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ISSUE 3: GUT HEALTH EDITION
APRIL 2024

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WELCOME

Clare Grundel
Managing Editor

WELCOME TO OUR BUMPER EDITION ON GUT HEALTH AND THE MICROBIOME -

- a massive, and increasingly mainstream topic, with substantial amounts of new research published daily. This 3rd edition of the NED Journal shines a light on the many and varied ways the microbiome interacts with human health, from different disease states and multiple life stages. It includes sections on the common diagnosis of irritable bowel disease, as well as the challenging autoimmune inflammatory bowel diseases.

NED Editorial Board member Dr Kate Lawrence specialises in nutritional psychology and neurodiversity, with a particular focus on dietary and microbiome influences on mental health and cognitive function. Having Crohn's Disease herself brings this NED Journal edition closer to Kate in many ways. She says,

"***My personal journey with Crohn's began after contracting a tropical parasite during travels in South East Asia, leading to gastrointestinal and immune system reactions and eventual diagnosis some twenty years later. Alongside conventional medicine, nutritional strategies play a key role in managing my condition. The emerging research on the microbiome and gut health is particularly exciting, offering insights into the causal factors of poor gut health and potential interventions to tackle the root causes. This issue of the journal features articles on probiotics, vitamin D, and the low FODMAP diet in Inflammatory Bowel Disease, all of which have been helpful, to some extent, in managing my own health. The journal aims to make such cutting-edge research accessible to health professionals, facilitating research-driven practice."***

The British Association of Nutrition and Lifestyle Medicine (BANT) is a professional membership body for nutrition practitioners, trained in nutrition sciences and the delivery of personalised nutrition services. BANT members are reading and interpreting nutrition and lifestyle sciences such as that found in this NED Journal on a routine basis to inform their clinical decision making.
You can find the BANT member practitioner listing here.

The Nutrition Evidence Database is one of the ways that BANT contributes to the evidence-based practice of precision nutrition. BANT is delighted to make this resource open access for all and encourages all healthcare practitioners interested in personalised healthcare to make use of the resource on a regular basis. **You can subscribe to receive monthly NED alerts here.**

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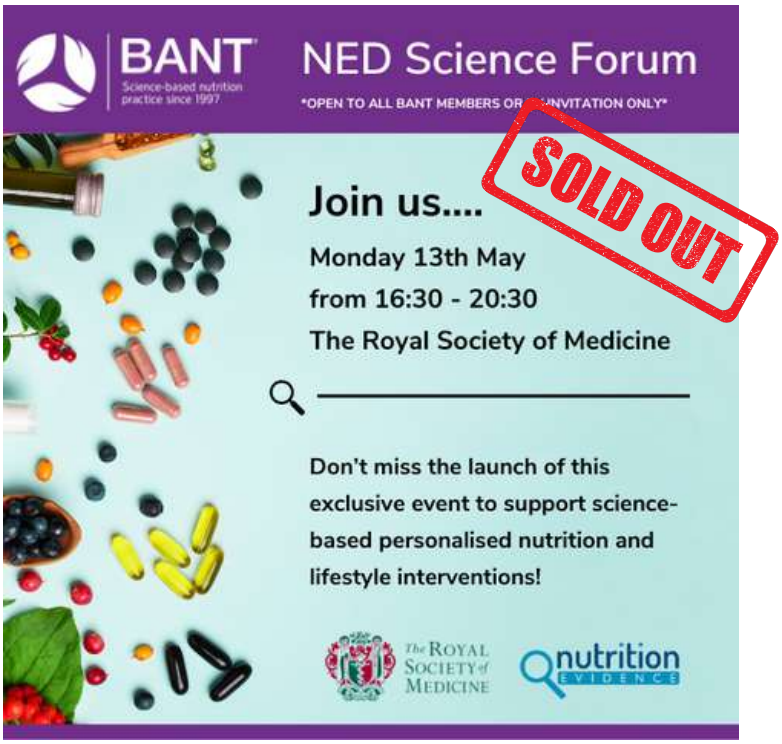

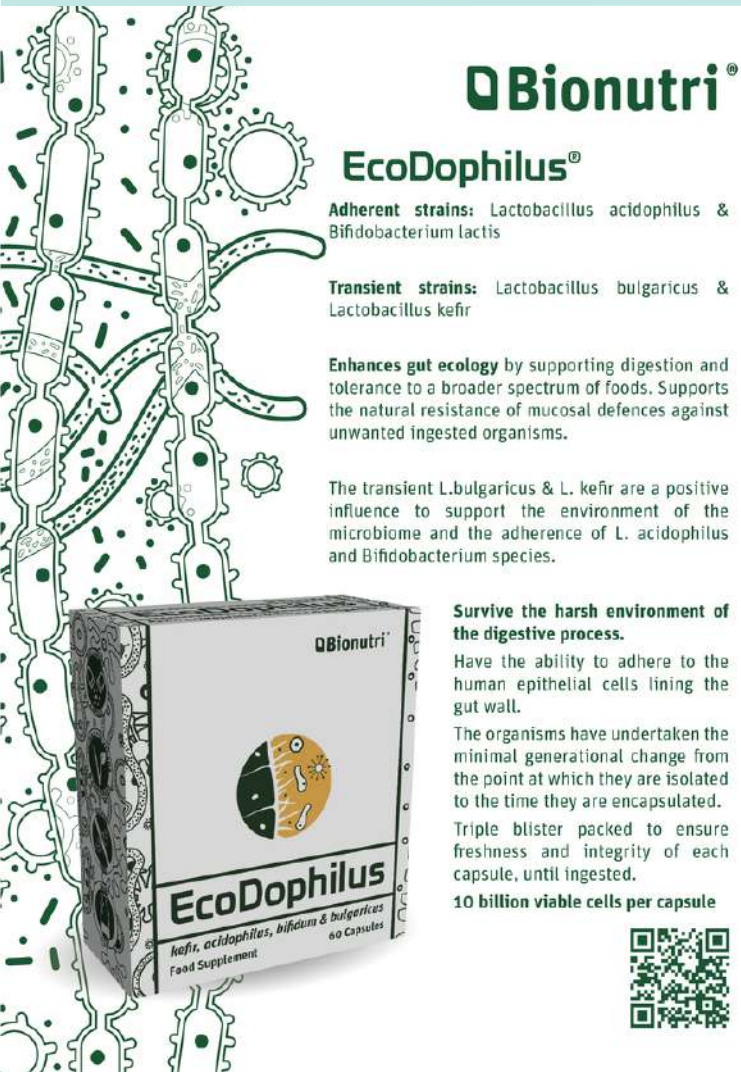

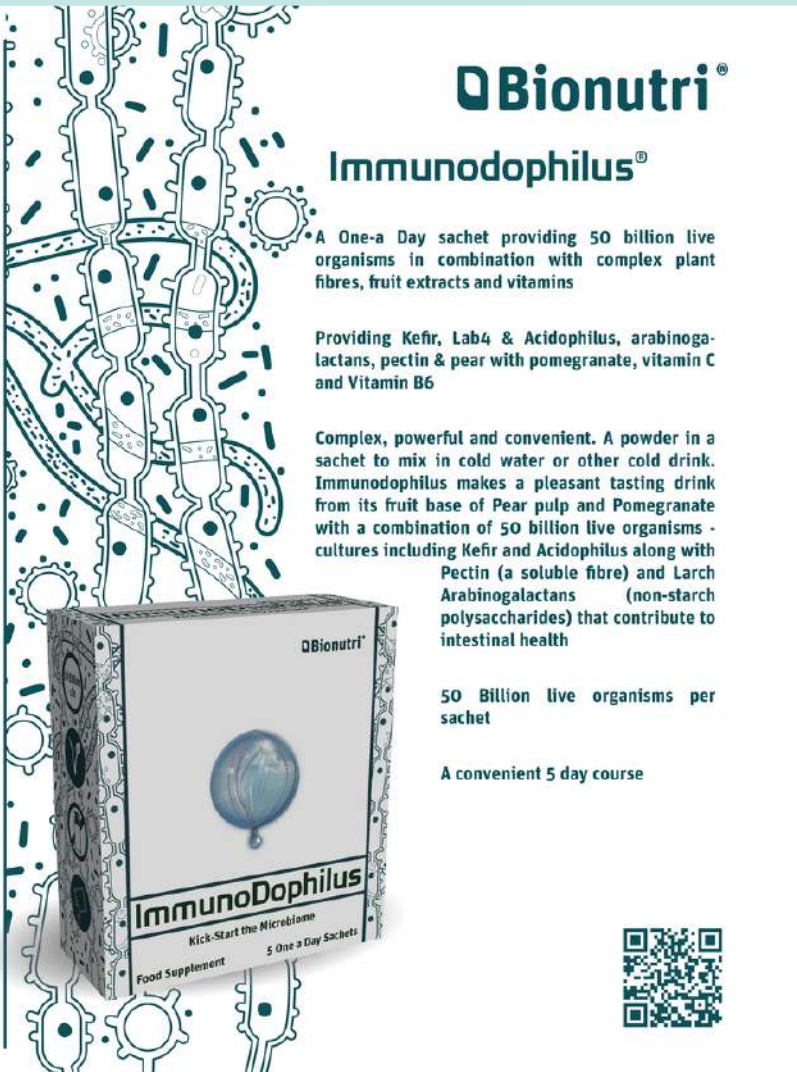

MEET THE NED EDITORIAL BOARD

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Dr Kate Lawrence - Editor, BA(Hons), PhD, FHEA

Dr Lawrence is a Senior Lecturer in psychology at St Mary's University, Twickenham. Kate's research specialises in neurodevelopmental disorders, with a particular focus on dietary and microbiome influences on mental health and cognitive function. She is published in many scientific journals, including Frontiers in Psychology, Neuropsychology, Neuropsychologia, Brain and Cognition.

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Our Expert Reviewers work within the nutrition industry in academia, research, clinical practice and wider healthcare, and provide unique and invaluable insights on the latest nutrition research to enable practitioners to apply the science to clinical practice.

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EXPERT REVIEWERS IN THIS ISSUE

(In alphabetical order from top left to right, bottom left to right)

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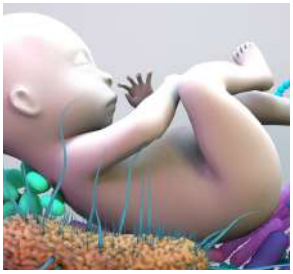
THE MICROBIOM

10 REVIEWS

THE MICROBIOME IN EARLY LIFE



THE GUT MICROBIOME IN EARLY LIFE STRESS: A SYSTEMATIC REVIEW.

Agusti, A ; Lamers, F ; Tamayo, M ; Benito-Amat, C ; Molina-Mendoza, GV ; Penninx, BWJH ; Sanz, Y
Nutrients. 2023;15(11)

INTRODUCTION:

A systematic review was conducted to consolidate clinical evidence examining the impact of early life stress (ELS) on the human intestinal microbiome.

METHOD:

Thirteen observational studies were included in the review, sourced from Pubmed, Scopus, Web of Science, and EMBASE. Methodological quality was assessed using the Newcastle-Ottawa Assessment Scale (NOS), with most studies scoring seven or eight out of nine stars.

Study designs varied, including prospective prenatal studies, postnatal longitudinal studies, case-control studies, and cross-sectional studies. Four prenatal studies were prospective in design. The other nine postnatal studies included one longitudinal study, five case-control studies, and three cross-sectional studies. All 13 studies were published between 2015 and 2022. Because study designs and outcome assessments varied, the results were presented in a narrative form. Data was extracted by 2 independent authors.

RESULTS:

The primary findings from the review were as follows:

- **Four longitudinal stress studies indicated that pregnant mothers experiencing psychological stress, increased cortisol levels, HIV, and lack of social support exhibited a lower abundance of beneficial Bifidobacterium and an increased abundance of Enterobacter genus.**
- **One postnatal stress longitudinal study (n=260) demonstrated lower depression and anxiety and improved internalising behaviour in patients with high microbiome diversity.**
- **. One postnatal stress case-control study (n=344) showed changes in the microbiome and an abundance of several bacterial taxa in stressed groups, including genera Prevotella, Bacteroides (Bacteroidetes), Coprococcus, Streptococcus, and Escherichia.**
- **One cross-sectional study of 128 adults without psychiatric conditions revealed that higher stress correlated with increased levels of Bacteroides, Parabacteroides, Rhodococcus, Methanobrevibacter, and Roseburia at the genus level, as well as lower Phascolarcto bacterium and Firmicutes at the phylum level.**
- **One large prospective study (n=446) found infants exposed to higher cumulative stress exhibited an increased relative abundance of Proteobacteria groups and lower Bifidobacterium.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **This systematic review consolidated and discussed existing evidence on the link between early life stress (ELS) and changes to the human microbiome.**
- **Exposure to ELS, prenatal or postnatal during childhood and adolescence, may impact mental and physical health.**

CLINICAL PRACTICE APPLICATIONS:

- Early life stress, and alterations in the gut microbiome, have been linked to mental health conditions
- Maternal prenatal stress may be linked to emotional, behavioural, and cognitive outcomes in infants.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research should standardise questionnaires, to ensure consistency and comparability across studies.
- Additionally, future studies should consider using standard procedures and specific species and strain resolution shotgun metagenomics sequencing.
- Consideration should be given to the influence of environmental variables (diet, physical activity, etc.) and sex in gut microbiome analysis.

CONCLUSION:

Due to the inconsistency of study designs and their results this review failed to find consensus microbiome signatures associated with pre- or postnatal stress, or both.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

EXPERT REVIEWER Ana-Paula Agrela

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University and holds a Health Coaching certificate from Zest for Life. She completed her Master's degree in Holistic Health and Nutritional Education through Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

SYNBIOTIC FORMULA EFFECTS

EARLY LIFE GUT MICROBIOTA PROFILES LINKED TO SYNBIOTIC FORMULA EFFECTS: A RANDOMIZED CLINICAL TRIAL IN EUROPEAN INFANTS.

Lagkouvardos, I ; Intze, E ; Schaubeck, M ; Rooney, JP ; Hecht, C ; Piloquet, H ; Clavel, T
The American journal of clinical nutrition. 2023;117(2):326-339

INTRODUCTION:

This randomised controlled intervention study compared gut health parameters with the use of a synbiotic pre- and probiotic strain enriched infant formula with human milk and standard formula at three intervals over a period of 2 years.

METHOD:

This was a double-blinded controlled study of 540 infants from France and Belgium. Participants were randomly allocated to 2 formula groups (n = 230 Control Formula (CF), n = 230 Intervention Formula (IF)) and the breastfed reference group (n = 80) as well as delivery mode (Cesarean and vaginal delivery). The synbiotic IF was a standard infant formula enriched with prebiotic GOS (0.02 g/g) and the probiotic strain L. fermentum CECT5716 (at least 1.0 × 106 cfu/g). Stool analysis was conducted at three time intervals, 4, 12, and 24 months (infant age). Biomarkers included short chain fatty acids, pH, secretory IgA, calprotectin, and various bacterial phyla via microbiota analysis.

RESULTS:

- **At 4 months, the IF group tested higher for Bifidobacterium spp., and Lactobacillaceae and lower occurrence of Blautia spp., as well as Ruminoccocus gnavus and relatives compared to CF. They also had lower fecal pH and butyrate levels.**
- **Both the formula cohorts had lower SigA and more basic pH values than the human milk cohort, as well as higher prevalence of anaerobes belonging to the bacterial genera Akkermansia, Collinsella, and Faecalibacterium.**
- **By age 24 months, the IF cohort exhibited increased levels of Akkermansia, Escherichia-Shigella, and R.gnavus. However there were no significant differences between the formula fed and human milk cohort at this time interval.**
- **The differences observed at 4 months disappeared over time, except for a significantly higher relative abundance of bifidobacteria and Faecalibacterium spp. in IF infants at 12 months compared with CF infants.**

CONCLUSION:

Although prominent differences between the cohorts were observed at 4 months, it appears that by the age of 2 years, there is little observable difference. This is most likely due to gut ecosystem maturation.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Infant gut colonisation differs in vaginal versus cesarean section deliveries and between breastfed and infant formula practices.**
- **Both enriched strain-specific probiotic and standard infant formula were shown to have a marked effect on microbiota colonisation in infants at age 4 months.**
- **By the age of 2 years, however, there is no significant difference between breastfed and formula fed infants.**

CLINICAL PRACTICE APPLICATIONS:

- Probiotic L.fermentum and prebiotic galacto-oligosaccharide enriched infant formula appears to the improve infant microbiome, when compared to that of breastfed infants.
- The most receptive infants were those born via cesarean section.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies need to include more diverse cultural and socio-economic cohorts to ascertain the potential influence of parental diet in baseline infant microbiome.
- It is imperative to establish what role solid food choices, generally introduced at 6 months, might have on gut ecosystem maturation.
- It would be useful to have a larger cesarean section birth cohort to compare to vaginal deliveries for more definitive results.

LIMITATIONS:

- The sample groups were from France and Belgium with no indications of culture, socio-economic, or sex distribution.
- The two infant formula groups were n=230 each with only 80 infants in the breastfed reference group.
- There was no indication of maternal diet practices pre-, during, and post- pregnancy.
- Stool samples were not collected from the infants at baseline visit prior to formula intervention.

EXPERT REVIEWER Wilma Kirsten

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Wilma has been in clinical practice since 2005. The topic for her MSc dissertation project was “The impact of Coenzyme Q10 deficiency in late-onset Alzheimer’s disease in patients who use cholesterol lowering medication”. She furthermore obtained two honours science degrees, one in Nutritional Therapy and the other in Molecular Cell Biology and Health Sciences. Wilma specialises in digestive disorders (IBS and IBD), female hormonal well-being (PMS and menopause), and mental health. She has successfully helped hundreds of patients address symptoms of ill health in her clinic. Wilma is the author of the popular science book, “Ideal Plate Composition - Choose Food to Help You Be Your Best Self”.

BIFIDOBACTERIUM & STRESS

BIFIDOBACTERIUM LONGUM SUBSP. LONGUM REDUCES PERCEIVED PSYCHOLOGICAL STRESS IN HEALTHY ADULTS: AN EXPLORATORY CLINICAL TRIAL.

Boehme, M ; Rémond-Derbez, N ; Lerond, C ; Lavalle, L ; Keddani, S ; Steinmann, M ; Rytz, A ; Dalile, B ; Verbeke, K ; Van Oudenhove, L ; Steiner, P ; Berger, B ; Vicario, M ; Bergonzelli, G ; Colombo Mottaz, S ; Hudry, J
Nutrients. 2023;15(14)

INTRODUCTION:

A randomised, placebo-controlled, two-arm, parallel, double-blind exploratory clinical trial was conducted to investigate the effect Bifidobacterium longum (BL) strain NCC3001 on stress-related psychological and physiological parameters and acute stress in healthy adults who typically experience mild-to-moderate-levels of stress.

METHOD:

47 Participants between the ages of 25-65 years old with mild-to-moderate psychological stress received 1x1010 CFU of Bifidobacterium longum (BL) strain NCC3001 daily or a placebo for 6 weeks.

Participants completed the Perceived Stress Scale (PSS), the Hospital Anxiety and Depression Scales (HAD-A and HADS-D), the Gastrointestinal Symptom Rating Scale (GSRA), the Pittsburgh Sleep Quality Index (PSQI) questionnaire, the Positive and Negative Affect Schedule (PANAS), the State Trait Anxiety Inventory (STAI-6), the Maastricht Acute Stress Test (MAST) and the Visual Analog Scales (VAS, which measures pain intensity) during the clinical study. The Depression, Anxiety and Stress Scale (DASS-42) questionnaire was also used to depict the progression of the participants through the study.

Faecal samples were taken at baseline and 6 weeks and awakening saliva samples were taken at baseline, 2, 4, 6 and 8 weeks. At the endpoint, 45/49 (91%) of the subjects completed the study. One participant reported an adverse event and the other withdrew without an explanation. Two participants were excluded from the full analysis.

RESULTS:

- **After 6-week of the probiotic intervention, there was a significant decrease in perceived stress in the probiotic group (21.4%) compared to the placebo group (-10.2%), p = 0.017.**
- **There was a significant improvement in subjective sleep in the probiotic group compared to the placebo group (p = 0.037).**
- **There was a significant decrease in the positive PANAS change score from the pre-stressor stage in the probiotic group compared to the placebo group (p = 0.01).**
- **There were lower pain values (VAS) scores from pre-stressor to post-stressor in the probiotic group compared to the placebo group (p = 0.05).**
- **There was no significant difference between groups in anxiety (HADS-A) and Depression (HADS_D) scores.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **There is mounting evidence to suggest that nutritional interventions can influence our stress responses. One of the routes by which nutrition can influence physiological and psychological stress responses involves the microbiota– gut–brain-axis.**
- **This exploratory trial suggests that supplementation with Bifidobacterium longum (BL) strain NCC3001 leads to a beneficial effect on stress relief and improves subjective sleep quality in a healthy adult population reporting moderate levels of psychological stress.**

CLINICAL PRACTICE APPLICATIONS:

- While the mechanism underlying the correlation between the microbiota and the gut-brain-axis is not fully understood, it is thought to play a critical role in the links between the microbiota, mood, stress, and brain health.
- This exploratory trial additionally supports the potential of specific probiotics being used to reduce perceived stress and improve subjective sleep quality in healthy adults.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger, powered clinical trials are needed to provide further insights into the mechanisms underlying the stress-relieving and sleep-improving effect of Bifidobacterium longum.
- Furthermore, the dosage and duration of the probiotics need further investigation in a larger healthy population.
- Comparative research is needed to help investigate the effect of different probiotic strains on stress relief and sleep quality.

CONCLUSION:

Oral supplementation with BL NCC3001 may have beneficial effects on stress relief and improves subjective sleep quality in a healthy adult population reporting moderate levels of psychological stress.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

EXPERT REVIEWER Ana-Paula Agrela

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University and holds a Health Coaching certificate from Zest for Life. She completed her Master's degree in Holistic Health and Nutritional Education through Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

PROBIOTICS & GLUCOSE DRUGS

COMPARATIVE ANALYSIS OF THE EFFICACIES OF PROBIOTIC SUPPLEMENTATION AND GLUCOSE-LOWERING DRUGS FOR THE TREATMENT OF TYPE 2 DIABETES: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Liang, T ; Xie, X ; Wu, L ; Li, L ; Yang, L ; Gao, H ; Deng, Z ; Zhang, X ; Chen, X ; Zhang, J ; Ding, Y ; Wu, Q
Frontiers in nutrition. 2022;9:825897

INTRODUCTION:

This meta-analysis compared the effects of probiotics and glucose-lowering drugs thiazolidinedione [TZD], glucagon-like pep-tide-1 receptor agonists [GLP-1 RA], dipeptidyl peptidase IV inhibitors, and sodium glucose co-transporter 2 inhibitors [SGLT-2i]) on various outcome measures in patients with type 2 diabetes (T2D).

METHOD:

25 randomised controlled trials (RCT) were included (2843 participants). 14 RCTs (842 participants) involved the administration of single probiotics, multi-strain probiotics, and probiotics with co-supplements, and 11 RCTs (2001 participants) involved TZD, GLP-1 RA, SGLT-2i, and DPP-4i. Participants in 7 of the studies had T2D, aged ≤ 55 years old. 8 RCTs included participants with a mean BMI ≥ 30 kg/m2, and 11 RCTs participants had a mean BMI < 30 kg/m2.

EFFECTS OF PROBIOTICS

- **Fasting Blood Sugar (FBS): A reduction (−1.42, −0.32 mg/dL, p=0.000).**
- **Glycated hemaglobin (HbA1c): No reduction (p = 0.000)**
- **Insulin Resistance (HOMA-IR): A decrease (−0.64, −0.31; p = 0.780), regardless of probiotic strain or with a co-supplement.**
- **Insulin: Not significant (p = 0.000). Subgroup analysis: no reduction.**
- **Total Cholesterol (TC): No difference (p = 0.941). Subgroup analysis: reduction from multi-species probiotics (−0.36, −0.01 mg/dL, p = 0.871).**
- **Triglycerides: Difference (−0.25 mg/dL, p = 0.958).**
- **LDL-C: No changes (p = 0.189).**
- **HDL-C: No increase (p = 0.014).**
- **Systolic Blood Pressure (SBP): A decrease (−6.44, −0.08 mmHg, p = 0.044).**
- **Diastolic Blood Pressure (DBP): A reduction (−4.53, −0.80 mmHg, p = 0.206).**

GLUCOSE LOWERING DRUGS

- **FBS: A decrease (−4.22 mg/dL, −1.24 mg/dL, p = 0.000).**
- **HbA1c: A decrease (−2.51%, −0.52%, p = 0.000) with TZD, GLP-1 RA, SGLT-2i, and DPP- 4i; a reduction with SGLT-2i (p = 0.003).**
- **TC: No difference (p = 0.000). Subgroup: no decrease with single species probiotics and probiotics with co-supplements, TZD, GLP-1 RA, and DPP-4i).**
- **TG: No difference (p = 0.000).**
- **HDL-C: No increase (p = 0.000). Subgroup: a decrease with TZDs (−2.37, −0.72 mg/dL). No difference with probiotic strains, or probiotics with co-supplements, GLP-1 RA, and DPP-4i.**
- **LDL-C: No changes (p = 0.000), Subgroups: no difference with probiotic strains, probiotics with co-supplements, TZD, GLP-1 RA, and DPP-4i).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Glucose-lowering drugs, except for DPP-4i, reduced FBS and HbA1c more than probiotics; and SGLT-2i induced the greatest decrease in HbA1c.**
- **A BMI ≥ 30 kg/m2 showed a significant decrease in FBS and the HOMA-IR index compared with those with lower BMI.**
- **Weight loss induced by glucose-lowering drugs and probiotic supplementation plays an important role in glycaemic control in obese patients with type 2 diabetes.**

CLINICAL PRACTICE APPLICATIONS:

- Probiotic supplementation reduced the HOMA-IR index.
- Multi-species probiotics were associated with reduction in TC and TG levels.
- DPP-4i only decreased TG levels.
- TZD was associated with decrease in HDL-C, whereas probiotic supplementation was associated with higher decrease in SBP and DBP and that GLP-1 RA increases the risk of hypoglycaemia.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Semaglutide was associated with an increased risk for hypoglycaemia compared with a placebo, indicating that the safety of semaglutide needs further study.
- Dietary and physical activity should be considered in future studies.
- Heterogeneity in some indicators may be due to differences in study baseline characteristics.
- Larger trials needed to support the results of this meta-analysis.

CONCLUSION:

Multi species probiotics are worth considering as an adjunct to glucose-lowering drugs, and for improving lipid profiles and hypertension.

EXPERT REVIEWER Kirsty Baxter

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, with a Master of Science in Nutrition (Advanced Research and Practice) and research project on the nutritional therapy approach to harnessing psychological aspects of obesity weight loss. from London South Bank University. She works collaboratively with a wide range of GPs and doctors, giving presentations to support awareness around the nutritional intervention for metabolic conditions.

PROBIOTICS ON MUSCLE MASS

IMPACT OF PROBIOTICS ON MUSCLE MASS, MUSCLE STRENGTH AND LEAN MASS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Prokopidis, K ; Giannos, P ; Kirwan, R ; Ispoglou, T ; Galli, F ; Witard, OC ; Triantafyllidis, KK ; Kechagias, KS ; Morwani-Mangnani, J ; Ticinesi, A ; Isanejad, M
Journal of cachexia, sarcopenia and muscle. 2023;14(1):30-44

INTRODUCTION:

This systematic review and meta-analysis evaluated the effect of probiotics on muscle mass, total lean mass and muscle strength in both young and older adults.

METHOD:

- The search encompassed PubMed, Scopus, Web of Science, and Cochrane Library databases, from inception up to June 2022; studies included spanned a period from 2013 to June 2022.
- The study adhered to Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines and included the Risk-of-Bias tool to assess study quality.
- The study focused on changes in muscle mass, total lean mass, and muscle strength.
- Inclusion criteria: randomised controlled trials (RCTs) with adult participants (>18 years); interventions involving any probiotics, and a control group receiving either no treatment or a placebo.

RESULTS:

- **24 RCTs were included (709 participants), with studies conducted in Europe, USA, and Asia. Intervention durations: ranged from 3 weeks to 12 months.**
- **Participants included overweight, untrained healthy and resistance-trained individuals, and those with specific conditions like metabolic syndrome and frailty.**
- **Body composition assessments were conducted using bioelectrical impedance (BIA) and/or dual-energy X-ray absorptiometry (DXA).**
- **Probiotic strains employed in the included studies varied, with Lactobacillus the most common, followed by Bifidobacterium; some combined both. 5 of 24 studies also used additional strains.**
- **Dosages: ranged from 2 × 10^9 to 11.2 × 10^10 colony-forming units (CFU).**
- **4 out of 24 studies used fermented food products like cheese and noodles as sources of probiotics.**
- **22 RCTs measured muscle mass and total lean mass; 6 RCTs measured global muscle strength.**
- **Probiotic supplementation (≥12 weeks) moderately increased muscle mass, with a standardised mean difference (SMD) of 0.42. This significant effect (95% CI: 0.10–0.74, P=0.009) was observed only in younger Asian adults (<50 years) after Bifidobacterium supplementation, based on a meta-analysis of 10 studies.**
- **Probiotic supplementation (≥12 weeks) significantly increased global muscle strength in older adults (>50 years; SMD: 0.69, 95% CI: 0.33–1.06, P = 0.0002).**
- **Probiotic supplementation showed no significant impact on lean mass (SMD: -0.03, 95% CI: 0.19 – 0.13, P = 0.69).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- This was a well-conducted meta-analysis based on its methodological approach that demonstrated that Lactobacillus and Bifidobacterium probiotic supplementation may contribute to improved muscle mass in younger adults and improved muscle strength in older adults.
- Bifidobacterium probiotic supplementation was associated with enhanced muscle mass in younger adults, a potential focus for those considering probiotic supplements.
- The duration of probiotic therapy matters, with longer-term (12 weeks or more) supplementation showing improvements in muscle mass and strength.

CLINICAL PRACTICE APPLICATIONS:

- Consumption of probiotics, mainly Lactobacillus and Bifidobacterium may contribute to improved muscle strength in older individuals (>50y).
- Consumption of Bifidobacterium strains was associated with improved muscle mass in younger individuals (<50y) in Asian countries, in a low number of studies (k=2).
- Bifidobacterium breve B-3 was associated with an improvement in muscle mass in older overweight individuals.
- Probiotics may enhance muscle mass or strength by enhancing protein digestion and amino acid absorption for muscle synthesis and function.
- Considering an individual's goals, a practitioner could consider probiotic supplementation as a complementary intervention when aiming to enhance muscle mass or strength.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research could focus on pinpointing which specific probiotic strains are most effective for muscle strength or muscle mass to tailor more precise interventions.
- Most studies did not exceed 12 weeks, highlighting the need for long-term research on probiotics sustained muscle impact.
- Future research could investigate the effects of probiotics across diverse demographic groups including different ages, sexes, and ethnic backgrounds to understand the impact in different populations.
- Delving deeper into the mechanisms by which probiotics influence muscle health could lead to targeted probiotic therapies that address specific physiological pathways.
- Finally, future research could explore how probiotics can be combined with other interventions, such as exercise or nutritional modifications, to synergistically improve muscle health and function.

EXPERT REVIEWER Anna Papoutsa

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Anna holds an MSc in Personalised Nutrition and a PGCert in Higher Education. Her dissertation delved into refined carbohydrates and the onset of gout in overweight individuals. Anna has a particular focus on cardio-metabolic and immune function disorders. Committed to staying at the forefront of nutritional science and technology, Anna integrates AI-driven tools and laboratory assessment insights into her practice to offer advanced, data-driven nutritional recommendations and support. Beyond her clinical work, she teaches and lectures at CNELM, where she leads BSc and MSc modules.

LACTOCOCCUS ON THE HPA AXIS

EFFECTS OF LACTOCOCCUS LACTIS SUBSP. CREMORIS YRC3780 DAILY INTAKE ON THE HPA AXIS RESPONSE TO ACUTE PSYCHOLOGICAL STRESS IN HEALTHY JAPANESE MEN.

Matsuura, N ; Motoshima, H ; Uchida, K ; Yamanaka, Y
European journal of clinical nutrition. 2022;76(4):574-580

INTRODUCTION:

A randomized, placebo-controlled, double-blind clinical trial was conducted to investigate the influence of Lactococcus lactis subsp. cremoris (YRC3780), isolated from kefir, on stress response, sleep quality, and mental health.

METHOD:

Twenty-seven healthy young men, with an average age of 23.5 years, and mean body mass index of 21.5 kg/m2 , were randomly assigned to either the YRC3780 group or the placebo group. Participants were administered YRC3780 or a placebo daily for 8 weeks.

Throughout the study, participants completed assessments, including the Athens Insomnia Scale (AIS), the Pittsburgh Sleep Quality Index (PSQI), the General Health Questionnaire (GHQ-28), and the Profile of Mood States 2nd Edition-Adult Short, Total Mood Disturbance subscale (POMS 2 TMD), every 2 weeks. Additionally, diurnal rhythms of HPA axis activity were assessed every 2 weeks through saliva samples collected at 2-hour intervals during the day. At the end of the 8-week supplementation period, participants underwent the Trier Social Stress Test (TSST) to evaluate the effects of daily YRC3780 intake on the HPA axis stress response. In addition, three fecal samples were collected to analyse the gut microbiome (on the last day of baseline, and at 4 and 8 weeks).
A total of 27 out of 33 subjects (81%) completed the study, with six participants withdrawing.

RESULTS:

- **At week 6 of YRC3780 supplementation, salivary cortisol levels at 2 hours and 6 hours after waking were significantly lower in the YRC3780 group compared to the placebo group (p=0.05).**
- **Salivary cortisol concentrations at 40 minutes after the TSST were significantly lower in the YRC3780 group (4.2 ± 4.4 nmol/L, mean ± SD) than in the placebo group (7.6 ± 4.7 nmol/L) (p=0.043).**
- **AIS scores at 6 weeks and GHQ-28 scores at 8 weeks were significantly lower in the YRC3780 group compared to the placebo group (AIS, p=0.031; GHQ-28, p=0.038) indicating better sleep quality and a better mental state.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Research indicates a bidirectional interaction between the gut microbiome and the central nervous system, affecting the functions of the brain and spinal cord.**
- **This clinical trial suggests that daily intake of Lactococcus lactis subsp. cremoris (YRC3780) may enhance the HPA axis response to acute psychological stress, potentially linked to a reduction in morning cortisol levels.**

CLINICAL PRACTICE APPLICATIONS:

- The precise mechanisms underlying the correlation between the gut microbiota and the gut-brain axis remain incompletely understood, emphasising the need for further research.
- This clinical trial demonstrated that daily intake of YRC3780 decreased morning salivary cortisol levels at 6 and 8 weeks and reduced the salivary cortisol response to acute psychological stress.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger, adequately powered clinical trials are required to provide deeper insights into the mechanisms responsible for the stress-reducing and sleep-improving effects of Lactococcus lactis subsp. cremoris.
- Furthermore, investigations into optimal dosage and duration of probiotic supplementation are warranted for a more comprehensive understanding, particularly in diverse demographic groups.
- Comparative research is needed to explore the effects of various probiotic strains on objective stress responses.

CONCLUSION:

Oral supplementation with YRC3780 may have beneficial effects on the HPA axis response to acute psychological stress, potentially associated with a decrease in morning cortisol levels. Additionally, the study suggests that the lower basal activity and stress reactivity of the HPA axis may lead to improvements in subjective sleep quality and mental health.

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University. She completed her Master's degree in Holistic Health and Nutritional Education at Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

85% CHOCOLATE & MICROBIOTA

CONSUMPTION OF 85% COCOA DARK CHOCOLATE IMPROVES MOOD IN ASSOCIATION WITH GUT MICROBIAL CHANGES IN HEALTHY ADULTS: A RANDOMIZED CONTROLLED TRIAL.

Shin, JH ; Kim, CS ; Cha, L ; Kim, S ; Lee, S ; Chae, S ; Chun, WY ; Shin, DM
The Journal of nutritional biochemistry. 2022;99:108854

INTRODUCTION:

The authors highlight that dark chocolate has been continually identified for its effects on mood. However, there is a dearth of evidence concerning the emotional impact of daily consumption of dark chocolate. Hence, the impact of dark chocolate consumption on daily mood, focusing on the gut-brain axis, is being investigated in this study.

METHOD:

- A randomised controlled trial was performed at Seoul National University from July to December 2017, This involved. consumption of two types of dark chocolate (70% and 85% cocoa content). Subjects in the treatment groups were blinded although investigators and the control cohort were unblinded.
- 117 participants were screened. However, 48 healthy males and females aged 20-30 years were eligible.
- Participants consumed (n=16) 30g/day of 70% cocoa chocolate, (n=18) 30g/day of 85% cocoa chocolate, (n=14) no chocolate for 3 weeks.
- Mood states were quantified via the Positive and Negative Affect Schedule in tandem with Microbiota analysis pre- and post-experiment. Body composition analysis and dietary assessment were also conducted pre- and post-intervention. Faecal 16S rRNA sequencing analysis of bacterial genomic DNA was conducted for the cohort who consumed 85% cocoa chocolate and the control arm to evaluate the association between the mood-altering effects of dark chocolate and the gut microbiota. Statistical tests were performed based on intention-to-treat analysis. The Chi-squared test, Kruskal-Wallis test, one-way ANOVA, unpaired t-test and Mann-Whitney U test were employed for inter-group analysis. Spearman's correlation analysis was used to assess the association between gut microbiota composition and mood scores and $P<.05$ was considered statistically significant.

RESULTS:

- **Daily intake of dark chocolate substantially diminished negative emotional states in the cohort consuming 85% cocoa content, but not in the 70% cocoa treatment arm**
- **Gut microbial diversity was substantially greater in the 85% cacao cohort than the control group ($P<.05$)**
- **Blautia obeum levels were significantly elevated and Faecalibacterium prausnitzii levels were decreased in the 85% cacao cohort than the control arm ($P<.05$).**
- **Furthermore, it was observed that changes in negative affect scores were inversely correlated with diversity and relative abundance of Blautia obeum ($P<.05$).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **To highlight the potential benefits of high cocoa content dark chocolate in relation to mental states.**
- **To promote more awareness of how dietary habits may impact emotional wellbeing.**
- **To emphasise the importance of microbiota and the gut-brain axis regarding dietary habits.**

CLINICAL PRACTICE APPLICATIONS:

- To inform practitioners of the benefits of 30g/day high (85%) cocoa chocolate consumption and its potential positive impact on mood through the gut-brain axis.
- To educate clients regarding the potential benefits of daily high cocoa content chocolate consumption and its possible favourable effect on emotional states associated with gut microbiota.

CONSIDERATIONS FOR FUTURE RESEARCH:

- More extensive research could investigate interventions of a longer period.
- Further studies could evaluate if any difference exists between cocoa and cacao consumption and emotional states via the gut-brain axis, and the strength of any associations.
- Interventions could investigate which strains of bacteria that high cocoa content dark chocolate may affect.

CONCLUSIONS:

The observations suggest that consumption of dark chocolate with a higher cocoa content may induce prebiotic effects due to its capacity to restructure the diversity and composition of the gut microbiota. Furthermore, consuming dark chocolate with a higher cocoa might exert a positive effect on negative emotional states through the gut-brain axis.

EXPERT REVIEWER Jennifer McCarthy

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Jennifer is a PhD candidate based in the Environmental Sustainability and Health Institute in TU Dublin and a freelance Scientific Editor. Her research integrates the areas of Environmental Health, Environmental Epidemiology, Food Science, Public Health, Agriculture, Microbiology, Food Safety, Risk Assessment, Mathematical Modelling and Statistics. She is a graduate member of The Nutrition Society and an associate member of the International Academy of Nutrition Educators with an MSc in Food, Nutrition and Health from UCD, MA in Translation Studies from DCU (scientific and technical writing/translation, translation technology, editing, etc.), and is a former third level Mathematics, Statistics and EAP Lecturer.

FEED MICROBES FOR STRESS

FEED YOUR MICROBES TO DEAL WITH STRESS: A PSYCHOBIOTIC DIET IMPACTS MICROBIAL STABILITY AND PERCEIVED STRESS IN A HEALTHY ADULT POPULATION.

Berding, K ; Bastiaanssen, TFS ; Moloney, GM ; Boscaini, S ; Strain, CR ; Anesi, A ; Long-Smith, C ; Mattivi, F ; Stanton, C ; Clarke, G ; Dinan, TG ; Cryan, JF
Molecular psychiatry. 2022

INTRODUCTION:

This RCT explored the impact of a psychobiotic diet, compared to a control diet, on perceived stress, sleep and gut microbiota. A high psychobiotic diet is one high in prebiotic and fermented foods. In this study, a psychobiotic diet included daily recommended consumption and servings of the following:

- High prebiotic fruit & veg (6-8)
- Grains (5-8)
- Fermented foods (2-3)
- Legumes (3-4 per week)

METHOD: A SINGLE-BLIND, RANDOMISED, CONTROLLED STUDY

- 45 healthy adults (18-59 years) with poor dietary habits. Sample size determined by previous microbiome research - target not reached due to introduction of covid restrictions.
- Active intervention (n=24) received dietitian advice to follow psychobitoic diet.
- Control intervention (n=21) received dietitian advice largely based on the Irish Healthy Eating food pyramid.
- Intervention duration 4 weeks.
- Assessed on questionnaire measures of perceived stress and sleep, pre and post-intervention.
- Shotgun microbiome analysis on stool samples, pre and post-intervention.

RESULTS:

- **Perceived stress improved in the psychobiotic diet group.**
- **Subjective sleep quality improved in the psychobiotic diet group.**
- **Only subtle changes in microbial composition and function.**
- **More stable microbiota throughout the study (regardless of diet) was correlated with greater changes in perceived stress.**
- **Neither cortisol awakening response nor measured immune markers were affected by dietary intervention.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Eating foods known to have a positive influence on gut microbial composition could elicit benefits in terms of reducing perceived stress and improving sleep quality.**

CLINICAL PRACTICE APPLICATIONS:

- Providing advice on dietary intake of foods known to positively impact gut microbiota may be helpful for individuals affected by stress or sleep problems.
- The inclusion of the following foods may be helpful:
  - High prebiotic fruit & veg (6-8 per day)
  - Grains (5-8 per day)
  - Fermented foods (2-3 per day)
  - Legumes (3-4 per week)

CONSIDERATIONS FOR FUTURE RESEARCH:

- Important to replicate these results in a larger sample.
- It might be helpful to investigate individual aspects of the diet separately, to assess their individual impact.
- Objective measures of sleep (such as actigraphy recordings) might provide additionally useful findings.
- It would be interesting to explore the effect of the psychobiotic diet in other conditions.
- Chronobiology or chrononutrition - i.e. looking at timing of the foods proposed in the section above.

CONCLUSIONS:

- **Using a diet targeted to positively modulate gut-brain communication may have the potential for reducing stress and improving sleep.**
- **Although improvements in stress were only observed for the intervention group – the post-intervention stress levels were not significantly different between the groups.**
- **Thus, we should interpret the results with some caution.**

EXPERT REVIEWER Dr. Kate Lawrence

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Dr Lawrence is a Senior Lecturer in psychology at St Mary's University, Twickenham. Kate's research specialises in neurodevelopmental disorders, with a particular focus on dietary and microbiome influences on mental health and cognitive function. She is published in many scientific journals, including Frontiers in Psychology, Neuropsychology, Neuropsychologia, Brain and Cognition.

PROBIOTICS & COVID19 VIRUS

PROBIOTIC IMPROVES SYMPTOMATIC AND VIRAL CLEARANCE IN COVID19 OUTPATIENTS: A RANDOMIZED, QUADRUPLE-BLINDED, PLACEBO-CONTROLLED TRIAL.

Gutiérrez-Castrellón, P ; Gandara-Martí, T ; Abreu Y Abreu, AT ; Nieto-Rufino, CD ; López-Orduña, E ; Jiménez-Escobar, I ; Jiménez-Gutiérrez, C ; López-Velazquez, G ; Espadaler-Mazo, J
Gut microbes. 2022;14(1):2018899

INTRODUCTION:

A quadruple-blinded, randomized trial was conducted in adults with symptomatic Coronavirus Disease 2019(Covid19) outpatients.

METHOD:

Three hundred subjects between the ages of 18 and 60 years, with a peripheral oxygen saturation (SpO2) ≥ 90% and in whom 42% had known metabolic risk factors for severe Covid19, were randomized to a oral probiotic containing Lactiplantibacillus plantarum KABP022, KABP023, and KAPB033, with Pediococcus acidilactici strain KABP021, totaling 2 x 109 colony-forming units (n=150), or placebo (n=150), for 30 days. At endpoint, 293/300 subjects finished the study.

RESULTS:

Primary clinical outcomes were:

- **Complete remission was achieved by 78 of 147 (53.1%) in probiotic group compared to 41 of 146 (28.1%) in placebo (P< .001).**
- **Adverse events were lower in the probiotic group (p=0.008), though not statistically significant in those taking ≥2 medications daily (risk ratio 0.66 (95%CI 0.29-1.48).**
- **No hospitalizations or deaths occurred during the study.**

Secondary clinical outcomes were:

- **The probiotic treatment was well-tolerated and reduce the duration of both digestive and non-digestive symptoms, compared to placebo.**
- **The probiotic treatment was associated with reduce nasopharyngeal viral load compared to placebo (P < .001) and reduce lung infiltrates (P < .001).**

Furthermore, the probiotic treatment:

- **Significantly increased specific IgM and IgG against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2).**
- **Lowered serum levels of high-sensitivity C-reactive protein (hsCRP) (P<00.1) and D-Dimer levels (P,00.1) compared to placebo.**
- **Shortened median recovery time by 5 days (p<0.001).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **It is advisable for those over 60 years old with a metabolic risk factor (BMI>30, diabetes and/or hypertension) to consult with their clinical practitioners if tested positive for Covid-19.**
- **Specific probiotic strains are reported to show positive results in reducing the duration and severity of Covid-19 symptoms in adults under 60 years old.**
- **These probiotics (Lactiplantibacillus plantarum KABP022, KABP023, and KAPB033, plus strain Pediococcus acidilactici KABP021) have also shown a positive effect on reducing inflammation and supporting remission of Covid-19.**

CLINICAL PRACTICE APPLICATIONS:

- General practitioners, pharmacists, and clinic nurses are generally the first point of contact for patients who are not feeling well. Especially, during a pandemic when hospitals are inundated with patients who need urgent care. It is therefore essential for clinicians to have outpatient treatment protocols available to support the community.
- The microbiome is reported to be the first line of defense and interacts with the human host's immune system. Therefore, probiotics may be useful as a preventative and supportive measure during a pandemic.
- Based on this study, practitioners could therefore consider a probiotic containing Lactiplantibacillus plantarum and Pediococcus acidilactici strains alone or in combination with other probiotic strains as a supportive measure.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies are needed to replicate these findings and elucidate its mechanism of action, particularly as fecal microbiome analysis in a subset of n=100 subjects did not detect a difference in fecal microbiome composition.
- Further studies are needed to identify specific probiotic strains that display immune effects, and their dosage.
- Further investigation of this probiotic formula in helping prevent thrombotic complications in Covid19 is warranted to explore elevated D-Dimer levels being associated with a higher risk of thrombotic events.
- All the subjects in the study were of Hispanic ethnicity, therefore further studies of other ethnicities are required.
- This study was capped at 60-year-olds, thus studies in older subjects are warranted.
- Conflict of interest statement: This study was fully funded by the manufacturer of the provided probiotic.

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University. She completed her Master's degree in Holistic Health and Nutritional Education at Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

PROBIOTICS & GASTROENTERITIS

EFFECTS OF PROBIOTICS IN ADULTS WITH GASTROENTERITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL TRIALS.

Mitra, AK ; Asala, AF ; Malone, S ; Mridha, MK
Diseases (Basel, Switzerland). 2023;11(4)

INTRODUCTION:

To date, evidence has been mixed for probiotic effectiveness in gastrointestinal syndromes associated with gastroenteritis. The aim of this study was to review current evidence on the effect of probiotics on gastroenteritis in adults.

METHOD:

This was a systematic review (n=35; total sample size 4577, median 44) and meta-analysis (n=22) of randomised controlled trials. Quality was assessed using CADIMA as per a rating scale (0 to 4) and standards of critical appraisal.

RESULTS:

- **All 35 studies on gastroenteritis included participants with chronic diarrhoea of diverse aetiologies such as IBD, antibiotic-associated, except one which had acute watery diarrhoea.**
- **51% (n=18) of studies assessed the effects of probiotics in the treatment of ulcerative colitis (UC) and Crohn's disease (CD). 60% (n=21) used multiple strains of probiotics while the rest used single strains. Lactobacilli, Bifidobacteria, Escherichia and Streptococcus were the most common and only a few studies administered probiotics with another conventional treatment.**
- **19 studies (55%) rated highly in terms of quality while 15 (43%) scored moderately. The majority (63%) of the 27 studies where probiotics were shown to be effective were of high quality.**

Systematic review results:

- **27/53 studies (77%) showed a favourable response after using probiotics (resolution, improvement, remission or no relapse), mostly in patients with IBDs.**
- **7 studies (20%) found probiotics to be ineffective.**
- **1 study was inconclusive.**
- **Multiple strain probiotics (VSL #3) was found to be most effective in IBD.**
- **All administered probiotics were well tolerated with no adverse side effects although caution in immunocompromised patients was mentioned in several studies.**

The meta-analysis results:

- **Overall effectiveness for 22 studies (p=0.37) highlighted there was not enough evidence that the intervention was more protective than controls.**
- **Probiotics were not effective in UC (p = 0.28), and adverse events caused by probiotics may outweigh the benefits in studies with UC patients.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **For chronic inflammatory gastroenteritis conditions in adults, probiotics were effective in treating and preventing relapse.**
- **In ulcerative colitis, probiotics were not effective and adverse events outweighed the benefits.**
- **No safety concerns were found for probiotic use in any studies.**
- **Aetiologies, disease severity and duration as well as the type of probiotics used were widely diverse.**

CLINICAL PRACTICE APPLICATIONS:

- Based on the systematic review, probiotics may be an effective treatment or adjuvant treatment for gastroenteritis but ineffective for around 20% of patients.
- It is worth noting that combined therapy with standard treatment showed effective results.
- Beneficial effects of probiotics in other key clinical outcomes including disease prevention, relapse, quality of life, morbidity were found.
- While the results are interesting it is difficult to apply them in practice as the type of probiotics used were widely different as were the causes, severity and duration of gastroenteritis.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Further and larger studies would be beneficial to understand the benefits of probiotics in terms of single therapy or in combination with standard treatment particularly for UC, CDs, gastroenteritis not due to viral infection.
- Individual-level data instead of aggregated data could give a better idea of effectiveness of probiotics in the future.
- In this study aetiologies and the type, dosage, duration of probiotics used were widely diverse therefore systematic reviews and meta-analysis on specific conditions, specific probiotic strains and combinations would be beneficial.

CONCLUSIONS:

While benefits of effectiveness were found for probiotic use in gastroenteritis in adults, results from the systematic review and meta-analysis showed a mixed effect.

EXPERT REVIEWER Georgie Murphy

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Georgie is a Registered Nutritional Therapist and BANT member. She studied Nutritional Therapy at CNM in London. Prior to this she completed her MSc in Nutrition at King's College London and BSc in Biomedical Science from University College Dublin. Georgie brings experience working as the Head of Nutrition at a personalised nutrition start-up. She has experience in supplement development, clinical research, biotech and early-stage clinical trials. Her areas of specialism include gut health and how it affects skin health.

SCIENCE TAKEAWAYS

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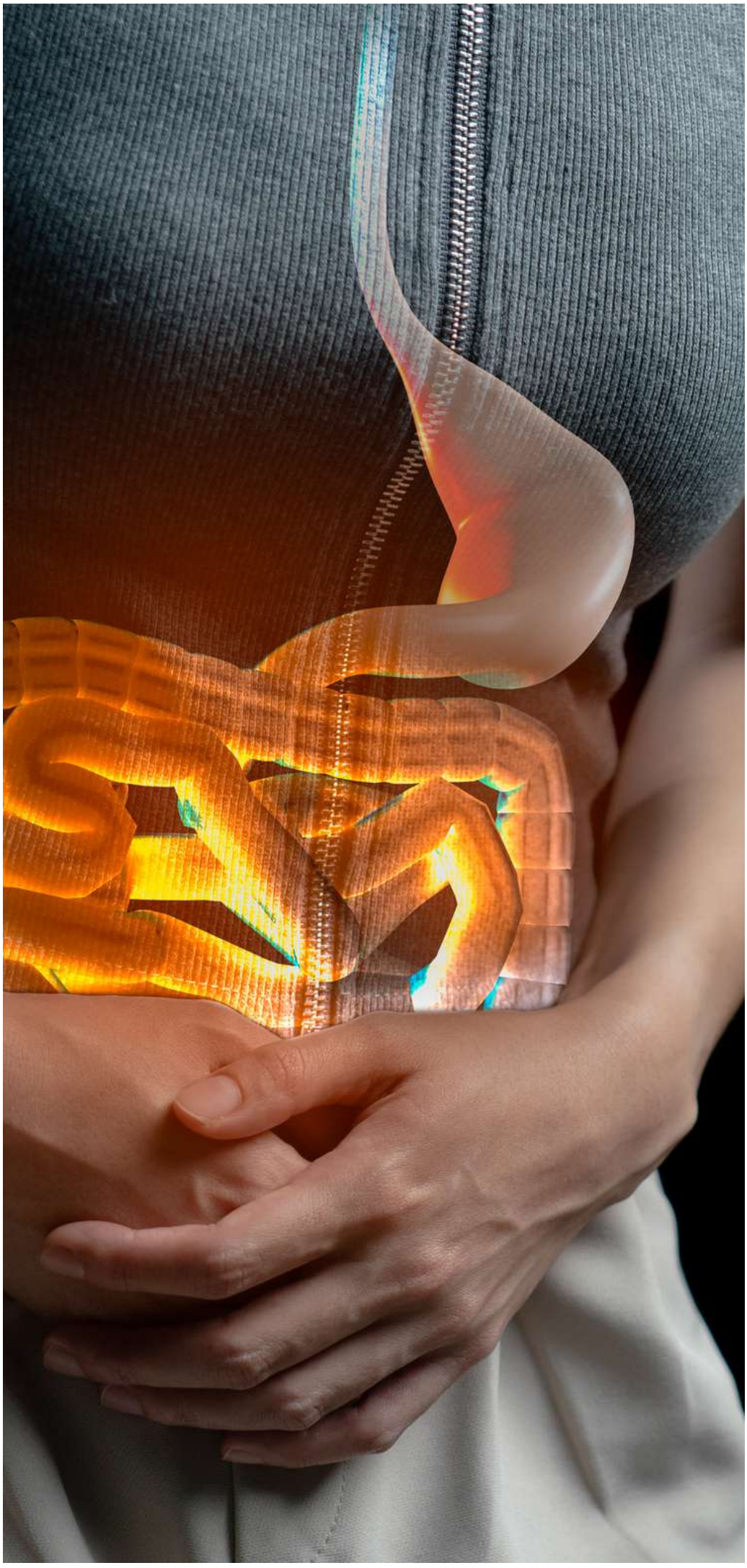
IBS & THE MICROBIOME



7 REVIEWS

PROBIOTICS & BARRIER FUNCTION

PROBIOTICS FORTIFY INTESTINAL BARRIER FUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED TRIALS.

Zheng, Y ; Zhang, Z ; Tang, P ; Wu, Y ; Zhang, A ; Li, D ; Wang, CZ ; Wan, JY ; Yao, H ; Yuan, CS
Frontiers in immunology. 2023;14:1143548

INTRODUCTION:

Probiotics are microorganisms that are considered beneficial to health. The aim of this study was to assess the role of probiotics in protecting intestinal barrier function as well as their effects on the composition of gut microbiota, inflammatory status, and immune function for reducing the risk of related diseases.

METHOD: THE TRIAL WAS BLINDED TO ALL PARTICIPANTS, PARENTS AND STUDY STAFF.

26 randomised controlled trials (RCTs) published between 2005-2021 with a total population of n=1891 (n = 955 Intervention, n = 936 controls)) were included in the meta-analysis. Outcome measures were categorised under indicators relating to intestinal barrier function, inflammatory markers, immune function and microbiota composition. Studies were conducted worldwide with participants being healthcare patients or athletes. Study durations ranged from 3 days to 6 months. Different dosages and forms of probiotics were used. Data was pooled for Bifidobacterium, Lactobacillus, Enterobacteriaceae and Enterococcus species.

RESULTS:

Gut barrier function in the probiotic groups was improved as measured by transepithelial resistance (TER) mean difference (MD) 5.27 {95% CI, 3.82 to 6.72, p = < 0.00001], lipopolysaccharide (LPS) standardised mean difference (SMD) -0.47 (95% CI, -0.85 to -0.09, p = 0.02), serum zonulin SMD -1.58 (95% CI,-2.49 to -0.66, p = 0.0007), and endotoxin SMD -3.20 (95% CI, -5.41 to - 0.98, p = 0.005).

The inflammatory markers interleukin 6 (IL-6), C-reactive protein (CRP) and tumour necrosis factor-alpha (TNF-a) were also improved compared to control groups. Lactobacillus (95% CI p=0.02) and Bifidobacterium (95% CI, p=0.01) enhanced microbial composition, however, Enterobacteriaceae and Enterococcus species did not. Immune function as measured by Immunoglobulin A (IgA), Immunoglobulin G IgG and Immunoglobulin M (IgM) were not improved.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- The probiotics Bifidobacterium and Lactobacillus may be beneficial for health by addressing imbalances in gut bacteria (dysbiosis), reducing inflammation in the gut and improving the integrity and function of the gut barrier.

CLINICAL PRACTICE APPLICATIONS:

The use of the probiotics Bifidobacterium and Lactobacillus may be beneficial for:

- supporting the integrity of gut barrier function.
- improving the composition of gut microbiota.
- lowering inflammation.

? CONSIDERATIONS FOR FUTURE RESEARCH:

High heterogeneity between studies may affect the applicability of the results. Future research development should focus on the following areas:

- testing methods.
- study durations.
- measuring indicators.
- the type and dose of probiotics.

CONCLUSIONS:

The findings of this study suggest that intestinal barrier function and microbial composition could be improved using probiotics. They were also found to help alleviate inflammation. Further studies of high quality are however needed to confirm these results.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Gail Brady

Gail is a Registered Nutritional Therapy Practitioner RCNHC MBANT. She qualified is 2013 from The Institute for Optimum Nutrition in London and has since furthered her studies and completed a Master's of Science (MSc) degree in Advanced Nutrition (Research and Practice). The topic for her MSc dissertation project was menopause and potential diet and lifestyle interventions that my help to prevent weight gain. In clinical practice, Gail specialises in female health and works 1:1 with clients using a Functional Medicine framework. She also runs an online course providing a tool kit for managing perimenopause and menopause.

LACTIPLANTIBACILLUS IN IBS

EFFICACY AND DOSE RESPONSE OF LACTIPLANTIBACILLUS PLANTARUM IN DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME.

Martoni, CJ ; Srivastava, S ; Damholt, A ; Leyer, GJ
World journal of gastroenterology. 2023;29(28):4451-4465

INTRODUCTION:

This study aimed to determine the tolerability and efficacy of varying supplemental doses of Lactiplantibacillus plantarum (Lpla33) in adults with irritable bowel syndrome of the diarrhoea predominant subtype (IBS-D).

METHOD:

- This randomised, double blind, placebo-controlled trial recruited 307 females and males aged 18-70 years with IBS-D based upon the Rome IV diagnostic criteria with Bristol Stool Scale stools of type 6 or 7.
- Individuals were randomised to receive an eight-week intervention in one of three study groups: Group 1B: Lpla33 at 1 × 109 vs group 10B: 1x1010 colony forming units (CFU) per day vs placebo.

RESULTS:

- **Improvement was seen in the primary outcome of IBS-D symptom severity (IBS-SSS) with both Lpla33 doses compared to placebo at the end of the trial (P=<0.001).**
- **Improvements with both doses compared to placebo were seen as quickly as 28 days (P=<0.01).**
- **At the end of the study the higher dose Lpla33 was more effective at improving IBS-SSS compared to the lower dose (P=<0.05).**
- **Improvements to IBS remission or mild IBS were seen in 48.1% in group 1B, 72.6% in group 10B and only 11.1% of placebo (P=<0.001).**
- **Specific improvements were seen in 10B group compared to placebo in abdominal pain severity and duration, abdominal distension, bowel habits, and quality of life (QoL) (P=<0.001).**
- **Post-hoc analysis showed that supplementation prevented symptom development compared to placebo with 2.9% of group 1B, 2.1% of group 10B and 18.2% of placebo individuals reporting increased symptom severity (P=<0.001).**
- **QoL and perceived stress were improved with supplementation compared to placebo (P=<0.001 for both), with the higher dose being more beneficial than the lower dose in QoL (P=<0.001).**
- **Compliance to Lpla33 was comparable to placebo (P=>0.05), with adverse events related to the supplement including nausea and vomiting.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- This randomised, double-blind, placebo controlled, multi-centre, parallel-arm and dose-ranging study showed that L. plantarum may be a strong candidate for the management of IBS-D symptoms and associated mental health effects.
- L. plantarum may be of particular benefit to individuals who are suffering from stress because of IBS-D.
- L. plantarum is well tolerated and may be of benefit to individuals who have ceased pharmaceutical treatments as a result of side-effects.

CLINICAL PRACTICE APPLICATIONS:

L. plantarum supplementation may be of benefit to the management and improvement of symptoms in individuals with IBS-D.

Improvements may be seen physically and in mental health parameters.

Metronidazole (400mg/day) was given as a rescue medication for individuals with severe pain and frequent loose stools and should be considered when interpreting results.

? CONSIDERATIONS FOR FUTURE RESEARCH:

The authors concluded that future research should focus on understanding the mechanisms of action that may be involved.

Studying the role of diet on the microbial community and metabolite profiles in IBS-D may be of interest.

CONCLUSIONS:

L. plantarum at doses of 1 × 109 and 1 × 1010 CFU/day is a well-tolerated and efficacious therapy for the improvement of symptoms related to IBS-D, with benefits seen as quickly as 28 days after commencing supplementation. Symptoms such as abdominal pain severity and duration, QoL and perceived stress may all be improved. Stool normalisation may be seen in certain individuals.

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: **A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)**

EXPERT REVIEWER Chloe Steele

Chloe has an MSc in Personalised Nutrition from the University of Middlesex, and specialises in cardiovascular disease, type 2 diabetes, and anxiety. Chloe started her career at BANT as a member of the Nutrition Evidence Database research team and now has over 5 years experience of research and writing. She has worked in several countries, and is currently in Australia, where she worked for Nutrition Australia and is currently the principal nutritionist for Heart Research Australia. She has published two papers in the Nutrition Medicine Journal, on gut microbiota and collagen. Chloe is a member of BANT and the Nutrition Society of Australia and sits on the editorial board for the Nutrition Medicine Institute in the UK.

PROBIOTICS & CONSTIPATION

EFFECT OF THE PROBIOTIC STRAIN, LACTIPLANTIBACILLUS PLANTARUM P9, ON CHRONIC CONSTIPATION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY.

Ma, T ; Yang, N ; Xie, Y ; Li, Y ; Xiao, Q ; Li, Q ; Jin, H ; Zheng, L ; Sun, Z ; Zuo, K ; Kwok, LY ; Zhang, H ; Lu, N ; Liu, W
Pharmacological research. 2023;191:106755

INTRODUCTION:

This study investigated the effect of a specific probiotic strain in alleviating Chronic Constipation (CC).

METHOD:

- The study employed a 42-day randomised control trial (RTC) double-blind, placebo-controlled design, with 163 patients, (mean age =22.68 ±5.66 years for the probiotic group and 21.59 ±4.59 years for the placebo group), diagnosed with CC (Rome IV criteria).
- The male to female ratio was 15–63 and 17–68 in probiotic and placebo groups respectively.
- Groups were standardised with no differences observed in baseline age, gender ratio, drug treatment, high-fibre diet and smoking between the two groups (P >0.18).
- Participants were randomly assigned to the probiotic Lactiplantibacillis plantarum P9 (n=78; 2 g per sachet, 1 ×1011 CFU/day) or the placebo (n =85; maltodextrin powder) groups.

RESULTS:

Primary outcomes: weekly mean complete spontaneous bowel movements (CSBMs):

- **At 28-days CSBM was 28% higher in the P9 group (P=0.039) compared with the placebo group**
- **At 42-days CSBM remained significantly higher in the P9 group (P=0.026) compared with the placebo group, and increased 2-fold compared with baseline (P <0.05) - benefits were maintained even after 14 days of not taking the supplement.**

Secondary outcomes: The effects of P9 supplementation on constipation-related parameters, including the weekly mean frequency of spontaneous bowel movements (SBMs) demonstrated:

- **After 28-days of P9 supplementation, SBMs were 12% higher than the placebo group (P=0.039)**
- **No differences were observed in the weekly mean stool consistency and straining scores between groups (P>0.05).**

Patients' quality of life and psychological state, using a PAC-QOL questionnaire related to: worries and concerns (WO), physical discomfort, psychosocial discomfort, and satisfaction and found:

- **At day 14 WO in the P9 group was 1.22-fold lower than those in the placebo group (P <0.05).**
- **No differences in the other 3 items between P9 and placebo groups (P >0.05) were observed.**
- **Supplementation resulted in a significant change in relative abundance of the P9 genome (≥0.01%).**
- **However, no differences were observed in alpha diversity after P9 consumption compared with placebo.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- This study suggested that P9-associated constipation symptom relief was not attributed to macroscopic changes in the host gut bacteriome and phageome.
- However, results supported that taking P9 could alleviate constipation, with the symptom relief effects linked to desired changes and interactions with different types of host microbes, including the gut commensal bacteria (L. plantarum, Ruminococcus_B gnavus, Oscillospiraceae sp., Lachnospiraceae sp.) and the bacteriophage family, Herelleviridae.

CLINICAL PRACTICE APPLICATIONS:

- In this study, the use of P9 administration significantly improved patients' defecation frequency which could have beneficial implications for patients suffering from chronic constipation.
- Probiotic effects are known to be strain- and host-specific, and based on this study P9 administration for relief of constipation needs to be taken for at least two weeks to improve aspects of patients' quality of life and 4 weeks for improvements in constipation.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Future trials should include factors that impact gut motility and constipation symptoms, such as: a detailed daily diet (dietary composition, fibre content, and water intake) and physical activity scale (intensity and duration), and longer term use of P9 or comparison across strains.
- The relatively small study size and short duration of this study, as well as the younger age groups included may be pertinent when considering future research.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Kirsty Baxter

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, with a Master of Science in Nutrition (Advanced Research and Practice) and research project on the nutritional therapy approach to harnessing psychological aspects of obesity weight loss. from London South Bank University. She works collaboratively with a wide range of GPs and doctors, giving presentations to support awareness around the nutritional intervention for metabolic conditions.

DIET FOR IBS SYMPTOMS

PREDICTORS OF SYMPTOM-SPECIFIC TREATMENT RESPONSE TO DIETARY INTERVENTIONS IN IRRITABLE BOWEL SYNDROME.

Colomier, E ; Van Oudenhove, L ; Tack, J ; Böhn, L ; Bennet, S ; Nybacka, S ; Störsrud, S ; Öhman, L ; Törnblom, H ; Simrén, M
Nutrients. 2022;14(2)

INTRODUCTION:

This randomised controlled intervention study of 67 individuals fulfilling the Rome III criteria for IBS drew comparisons between the efficacy of the traditional IBS diet - as directed by the British Dietetic Association and National Institute for Health and Care Excellence (NICE) - and the low fermentable oligo-, di-, monosaccharides, and polyols (FODMAPs) diet on specific IBS-related symptoms (pain, constipation, diarrhoea, and bloating).

METHOD:

A 10-day screening period included faecal sample analysis, 4-day food diary (pre-randomisation and last week of intervention), and daily stool diary (Bristol Stool Form scale). After 10 days, patients compiled several GI and non-GI related questionnaires, inclusive of IBS severity scoring system (IBS-SSS). Patients who scored ≥175 for the IBS-SSS were randomly allocated to follow either a low-FODMAP or traditional IBS diet for a period of 4-weeks. Thorough explanations were provided by trained Dietitians. During intervention, patients compiled symptom questionnaires (Gastrointestinal Symptoms Rating Scale-IBS) on a weekly basis.

RESULTS:

- **Both diets reduced symptoms of pain, diarrhoea and bloating (all p<0.0001), but not constipation (p=0.15).**
- **There was no difference between following the traditional IBS diet and low-FODMAP diet in terms of pain (p=0.80), constipation (p=0.63), diarrhoea (p=0.96) and bloating (p=0.35).**
- **Less severe gut dysbiosis was weakly associated with better dietary response and improvement of constipation (p=0.05).**
- **Higher energy intake at baseline predicted better pain improvement with both dietary types compared to lower energy intake (p=0.03).**
- **More severe psychological distress predicted worse intervention response for bloating (p=0.03).**
- **Higher baseline oligosaccharide intake predicted a worse response to the low FODMAP diet (p=0.01) but not the traditional IBS diet (p=0.16).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Dietary intervention for IBS related symptoms was efficacious for up to 75% of patients in this study.**
- **Recommendation for a traditional IBS dietary intervention should supersede the low-FODMAP diet, with the latter only implemented when symptoms persist.**

CLINICAL PRACTICE APPLICATIONS:

- Even a short 4-week specific dietary intervention (low FODMAP or traditional IBS diet) can result in IBS-related symptomatic improvement for pain, bloating, and diarrhoea, but not constipation.
- The preferred starting point for dietary intervention should be the traditional IBS diet given its relative ease to follow.
- The more restrictive low FODMAP protocol could be considered if symptoms persist.
- More bespoke interventions are required for patients who suffer with severe psychological stress, have tested and found gut dysbiosis, and individuals who already follow a restrictive diet.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies need to include not only larger but more diverse cultural and socio-economic cohorts to ascertain the efficacy of IBS symptom-related dietary interventions.
- Longer periods of intervention are needed to confirm dietary intervention efficacy.

CONCLUSION:

This study demonstrated that based on 4 distinct IBS-related symptomatology, better treatment response to 2 different dietary strategies was noted in patients with less severe clinical characteristics. Higher energy intake at baseline and gut dysbiosis scores that were similar to healthy controls were associated with better improvements following dietary interventions. Thus patients who already follow a calorie restricted diet and who have more significant gut dysbiosis profiles might need more bespoke intervention. Severe psychological distress patients responded worse to both diets.

EXPERT REVIEWER Wilma Kirsten

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Wilma has been in clinical practice since 2005. The topic for her MSc dissertation project was “The impact of Coenzyme Q10 deficiency in late-onset Alzheimer’s disease in patients who use cholesterol lowering medication”. She furthermore obtained two honours science degrees, one in Nutritional Therapy and the other in Molecular Cell Biology and Health Sciences. Wilma specialises in digestive disorders (IBS and IBD), female hormonal well-being (PMS and menopause), and mental health. She has successfully helped hundreds of patients address symptoms of ill health in her clinic. Wilma is the author of the popular science book, “Ideal Plate Composition - Choose Food to Help You Be Your Best Self”.

FODMAP REDUCES IBS SYMPTOMS

LOW FODMAP DIET REDUCES GASTROINTESTINAL SYMPTOMS IN IRRITABLE BOWEL SYNDROME AND CLINICAL RESPONSE COULD BE PREDICTED BY SYMPTOM SEVERITY: A RANDOMIZED CROSSOVER TRIAL.

Algera, JP ; Demir, D ; Törnblom, H ; Nybacka, S ; Simrén, M ; Störsrud, S
Clinical nutrition (Edinburgh, Scotland). 2022;41(12):2792-2800

INTRODUCTION:

The aim of this paper was to investigate the effects of diets with low vs. moderate FODMAP content on gastrointestinal (GI) symptoms and bowel habits, and to identify possible predictors of clinical response to a low FODMAP diet and FODMAP sensitivity in Irritable Bowel Syndrome (IBS).

METHOD:

- This study involved a double-blind, randomised, controlled, crossover trial of 29 participants (18-75 years), mostly female, diagnosed with IBS (Rome IV).
- Primary outcome - assess the effects of a low (4 g/day) vs. moderate (23 g/day) FODMAP diet over a 7-day period.
- Secondary outcomes - assess the effects of low vs. moderate FODMAP diets on i) somatic symptoms, ii) psychological distress, iii) predictors of clinical and IBS-Severity Scoring System (IBS-SSS) sensitivity to FODMAP.
- Breakfast was standardised, with prescribed low FODMAP list deviations recorded.
- GI symptoms and bowel habits were recorded during the 7-day screening period, then participants undertook a Lactulose Nutrient Challenge Test (LNCT). The first 7-day diet started one day after the LNCT.
- A 14-day wash-out period allowed participants to eat and drink as usual, thereafter following the second 7-day diet period as part of the cross over design.

RESULTS:

A low FODMAP intervention (compared to a moderate FODMAP diet); resulted in:

- **Reduced overall IBS rating (10 ± 72 vs. 57 ± 108, P=0.04).**
- **Improved abdominal pain frequency (10 ± 32 vs. 18 ± 29 (P=0.02).**
- **Improved stool consistency (0.2 ± 1.0 vs. 0.6 ± 1.2, P= 0.01) and frequency (0.1 ± 0.7 vs. 0.4 ± 0.7, P= 0.01).**
- **Overall, 34% of participants positively responded to the low FODMAP diet, which could be predicted based on higher baseline IBS-SSS scores (P=0.02).**
- **Participants sensitive to FODMAPs had increased pre- and postprandial ratings of gas, abdominal pain and bloating and higher exhaled methane concentrations compared to non-sensitive participants to FODMAPs.**
- **Authors highlighted a non-significant association between FODMAP sensitivity and GI symptoms during the LNCT, with higher visceral hypersensitivity (45 ± 20, P=0.73) after ingestion of poorly absorbed and fermentable carbohydrates, with no independent predictors identified.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- A low (4 g/day) FODMAP diet could provide clinical benefits in the context of an acute strategy for IBS clients with frequent loose stools (IBS-Diarrhoea and/or IBS-Mixed) compared to those with hard and less frequent stools (IBS-Constipation) to improve the severity of GI symptoms, including lower abdominal pain intensity and frequency, bowel habits, daily life interference, and psychological distress.

CLINICAL PRACTICE APPLICATIONS:

- While this was a short term study, a low FODMAP diet reduced GI symptoms and affected bowel habits (more firm and less frequent stools) in IBS, compared with a diet containing moderate amounts of FODMAPs.
- Knowing the above, an assessment of overall IBS severity and predominant bowel habits before the intervention may be helpful for clinicians working with younger females in their IBS management before considering a trial period with the low FODMAP diet as a treatment option.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future trials could target a larger sample size with a more representative population, as well as assessing low FODMAP interventions over longer timeframes.
- Additionally, the assessment of biological measures such as microbiota diversity and stability, as well as metabolites (such as short chain fatty acids) could be important to understand mechanistic attributes of low FODMAP diets in IBS.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Kirsty Baxter

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, with a Master of Science in Nutrition (Advanced Research and Practice) and research project on the nutritional therapy approach to harnessing psychological aspects of obesity weight loss. from London South Bank University. She works collaboratively with a wide range of GPs and doctors, giving presentations to support awareness around the nutritional intervention for metabolic conditions.

LACTOBACILLUS FOR IBS

EFFICACY OF A SYNBIOTIC CONTAINING LACTOBACILLUS PARACASEI DKGF1 AND OPUNTIA HUMIFUSA IN ELDERLY PATIENTS WITH IRRITABLE BOWEL SYNDROME: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

Oh, JH ; Jang, YS ; Kang, D ; Kim, HS ; Kim, EJ ; Park, SY ; Kim, CH ; Min, YW ; Chang, DK
Gut and liver. 2023;17(1):100-107

INTRODUCTION:

This study involved a randomized, double-blind, placebo-controlled trial to investigate the impact of a synbiotic combination, comprising of L. paracasei DKGF1 and prebiotics extracted from Optuntia humifusa, on Irritable Bowel Syndrome (IBS) in elderly patients.

METHOD:

- Sixty-seven IBS patients (mean age: 64 years) were randomly assigned to either a synbiotic group (n=33) or a placebo group (n=34) for a 4-week intervention. The synbiotic group received a daily sachet containing one billion colony-forming units of L. paracasei DKGF1, 0.2g of O. humifusa extract and 1.59 grams of maltodextrin, while the placebo group received an identical sachet containing only maltodextrin.

During the study period:

- Participants recorded the degree of symptom improvement using a Subject Global Assessment (SGA) scale.
- IBS symptoms, abdominal pain, gas, bloating, and psychological well-being were recorded using a VAS scale.
- Stool form and consistency were assessed using a Bristol Stool Chart (BSC).

RESULTS:

The primary findings from the study were as follows:

- **There was significant improvement in IBS symptoms as measured by the SGA score, in the synbiotic group versus the placebo group (+50.5% vs +23.5%, p=0.017). The synbiotic group consistently demonstrated improved response rates.**

The secondary findings were as follows:

- **Participants also reported an improvement in psychological well-being in the synbiotic group (from 1.3 to 1.0) compared to the placebo group (from 3.0 to 2.0) (p=0.003).**
- **Responders reported a significant improvement in stool form and consistency in the synbiotic group (+85.7%) compared to the placebo group (+22.2%) (p=0.04).**
- **Among the patients with IBS constipation, patients in the synbiotic group reported a positive response compared to the placebo group (0% and +100%, p=0.029).**
- **. However, there was no significant improvement among the patients with IBS diarrhoea in the synbiotic group compared to the placebo group (+33.3% and +66.6%,, p=0.52).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- The management of IBS in elderly people is more complicated than in younger populations.
- Synbiotic formulations containing both probiotics and prebiotics have reported gastrointestinal health benefits.
- This randomized controlled trial indicated that the synbiotic containing L. paracasei DKGF1 and Optuntia humifusa extracts might be effective and safe for treating IBS symptoms in elderly patients.

CLINICAL PRACTICE APPLICATIONS:

- The human microbiota undergoes changes in diversity and variation with age, emphasising the importance of understanding age-specific interventions.
- Managing IBS in the elderly is challenging, and synbiotics, containing both probiotics and prebiotics, have reported gastrointestinal health benefits.
- Most clinical trials have excluded elderly patients, and there has been uncertainty about whether synbiotic use is safe for the elderly.
- This study focused exclusively on elderly patients with IBS, indicating the potential safety and effective use of a synbiotic containing L. paracasei DKGF1 and Optuntia humifusa in improving IBS symptoms.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Only elderly patients were included in this study, therefore further investigation is needed to explore the effects of synbiotics on participants of different age groups.
- Microbial analysis was not done in this study. It would be useful to include this in future research to gain more insight into the microbiome's diversity in elderly patients with IBS.
- The study did not quantify food intake or variety which might have impacted the results, therefore future research needs to consider the impact diet has on the microbiome and IBS.
- Since patient reports are subjective, future research should consider involving researchers during patient-reported assessments to enhance the accuracy and reliability of the data.

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University. She completed her Master's degree in Holistic Health and Nutritional Education at Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

DIETARY THERAPIES IN IBS

EFFICACY AND ACCEPTABILITY OF DIETARY THERAPIES IN NON-CONSTIPATED IRRITABLE BOWEL SYNDROME: A RANDOMIZED TRIAL OF TRADITIONAL DIETARY ADVICE, THE LOW FODMAP DIET, AND THE GLUTEN-FREE DIET.

Rej, A ; Sanders, DS ; Shaw, CC ; Buckle, R ; Trott, N ; Agrawal, A ; Aziz, I
Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2022;20(12):2876-2887.e15

INTRODUCTION:

The aim of this study was to compare the effectiveness and patient acceptability of traditional dietary advice (TDA) vs a low FODMAP diet (LFD) vs a gluten-free diet (GFD, cross-contamination allowed) in patients with non-constipation irritable bowel syndrome (IBS). TDA definition: healthy, sensible eating pattern, including regular meals, not eating too little/too much, adequate hydration, and reducing the intake of: alcohol/caffeine/fizzydrinks/fatty/spicy/ processed foods; fresh fruit (maximum of 3 per day); fibre/gas-producing foods and perceived food intolerances.

METHOD:

This was a randomised dietary trial over 4 weeks. Dietary advice was provided by a specialist dietitian in a session lasting 45-60 minutes. 99 patients completed the study (33 in each group). Stool analysis was performed in “around half“ (study authors terminology) of participants due to disruption of trial caused by COVID-19.

RESULTS:

- **Primary endpoint (reduction of 50+ points on IBS symptom severity score) was met by 42% of patients on the TDA, 55% on LFD and 58% on GFD. The differences between groups were not statistically significant, p=0.43.**
- **Patients on the LFD had greater improvements in mood compared to the other diets under examination, reaching statistical significance (p=0.03) for Hospital Anxiety and Depression scale and (p<0.01) for dysphoria score on IBS-QOL scale.**
- **Patients on TDA found their diet cheaper (p<0.01), less time consuming to shop (p<0.01) and easier to follow when eating out with family and friends (p=0.03), whilst TDA and GFD were considered easier to incorporate into daily diet than LFD (p=0.02).**
- **No significant differences were found between groups in changes to macro- and micronutrient composition, except a trend to lower fibre intake with LFD (p=0.06).**
- **There was a significant reduction in intake of FODMAPs in all groups, with greatest reduction in LFD (27.7 to 7.6 g/day, p<0.01), followed by TDA (24.9 to 15.2 g/day, p<0.01) and GFD (27.4 to 22.4 g/day, p=0.03). Differences between groups were statistically significant (p<0.01).**
- **No differences were noted in change to the dysbiosis index between groups.**
- **Neither clinical characteristics nor dysbiosis index predicted response to any of the diets.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- TDA, LFD and GFD can all lead to significant improvements in non-constipation IBS with no statistically significant difference in effectiveness between the diets.
- Most patients find a TDA easier and cheaper to implement than a LFD or GFD.
- TDA is therefore recommended as a first line approach in non-constipation IBS.

CLINICAL PRACTICE APPLICATIONS:

- When working with clients with non-constipation IBS, a TDA approach may be favoured over LFD and GFD as a first line intervention if the patient has not already tried a TDA diet.
- Patient preferences, budget, time and living situation should be taken into account when deciding on best dietary advice for IBS.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- As all 3 approaches led to reduction in FODMAPs, trials comparing different levels of FODMAP exclusion could lead to valuable information, as a strict FODMAP exclusion, which is commonly recommended in IBS, is difficult and may not be necessary.
- Studies of longer duration would be valuable to confirm that benefits observed with the 3 approaches are not short-term only.
- Comparing individual approaches to appropriate control group would ensure that improvements are not due to a placebo effect.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Karin Elgar

Following the completion of a PhD in Physiology and a career in the pharmaceutical industry, Karin graduated as a nutritional therapist from the Institute of Optimum Nutrition in 2004. She has since been practicing in the Greater Manchester area, specialising in women's health and autoimmunity. Karin has written a number of literature reviews and carried out a variety of research and editing projects. She has also delivered CPD seminars and webinars on various topics.

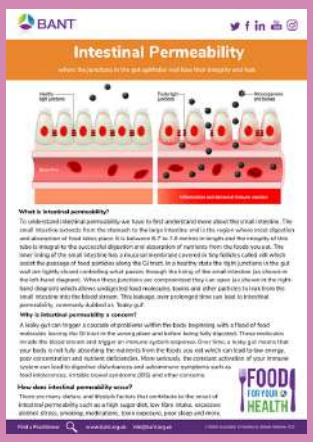
GUT HEALTH & IBS RESOURCES

DEDICATED GUT HEALTH & IBS RESOURCES

BANT has developed a dedicated range of Gut Health resources to support practitioners to help educate on common symptoms, gastrointestinal processes, and dietary and lifestyle approaches. These are suitable to share with clients in clinical consultations and group programmes.

CLIENT-FRIENDLY GUIDES:

Providing practitioners with gut health resources to support their clinical recommendations.



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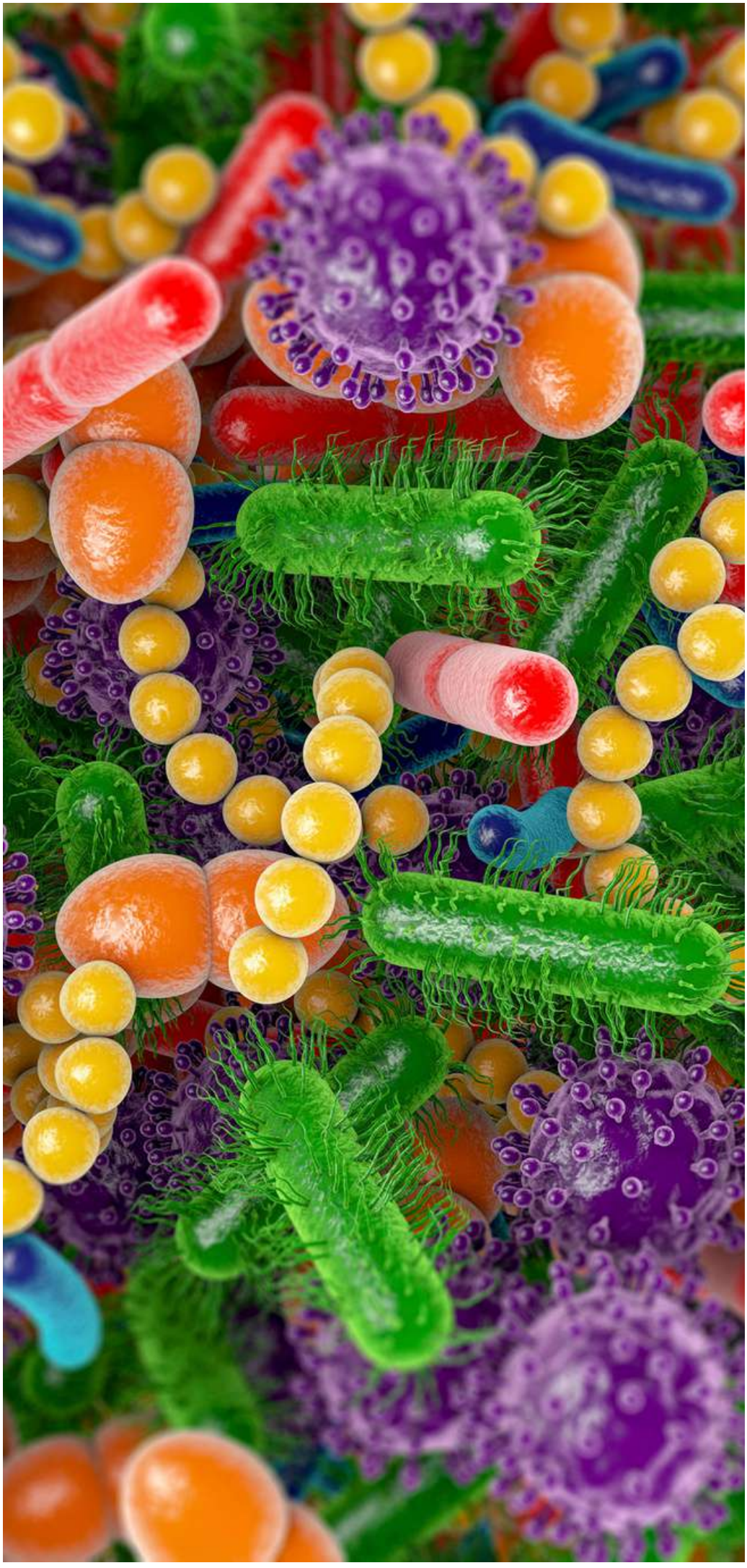
IBD & THE MICROBIOME

6 REVIEWS



ANIMAL PROTEIN SOURCES AND IBD

THE ASSOCIATION BETWEEN TOTAL PROTEIN, ANIMAL PROTEIN, AND ANIMAL PROTEIN SOURCES WITH RISK OF INFLAMMATORY BOWEL DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT STUDIES.

Talebi, S ; Zeraattalab-Motlagh, S ; Rahimlou, M ; Naeini, F ; Ranjbar, M ; Talebi, A ; Mohammadi, H
Advances in nutrition (Bethesda, Md.). 2023;14(4):752-761

INTRODUCTION:

The authors conducted a dose-dependent meta-analysis of prospective cohort studies which examined the relation between total protein, animal protein, and animal protein sources with inflammatory bowel disease (IBD) in adults because the prevalence and incidence of IBD have exceeded globally.

METHOD:

Cochrane methodology was undertaken for the systematic review. Data from 11 prospective cohort studies with 8067 cases and 4,302,554 participants was extracted by 2 independent investigators. Evaluation of the quality and possible biases of included studies was performed. Risk ratios (RR) with 95% confidence intervals were chosen as the effect estimate. Various subgroup analyses were undertaken as well as metaregression analyses.

RESULTS:

- **Seven cohort studies (7232 cases, 1,097,040 participants) were included in the analysis of dairy intake. Higher intakes of dairy was associated with a lower risk of IBD (RR: 0.81; 95% CI: 0.72, 0.90; n = 7).**
- **Consumption of protein from dairy products was found to be protective against IBD risk (RR = 0.77; 95% CI: 0.68, 0.88).**
- **Three prospective cohort studies with 1214 cases of IBD among a total of 535,738 subjects were included in the total meat analyses. Higher dietary total meat intake was not associated with the risk of IBD (RR: 1.24; 95% CI: 0.90, 1.70; n = 4).**
- **A positive linear association was found between total meat intake and risk of IBD. 100 g/d increment in dietary total meat consumption was associated with a 38% greater risk of IBD (RR: 1.38, 95% CI: 1.13, 1.68).**
- **Three prospective cohorts, among 492,497 participants and 4025 cases were included in the egg analysis. No association was found between egg consumption and IBD risk (RR: 0.92; 95% CI: 0.81, 1.04; n = 4).**

CONCLUSION:

The findings indicated no notable correlation between the intake of the majority of dietary protein sources and the incidence of IBD. IBD risk only escalated with higher total meat consumption, while the intake of protein from dairy products emerged as a protective factor against the risk of IBD.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **According to the researchers, the effect of the high consumption of meat in increasing the risk of IBD is not related to the type of protein contained in it but could be due to cooking meat at high temperatures.**
- **Other studies have reported that the consumption of animal proteins, especially processed and red meat, increases the risk of IBD.**
- **Other studies related to dairy intake have been contradictory. There is also evidence reported of a positive effect from dairy exclusion in IBD patients.**
- **Further research is required to corroborate the findings of this systematic review.**

CLINICAL PRACTICE APPLICATIONS:

- Dairy product consumption may be protective against IBD. However the studies included with statistically significant results did not control for alcohol intake and other confounding factors. The type of dairy product consumed, as well as a personalised approach, should be considered.
- This study did not find any association between red or processed meat consumption and risk of IBD. However the subgroup analysis did find a significant association between red meat intake and IBD risk. This difference in results may be caused by differences in cooking methods, genetic factors, amount of meat consumption, confounding factors, and other environmental factors.
- Total meat intake, as well as type of meat intake, and how meat is cooked, should be reviewed in clients with IBD, Crohn's Disease and Ulcerative Colitis.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Intervention studies would need to be conducted to corroborate the findings of this systematic review.
- Future research should fully consider cofounding factors, such as alcohol intake and body mass index (BMI).
- Future studies should further consider types of protein as well as dose and cooking implications.

EXPERT REVIEWER Dr. Michelle Barrow

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Dr Michelle Barrow is the Academic Team Director and Clinical Director at CNELM. Michelle completed a Doctorate in Professional Studies (DProf) in 2019, titled "Leading transformation in Personalised Nutrition Practice". Her doctoral research included the construction of clinical tools to enable the development of a new evidence base for personalised nutrition practice in obesity management. She strives to develop the evidence base to support personalised nutrition practice through her academic work, research supervision, post-doctoral research, and publication.

VITAMIN D & IBD IN CHILDREN

THE ASSOCIATION BETWEEN VITAMIN D STATUS AND INFLAMMATORY BOWEL DISEASE AMONG CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Fatahi, S ; Alyahyawi, N ; Albadawi, N ; Mardali, F ; Dara, N ; Sohouli, MH ; Prabahar, K ; Rohani, P ; Koushki, N ; Sayyari, A ; Hosseini, AH ; Abu-Zaid, A
Frontiers in nutrition. 2022;9:1007725

INTRODUCTION:

The aim of the study was to determine the relationship between serum vitamin D levels and paediatric inflammatory bowel disease (IBD).

METHOD:

- This systematic review and meta-analysis of 35 case-control, cross-sectional or cohort studies followed PRISMA and MOOSE guidelines.
- Five different libraries were searched.
- 4803 children were included with the majority from the United States, and the remainder from Australia, Finland, Denmark, Italy, South Korea, and Israel.

RESULTS:

- **16 studies were appropriate for meta-analysis and showed a trend of lower vitamin D levels in children with IBD compared to healthy controls, but this was not statistically significant (-1.159 ng/ml; 95% CI: -2.783, 0.464).**
- **18 studies with 2602 children showed that the prevalence of vitamin D deficiency or insufficiency was 44% (95% CI: -0.34- 0.54).**
- **There was significant heterogeneity between the prevalence studies (P=<0.001; I2=97.31%) as they included children with different classifications of IBD such as ulcerative colitis and Crohn's Disease and used different assessments of serum vitamin D levels.**
- **A strength was that most studies included in the systematic review and meta-analysis were of high quality.**

CONCLUSION:

There is a non-significant trend towards lower serum vitamin D levels in children with IBD.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Without further research, justification to measure vitamin D levels in children with IBD would require other clinical signs of deficiency.

CLINICAL PRACTICE APPLICATIONS:

- Practitioners could consider measuring serum vitamin D levels in children with IBD.
- However, as vitamin D levels were not lower in children with IBD in the present paper, practitioners should be aware that lower vitamin D concentrations may be due to other factors.
- Furthermore, heterogeneity in the study means that it is unclear as to how different forms of the disease may affect levels.
- Vitamin D regulates the immune response and as this is an immune disease, a better understanding of levels may be beneficial.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research could consider the effect of supplementary vitamin D intakes on IBD symptoms.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Chloe Steele

Chloe has an MSc in Personalised Nutrition from the University of Middlesex, and specialises in cardiovascular disease, type 2 diabetes, and anxiety. Chloe started her career at BANT as a member of the Nutrition Evidence Database research team and now has over 5 years experience of research and writing. She has worked in several countries, and is currently in Australia, where she worked for Nutrition Australia and is currently the principal nutritionist for Heart Research Australia. She has published two papers in the Nutrition Medicine Journal, on gut microbiota and collagen. Chloe is a member of BANT and the Nutrition Society of Australia and sits on the editorial board for the Nutrition Medicine Institute in the UK.

BENEFITS OF FODMAP IN IBD

A LOW-FODMAP DIET PROVIDES BENEFITS FOR FUNCTIONAL GASTROINTESTINAL SYMPTOMS BUT NOT FOR IMPROVING STOOL CONSISTENCY AND MUCOSAL INFLAMMATION IN IBD: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Peng, Z ; Yi, J ; Liu, X
Nutrients. 2022;14(10)

INTRODUCTION:

This meta-analysis assesses the efficacy of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet (LFD) in inflammatory bowel disease [IBD: ulcerative colitis (UC) and Crohn's disease (UC)] participants with functional gastrointestinal symptoms (FGSs).

METHOD:

- A search was performed on PubMed, Web of Science, EMBASE, Cochrane Central Register of Controlled Trials, Chinese National Knowledge Infrastructure (CNKI), WanFang (Chinese) Database up to March 2022. Quality assessment of all included studies was performed.

RESULTS:

9 studies (4 randomised controlled trials, 5 non-randomised studies) with a total of 351 participants diagnosed with IBD were included, and compared LFD with a placebo diet or normal diet (ND).

LFD effects of FGS:

- Overall 9 studies: an improvement (0.47, 0.33–0.66, p = 0.0000).
- No difference in the subgroup classified by disease type.
- CD and UC: no improvement.

Individual improvement:

- Bloating (0.37, 0,24-0,57, p=0.0000); wind or flatulence (0.38, 0,28-0,51, p=0.0000); borborygmi (0.48, 0,26-0,89, p=0.0000), abdominal pain (0.5, 0,37-0,68, p=0.0000), fatigue/lethargy (0.71, 0,61-0,82, p=0.0000).
- No difference in nausea and vomiting (0.54, 0,22-1,32, p=018).

Faecal calprotectin:

- 2 studies: no change (-16.03, -36,78-4.73, p=0.13).

IBS Quality of Life Score:

- 2 studies: reduced Short IBD Questionnaire (SIBDQ) score (11.24, 6.61-15.87, p=0.0000).

Bristol Stool Form Chart:

- 2 studies: normal stool consistency (type 3-4); no difference (5.99, 0.17-216.51, p=0.33).
- 2 other studies: no difference (-0.17, 0.48 - 0.15, p=0.30).

Diseases activity (Harvey-Bradshaw index):

- 2 studies using the Mayo score: no difference (-32, -1,09-0.45, p=0.41).
- 3 studies using BHi score: reduction (-1.09, -1,77-0.42, p=0.002).

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- LFD use in IBD improved symptoms of bloating, wind or flatulence, borborygmi, abdominal pain, and fatigue or lethargy, but not nausea and vomiting.

CLINICAL PRACTICE APPLICATIONS:

- This study suggests that IBD patients with FGSs may benefit from LFD treatment with the assistance of a healthcare professional.

CONSIDERATIONS FOR FUTURE RESEARCH:

- This study has shown that LFD can improve FGSs in IBD, but further research with a larger sample size and more comprehensive analysis is warranted to replicate the results.
- The description of the findings and Quality of Life data are a little unclear. The impact on Quality of Life warrants further investigation, as clinicians need to consider the impact of following a restrictive diet on Quality of Life.

CONCLUSION:

While the study found inconsistent definition standards for FGS, all the nine studies showed that LFD was associated with an improvement in some symptoms.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Kirsty Baxter

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, with a Master of Science in Nutrition (Advanced Research and Practice) and research project on the nutritional therapy approach to harnessing psychological aspects of obesity weight loss. from London South Bank University. She works collaboratively with a wide range of GPs and doctors, giving presentations to support awareness around the nutritional intervention for metabolic conditions.

DIET AS OPTIONAL TREATMENT IN IBD

DIET AS AN OPTIONAL TREATMENT IN ADULTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW OF THE LITERATURE.

Jaramillo, AP ; Abaza, A ; Sid Idris, F ; Anis, H ; Vahora, I ; Moparthi, KP ; Al Rushaidi, MT ; Muddam, M ; Obajeun, OA
Cureus. 2023;15(7):e42057

INTRODUCTION:

This systematic review evaluated the efficacy of diet as a preventative therapeutic treatment for Inflammatory Bowel Disease (IBD).

METHOD:

A total of 9 studies (published in the last 5 years) were chosen. The articles included 6 randomised controlled trials (RCT), one systematic literature review (SLR) and two SLR and meta-analysis. The authors used the Assessment Systematic Reviews (AMSTAR) approach and an unspecified Cochrane Risk of Bias assessment tool.

RESULTS:

The following refers to the original RCT articles as the review article data was sparse.

- **A 6-month, open-label, randomised, placebo-controlled trial of 53 adult Ulcerative Colitis (UC) patients compared response to an Anti-inflammatory Diet (AID) with Canada's Food Guide (CFG). The outcome showed that the faecal calprotectin value (<150 µg/g at the endpoint) was significantly higher in the AID group (69.2 vs. 37.0%, p = 0.02) (Keshteli et al., 2022).**
- **The Specific Carbohydrate Diet (SCD) was not superior to the Mediterranean Diet (MD) in terms of achieved symptomatic remission at 6 weeks (SCD 46.5%, MD 43.5%; p = .77) (Lewis et al., 2022).**
- **A single-blind, 4-week trial concluded significant relief from gut symptoms was achieved when comparing a low FODMAP diet (14/27, 52% of positive patient feedback) to a control diet (4/25, 16%, p=.007) (Cox et al., 2020).**
- **A 7-day trial of 28 volunteers compared individualised food-based diet (CD-TREAT), with similar composition to Exclusive Enteral Nutrition (EEN) and found a change in relative abundance in faecal microbiome genera of 58 (49.3%) and 38 (32.3%) following both feeding practices respectively (Svolos et al., 2019).**
- **Substantial reduction in red and processed meat was not significant in reducing time to symptomatic relapse in Crohn's Disease (CD) patients when comparing 115 high red meat consumers with 87 low red meat CD patients (p = 0.61 any relapse and p = 0.50 for moderate to severe relapse) (Aldenberg et al., 2019).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Whilst concise, this limited review highlights the current lack of evidence supporting stand alone dietary strategies in preventing relapse for IBD patients. At the very least an anti-inflammatory diet should ideally be implemented alongside specific medical care and counselling to minimise risk of disease relapses.

CLINICAL PRACTICE APPLICATIONS:

- In order to delay relapse in IBD it is imperative that foods that support anti-inflammatory mechanisms are incorporated and maintained.
- Whilst limited, the papers reviewed highlight potential for an initial low FODMAP diet followed by a longer term MD or SCD combined with constant monitoring.
- From one study, red meat consumption did not appear to exacerbate symptoms.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies need to include larger cohorts to ascertain the efficacy of dietary interventions as a stand alone treatment option for IBD.
- Longer periods of intervention are needed to confirm dietary intervention efficacy and safety in this population.

CONCLUSION:

An anti-inflammatory diet may prolong clinical remission for UC patients. CD patients, with mild to severe symptoms, may tolerate both the MD and SCD equally well. The authors advise a low FODMAP diet for a 4-week period combined with professional counselling and regular follow-up sessions to delay flare-up episodes. However the findings were based on a very limited number of scientific material that requires extensive further assessment prior to deriving any firm conclusions.

EXPERT REVIEWER Wilma Kirsten

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Wilma has been in clinical practice since 2005. The topic for her MSc dissertation project was “The impact of Coenzyme Q10 deficiency in late-onset Alzheimer’s disease in patients who use cholesterol lowering medication”. She furthermore obtained two honours science degrees, one in Nutritional Therapy and the other in Molecular Cell Biology and Health Sciences. Wilma specialises in digestive disorders (IBS and IBD), female hormonal well-being (PMS and menopause), and mental health. She has successfully helped hundreds of patients address symptoms of ill health in her clinic. Wilma is the author of the popular science book, “Ideal Plate Composition - Choose Food to Help You Be Your Best Self”.

GENETICALLY ENGINEERED PROBIOTICS IN IBD

THE ROLE OF GENETICALLY ENGINEERED PROBIOTICS FOR TREATMENT OF INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW.

Zhang, T ; Zhang, J ; Duan, L
Nutrients. 2023;15(7)

INTRODUCTION:

This paper summarises the efficacy of specific genetically modified (GM) probiotic formulations for Inflammatory Bowel Disease (IBD) when compared to wild type probiotics. The aim was to ascertain what specific effects and mechanisms such probiotics have on IBD symptomatology.

METHOD:

- A total of 46 published articles were included; 45 mouse experimental models (induced acute or chronic colitis) (n=15-130) and 1 human IBD population clinical trial (n=10).
- The effect of GM probiotics were compared to placebo and wild-type probiotics in trials including preclinical studies, randomised controlled trials and cohort studies.
- Animals received probiotics via gastric gavage (105 - 4 x 1012 CFU) for 3-6 weeks.
- The human placebo-uncontrolled trial lasted 7 days and patients received 10 GM capsules of L.lactis (1 x 1010 CFU) twice daily.

RESULTS:

- **GM probiotics that secrete immunoregulatory cytokines such as IL-10 appear to reduce intestinal damage.**
- **The human trial using GM L.lactis resulted in 5 patients who went into complete clinical remission (CDAI, <150) with 3 patients exhibiting a clinical response (decrease in CDAI, >70). with only minor adverse events (flatulence).**
- **However, human cytokines that promote intestinal barrier function and epithelial restitution were not enhanced with oral administration of probiotics.**
- **Two studies concluded that GM L.lactis and S.boulardii, that secrete atrial natriuretic peptide, might be the most effective options in supporting colitis.**
- **GM L.casei resulted in faster recovery from weight loss in acute colitis models.**
- **Superoxide dismutase (SOD) producing GM L.fermentum increased SOD activity by almost eightfold compared to the wild type.**
- **GM Lact. fermentum furthermore showed a higher survival rate and lower disease activity index (P <0·05) in colitis models.**
- **GM L.lactis improved gut microbial composition and GM S.cerevisiae improved microbial diversity whilst reducing the Firmicutes to Bacteroides ratio.**
- **GM E.coli significantly reduced weight loss, colon shortening plus lower disease activity and histological changes (P < 0.05).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Conclusions of this review were largely based on mouse models and although treatment using probiotics is generally considered safe in humans, with only minor side-effects (flatulence), practitioners need to be aware that in an IBD population the use of GM formulations might not be completely without risk.

CLINICAL PRACTICE APPLICATIONS:

- Probiotics species used in the trials included S.thermophilus, E.coli, L.lactis, B.ovatus, S.boulardii, L.fermentum, B.longhum, L.casei, L.plantarum, and S.cerevisiae. Wild-types of some of these are already available to use in clinical practice.
- Note that oral administration in the human trial showed no significant health outcome, therefore efficacy and safety need to be ascertained on an individual patient level.
- Colonisation of beneficial bacteria in the gut of IBD patients might be difficult and any form of supplementation therefore needs to be closely monitored.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- More evidence is needed to demonstrate that GM probiotic formulations result in significantly improved outcomes when compared to wild-types.
- Future randomised placebo-controlled trials need to include larger cohorts to determine supplement efficacy.
- Longer periods of intervention are needed to confirm efficacy, safety, and tolerance for both Crohn's Disease and Colitis.
- Optimal GM probiotic formulation, doses, and means of application need to be identified.

CONCLUSION:

Despite the heterogeneity of the trials, GM probiotics appear to play a notable part in ameliorating IBD symptomatology and disease severity when compared to wild-type probiotics. Human efficacy and potential adverse effects require more in-depth trials to ascertain safety and optimal dosages.

EXPERT REVIEWER Wilma Kirsten

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Wilma has been in clinical practice since 2005. The topic for her MSc dissertation project was "The impact of Coenzyme Q10 deficiency in late-onset Alzheimer's disease in patients who use cholesterol lowering medication". She furthermore obtained two honours science degrees, one in Nutritional Therapy and the other in Molecular Cell Biology and Health Sciences. Wilma specialises in digestive disorders (IBS and IBD), female hormonal well-being (PMS and menopause), and mental health. She has successfully helped hundreds of patients address symptoms of ill health in her clinic. Wilma is the author of the popular science book, "Ideal Plate Composition - Choose Food to Help You Be Your Best Self".

TRAINING DIET & FATIGUE IN IBD

PHYSICAL TRAINING AND HEALTHY DIET IMPROVED BOWEL SYMPTOMS, QUALITY OF LIFE, AND FATIGUE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE.

Scheffers, LE ; Vos, IK ; Utens, EMWJ ; Dieleman, GC ; Walet, S ; Escher, JC ; van den Berg, LEM
Journal of pediatric gastroenterology and nutrition. 2023;77(2):214-221

INTRODUCTION:

A randomised semi-crossover controlled trial was conducted to investigate the impact of a 12-week lifestyle program (3 physical training sessions per week plus personalised healthy dietary advice) in children with Inflammatory Bowel Disease (IBD).

METHOD:

- Sixteen children with a median age of 15 [IQR: 12–16]) that were diagnosed with IBD (CD, UC, or IBD-unclassified) were randomized to group A (start exercise) or group B (start control period). Group A started the intervention immediately after the first assessment and did not have a control period. Group B started after a control period (this was planned to last for 6 weeks but due to the COVID-19 lockdown extended to 6 months).
- The lifestyle intervention lasted 12 weeks and consisted of 3 physiotherapist-supervised training sessions per week, lasting 60 minutes each. In addition, all participants received a recommended caloric intake per day based on measured rest energy expenditure and a brochure regarding healthy diet in children.
- Endpoints were physical fitness (maximal and submaximal exercise capacity, strength, and core stability), patient-reported outcomes (quality of life, fatigue, and fears for exercise), clinical disease activity (faecal calprotectin and disease activity scores), and nutritional status (energy balance and body composition).
- A total of 15 out of 16 participants (93%) completed the program, one patient dropped out after one training session due to motivational problems.

RESULTS:

- **While medical treatment remained unchanged, Paediatric Crohn's Disease Activity Index decreased versus the control period (15 [3–25] vs 2.5 [0–5], P = 0.012).**
- **The number of patients in clinical remission increased from 5 to 12 (P < 0.001), compared to the control period.**
- **Quality of life (IMPACT-III) improved on 4 out of 6 domains and the total score (+13 points) versus the control period including a large improvement in bowel-related symptoms, P= 0.029).**
- **Fecal calprotectin decreased, but not compared to the control period, mainly due to relatively large intra-patient fluctuations (400 µg/g [57.1–1662.7] vs 128 µg/g [23.8–642.3], P = 0.016).**
- **Parents reported an improvement in the quality of life versus the control period on the child health questionnaire and total fatigue score (PedsQoL • Multidimensional Fatigue Scale) (+14 points, P = 0.048).**
- **Walking distance improved after the 12-week program, compared to the control period (P = 0.001).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **IBD is a chronic inflammatory disease of the gastrointestinal tract, characterised by periods of abdominal pain, severe diarrhoea, and fatigue.**
- **This clinical trial suggests that a 12-week program of physical training plus personalised healthy dietary advice may improve physical fitness, quality of life, and fatigue in children with IBD.**

CLINICAL PRACTICE APPLICATIONS:

- The mechanism behind the anti-inflammatory effects of exercise has not been clarified.
- Multiple theories have been suggested in previously published studies such as a reduced release of adipokines due to less visceral fat, increased secretion of anti-inflammatory cytokines such as interleukin (IL)-6, and reduced transient stool time.
- This clinical trial demonstrated that a 12-week program of physical training sessions plus personalised healthy dietary advice resulted in improved physical fitness, quality of life, and parent-reported fatigue.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- A sample size calculation was not provided in the study report and it is therefore assumed that the sample size of 16 children in this trial was too small to draw a definite conclusion. A larger study over a longer period is therefore needed across diverse age and ethnic population groups to draw better conclusions.
- This study did not measure mucosal inflammation before and after the intervention due to the invasive nature of the procedure. It would however be useful that future research investigate this to gain more insight into the effect of lifestyle interventions on IBD.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

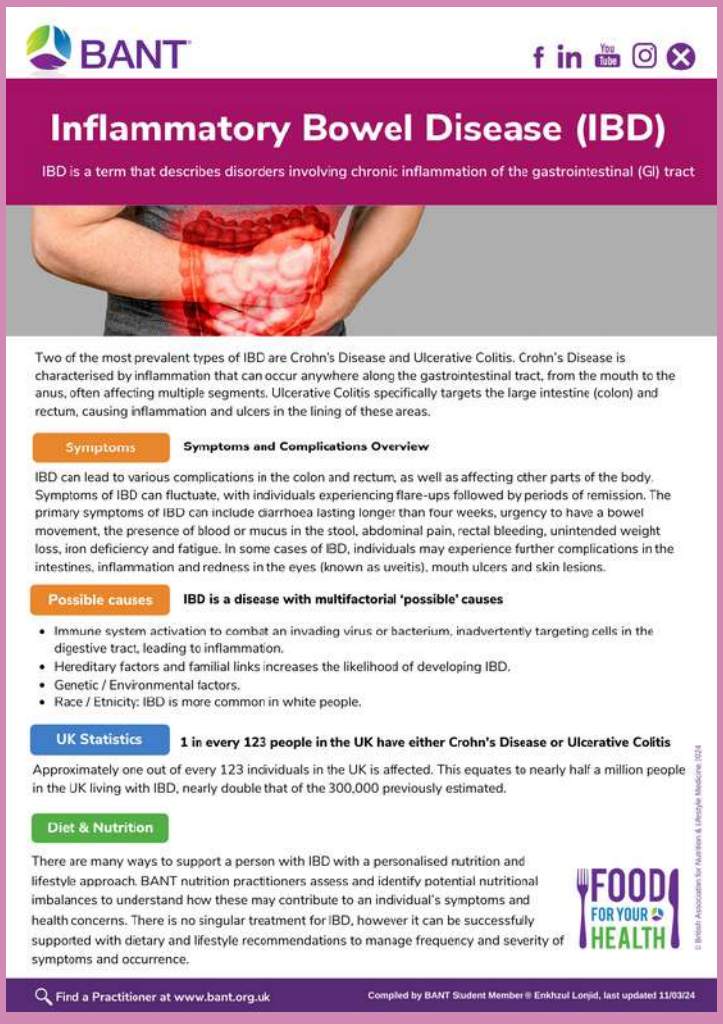
EXPERT REVIEWER Ana-Paula Agrela

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University. She completed her Master's degree in Holistic Health and Nutritional Education at Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

GUT HEALTH & IBD RESOURCES

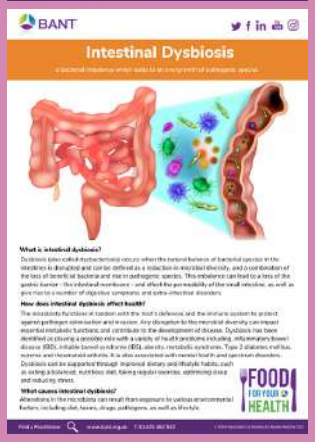
DEDICATED GUT HEALTH & IBD RESOURCES

BANT has developed a dedicated range of Gut Health resources to support practitioners to help educate on common symptoms, gastrointestinal processes, and dietary and lifestyle approaches. These are suitable to share with clients in clinical consultations and group programmes.



CLIENT-FRIENDLY GUIDES:

Translating the science into clinical take-aways to facilitate client's understanding of gut health.



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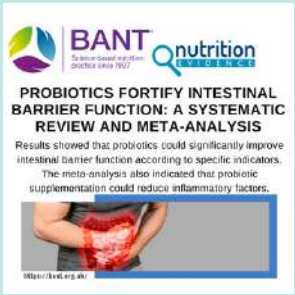
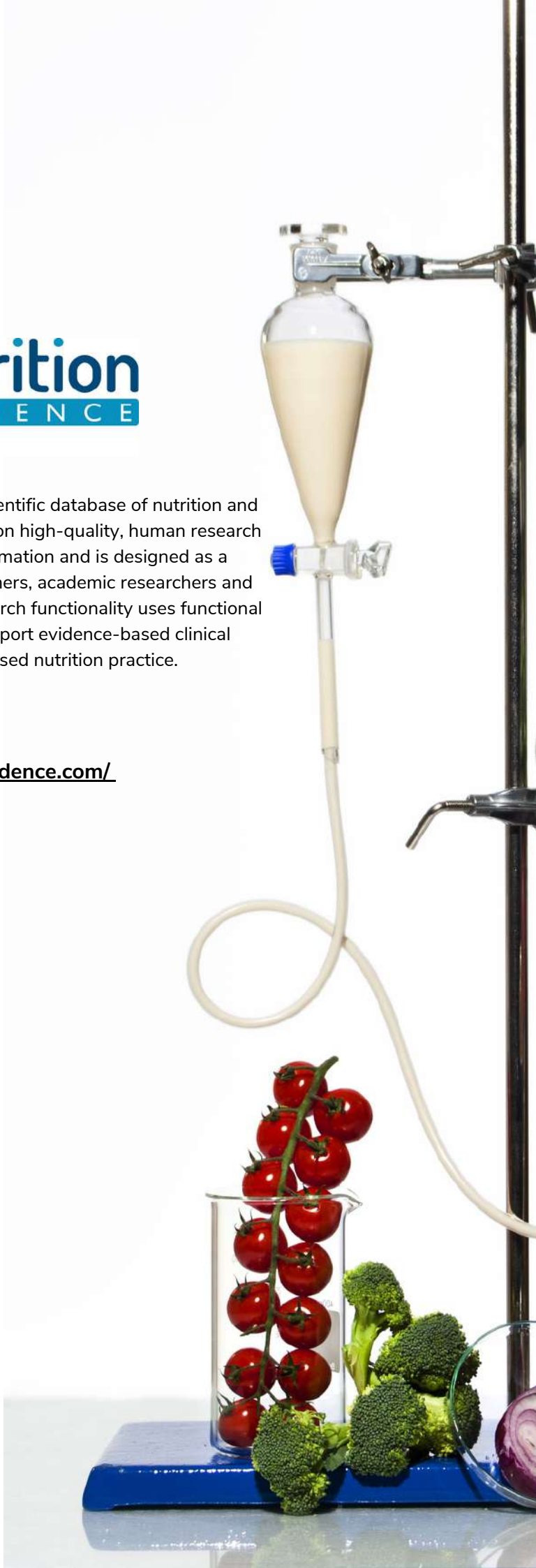


BANT on Social Media

BANT is committed to promoting the nutritional therapy profession across all channels so if you're not yet following us on social media, please come and join the conversation. The more you engage, like, comment, and share our BANT content, news and resources, the more we can grow our nutritional credibility and drive awareness of our profession.

Nutrition Evidence is the UK's first scientific database of nutrition and lifestyle medicine research. It focuses on high-quality, human research and other science-supported information and is designed as a comprehensive platform for practitioners, academic researchers and students. The powerful, yet simple search functionality uses functional and lifestyle medicine filters to support evidence-based clinical decision making in personalised nutrition practice.

www.nutrition-evidence.com/



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Science-based nutrition practice since 1997