IBS). This new evidence is unlikely to change the direction of the current guideline recommendation which states that referral for psychological interventions CBT, hypnotherapy and/or psychological therapy) should be considered for people with IBS who do not respond to	New evidence is consistent with guideline recommendations.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
		pharmacological treatments after 12 months and who develop a continuing symptom profile (described as refractory IBS).	
Does hypnotherapy have a role in managing IBS symptoms?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
Does relaxation therapy have a role in managing symptoms? / Does bio-feedback have a role in managing symptoms?			
Both questions were reviewed separately in CG61 but were considered together in the last review of the guideline in 2011. The current guideline makes no recommendations about relaxation and biofeedback. Through a focused literature search 3 studies were identified that were relevant to this research recommendation, finding that relaxation does have a beneficial effect on IBS related symptoms. It was concluded that a limited amount of new evidence was found that may potentially enable a recommendation to be made therefore, this review question is now scheduled to be updated using the rapid update process.	Questions not reviewed	Questions not reviewed	Review question scheduled for rapid update
What is the cost effectiveness of CBT, psychotherapy and hypnotherapy as 'one-off' interventions for IBS?			
No relevant evidence identified –	Yes	No	No relevant evidence identified.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
question does not need to be updated.			
Is acupuncture an effective intervention in managing IBS symptoms?			
Through a high-level RCT search two studies evaluating the use of acupuncture for IBS were identified. The results of the studies were conflicting therefore, it was concluded that there was insufficient consistent new evidence to change the direction of the current recommendation which states that the use of acupuncture should not be encouraged for the treatment of IBS.	Yes	No: Three systematic reviews investigating the use of acupuncture for IBS were identified. However, the evidence for the use of acupuncture in IBS remains conflicting depending on the control treatment used in the trial. Currently, there is insufficient consistent new evidence to change the direction of the current recommendation which states that the use of acupuncture should not be encouraged for the treatment of IBS.	Insufficient conclusive new evidence to change the direction of guideline recommendations.
Is reflexology an effective intervention in managing IBS symptoms?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
Is herbal medicine an effective intervention in managing IBS symptoms?			
Through a high-level RCT search 5 studies evaluating the use of herbal medicines for management of IBS were identified. Different herbal medicines were used in each study whilst the evidence for effectiveness was conflicting. It was concluded that this evidence was too conflicting to enable a recommendation to be made.	Yes	No: The guideline does not include any recommendations on herbal medicines for IBS because the GDG felt there were too many uncertainties regarding type and dose of herbal medicines to make a recommendation for practice. The identified new evidence (one systematic review which found no beneficial effect of the herbs Curcuma xanthorrhiza and Fumaria officinalis in IBS) is unlikely to add to the evidence base sufficiently to enable a recommendation to be made in this area.	Insufficient conclusive new evidence identified to enable a recommendation to be made in this area.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
Do psychosocial interventions have a role in managing IBS symptoms? / Do self-help/support groups have a role in managing IBS symptoms?			
One study was identified through a high-level RCT search which indicated that a comprehensive self-management program is efficacious whether delivered primarily by telephone or in person. However, as the recommendations don't specifically state how self-help should be delivered it was decided that this study was unlikely to impact on the recommendations.	Yes	No	No relevant evidence identified.
What role does patient information play in IBS?			
No relevant evidence identified – question does not need to be updated.	Yes	No	No relevant evidence identified.
NEW DRUGS NOT CURRENTLY COVERED BY THE GUIDELINE			
Through the high-level RCT search evidence was identified for the following drugs: <u>Melatonin</u> One study was identified which indicated that melatonin may be a promising candidate for the future research of agents that can modulate bowel motility. This evidence was considered insufficient to warrant	No	<u>Antiemetics</u> Two systematic reviews evaluated the efficacy and safety of antiemetics in IBS. The evidence for effectiveness was inconclusive and therefore this drug class does not warrant inclusion in the guideline at this time. <u>Asimadoline</u> One systematic review reported on the efficacy and safety of asimadoline for diarrhoea predominant IBS. However, this evidence is	There is some literature on drug classes other than laxatives, antimotility agents, antispasmodics and antidepressants. However, this evidence is currently insufficient to warrant inclusion of these drugs in the guideline at this time.

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
inclusion of this drug in the guideline at that time.		<p>currently insufficient to warrant inclusion of this drug in the guideline at this time.</p> <p><u>Antibiotics</u> Six reviews have highlighted the benefits of antibiotics, in particular rifaximin (5 reviews), in improving IBS symptoms. However, currently antibiotics are not licensed for use in IBS, side effects are common and antibiotic resistance levels are increasing rapidly therefore further evidence of effectiveness is required before considering antibiotics for management of IBS.</p> <p><u>Melatonin</u> One systematic review found that melatonin treatment decreased abdominal pain and improved overall IBS symptom scores. However, this evidence is currently insufficient to warrant inclusion of this drug in the guideline at this time.</p> <p><u>Benzodiazepine receptor modulators</u> One systematic review was identified which concluded that benzodiazepine receptor modulators may be beneficial in diarrhoea predominant IBS. However, this evidence is currently insufficient to warrant inclusion of this drug in the guideline at this time.</p> <p><u>Anticonvulsants</u></p>	

Conclusions from previous review (3 year; 2011)	Is this conclusion still supported by the evidence / still valid?	Has there been any new evidence / intelligence that may change this conclusion? If yes, please provide references	Comments
		<p>One systematic review found a benefit of pregabalin for IBS. However, this evidence is currently insufficient to warrant inclusion of this drug in the guideline at this time.</p> <p><u>Antiepileptics</u> One systematic review found a benefit of gabapentin for IBS. However, this evidence is currently insufficient to warrant inclusion of this drug in the guideline at this time.</p> <p><u>Antimigraine drugs</u> One systematic review found a benefit of clonidine for IBS. However, this evidence is currently insufficient to warrant inclusion of this drug in the guideline at this time.</p>	