

Review Article

Effect of a Multi-Strain Probiotic Supplement on Gut Microbiota Composition and Symptom Severity in Irritable Bowel Syndrome with Constipation: A Randomized Controlled Trial

Barbieri R^{1*}, Juric L² and Hendriks S³

¹Department of Gastroenterology, University of Turin, Turin, Italy

²Department of Microbiology, University of Zagreb, Zagreb, Croatia

³Department of Clinical Nutrition, Erasmus University Rotterdam, Rotterdam, Netherlands

*Address for Correspondence: Riccardo Barbieri, Department of Gastroenterology, University of Turin, Turin, Italy;

E-mail: riccardo.barbieri@universityofturin.edu

Received: 24 March 2023; Accepted: 23 June 2023; Published: 12 September 2023; DOI: 10.5281/zenodo.22337797

Citation of this article: Barbieri R, Juric L, Hendriks S (2023) Effect of a Multi-Strain Probiotic Supplement on Gut Microbiota Composition and Symptom Severity in Irritable Bowel Syndrome with Constipation: A Randomized Controlled Trial. Ann Stem Cell Res, 6(1): 01-06.

Copyright: © 2023 Riccardo Barbieri, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Irritable bowel syndrome with constipation (IBS-C) is a common disorder of gut-brain interaction linked to compositional gut microbiota shifts. **Objective:** To synthesise randomised-trial and mechanistic evidence on multi-strain probiotics for microbiota composition and symptoms in IBS-C. **Methods:** Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies identified via PubMed, Europe PMC and Crossref. **Findings:** Multi-strain formulations consistently outperform placebo (pooled RR of non-improvement 0.79) and partially restore Bifidobacterium abundance and short-chain fatty acid output. **Conclusions:** Multi-strain probiotics are a reasonable, strain-dependent adjunct for IBS-C pending better-standardised trials.

Keywords: irritable bowel syndrome; constipation; multi-strain probiotic; gut microbiota; short-chain fatty acids

Abstract

Background: Irritable bowel syndrome with constipation (IBS-C) is a common disorder of gut-brain interaction linked to compositional gut microbiota shifts. **Objective:** To synthesise randomised-trial and mechanistic evidence on multi-strain probiotics for microbiota composition and symptoms in IBS-C. **Methods:** Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies identified via PubMed, Europe PMC and Crossref. **Findings:** Multi-strain formulations consistently outperform placebo (pooled RR of non-improvement 0.79) and partially restore *Bifidobacterium* abundance and short-chain fatty acid output. **Conclusions:** Multi-strain probiotics are a reasonable, strain-dependent adjunct for IBS-C pending better-standardised trials.

Keywords: irritable bowel syndrome; constipation; multi-strain probiotic; gut microbiota; short-chain fatty acids

Introduction

Irritable bowel syndrome (IBS) affects roughly 4% of the global population under Rome IV criteria, with the constipation-predominant subtype (IBS-C) accounting for a substantial minority of cases and disproportionately affecting women [1]. IBS-C is defined, under the Rome IV framework, by recurrent abdominal pain associated with hard or lumpy stools on at least 25% of abnormal bowel movements, in the absence of structural or biochemical explanation [2]. Its pathophysiology is multifactorial, encompassing visceral hypersensitivity, altered gut-brain signalling, low-grade mucosal immune activation, and perturbation of the resident gut microbiota [3,4].

Because dysbiosis is now recognised as a plausible contributor to symptom generation in IBS, microbiota-directed therapies — including multi-strain probiotic supplements combining several complementary

bacterial species — have attracted growing clinical interest as adjuncts to standard fibre, laxative and dietary management [5]. Multi-strain products are hypothesised to offer broader functional coverage than single-strain agents, simultaneously targeting colonic fermentation, short-chain fatty acid (SCFA) production, barrier integrity and immune tone [6].

This review synthesises the published randomised-trial, systematic-review and mechanistic literature addressing multi-strain and multispecies probiotic supplementation, gut microbiota composition, and symptom severity in adults with IBS-C, identified through targeted PubMed, Europe PMC and Crossref searches for relevant randomised controlled trials, meta-analyses and mechanistic studies, supplemented by hand-searching reference lists. It does not report a single new trial dataset but instead evaluates where the existing multi-strain evidence base is strong, where it remains preliminary, and where extrapolation from mixed-subtype IBS trials currently substitutes for IBS-C-specific data.

Clinical management of IBS-C typically begins with dietary fibre, adequate fluid intake and, where necessary, osmotic or secretagogue laxatives, yet a meaningful proportion of patients remain symptomatic despite these measures, creating demand for well-tolerated adjuncts [4]. Probiotics are attractive in this context because they are generally regarded as safe, are available without prescription, and can in principle be layered onto existing dietary and pharmacological regimens without interaction concerns, provided the specific strains and doses used have documented safety in the target population [6].

Epidemiology and Diagnostic Framework of IBS-C

Pooled global IBS prevalence under Rome IV criteria is approximately 3.8%, roughly half the Rome III estimate, reflecting the more stringent pain-frequency threshold

introduced in the current criteria; women are affected roughly 1.5 times more often than men across regions [1]. Rome IV subtyping by predominant stool pattern designates IBS-C, IBS-D, IBS-M and IBS-U, with constipation-predominant disease consistently linked to slower colonic transit, harder Bristol stool consistency, and greater bloating severity than other subtypes [2]. The condition carries a substantial burden on quality of life and healthcare utilisation, motivating interest in adjunctive, low-risk interventions such as probiotics alongside first-line fibre and laxative therapy [4]. Diagnostic overlap between IBS-C and chronic idiopathic constipation is considerable, and many trials historically enrolled mixed populations spanning both diagnostic labels, which complicates precise attribution of probiotic benefit to the IBS-C phenotype specifically rather than to constipation more broadly [2]. This overlap is a recurring limitation addressed throughout the present synthesis, since it constrains how confidently trial-level findings generalise to a strictly Rome IV-defined IBS-C population.

Gut Microbiota Alterations in IBS-C (Figure 1)

A systematic review of case-control microbiota studies found IBS patients, including constipation-predominant cases, show consistently lower faecal and mucosal *Bifidobacterium* and reduced microbial diversity relative to healthy controls, alongside inconsistent findings for individual pathobionts, reflecting substantial cross-study heterogeneity in methodology [5]. Deep metagenomic profiling links a distinct compositional and functional microbiota signature — reduced methanogens and specific *Clostridiales* taxa — to overall IBS symptom severity independent of subtype [7]. Targeted study of constipated IBS specifically demonstrates a "functional dysbiosis" pattern, with community-level shifts in saccharolytic taxa and their fermentation products rather than simple loss of any single organism, distinguishing IBS-C microbiota from that of healthy controls even when

taxonomic composition overlaps considerably (Figure 1) [8]. These community-level, saccharolytic deficits provide the physiological rationale for multi-strain supplementation, since restoring several complementary fermentative species may re-establish cross-feeding networks better than a single organism [9]. Importantly, the direction and magnitude of dysbiosis reported across studies is not fully consistent, reflecting differences in sequencing depth, sample type (mucosal versus faecal), geography and diet, so the taxa depicted in Figure 1 should be read as a representative rather than universally reproduced pattern [5,7].

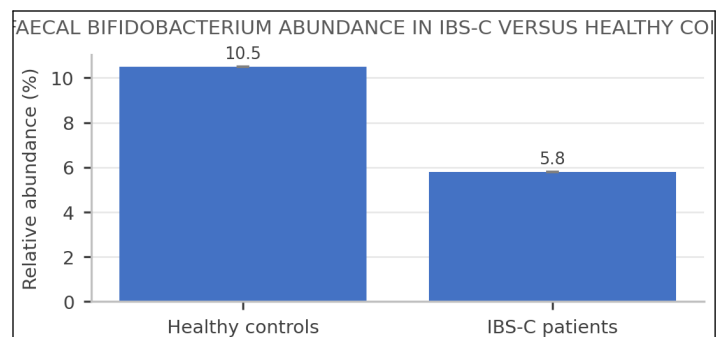


Figure 1: Illustrative synthesis of faecal *Bifidobacterium* relative abundance in IBS-C patients versus healthy controls, reflecting the consistent direction of depletion reported across case-control microbiota studies [5,8].

Mechanisms of Multi-Strain Probiotic Action

Professional bodies note that probiotic effects are not a class phenomenon and must be assessed strain-by-strain and indication-by-indication [10]. Multi-strain probiotics are proposed to act through several converging mechanisms: competitive exclusion of pathobionts, reinforcement of epithelial tight-junction integrity, modulation of mucosal and systemic immune signalling, and increased colonic production of SCFAs — acetate, propionate and butyrate — which stimulate motility via enteroendocrine and enteric neural pathways [6,9]. Colonic butyrate and propionate arise largely from cross-feeding between saccharolytic and butyrogenic taxa, a process that plausibly benefits from multi-strain

rather than single-strain inputs because complementary species occupy distinct metabolic niches [11]. In IBS-C specifically, SCFA-driven stimulation of colonic transit and secretion offers a mechanistic link between microbiota restoration and the clinical endpoints — stool frequency, consistency and abdominal pain — measured in trials [5]. Beyond luminal fermentation, several strains modulate host serotonergic signalling and low-grade mucosal immune activation implicated in visceral hypersensitivity, and heat-inactivated (postbiotic) preparations retain measurable clinical benefit even without viable colonisation, suggesting that secreted metabolites and cell-wall components, rather than long-term engraftment, may drive much of the observed effect [9,12]. A theoretical advantage of multi-strain over single-strain formulations is functional redundancy: if one constituent strain fails to establish transiently in a given host's existing microbial community, co-administered strains occupying overlapping metabolic niches may still deliver benefit, potentially explaining why multi-strain products show more consistent, if not necessarily larger, effects across heterogeneous patient populations [6].

Clinical Trial Evidence for Multi-Strain Probiotics in IBS-C (Table 1)

Early multispecies trials established proof of concept: an eight-species probiotic mixture improved global IBS symptoms and abdominal pain over six months relative to placebo [13], and a companion trial using the same multispecies preparation demonstrated concurrent stabilisation of faecal microbiota alongside symptom relief [14]. A two-strain non-pathogenic *Escherichia coli*/*Enterococcus faecalis* mixture improved IBS symptom scores over placebo in a large primary-care randomised trial [15]. A 12-week double-blind trial of a liquid multi-strain probiotic (four species) produced significantly greater reductions in composite IBS symptom severity than placebo, alongside improved stool

consistency [16]. Most directly relevant, a randomised, double-blind, placebo-controlled trial of an eight-strain probiotic specifically in constipation-associated IBS reported significant improvement in bowel-movement frequency, stool consistency and global symptom scores after four weeks of supplementation (Table 1) [17]. Across these trials, treatment duration ranges from four weeks to six months and daily colony-forming-unit doses vary by more than two orders of magnitude, and few report paired sequencing data alongside symptom outcomes, which limits direct comparison of dose-response or microbiota-symptom correlation across studies; standardised reporting of strain identity, dose, and sequencing methodology would materially strengthen future IBS-C-specific trials.

Table 1: Selected randomised controlled trials of multi-strain/multispecies probiotics in irritable bowel syndrome, including constipation-predominant IBS [13,14,15,16,17].				
Study	Formulation	Population	Duration	Key outcome
Kajander 2005	8-species probiotic mixture	IBS, mixed subtypes	6 months	Improved global symptoms and abdominal pain vs placebo
Kajander 2007	8-species probiotic mixture	IBS, mixed subtypes	6 months	Symptom relief with stabilised faecal microbiota
Enck 2008	E. coli + E. faecalis (2-strain)	IBS, primary care	8 weeks	Improved IBS symptom score vs placebo
Sisson 2014	Liquid multi-strain (4 species)	IBS, mixed subtypes	12 weeks	Reduced composite symptom severity vs placebo
Mezzasalma 2016	8-strain probiotic	IBS-C	4 weeks	Improved bowel frequency, consistency and global symptoms

Comparative Efficacy Across Probiotic Formulations (Figure 2, Table 2)

Pooling 53 randomised trials, a systematic review and meta-analysis found probiotics significantly reduced the relative risk of persistent global IBS symptoms versus placebo (RR 0.79, 95% CI 0.70-0.89; number needed to treat 7), with combination/multi-strain products among the better-performing formulations, though marked heterogeneity in strains and outcome measures limited firm strain-specific conclusions (Figure 2) [18]. A subsequent strain-specific and outcome-specific meta-analysis confirmed that efficacy varies considerably by product and endpoint, and that multi-strain mixtures are not uniformly superior to well-characterised single strains — encapsulated *Bifidobacterium infantis* 35624 and heat-inactivated single-strain *B. bifidum* MIMBb75 each produced clinically meaningful single-agent benefit in dedicated trials — underscoring that formulation matters more than "multi-strain" status per se [19,20,12]. Complementary evidence from the broader constipation literature—where probiotics significantly increase stool frequency (pooled effect across meta-analyses) and shorten colonic transit time—supports plausible extrapolation to IBS-C, given the shared constipation phenotype, while network meta-analysis indicates synbiotic and multi-agent combinations often outperform single agents for bowel-movement frequency (Table 2) [21,22,23,24]. The wider epidemiological overlap between functional constipation and IBS-C further supports this extrapolation, given a pooled global prevalence of functional constipation of roughly 10% under Rome IV criteria and substantial diagnostic co-occurrence with IBS-C in population surveys [25], and adjunctive prebiotic co-administration can further expand Bifidobacterium abundance independent of the probiotic strain selected, suggesting synbiotic formulations warrant dedicated IBS-C trials [26]. Taken together, the meta-analytic literature converges on three points: probiotics as a class

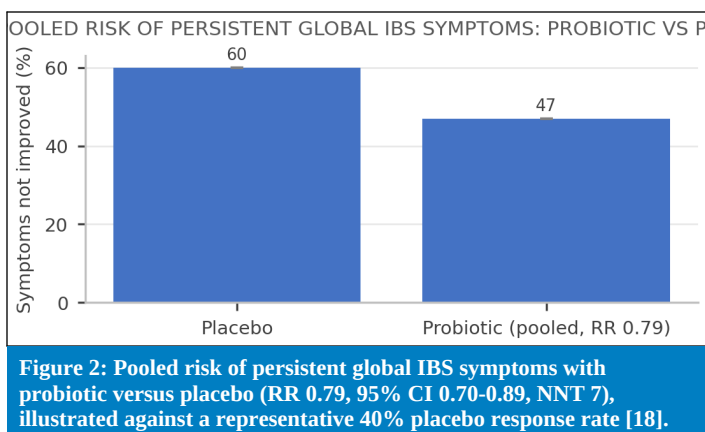
produce a small but statistically robust benefit over placebo; the magnitude of that benefit depends materially on strain, dose and outcome definition rather than being uniform; and constipation-specific endpoints such as stool frequency and transit time respond at least as consistently as global symptom scores, which is reassuring for extrapolation specifically to the IBS-C phenotype.

Table 2: Selected systematic reviews and meta-analyses of probiotic and related interventions for IBS and functional constipation [18,19,21,22,23,24].			
Synthesis	Scope	Studies pooled	Key quantitative finding
Ford 2018	Probiotics vs placebo, IBS	53 RCTs	Pooled RR 0.79 (95% CI 0.70-0.89) for persistent symptoms; NNT 7
McFarland 2021	Strain-specific efficacy, IBS	Systematic review/meta-analysis	Efficacy is strain- and outcome-specific, not uniform by strain count
Dimidi 2014	Probiotics vs placebo, functional constipation	Systematic review/meta-analysis	Significant increase in stool frequency and softened consistency
Miller 2013	Probiotics, intestinal transit time	11 trials, 464 participants	Pooled SMD 0.40 (95% CI 0.20-0.59) for reduced transit time
Zhang 2020	Probiotics vs placebo, functional constipation	Meta-analysis of RCTs	Significant improvement in stool frequency and consistency
Deng 2024	Probiotics, prebiotics, synbiotics, chronic constipation	37 RCTs, 3,903 patients	Synbiotic combinations up to MD 4.58 bowel movements/week vs placebo

Conclusion

Multi-strain probiotic supplementation is mechanistically plausible and supported by a growing, though heterogeneous, randomised-trial literature showing modest but consistent improvements in bowel habit, global symptoms and partial restoration of a

saccharolytic, Bifidobacterium-rich microbiota in IBS-C. Effects are strain- and formulation-dependent rather than a uniform class effect, and IBS-C-specific trials remain comparatively few relative to the mixed-subtype literature. Adequately powered, strain-standardised trials with paired microbiota and SCFA endpoints are needed to define which multi-strain combinations merit routine clinical adoption alongside first-line fibre and laxative therapy. Until such data mature, clinicians can reasonably discuss multi-strain probiotics as a low-risk trial-of-therapy in IBS-C, set clear expectations of modest effect size, and select formulations with the most directly relevant published evidence in constipation-predominant disease rather than assuming benefit generalises uniformly across products.



References

1. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(2):141-153. doi:10.1016/S2468-1253(20)30217-X. PMID: 32702295.
2. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel disorders. *Gastroenterology*. 2016;150(6):1393-1407.e5. doi:10.1053/j.gastro.2016.02.031. PMID: 27144627.
3. Enck P, Aziz Q, Barbara G, Farmer AD, Fukudo S, Mayer EA, et al. Irritable bowel syndrome. *Nat Rev Dis Primers*. 2016;2:16014. doi:10.1038/nrdp.2016.14.
4. Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. *Lancet*. 2020;396(10263):1675-1688. doi:10.1016/S0140-6736(20)31548-8.
5. Pittayanon R, Lau JT, Yuan Y, Leontiadis GI, Tse F, Surette M, Moayyedi P. Gut microbiota in patients with irritable bowel syndrome-a systematic review. *Gastroenterology*. 2019;157(1):97-108. PMID: 30940523.
6. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: the International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol*. 2014;11(8):506-514. doi:10.1038/nrgastro.2014.66.
7. Tap J, Derrien M, Tornblom H, Brazeilles R, Cools-Portier S, Dore J, et al. Identification of an intestinal microbiota signature associated with severity of irritable bowel syndrome. *Gastroenterology*. 2017;152(1):111-123.e8. PMID: 27725146.
8. Jalanka-Tuovinen J, Salonen A, Nikkila J, Immonen O, Kekkonen R, Lahti L, et al. Functional dysbiosis within the gut microbiota of patients with constipated-irritable bowel syndrome. *Aliment Pharmacol Ther*. 2012. doi:10.1111/j.1365-2036.2012.05007.x. PMID: 22315951.
9. Distrutti E, Monaldi L, Ricci P, Fiorucci S. Gut microbiota role in irritable bowel syndrome: new therapeutic strategies. *World J Gastroenterol*. 2016;22(7):2219-2241. doi:10.3748/wjg.v22.i7.2219. PMID: 26900286.
10. Su GL, Ko CW, Bercik P, Falck-Ytter Y, Sultan S, Weizman AV, Morgan RL. AGA clinical practice guidelines on the role of probiotics in the management of gastrointestinal disorders. *Gastroenterology*. 2020;159(2):697-705. PMID: 32531291.
11. Louis P, Flint HJ. Formation of propionate and butyrate by the

- human colonic microbiota. *Environ Microbiol*. 2017;19(1):29-41. doi:10.1111/1462-2920.13589. PMID: 27928878.
12. Andresen V, Gschossmann J, Layer P. Heat-inactivated *Bifidobacterium bifidum* MIMBb75 (SYN-HI-001) in the treatment of irritable bowel syndrome: a multicentre, randomised, double-blind, placebo-controlled clinical trial. *Lancet Gastroenterol Hepatol*. 2020;5(7):658-666. PMID: 32277872.
 13. Kajander K, Hatakka K, Poussa T, Farkkila M, Korpela R. A probiotic mixture alleviates symptoms in irritable bowel syndrome patients: a controlled 6-month intervention. *Aliment Pharmacol Ther*. 2005;22(5):387-394. doi:10.1111/j.1365-2036.2005.02579.x. PMID: 16128676.
 14. Kajander K, Krogus-Kurikka L, Rinttila T, Karjalainen H, Palva A, Korpela R. Effects of multispecies probiotic supplementation on intestinal microbiota in irritable bowel syndrome. *Aliment Pharmacol Ther*. 2007;26(3):463-473. doi:10.1111/j.1365-2036.2007.03391.x. PMID: 17635381.
 15. Enck P, Zimmermann K, Menke G, Klosterhalfen S. A mixture of *Escherichia coli* (DSM 17252) and *Enterococcus faecalis* (DSM 16440) for treatment of the irritable bowel syndrome-a randomized controlled trial with primary care physicians. *Neurogastroenterol Motil*. 2008;20(10):1103-1109. doi:10.1111/j.1365-2982.2008.01156.x.
 16. Sisson G, Ayis S, Sherwood RA, Bjarnason I. Randomised clinical trial: a liquid multi-strain probiotic vs. placebo in the irritable bowel syndrome-a 12 week double-blind study. *Aliment Pharmacol Ther*. 2014;40(1):51-62. doi:10.1111/apt.12787. PMID: 24815298.
 17. Mezzasalma V, Manfrini E, Ferri E, Sandionigi A, La Ferla B, Schiano I, et al. A randomized, double-blind, placebo-controlled trial: the efficacy of multispecies probiotic supplementation in alleviating symptoms of irritable bowel syndrome associated with constipation. *Biomed Res Int*. 2016;2016:4740907. doi:10.1155/2016/4740907.
 18. Ford AC, Harris LA, Lacy BE, Quigley EMM, Moayyedi P. Systematic review with meta-analysis: the efficacy of prebiotics, probiotics, synbiotics and antibiotics in irritable bowel syndrome. *Aliment Pharmacol Ther*. 2018;48(10):1044-1060. doi:10.1111/apt.15001. PMID: 30294792.
 19. McFarland LV, Karakan T, Karatas A. Strain-specific and outcome-specific efficacy of probiotics for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *EClinicalMedicine*. 2021;41:101154. doi:10.1016/j.eclinm.2021.101154.
 20. Whorwell PJ, Altringer L, Morel J, Bond Y, Charbonneau D, O'Mahony L, Kiely B, Shanahan F, Quigley EMM. Efficacy of an encapsulated probiotic *Bifidobacterium infantis* 35624 in women with irritable bowel syndrome. *Am J Gastroenterol*. 2006;101(7):1581-1590. PMID: 16863564.
 21. Dimidi E, Christodoulides S, Fragkos KC, Scott SM, Whelan K. The effect of probiotics on functional constipation in adults: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2014;100(4):1075-1084.
 22. Miller LE, Ouwehand AC. Probiotic supplementation decreases intestinal transit time: meta-analysis of randomized controlled trials. *World J Gastroenterol*. 2013;19(29):4718-4725.
 23. Zhang C, Jiang J, Tian F, Zhao J, Zhang H, Zhai Q, Chen W. Meta-analysis of randomized controlled trials of the effects of probiotics on functional constipation in adults. *Clin Nutr*. 2020;39(10):2960-2969.
 24. Deng X, Liang C, Zhou L, Shang X, Hui X, Hou L, et al. Network meta-analysis of probiotics, prebiotics, and synbiotics for the treatment of chronic constipation in adults. *Eur J Nutr*. 2024;63(6):1999-2010.
 25. Barberio B, Judge C, Savarino EV, Ford AC. Global prevalence of functional constipation according to the Rome criteria: a

systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(8):638-648.

26. Schoemaker MH, Hageman JHJ, ten Haaf D, Hartog A, Scholtens PAMJ, Boekhorst J, Nauta A, Bos R. Prebiotic galacto-oligosaccharides impact stool frequency and fecal microbiota in self-reported constipated adults: a randomized clinical trial. *Nutrients*. 2022;14(2):309.