An updated ACG Systematic Review on the Management of Chronic Idiopathic Constipation and Irritable Bowel Syndrome will publish in 2014 as a supplement to The American Journal of Gastroenterology. This treatment matrix will be updated at that time.

Linaclotide

Linaclotide is a 14 amino acid peptide structurally similar to hormones in the guanylin peptide family. Guanylin peptides are endogenous hormones that assist in the regulation of intestinal fluid and electrolyte homeostasis by binding to, and activating, guanylate cyclase-C receptors on the lumen of intestinal epithelium. Linaclotide is superior to placebo for the treatment of constipation-predominant IBS with a high quality of evidence.

Symptoms: Constipation-predominant IBS

Level of Evidence: V+

Quality of Supporting Evidence and ACG Graded Recommendations: Three randomized clinical trials in IBS patients demonstrated a statistically significant effect in favor of linaclotide compared with placebo for constipation-predominant IBS with no significant heterogeneity between studies. There was a statistically significant effect in favor of linaclotide compared with placebo on abdominal pain but with significant heterogeneity between individual trial results. Data on overall adverse events were provided by two of the three trials. Overall, adverse event rates were not higher among those taking linaclotide compared with Placebo. However, diarrhea, reported in all three trials, was significantly more likely with linaclotide, compared with placebo. Flatulence, reported in two trials, was also significantly more common with active therapy.

ACG Grade
Recommendation: STRONG
Quality of Evidence: HIGH

Lubiprostone (Selective C-2 Chloride Channel Activators)

Selective C-2 chloride channel activators are effective in constipation-predominant IBS with moderate quality of evidence.

Symptoms: Constipation; Overall Symptoms; Abdominal Pain

Level of Evidence: V+

Quality of Supporting Evidence and ACG Graded Recommendations: Two well-designed, large clinical trials demonstrated that lubiprostone is effective in relieving IBS symptoms for women with IBS-C. It is important to note that women capable of bearing children should have documented negative pregnancy test before starting therapy and should be advised to use contraception while taking lubiprostone. Additional studies need to be conducted in men before lubiprostone can be recommended to treat male IBS symptoms. Still, lubiprostone is strongly recommended for women with IBS-C in most circumstances.

ACG Grade
Recommendation: STRONG
Quality of Evidence: MODERATE
Antibiotic Therapy

Non-absorbable antibiotics are particularly effective in diarrhea-predominant IBS with moderate quality of evidence.

**Symptoms:** Bloating; Diarrhea; Overall Symptoms; Abdominal Pain

**Level of Evidence:** V+

**Quality of Supporting Evidence and ACG Graded Recommendations:** A short term course of non-absorbable antibiotics is more effective than placebo (sugar pill) for improving all IBS symptoms and for bloating. More studies need to be conducted to understand the long term safety and effectiveness of non-absorbable antibiotics for the management of IBS symptoms. However, non-absorbable antibiotics are strongly recommended for short term use and can be used by most patients in most circumstances.

**ACG Grade**
**Recommendation:** STRONG
**Quality of Evidence:** MODERATE

Antidepressants

Tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) have been shown to be effective in IBS patients of all subtypes. The trials generally are of good quality, but the limited number of patients included in the studies means the quality of evidence was graded as moderate.

**Symptoms:** Overall Symptoms; Abdominal Pain

**Level of Evidence:** V+

**Quality of Supporting Evidence and ACG Graded Recommendations:** Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are effective at reducing global IBS symptoms, and appear to reduce abdominal pain. The safety of using antidepressants in IBS remains poorly documented, although studies suggest that SSRIs are tolerated better than TCAs. Therefore, use of antidepressants can be strongly recommended for most patients in most circumstances.

**ACG Grade**
**Recommendation:** STRONG
**Quality of Evidence:** MODERATE

Psychological Therapies

Psychological therapies may provide benefit to IBS patients, although the quality of evidence is moderate.

**Symptoms:** Overall Symptoms

**Level of Evidence:** V+

**Quality of Supporting Evidence and ACG Graded Recommendations:** In 20 randomized clinical trials that compared various psychological therapies with usual care, there was a benefit for cognitive behavioral therapy, dynamic psychotherapy and hypnotherapy in relieving IBS symptoms. Relaxation therapy did not show any benefit. Psychological therapies are not documented to have any serious adverse events although how and why they provide relief remains unclear. Still, use of psychological therapies can be strongly recommended for most patients in most circumstances.

**ACG Grade**
**Recommendation:** STRONG
**Quality of Evidence:** MODERATE
### 5-HT3 Antagonists (alosetron) for Women

A class of drugs known as 5-HT3 antagonists (alosetron) is effective in IBS patients with diarrhea and the quality of evidence is good. Patients need to be carefully selected, however, because of the risk of potentially serious complications, including ischemic colitis.

**Symptoms:** Diarrhea; Overall Symptoms; Abdominal Pain

**Level of Evidence:** V

**Quality of Supporting Evidence and ACG Graded Recommendations:** Alosetron is the only 5-HT3 receptor antagonist approved for the treatment of women with severe IBS-D in the United States. In clinical trials, potentially serious side effects including constipation and colon ischemia occurred more commonly in patients treated with alosetron than placebo (sugar pill). As a result, current use of alosetron is regulated by a prescribing program set forth by the FDA and administered by the manufacturer.

**ACG Grade**
**Recommendation:** WEAK

**Quality of Evidence:** HIGH

### 5-HT3 Antagonists (alosetron) for Men

A class of drugs known as 5-HT3 antagonists (alosetron) are effective in IBS patients with diarrhea and the quality of evidence is good. Patients need to be carefully selected, however, because of the risk of potentially serious side effects, including ischemic colitis.

**Symptoms:** Diarrhea; Overall Symptoms

**Level of Evidence:** V

**Quality of Supporting Evidence and ACG Graded Recommendations:** In clinical studies, alosetron was shown to be effective at relieving global IBS symptoms in male IBS patients with diarrhea (IBS-D). However, potentially serious side effects including constipation and colon ischemia occurred more commonly in patients treated with alosetron than with placebo (sugar pill). As a result, current use of alosetron is regulated by a prescribing program set forth by the FDA and administered by the manufacturer.

**ACG Grade**
**Recommendation:** WEAK

**Quality of Evidence:** MODERATE

### Probiotic Therapy

Evidence suggests that some probiotics may be effective in reducing overall IBS symptoms but more data are needed.

**Symptoms:** Overall Symptoms

**Quality of Supporting Evidence and ACG Graded Recommendations:** Probiotics possess a number of properties that may prove of benefit to patients with IBS. However, probiotics vary widely in terms of species, strains, preparations and quality; making comparison of studies difficult. Lactobacilli do not appear effective for patients with IBS. Bifidobacteria and some combinations of probiotics demonstrate some efficacy for patients with IBS. According to the available safety data, probiotics are well tolerated and free from serious adverse side effects among people with IBS. Still, other treatment alternatives may be equally reasonable.

**ACG Grade**
**Recommendation:** WEAK

**Quality of Evidence:** LOW OR VERY LOW
Diet

There is not enough evidence that either food allergy testing or excluding certain foods from the diet is an effective treatment for IBS. Neither can be recommended.

Symptoms: Overall Symptoms
Level of Evidence: V-

Quality of Supporting Evidence and ACG Graded Recommendations: Patients often believe that certain foods make their IBS symptoms worse. However, there is not enough evidence that either food allergy testing or excluding certain foods from the diet is an effective treatment for IBS. Therefore, neither can be recommended.

ACG Grade
Recommendation: WEAK
Quality of Evidence: LOW OR VERY LOW

Bulking Agents (psyllium, hydrophilic mucilloid, ispaghula husk)

Trials suggest psyllium fiber is effective in IBS patients although the quality of evidence is poor.

Symptoms: Overall Symptoms
Level of Evidence: V-

Quality of Supporting Evidence and ACG Graded Recommendations: In four out of six studies evaluated, the use of psyllium improved global IBS symptoms for some patients. It is important to note that these studies were performed many years ago and do not comply with the standards of modern study design. In addition, any adverse events as a result of using psyllium were not recorded. Still, psyllium is moderately effective for some people and can be given a conditional recommendation. However, other alternatives may be equally beneficial.

ACG Grade
Recommendation: WEAK
Quality of Evidence: LOW OR VERY LOW

Dietary Fiber Supplements (wheat or corn bran)

In studies, neither wheat bran nor corn bran were effective at reducing global IBS symptoms. Neither is recommended.

Symptoms: Overall Symptoms
Level of Evidence: V-

Quality of Supporting Evidence and ACG Graded Recommendations: In studies, neither wheat bran nor corn bran were effective at reducing global IBS symptoms. Wheat bran or corn bran is not recommended for routine use.

ACG Grade
Recommendation: WEAK
Quality of Evidence: LOW OR VERY LOW

Laxatives (polyethylene glycol (PEG))

Routine use of laxatives in the treatment of IBS cannot be recommended as other alternatives may be equally reasonable.

Symptoms: Stool Frequency; Abdominal Pain
Level of Evidence: V-

Quality of Supporting Evidence and ACG Graded Recommendations: In one small study PEG was shown to improve stool frequency but not abdominal pain. The quality of this one study is poor and there are no additional long term, more complete studies of laxatives in IBS treatment. Therefore routine use of laxatives in the treatment of IBS cannot be recommended as other alternatives may be equally reasonable.

ACG Grade
Recommendation: WEAK
Quality of Evidence: LOW OR VERY LOW
**Antispasmodics (Hyoscine, Cimetropium, Pinaverium)**

Trials suggest certain antispasmodics are effective in IBS although the quality of evidence is poor. Availability of antispasmodics varies greatly around the world.

**Symptoms:** Overall Symptoms

**Level of Evidence:** V-

**Quality of Supporting Evidence and ACG Graded Recommendations:** Many antispasmodics have demonstrated effectiveness in treating IBS, however the availability of antispasmodics varies greatly around the world. Furthermore, the research into antispasmodics differs greatly; it does not distinguish between global IBS symptoms and individual symptoms and does not provide detail of adverse events. Because there is no evidence to support the long-term effectiveness or the long term safety of antispasmodics, they cannot be recommended for routine treatment of IBS symptoms.

**ACG Grade**
**Recommendation:** WEAK
**Quality of Evidence:** LOW OR VERY LOW

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**Peppermint Oil**

Trials suggest that peppermint oil is effective in IBS patients although the quality of evidence is poor.

**Symptoms:** Overall Symptoms

**Level of Evidence:** V-

**Quality of Supporting Evidence and ACG Graded Recommendations:** Some peppermint oil preparations seem to be effective at relieving IBS symptoms, however, preparations and quality vary greatly. Because there is no evidence to support the long-term effectiveness or the long-term safety of using peppermint oil preparations, they cannot be recommended for routine treatment of IBS symptoms.

**ACG Grade**
**Recommendation:** WEAK
**Quality of Evidence:** LOW OR VERY LOW

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**Antidiarrheal Agents (loperamide)**

Antidiarrheals reduce the frequency of stools but do not affect the overall symptoms of IBS.

**Symptoms:** Diarrhea; Abdominal Pain; Bloating; Overall Symptoms

**Level of Evidence:** V-

**Quality of Supporting Evidence and ACG Graded Recommendations:** In clinical studies, the antidiarrheal agent loperamide was no more effective than placebo (sugar pill) at reducing pain, bloating or global symptoms of IBS. However loperamide is effective in treating diarrhea, reducing stool frequency and improving stool consistency. No clinical trials have been performed comparing loperamide with other antidiarrheal agents and loperamide has not been broadly tested in terms of safety and long term tolerance. Still, loperamide can be considered an effective therapy for diarrhea.

**ACG Grade**
**Recommendation:** WEAK
**Quality of Evidence:** LOW OR VERY LOW
Antidiarrheal Agents (loperamide)

Antidiarrheals reduce the frequency of stools but do not affect the overall symptoms of IBS.

Symptoms:
- Diarrhea
- Abdominal Pain
- Bloating
- Overall Symptoms

Level of Evidence:

Quality of Supporting Evidence and ACG Graded Recommendations:

In clinical studies, the antidiarrheal agent loperamide was no more effective than placebo (sugar pill) at reducing pain, bloating or global symptoms of IBS. However, loperamide is effective in treating diarrhea, reducing stool frequency and improving stool consistency. No clinical trials have been performed comparing loperamide with other antidiarrheal agents and loperamide has not been broadly tested in terms of safety and long term tolerance. Still, loperamide can be considered an effective therapy for diarrhea.

ACG Grade Recommendation: WEAK
Quality of Evidence: LOW OR VERY LOW

5-HT4 Agonists (tegaserod)

Currently there are no 5-HT4 receptor agonists available for use in the United States. Although they are modestly effective in IBS patients with constipation, and the quality of evidence is good, the possible risk of cardiovascular events associated with these drugs may limit their usefulness.

Symptoms:
- N/A

Level of Evidence:

Quality of Supporting Evidence and ACG Graded Recommendations:

Currently there are no 5-HT4 receptor agonists available for use in the United States. In extensive clinical trials, tegaserod was shown to be effective at relieving global IBS symptoms in female IBS-C and IBS-M patients. The most common side effect of tegaserod is diarrhea. A small number of cardiovascular events were reported among patients who had received tegaserod in clinical trials. As a result, tegaserod was removed from the U.S. market in March 2007.

Recommendation: SPECIAL NOTE: While the recommendation is strong and the evidence is high quality, the therapy is not available for use in the U.S.
Quality of Evidence: N/A

Herbal Therapies and Acupuncture

Further study is needed before any recommendations on acupuncture or herbal therapy can be made.

Symptoms: N/A
Level of Evidence: Ø

Quality of Supporting Evidence and ACG Graded Recommendations: Although the available clinical studies of unique Chinese herbal mixtures appear to show benefit, it is not possible to compare these studies. Any benefit from Chinese herbal therapy in IBS is suspect due to the variations in purity and the components used in each mixture. There are significant concerns about toxicity, especially liver failure, with the use of any Chinese herbal mixture. A review of acupuncture trials was inconclusive. Further study is needed before any recommendations on acupuncture or herbal therapy can be made.

ACG Grade Recommendation: NONE
Quality of Evidence: N/A

The American College of Gastroenterology (ACG) evaluated a broad spectrum of medical research and conducted a rigorous review of the evidence regarding the effectiveness of testing and treatments for IBS. The results were graded by physician experts based on the quality of the scientific studies, including study design and findings and published in The American Journal of Gastroenterology in January 2009.

The IBS Treatment Matrix was developed based on this evidence-based review. Each studied IBS treatment is graded according to the quality of the scientific evidence supporting its use and its safety and effectiveness at treating overall IBS symptoms.

Reviewed by Brian Lacy, MD, FACG 3/18/2014