

**NMI Summit 2023. Author, Benjamin Brown.**

**Table:** Diets used in clinical practice for symptoms of irritable bowel syndrome and corresponding biomarker tests.

<b>Diet</b>	<b>Diet description</b>	<b>Evidence for efficacy</b>	<b>Biomarkers</b>	<b>Biomarker evidence</b>
Traditional dietary advice	Recommendations include regular meals, adequate fluids, restrict caffeine, alcohol, fizzy drinks, limit fat, gas producing foods (e.g., onions, beans), fiber, resistant starch, spicy foods, and fruit, increase soluble fiber. <sup>1 2</sup>	Head-to-head comparisons suggest similar efficacy to other dietary approaches (GFD, LFD) with better acceptance. <sup>3</sup>	N/A	N/A
Low-FODMAP diet	A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) present in foods including certain grains, fruit, vegetables, legumes and sweeteners. The diet consists of three phases: a period of FODMAP restriction, reintroduction of individual food items to determine tolerance, and personalisation to create a modified FODMAP-	The LFD reduces global symptoms and has been found to be generally more effective than traditional dietary advice. <sup>5</sup>	Microbiome	Microbiome signatures, including a 'pathogenic' profile and 'dysbiosis index,' may predict response to diet in some, <sup>6 7 8 9 10</sup> but not all studies. <sup>11</sup> Relationships between dysbiosis and symptom improvement are contradictory.
			Faecal and urine metabolites	Pattern of 15 volatile organic compounds predicted response to diet with good accuracy, <sup>12</sup> while faecal propionate, cyclohexanecarboxylic acid esters, and urine metabolite profile also predicted clinical response. <sup>13</sup>

	containing diet based on individual tolerance. <sup>4</sup>			
Gluten-free diet	Complete exclusion of wheat, rye, and barley from the diet independent of wheat allergy and celiac disease (non-celiac wheat sensitivity), assessing clinical response and response to gluten challenge. <sup>14</sup>	Gluten elimination has been shown to reduce symptoms, and blinded gluten challenge to aggravate symptoms. <sup>15 16 17 18 19</sup> A GFD showed comparative efficacy to an LFD or traditional Mediterranean diet. <sup>20</sup>	HLA-DQ2 and HLA-DQ8	Predicted greater reduction in symptoms of depression and improvements in vitality, but not GI symptoms. <sup>21</sup> Only 50% of NCWS patients express the HLA-DQ2 and/or HLA-DQ8 genotype. <sup>22</sup>
			Antigliadin antibodies	Predicted greater reductions in symptoms, particularly diarrhoea. <sup>23</sup>
			Confocal laser endomicroscopy	Poor diagnostic accuracy. <sup>24</sup>
Elimination diets	Empirical elimination diets involve initial short-term restriction followed by re-challenge to assess tolerance to each food. Commonly restricted foods include seafood, wheat, corn, eggs, dairy, soy, nuts, citrus, and yeast. <sup>25 26 27 28 29</sup> Testing-led elimination diets follow the same procedure, but elimination is personalised based on test results. <sup>30</sup>	There is mixed evidence for empirical elimination re-challenge diets. <sup>31 32 33 34</sup>  IgG antibody-led elimination diets reduce symptoms and improve quality of life but suffer from low evidence. <sup>35</sup> An IgG guided diet was superior to a LFD. <sup>36</sup>	IgG antibodies	IgG antibody-led elimination diets result in clinical improvement in symptoms. <sup>37 38 39 40 41 42 43</sup>
			Confocal laser endomicroscopy	Confocal laser endomicroscopy (CLE)-led elimination diets result in significant symptom improvement. <sup>44 45 46</sup> CLE is expensive, invasive and may lack accuracy. <sup>47</sup>
			Leukocyte activation assay	Leukocyte activation test-led elimination diets reduce symptoms. <sup>48 49</sup>

SIBO diet	Small intestinal bacterial overgrowth (SIBO) has controversially been proposed as a cause of IBS. <sup>50</sup> The LFD has been recommended during SIBO management with antibiotic therapy. <sup>51</sup>	A case report described benefit of a LFD and herbal antibiotic therapy, <sup>52</sup> no clinical trials have assessed the LFD for SIBO. A single study examined a short-term elemental diet. <sup>53</sup>	Hydrogen and methane breath testing	Breath testing has important limitations; it may not correlate with bacterial overgrowth (jejunal aspirate culture) or differentiate symptomatic subjects from healthy controls. <sup>54</sup> Breath testing has not yet been studied in relation to dietary management. <sup>55</sup>
Histamine diet	Recommendations vary but most often include restriction of cured and semi cured cheese, grated cheese, oily fish, canned and semi preserved oily fish derivatives, dry-fermented meat products, spinach, tomatoes, fermented cabbage, strawberries, citrus, wine, and beer. <sup>56</sup>	Histamine intolerance has been suggested in a subgroup of IBS patients. <sup>57 58</sup> A histamine diet has been shown to reduce symptoms in patients presenting primarily with functional abdominal symptoms. <sup>59</sup> This is supported by benefit of DAO enzyme intervention on GI symptoms. <sup>60</sup>  FODMAPs may favour the production of faecal histamine by <i>Klebsiella aerogenes</i> in a subgroup of IBS patients. <sup>61</sup> A moderate correlation was found between visceral pain severity and urinary histamine with an LFD. <sup>62</sup>	Serum DAO	Does not have reliable diagnostic value. <sup>63 64</sup> Despite uncertainty, may be useful to complement diagnosis and prediction of clinical response to treatment. <sup>65 66</sup>
			Urinary histamine	Methylhistamine in urine is emerging as a potential biomarker. <sup>67 68</sup>
			DAO gene variants	The relevance of gene variants to histamine intolerance is unknown. <sup>69</sup> DAO gene variants were associated with lower serum DAO in a subgroup of people with histamine intolerance, but not with clinical histamine intolerance phenotype. <sup>70</sup>

Low sucrose diet	Modified dietary guidelines for patients with congenital sucrase-isomaltase deficiency including avoiding sucrose containing foods, foods with added sugars, and replacing refined grain product with high fiber alternatives. <sup>71 72</sup>	Low sucrose diets have been shown to reduce symptoms. <sup>73 74 75 76</sup> Congenital sucrase-isomaltase deficiency may also masquerade as adult IBS and respond to diet. <sup>77</sup>	Sucrase-isomaltase gene variants	Predict a moderately better response to a low sucrose in IBS-D. <sup>78</sup> May predict poor response to a LFD. <sup>79 80</sup> Positive test does not rule out congenital deficiency as not all gene variants have been identified. <sup>81</sup>
Specific carbohydrate diet	The SCD restricts grains, refined sugars except for honey, processed foods, and most milk products except for fully fermented yogurt and some hard cheeses. <sup>82</sup>	The SCD has primarily been studied in IBD. <sup>83</sup> A clinical trial found no significant improvement in IBS symptoms with a SCD. <sup>84</sup>	N/A	N/A
Low nickel diet	The low nickel diet was constructed to manage adverse reactions to nickel containing foods and restricts foods high in nickel such as oats, almonds, chickpeas, tomato, cocoa, peanuts, walnuts and many others. <sup>85</sup>	A low nickel diet improves gastrointestinal symptoms in patients with nickel sensitivity and IBS or IBS-like symptoms. <sup>86 87 88 89 90</sup>	Oral mucosa patch test	The oral mucosa patch test complements clinical diagnosis of nickel sensitivity and predicts treatment response. <sup>91</sup>
Microbiome-targeted diet	Targeting the gut microbiota with dietary changes such as improving dietary quality, <sup>92</sup> increasing intake of fermented foods, <sup>93</sup> polyphenol rich foods, <sup>94</sup> and reduction of artificial food	Intervention studies have found symptom reductions with polyphenol rich food (blueberries), <sup>96</sup> fermented foods (sauerkraut, kimchi), <sup>97 98</sup> and elimination of artificial sweeteners, <sup>99</sup> and	Microbiome	Microbiome testing-based dietary advice is limited by considerable inter-individual variability and lack of evidence linking microbiota signatures to disease phenotypes and treatment responses. <sup>102 103 104</sup>

	additives <sup>95</sup> has been proposed but lacks a defined dietary approach.	monosodium glutamate. <sup>100</sup> A traditional Mediterranean diet showed comparative efficacy to an LFD or GFD. <sup>101</sup>		
Ayurvedic diet	Ayurvedic nutritional therapy based on general concepts to support digestive health including warm food, regular timings of meals, and foods which are generally light on digestion but nourishing with additional personalization based on symptoms.	Personalised Ayurvedic nutritional therapy was as effective as a traditional diet and LFD. <sup>105</sup>	N/A	N/A

Key: Gluten free diet, GFD; Low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet, LFD; Confocal laser endomicroscopy, CLE; Specific carbohydrate diet, SCD; irritable bowel syndrome, IBS; diarrhoea predominant irritable bowel syndrome, IBS-D; Inflammatory bowel disease, IBD; Diamine oxidase, DAO; Gastrointestinal, GI; Small intestinal bacterial overgrowth, SIBO.

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