

## **Supplementary Materials**

### **Search strategy:**

“irritable bowel syndrome” OR “IBS”

AND

“microbiota” OR “microbes” OR “microbiome” OR “microflora”

AND

“sequence” OR “sequencing” OR “pyrosequencing” OR “high through put” OR “16S rRNA” OR

“16S ribosomal RNA”

**Supplementary Table 1:** Quality assessment of the included studies

Author	Selection criteria				Comparability criteria	Exposure criteria			Total	
	Case definition	Representativeness of the cases	Selection of controls	Definition of controls		Ascertainment of exposure	Same method for cases and controls	Non-response rate		
Li et al. <sup>17</sup>	1	0	0	1	1	0	1	1	0	5
Labus et al. <sup>18</sup>	1	0	1	1	1	0	1	1	1	7
Tap et al. <sup>19</sup>	1	1	0	1	1	0	1	1	0	6
Gobert et al. <sup>20</sup>	1	0	0	1	1	0	1	1	1	6
Liu et al. <sup>21</sup>	1	1	0	1	1	0	1	1	1	7
Zeber-Lubecka et al. <sup>22</sup>	1	1	0	1	1	0	1	1	1	7
Nagel et al. <sup>23</sup>	1	1	0	1	1	0	1	1	0	6
Ringel-Kulka et al. <sup>24</sup>	1	0	1	1	1	0	1	1	0	6
Chung et al. <sup>25</sup>	1	0	1	1	1	0	1	1	0	6
Pozuelo et al. <sup>26</sup>	1	0	1	1	1	0	1	1	1	7
Giamarellos-Bourboulis et al. <sup>27</sup>	1	1	0	1	1	0	1	1	0	6
Dlugosz et al. <sup>28</sup>	1	0	0	1	1	0	1	1	1	6
Ng et al. <sup>29</sup>	1	1	1	1	1	0	1	1	0	7
Jeffery et al. <sup>30</sup>	1	1	0	1	1	0	1	1	1	7
Carroll et al. <sup>31</sup>	1	0	0	1	1	0	1	1	1	6
Durbán et al. <sup>32</sup>	1	0	0	1	1	0	1	1	1	6

Note: The Newcastle-Ottawa Scale for case-control studies contains nine items. The selection criteria include four items: (1) is the case definition adequate? (2) representativeness of the cases, (3) selection of controls, and (4) definition of controls. The comparability criteria include comparability of cases and controls on the basis of the design or analysis. The exposure criteria include three items: (1) ascertainment of exposure, (2) same method of ascertainment for cases and controls, and (3) non-response rate.

**Supplementary Table 2:** The mean relative abundances of *Firmicutes* and *Bacteroidetes*, and F/B ratio in relevant studies

Author	<i>Firmicutes</i>		<i>Bacteroidetes</i>		F/B ratio	
	IBS patients	HCs	IBS patients	HCs	IBS patients	HCs
Labus et al. <sup>18</sup>	IBS1: 76.0%	54.6%	IBS1: 20.5%	44.3%	IBS1: 1.5-2	0-0.5
	HC-like IBS: 62.4%		HC-like IBS: 36.8%		HC-like IBS: 0.5-1	
Jeffery et al. <sup>30</sup>	Normal-like IBS: 56.1%	55.7%	Normal-like IBS: 40.1%	40.6%	NA	NA
	IBS cluster 1: 81.4%		IBS cluster 1: 13.8%			
	IBS cluster 2: 80.4%		IBS cluster 2: 10.2%			
Nagel et al. <sup>23</sup>	49.812%	41.431%	34.623%	47.700%	7.13	2.28
Chung et al. <sup>25</sup>	40.7%	38.2%	41.3%	45.8%	IBS-D: 17.15	6.43
					IBS-M: 13.42	
					IBS-C: 0.73	
Zeber-Lubecka et al. <sup>22</sup>	NA	NA	NA	NA	NA	NA
Liu et al. <sup>21</sup>	NA	NA	NA	NA	NA	NA
Pozuelo et al. <sup>26</sup>	39.8%	49%	52.6%	42.7%	NA	NA

IBS, irritable bowel syndrome; HC, healthy control; NA, not available.

**Supplementary Table 3:** Alterations of fecal microbiota composition in irritable bowel syndrome (IBS) patients at the genus level

Author	Genus
Labus et al. <sup>18</sup>	<i>Holdemania</i> ↑
	<i>Parabacteroides</i> ↓
Tap et al. <sup>19</sup>	<i>Bacteroides</i> ↑
	<i>Prevotella</i> ↓
Gobert et al. <sup>20</sup>	<i>Roseburia</i> ↓
	<i>Prevotella</i> ↑
	<i>Alistipes</i> ↑
	<i>Desulfovibrio</i> ↑
Liu et al. <sup>21</sup>	<i>Akkermensia</i> ↑
	<i>Faecalibacterium</i> ↓
	<i>Lachnospiracea_incertae_sedis</i> ↓
	<i>Blautia</i> ↓
	<i>Coprococcus</i> ↓
	<i>Ruminococcus</i> ↓
	<i>Mitsuokella</i> ↓
	<i>Megamonas</i> ↓
	<i>Clostridium XI</i> ↓
	<i>Dialister</i> ↓
	<i>Oscillibacter</i> ↓
	<i>Clostridium sensu stricto</i> ↓
	<i>Clostridium IV</i> ↓
	<i>Catenibacterium</i> ↑
	<i>Clostridium XIVb</i> ↓
	<i>Prevotella</i> ↑
	<i>Bacteroides</i> ↑
	<i>Barnesiella</i> ↓
	<i>Paraprevotella</i> ↑
	<i>Odoribacter</i> ↓
	<i>Butyricimonas</i> ↓
	<i>Alistipes</i> ↓
	<i>Escherichia/Shigella</i> ↓
	<i>Parasutterella</i> ↓
	<i>Gemmiger</i> ↓
	<i>Comamonas</i> ↓
	<i>Bifidobacterium</i> ↓
<i>Fusobacterium</i> ↓	

Author	Genus	
Zeber-Lubecka et al. <sup>22</sup>	IBS-C:	
	<i>Eubacterium</i> ↑	
	<i>Acetanaerobacterium</i> ↑	
	<i>Catenibacterium</i> ↑	
	<i>Uncultured Ruminococcaceae</i> ↑	
	<i>Bacteroides</i> ↓	
	<i>Granulicatella</i> ↑	
	<i>Parabacteroides</i> ↓	
	IBS-D:	
	<i>Alistipes</i> ↓	
Nagel et al. <sup>23</sup>	<i>Enterococcus</i> ↑	
	<i>Streptococcus</i> ↑	
	<i>Anaerostipes</i> ↑	
	<i>Blautia</i> ↑	
	<i>Lachnospiracea_incertae_sedis</i> ↑	
	<i>Peptococcus</i> ↓	
	<i>Papillibacter</i> ↑	
	<i>Cantenibacterium</i> ↓	
	<i>Allisonella</i> ↓	
	<i>Dialister</i> ↓	
	<i>Butyricimonas</i> ↓	
	<i>Parabacteroides</i> ↓	
	<i>Gemmiger</i> ↑	
	<i>Actinomyces</i> ↑	
	<i>Eggethella</i> ↑	
	<i>Gordonibacter</i> ↑	
	<i>Olsenella</i> ↓	
	<i>Methanobrevibacter</i> ↑	
	Ringel-Kulka et al. <sup>24</sup>	<i>Lactobacillus</i> ↑
		<i>Streptococcus</i> ↑
<i>Actinomyces</i> ↑		
IBS-D/M:		
several members of the <i>Clostridiales</i> , <i>Oscillibacter</i> , <i>Anaerovorax</i> , and a member of the <i>Incertae sedis XIII</i> ↓		
IBS-M:		
<i>Eubacterium</i> ↓		
IBS-C:		
<i>Anaerovorax</i> ↑		
<i>Collinsiella</i> ↑		

Author	Genus
Chung et al. <sup>25</sup>	<i>Faecalibacterium</i> ↑
	<i>Bacteroides</i> ↓
	<i>Prevotella</i> ↑
	<i>Escherichia</i> ↑
	<i>Klebsiella</i> ↑
Pozuelo et al. <sup>26</sup>	IBS-D:
	unknown <i>Ruminococcaceae</i> ↓
	IBS-D/IBS-M vs IBS-C/HCs:
	unknown <i>Ruminococcaceae</i> ↓
	unknown <i>Christensenellaceae</i> ↓
	<i>Akkermansia</i> ↓
Jeffery et al. <sup>30</sup>	<i>Methanobrevibacter</i> ↓
	<i>Papillibacter</i> ↑
	<i>Dorea</i> ↑
	<i>Blautia</i> ↑
	<i>Dialister</i> ↑
	<i>Bacteroides</i> ↓
	<i>Alistipes</i> ↓
	<i>Odoribacter</i> ↓
	<i>Escherichia</i> ↑
	<i>Actinomyces</i> ↑
	<i>Bifidobacterium</i> ↑
	Carroll et al. <sup>31</sup>
<i>Pediococcus</i> ↑	
<i>Faecalibacterium</i> ↓	
Unclassified <i>Lactobacillaceae</i> ↑	
Unclassified <i>Enterobacteriaceae</i> ↑	
<i>Fusobacterium</i> ↑	
V6:	
<i>Ethanoligenens</i> ↑	
<i>Enterococcus</i> ↑	
<i>Veillonella</i> ↑	
Unclassified <i>Enterobacteriaceae</i> ↑	
Durbán et al. <sup>32</sup>	IBS-D:
	<i>Leuconostoc</i> ↑
	<i>Odoribacter</i> ↑
	<i>Acinetobacter</i> ↑
	<i>Butyricimonas</i> ↑
	IBS-C:
	<i>Alistipes</i> ↑
	<i>Butyricimonas</i> ↑

IBS, irritable bowel syndrome; HCs, healthy controls; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-C, constipation-predominant irritable bowel syndrome; IBS-M, mixed irritable bowel syndrome.

**Supplementary Table 4:** Alterations of fecal microbiota composition in different subtypes of irritable bowel syndrome (IBS) patients

Author	Phylum	Class	Order	Family	Genus
<b>Studies involving IBS-D patients</b>					
Liu et al. <sup>21</sup>	<i>Firmicutes</i> ↓				<i>Faecalibacterium</i> ↓
	<i>Bacteroidetes</i> ↑				<i>Lachnospiraceae_incertae_sedis</i> ↓
					<i>Blautia</i> ↓
					<i>Coproccoccus</i> ↓
					<i>Ruminococcus</i> ↓
					<i>Mitsuokella</i> ↓
					<i>Megamonas</i> ↓
					<i>Clostridium XI</i> ↓
					<i>Dialister</i> ↓
					<i>Oscillibacter</i> ↓
					<i>Clostridium sensu stricto</i> ↓
					<i>Clostridium IV</i> ↓
					<i>Catenibacterium</i> ↑
					<i>Clostridium XIVb</i> ↓
					<i>Prevotella</i> ↑
					<i>Bacteroides</i> ↑
					<i>Barnesiella</i> ↓
					<i>Paraprevotella</i> ↑
					<i>Odoribacter</i> ↓
					<i>Butyricimonas</i> ↓
					<i>Alistipes</i> ↓
					<i>Escherichia/Shigella</i> ↓
					<i>Parasutterella</i> ↓
					<i>Gemmiger</i> ↓
					<i>Comamonas</i> ↓
					<i>Bifidobacterium</i> ↓
					<i>Fusobacterium</i> ↓
Zeber-Lubecka et al. <sup>22</sup>				<i>Porphyromonadaceae</i> ↓	<i>Alistipes</i> ↓

Author	Phylum	Class	Order	Family	Genus
Nagel et al. <sup>23</sup>	F/B ratio ↑	<i>Clostridia</i> ↑	<i>Clostridiales</i> ↑	<i>Streptococcaceae</i> ↑	<i>Enterococcus</i> ↑
		<i>Firmicutes</i> ↑	<i>Selenomonadales</i> ↓	<i>Lachnospiraceae</i> ↑	<i>Streptococcus</i> ↑
		<i>Bacteroidetes</i> ↓	<i>Bacteroidales</i> ↓	<i>Peptococcaceae I</i> ↓	<i>Anaerostipes</i> ↑
		<i>Proteobacteria</i> ↑	<i>Rhizobiales</i> ↑	<i>Veillonellaceae</i> ↓	<i>Blautia</i> ↑
		<i>Actinobacteria</i> ↑	<i>Actinomycetales</i> ↑	<i>Hyphomicrobiaceae</i> ↑	<i>Lachnospiraceae_incertae_sedis</i> ↑
			<i>Methanobacteriales</i> ↑	<i>Actinomycetaceae</i> ↑	<i>Peptococcus</i> ↓
				<i>Methanobacteriaceae</i> ↑	<i>Papillibacter</i> ↑
					<i>Cantenibacterium</i> ↓
					<i>Allisonella</i> ↓
					<i>Dialister</i> ↓
					<i>Butyricimonas</i> ↓
					<i>Parabacteroides</i> ↓
					<i>Gemmiger</i> ↑
					<i>Actinomyces</i> ↑
					<i>Eggethella</i> ↑
					<i>Gordonibacter</i> ↑
					<i>Olsenella</i> ↓
				<i>Methanobrevibacter</i> ↑	
Ringel-Kulka et al. <sup>24</sup>			<i>Lactobacillales</i> ↑	<i>Lactobacillaceae</i> ↑	<i>Lactobacillus</i> ↑
			<i>Actinomycetales</i> ↑	<i>Actinomycetaceae</i> ↑	<i>Streptococcus</i> ↑
				<i>Incertae sedis XIII</i> ↓	<i>Actinomyces</i> ↑
					several members of the <i>Clostridiales</i> , <i>Oscillibacter</i> , <i>Anaerovorax</i> , and a member of the <i>Incertae sedis XIII</i> ↓
Pozuelo et al. <sup>26</sup>				<i>Ruminococcaceae</i> ↓	unknown <i>Ruminococcaceae</i> ↓
				unknown <i>Clostridiales</i> ↓	
				<i>Erysipelotrichaceae</i> ↓	
				<i>Methanobacteriaceae</i> ↓	
Carroll et al. <sup>31</sup>	V6:	V3:	V3:	V3:	V3:
	<i>Proteobacteria</i> ↑	<i>Gammaproteobacteria</i> ↑	<i>Clostridiales</i> ↓	<i>Incertae Sedis XII</i> ↓	<i>Pediococcus</i> ↑
		V6:	<i>Enterobacteriales</i> ↑	<i>Peptococcaceae</i> ↑	<i>Faecalibacterium</i> ↓
		<i>Gammaproteobacteria</i> ↑	<i>Pseudomonadales</i> ↑	<i>Ruminococcaceae</i> ↓	<i>Unclassified Lactobacillaceae</i> ↑
			<i>Fusobacteriales</i> ↑	<i>Lactobacillaceae</i> ↑	<i>Unclassified Enterobacteriaceae</i> ↑
			V6:	<i>Enterobacteriaceae</i> ↑	<i>Fusobacterium</i> ↑
			<i>Lactobacillales</i> ↑	<i>Pseudomonadaceae</i> ↑	V6:
			<i>Enterobacteriales</i> ↑	<i>Fusobacteriaceae</i> ↑	<i>Ethanoligenens</i> ↑
				V6:	<i>Enterococcus</i> ↑
				<i>Ruminococcaceae</i> ↑	<i>Veillonella</i> ↑
				<i>Enterococcaceae</i> ↑	<i>Unclassified Enterobacteriaceae</i> ↑
			<i>Veillonellaceae</i> ↑		
			<i>Enterobacteriaceae</i> ↑		



Author	Phylum	Class	Order	Family	Genus
Durbán et al. <sup>32</sup>				<i>Ruminococcaceae</i> ↓	<i>Leuconostoc</i> ↑
				<i>Rikenellaceae</i> ↑	<i>Odoribacter</i> ↑
				<i>Porphyromonadaceae</i> ↑	<i>Acinetobacter</i> ↑
					<i>Butyricimonas</i> ↑
<b>Studies involving IBS-C patients</b>					
Gobert et al. <sup>20</sup>	<i>Proteobacteria</i> ↑				<i>Roseburia</i> ↓
					<i>Prevotella</i> ↑
					<i>Alistipes</i> ↑
					<i>Desulfovibrio</i> ↑
					<i>Akkermensia</i> ↑
Zeber-Lubecka et al. <sup>22</sup>	<i>Firmicutes</i> ↑	<i>Clostridia</i> ↑	<i>Clostridiales</i> ↑	<i>Incertae Sedis XIII</i> ↑	<i>Eubacterium</i> ↑
				<i>Lachnospiraceae</i> ↑	<i>Acetanaerobacterium</i> ↑
				<i>Ruminococcaceae</i> ↑	<i>Catenibacterium</i> ↑
				<i>Rhodospirillaceae</i> ↑	<i>Uncultured Ruminococcaceae</i> ↑
				<i>Coriobacteriaceae</i> ↑	<i>Bacteroides</i> ↓
					<i>Granulicatella</i> ↑
					<i>Parabacteroides</i> ↓
Ringel-Kulka et al. <sup>24</sup>	<i>Actinobacteria</i> ↑		<i>Lactobacillales</i> ↑	<i>Lactobacillaceae</i> ↑	<i>Lactobacillus</i> ↑
			<i>Actinomycetales</i> ↑	<i>Actinomycetaceae</i> ↑	<i>Streptococcus</i> ↑
			<i>Coriobacteriales</i> ↑	<i>Incertae sedis XIII</i> ↑	<i>Actinomyces</i> ↑
				<i>Coriobacteriaceae</i> ↑	<i>Anaerovorax</i> ↑
					<i>Collinsiella</i> ↑
Durbán et al. <sup>32</sup>				<i>Ruminococcaceae</i> ↓	<i>Alistipes</i> ↑
				<i>Rikenellaceae</i> ↑	<i>Butyricimonas</i> ↑
				<i>Porphyromonadaceae</i> ↑	
<b>Studies involving IBS-M patients</b>					
Pozuelo et al. <sup>26</sup>				<i>Erysipelotrichaceae</i> ↓	
Ringel-Kulka et al. <sup>24</sup>			<i>Lactobacillales</i> ↑	<i>Lactobacillaceae</i> ↑	<i>Lactobacillus</i> ↑
			<i>Actinomycetales</i> ↑	<i>Actinomycetaceae</i> ↑	<i>Streptococcus</i> ↑
				<i>Eubacteriaceae</i> ↓	<i>Actinomyces</i> ↑
				<i>Incertae sedis XIII</i> ↓	several members of the <i>Clostridiales</i> , <i>Oscillibacter</i> , <i>Anaerovorax</i> , and a member of the <i>Incertae sedis XIII</i> ↓
					<i>Eubacterium</i> ↓

IBS, irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-C, constipation-predominant irritable bowel syndrome; IBS-M, mixed irritable bowel syndrome.