Microbiome, diet, and cardiometabolic health

Supplementary Text as supplied by author

Systematic Search of Interventions targeting Cardiometabolic Diseases/Disorders

Systematic PubMed Search

We have aimed to systematically cover the evidence for dietary interventions on cardiometabolic outcomes by targeting the gut microbiome. To do so we have carried out a systematic search on PubMed using the search terms "probiotics" OR "prebiotics" OR "synbiotics" OR "paraprobiotics" OR "postbiotics") AND ("cardiometabolic" OR "blood pressure" OR "obesity" OR "diabetes" OR "heart disease" OR "metabolic syndrome" OR "atherosclerosis" OR "hypertension") AND ("microbiota" OR "clinical trials" OR "prevention" OR "treatment" OR "therapy").

The search yielded a total of 385 abstracts. Each abstract and the associated published paper (if freely available) were thoroughly searched and to retain only those studies satisfying the following criteria:

1. The study focused on a Randomized Controlled Trial.
2. The focus of the study (i.e. identified from the focus population or the clinical parameters profiled) was a specific disorder associated with cardiometabolic health. Specifically, this list of disorders was broadly divided into namely categories namely, InsRes/T2D/GDM (Insulin Resistance, Type II Diabetes, Gestational Diabetes Mellitus), Obesity, Liver Disorders (including NAFLD, Hepatic Disorders, Cirrhosis), MetS/CMD risk (Metabolic Syndrome and General Cardiometabolic Risk), Cardiovascular Disease (including Atherosclerosis, Hypertension, Stroke, Coronary Artery Disease).
3. We excluded all studies focusing on pediatric populations (that is the study population with age less than or equal to 18 years).

Out of 385 summaries, 214 were interventions that had as outcomes one or more clinical traits related to cardiometabolic health, and that also measured gut microbiome composition or gut microbial metabolites or, if neither was measured, the intervention specifically related to gut microbes (i.e. probiotics) (**Supplementary Table S1**).

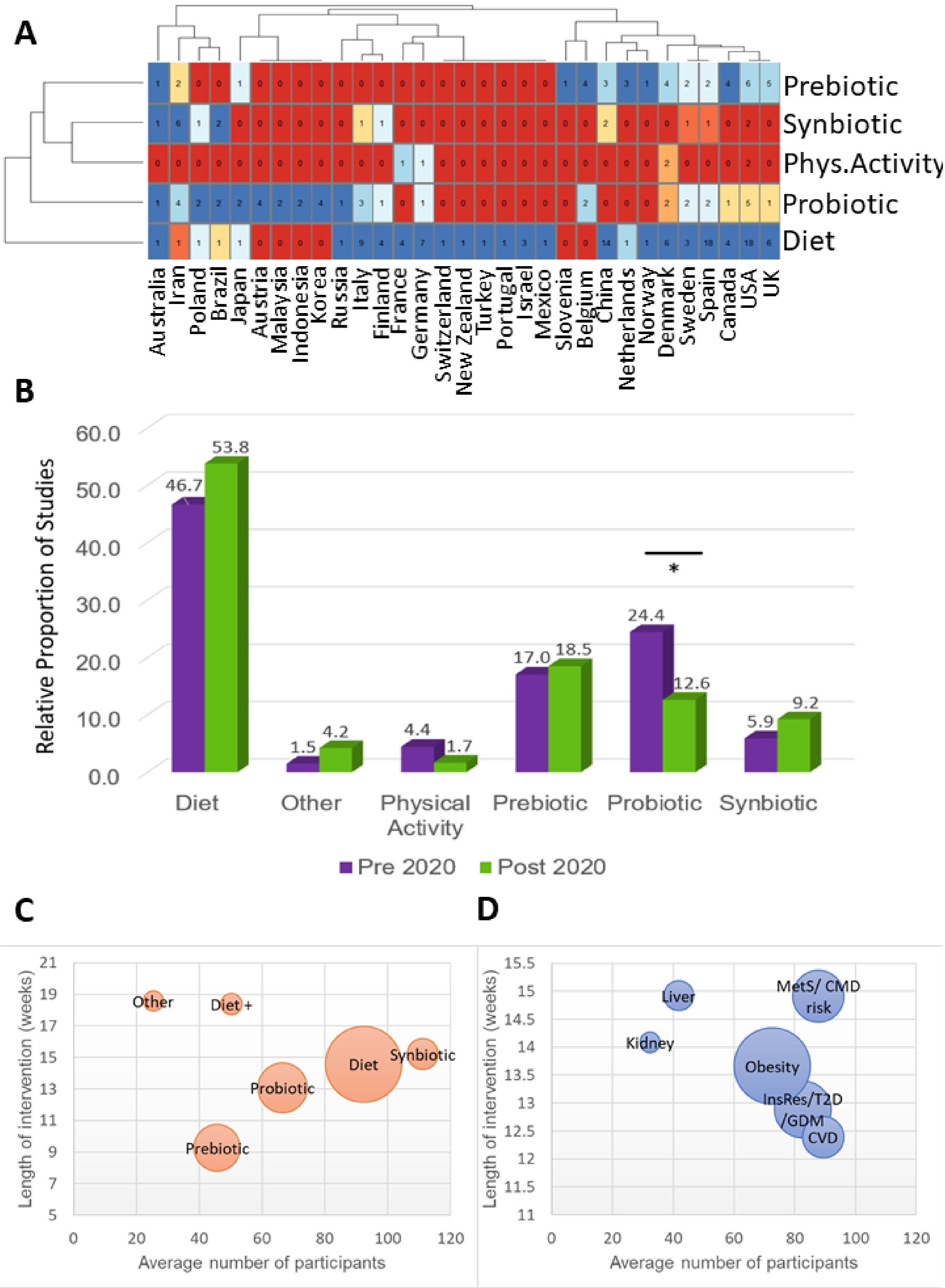
Classification of studies

A study associated with significant changes in host clinical phenotypes and gut microbiome compositions were tagged as those with significant effects on host health and gut microbiome. A study tagged as those having gut microbiome mediated effects were those having at least one or more of the following features:

- The baseline gut microbiome composition was observed to have an influence on the effect of the intervention on the host health.
- Associations between the host clinical phenotype and the gut microbiome composition were observed, but no such association of the corresponding host phenotype were observed directly with intervention status.
- Associations of the gut microbiome composition with the different host clinical phenotypes that were independent of the intervention status.

Descriptive characteristics and geographical distribution of the intervention studies

The average sample size was 76.7 participants per study (median = 45, range = 5 to 1065 research participants). The average duration of each intervention was 13.2 weeks, (median = 12 weeks, range = 0.14 to 156 weeks). The intervention studies were performed in 31 different countries. In terms of geographical origin 52.8% of studies originated in Europe, 18.7% in North America, 9.3% in China, 7.9% in the Middle East, 5.6% in East Asia, 2.8% in Central and South America and 2.8% in Australia and New Zealand. There were no studies from South Asia or Africa, despite these two regions having around 20% of world's diabetic populations (diabetesatlas.org) and one of the highest disability-adjusted life years (DALYs) for people suffering from cardiovascular diseases [1].



A
Prebiotic
Synbiotic
Phys.Activity
Probiotic
Diet
Australia
Iran
Poland
Brazil
Japan
Austria
Malaysia
Indonesia
Korea
Russia
Italy
Finland
France
Germany
Switzerland
New Zealand
Turkey
Portugal
Israel
Mexico
Slovenia
Belgium
China
Netherlands
Norway
Denmark
Sweden
Spain
Canada
USA
UK
B
Relative Proportion of Studies
60.0
50.0
40.0
30.0
20.0
10.0
0.0
46.7
53.8
1.5
4.2
4.4
1.7
17.0
18.5
24.4
12.6
5.9
9.2
*
Diet
Other
Physical Activity
Prebiotic
Probiotic
Synbiotic
Pre 2020
Post 2020
C
Length of intervention (weeks)
Average number of participants
Other
Diet +
Diet
Synbiotic
Probiotic
Prebiotic
D
Length of intervention (weeks)
Average number of participants
Liver
MetS/ CMD risk
Kidney
Obesity
InsRes/T2D /GDM
CVD

Supplementary Figure S1. A. *Heatmaps showing the pattern of relative numbers of different kinds of intervention studies from various countries. The number of studies of each kind are provided in each cell corresponding to the interventions of each type (determined from the rows) performed from a given country given by the column. The cells are colored based on the relative proportion of each intervention types per country.* ***B.*** *Representations of the different kinds of intervention studies pre- and post- 2020. The proportions are represented above each bar. The significant difference in the proportions of the probiotic-based interventions is also indicated.* ***C.*** *Bubble plot showing the average number of participants and the length of interventions of different types.* ***D.*** *Bubble plot showing the average number of participants and the duration of the interventions targeting different kinds of disorders. The size of the bubble represents the number of studies in each category.*

In terms of the relative proportions of the different kinds of intervention studies performed, the countries could be divided into three further different groups. The first group consisted of UK, USA, Canada, Spain, Sweden, Denmark, Norway, Netherlands, China, where the interventions were dominated by Diet, Prebiotic and Probiotic (in the same order). The second group consisted of Mexico, Israel, Portugal, Turkey, New Zealand, Switzerland, Germany, France, Finland, Italy, Russia, where the interventions were predominantly diet. The third group consisted of Australia, Iran, Poland, Brazil, Japan, Austria, Malaysia, Indonesia, Korea, where the proportion of probiotic driven intervention studies were the highest.

Types of interventions:

Over 50% of studies were dietary interventions, 47.2% were diet alone and 3.7% were diet plus prebiotics, probiotics or physical activity. 20% of studies were probiotic interventions, 17.8% were prebiotic interventions, 8% were synbiotics (prebiotic and probiotics), the rest of the interventions included physical activity (1.4%), one fecal matter transplantation (FMT) and two surgical interventions. Of the 104 diet interventions (with or without another intervention) 19.3% involved reducing caloric intake, 14.7% involved supplementation with fibre (via whole grains or another method), 13.8% were some form of Mediterranean diet, 11.9% involved flavonoid or polyphenol intervention using some form of fruit or vegetable supplementation, 6.4% included higher protein intake, 5.5% involved additional intake of poly or monounsaturated fatty acids via fish oil, higher fish intake or higher olive oil intake, 4.6% involved higher intake of nuts (walnuts, almonds, pistachios etc) and the remainder were a mix of strategies including traditional diets, meal timing, specific diary products, lower carbohydrate or fat intake, etc.

With regards to the different kinds of interventions, we observed a significant decrease in the proportion of probiotics-based interventions post-2020 (Fishers' exact test P-value = 0.034). This decrease was accompanied by an increase in the number of dietary and synbiotic interventions which are aimed at facilitating broader modifications of the microbiome.

Clinical outcomes:

The Sankey plot in f**ig 2 of the main article** summarizes the overall pattern of the various kinds of intervention studies targeted for the different clinical disorders. 29 of the 214 studies dealt with more than one clinical condition. 46.7% of all studies were concerned with obesity, 21.5% with insulin resistance or type II diabetes, 14% with metabolic syndrome, 6% with NAFLD and other liver diseases, 5.1% with general cardiometabolic risk. 4.75% with cardiovascular diseases, 4.2% with hypertension and blood pressure, 3.3% with dyslipidemia, 2.8% with kidney disease and there was a single study for stroke and Atherosclerosis.

The detailed comparison of the efficacies of the different intervention types with respect to cardiometabolic improvements in the host as well as with respect to improvements in the gut microbiome is provided in **Box 2**. Besides these observed variations in efficacies across intervention types, we also observed differences in the intervention cohort size and the study duration across the various intervention types. Whereas the average sample size and duration of the intervention was similar for diet and probiotic interventions, both were significantly smaller and shorter for prebiotic interventions. The duration of probiotic and synbiotic was 13.7 (std dev 14.1) weeks, for dietary interventions (alone or with another intervention) it was 14.8, standard deviation (sd) = 20.1

weeks. For prebiotic interventions the mean duration was 9.3 weeks (sd=7.5; p<0.0004 from a t-test with unequal variances). The average sample size for prebiotic interventions (mean n=45.6 sd=32.8) was also significantly smaller than for probiotic (mean n=79.1 sd 83.7) and diet (mean n=89.1 sd=136.7).

Supplementary Table 1. Interventional studies identified with cardiometabolic outcomes measuring gut microbiome composition or surrogates or containing probiotics.

References:

1 Vaduganathan M, Mensah GA, Turco JV, *et al.* The Global Burden of Cardiovascular Diseases and Risk: A Compass for Future Health. *J Am Coll Cardiol* 2022;**80**:2361–71.

2 Sergeev IN, Aljutaily T, Walton G, *et al.* Effects of Synbiotic Supplement on Human Gut Microbiota, Body Composition and Weight Loss in Obesity. *Nutrients* 2020;**12**. doi:10.3390/nu12010222

3 Zhang Y, Gu Y, Ren H, *et al.* Gut microbiome-related effects of berberine and probiotics on type 2 diabetes (the PREMOTE study). *Nat Commun* 2020;**11**:5015.

4 Zhao L, Zhang F, Ding X, *et al.* Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. *Science* 2018;**359**:1151–6.

5 Guo Y, Luo S, Ye Y, *et al.* Intermittent Fasting Improves Cardiometabolic Risk Factors and Alters Gut Microbiota in Metabolic Syndrome Patients. *J Clin Endocrinol Metab* 2021;**106**:64–79.

6 Meslier V, Laiola M, Roager HM, *et al.* Mediterranean diet intervention in overweight and obese subjects lowers plasma cholesterol and causes changes in the gut microbiome and metabolome independently of energy intake. *Gut* 2020;**69**:1258–68.

7 Depommier C, Everard A, Druart C, *et al.* Supplementation with Akkermansia muciniphila in overweight and obese human volunteers: a proof-of-concept exploratory study. *Nat Med* 2019;**25**:1096–103.

8 Djekic D, Shi L, Brolin H, *et al.* Effects of a Vegetarian Diet on Cardiometabolic Risk Factors, Gut Microbiota, and Plasma Metabolome in Subjects With Ischemic Heart Disease: A Randomized, Crossover Study. *J Am Heart Assoc* 2020;**9**:e016518.

9 Kahleova H, Rembert E, Alwarith J, *et al.* Effects of a Low-Fat Vegan Diet on Gut Microbiota in Overweight Individuals and Relationships with Body Weight, Body Composition, and Insulin Sensitivity. A Randomized Clinical Trial. *Nutrients* 2020;**12**. doi:10.3390/nu12102917

10 Dong TS, Luu K, Lagishetty V, *et al.* A High Protein Calorie Restriction Diet Alters the Gut Microbiome in Obesity. *Nutrients* 2020;**12**. doi:10.3390/nu12103221

11 Yaskolka Meir A, Rinott E, Tsaban G, *et al.* Effect of green-Mediterranean diet on intrahepatic fat: the DIRECT PLUS randomised controlled trial. *Gut* 2021;**70**:2085–95.

12 Roager HM, Vogt JK, Kristensen M, *et al.* Whole grain-rich diet reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial. *Gut* 2019;**68**:83–93.

13 Stanislawski MA, Frank DN, Borengasser SJ, *et al.* The Gut Microbiota during a Behavioral Weight Loss Intervention. *Nutrients* 2021;**13**. doi:10.3390/nu13093248

14 Wan Y, Wang F, Yuan J, *et al.* Effects of dietary fat on gut microbiota and faecal metabolites, and their relationship with cardiometabolic risk factors: a 6-month randomised controlled-feeding trial. *Gut* 2019;**68**:1417–29.

15 Muralidharan J, Moreno-Indias I, Bulló M, *et al.* Effect on gut microbiota of a 1-y lifestyle intervention with Mediterranean diet compared with energy-reduced Mediterranean diet and physical activity promotion: PREDIMED-Plus Study. *Am J Clin Nutr* 2021;**114**:1148–58.

16 Tettamanzi F, Bagnardi V, Louca P, *et al.* A High Protein Diet Is More Effective in Improving Insulin Resistance and Glycemic Variability Compared to a Mediterranean Diet-A Cross-Over Controlled Inpatient Dietary Study. *Nutrients* 2021;**13**. doi:10.3390/nu13124380

17 Ren M, Zhang H, Qi J, *et al.* An Almond-Based Low Carbohydrate Diet Improves Depression and Glycometabolism in Patients with Type 2 Diabetes through Modulating Gut Microbiota and GLP-1: A Randomized Controlled Trial. *Nutrients* 2020;**12**. doi:10.3390/nu12103036

18 Mayengbam S, Lambert JE, Parnell JA, *et al.* Impact of dietary fiber supplementation on modulating microbiota-host-metabolic axes in obesity. *J Nutr Biochem* 2019;**64**:228–36.

19 Xue L, Deng Z, Luo W, *et al.* Effect of Fecal Microbiota Transplantation on Non-Alcoholic Fatty Liver Disease: A Randomized Clinical Trial. *Front Cell Infect Microbiol* 2022;**12**:759306.

20 Zhang S, Wu P, Tian Y, *et al.* Gut Microbiota Serves a Predictable Outcome of Short-Term Low-Carbohydrate Diet (LCD) Intervention for Patients with Obesity. *Microbiol Spectr* 2021;**9**:e0022321.

21 Tonucci LB, Olbrich Dos Santos KM, Licursi de Oliveira L, *et al.* Clinical application of probiotics in type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled study. *Clin Nutr* 2017;**36**:85–92.

22 Nicolucci AC, Hume MP, Martínez I, *et al.* Prebiotics Reduce Body Fat and Alter Intestinal Microbiota in Children Who Are Overweight or With Obesity. *Gastroenterology* 2017;**153**:711–22.

23 Wang S, Ren H, Zhong H, *et al.* Combined berberine and probiotic treatment as an effective regimen for improving postprandial hyperlipidemia in type 2 diabetes patients: a double blinded placebo controlled randomized study. *Gut Microbes* 2022;**14**:2003176.

24 Deehan EC, Zhang Z, Riva A, *et al.* Elucidating the role of the gut microbiota in the physiological effects of dietary fiber. *Microbiome* 2022;**10**:77.

25 Rinott E, Meir AY, Tsaban G, *et al.* The effects of the Green-Mediterranean diet on cardiometabolic health are linked to gut microbiome modifications: a randomized controlled trial. *Genome Med* 2022;**14**:29.

26 Dupuit M, Rance M, Morel C, *et al.* Effect of Concurrent Training on Body Composition and Gut Microbiota in Postmenopausal Women with Overweight or Obesity. *Med Sci Sports Exerc* 2022;**54**:517–29.

27 Heianza Y, Sun D, Li X, *et al.* Gut microbiota metabolites, amino acid metabolites and improvements in insulin sensitivity and glucose metabolism: the POUNDS Lost trial. *Gut* 2019;**68**:263–70.

28 Mokkala K, Paulin N, Houttu N, *et al.* Metagenomics analysis of gut microbiota in response to diet intervention and gestational diabetes in overweight and obese women: a randomised, double-blind, placebo-controlled clinical trial. *Gut* 2021;**70**:309–18.

29 Cotillard A, Kennedy SP, Kong LC, *et al.* Dietary intervention impact on gut microbial gene richness. *Nature* 2013;**500**:585–8.

30 Callaway LK, McIntyre HD, Barrett HL, *et al.* Probiotics for the Prevention of Gestational Diabetes Mellitus in Overweight and Obese Women: Findings From the SPRING Double-Blind Randomized Controlled Trial. *Diabetes Care* 2019;**42**:364–71.

31 Hibberd AA, Yde CC, Ziegler ML, *et al.* Probiotic or synbiotic alters the gut microbiota and metabolism in a randomised controlled trial of weight management in overweight adults. *Benef Microbes* 2019;**10**:121–35.

32 Birkeland E, Gharagozlian S, Birkeland KI, *et al.* Prebiotic effect of inulin-type fructans on faecal microbiota

and short-chain fatty acids in type 2 diabetes: a randomised controlled trial. *Eur J Nutr* 2020;**59**:3325–38.

33 Chambers ES, Byrne CS, Morrison DJ, *et al.* Dietary supplementation with inulin-propionate ester or inulin improves insulin sensitivity in adults with overweight and obesity with distinct effects on the gut microbiota, plasma metabolome and systemic inflammatory responses: a randomised cross-over trial. *Gut* 2019;**68**:1430–8.

34 Basciani S, Camajani E, Contini S, *et al.* Very-Low-Calorie Ketogenic Diets With Whey, Vegetable, or Animal Protein in Patients With Obesity: A Randomized Pilot Study. *J Clin Endocrinol Metab* 2020;**105**. doi:10.1210/clinem/dgaa336

35 Rein M, Ben-Yacov O, Godneva A, *et al.* Effects of personalized diets by prediction of glycemic responses on glycemic control and metabolic health in newly diagnosed T2DM: a randomized dietary intervention pilot trial. *BMC Med* 2022;**20**:56.

36 Gomes AC, Hoffmann C, Mota JF. Gut microbiota is associated with adiposity markers and probiotics may impact specific genera. *Eur J Nutr* 2020;**59**:1751–62.

37 Guevara-Cruz M, Flores-López AG, Aguilar-López M, *et al.* Improvement of Lipoprotein Profile and Metabolic Endotoxemia by a Lifestyle Intervention That Modifies the Gut Microbiota in Subjects With Metabolic Syndrome. *J Am Heart Assoc* 2019;**8**:e012401.

38 Crovesy L, El-Bacha T, Rosado EL. Modulation of the gut microbiota by probiotics and symbiotics is associated with changes in serum metabolite profile related to a decrease in inflammation and overall benefits to metabolic health: a double-blind randomized controlled clinical trial in women with obesity. *Food Funct* 2021;**12**:2161–70.

39 Biolato M, Manca F, Marrone G, *et al.* Intestinal permeability after Mediterranean diet and low-fat diet in non-alcoholic fatty liver disease. *World J Gastroenterol* 2019;**25**:509–20.

40 Perraudeau F, McMurdie P, Bullard J, *et al.* Improvements to postprandial glucose control in subjects with type 2 diabetes: a multicenter, double blind, randomized placebo-controlled trial of a novel probiotic formulation. *BMJ Open Diabetes Res Care* 2020;**8**. doi:10.1136/bmjdrc-2020-001319

41 Sato J, Kanazawa A, Azuma K, *et al.* Probiotic reduces bacterial translocation in type 2 diabetes mellitus: A randomised controlled study. *Sci Rep* 2017;**7**:12115.

42 Jian C, Silvestre MP, Middleton D, *et al.* Gut microbiota predicts body fat change following a low-energy diet: a PREVIEW intervention study. *Genome Med* 2022;**14**:54.

43 Razmpoosh E, Javadi A, Ejtahed HS, *et al.* The effect of probiotic supplementation on glycemic control and lipid profile in patients with type 2 diabetes: A randomized placebo controlled trial. *Diabetes Metab Syndr* 2019;**13**:175–82.

44 Rahayu ES, Mariyatun M, Putri Manurung NE, *et al.* Effect of probiotic Lactobacillus plantarum Dad-13 powder consumption on the gut microbiota and intestinal health of overweight adults. *World J Gastroenterol* 2021;**27**:107–28.

45 Cuevas-Sierra A, Romo-Hualde A, Aranaz P, *et al.* Diet- and sex-related changes of gut microbiota composition and functional profiles after 4 months of weight loss intervention. *Eur J Nutr* 2021;**60**:3279–301.

46 Stenman LK, Lehtinen MJ, Meland N, *et al.* Probiotic With or Without Fiber Controls Body Fat Mass, Associated With Serum Zonulin, in Overweight and Obese Adults-Randomized Controlled Trial. *EBioMedicine* 2016;**13**:190–200.

47 Kobyliak N, Abenavoli L, Mykhalchyshyn G, *et al.* A Multi-strain Probiotic Reduces the Fatty Liver Index,

Cytokines and Aminotransferase levels in NAFLD Patients: Evidence from a Randomized Clinical Trial. *J Gastrointestin Liver Dis* 2018;**27**:41–9.

48 Su L, Hong Z, Zhou T, *et al.* Health improvements of type 2 diabetic patients through diet and diet plus fecal microbiota transplantation. *Sci Rep* 2022;**12**:1152.

49 Sowah SA, Milanese A, Schübel R, *et al.* Calorie restriction improves metabolic state independently of gut microbiome composition: a randomized dietary intervention trial. *Genome Med* 2022;**14**:30.

50 Pedret A, Valls RM, Calderón-Pérez L, *et al.* Effects of daily consumption of the probiotic Bifidobacterium animalis subsp. lactis CECT 8145 on anthropometric adiposity biomarkers in abdominally obese subjects: a randomized controlled trial. *Int J Obes* 2019;**43**:1863–8.

51 Derkach A, Sampson J, Joseph J, *et al.* Effects of dietary sodium on metabolites: the Dietary Approaches to Stop Hypertension (DASH)-Sodium Feeding Study. *Am J Clin Nutr* 2017;**106**:1131–41.

52 McFarlane C, Krishnasamy R, Stanton T, *et al.* Synbiotics Easing Renal Failure by Improving Gut Microbiology II (SYNERGY II): A Feasibility Randomized Controlled Trial. *Nutrients* 2021;**13**. doi:10.3390/nu13124481

53 Ismael S, Silvestre MP, Vasques M, *et al.* A Pilot Study on the Metabolic Impact of Mediterranean Diet in Type 2 Diabetes: Is Gut Microbiota the Key? *Nutrients* 2021;**13**. doi:10.3390/nu13041228

54 Janczy A, Aleksandrowicz-Wrona E, Kochan Z, *et al.* Impact of diet and synbiotics on selected gut bacteria and intestinal permeability in individuals with excess body weight - A Prospective, Randomized Study. *Acta Biochim Pol* 2020;**67**:571–8.

55 Leyrolle Q, Cserjesi R, D G H Mulders M, *et al.* Prebiotic effect on mood in obese patients is determined by the initial gut microbiota composition: A randomized, controlled trial. *Brain Behav Immun* 2021;**94**:289–98.

56 Thomas MS, DiBella M, Blesso CN, *et al.* Comparison between Egg Intake versus Choline Supplementation on Gut Microbiota and Plasma Carotenoids in Subjects with Metabolic Syndrome. *Nutrients* 2022;**14**. doi:10.3390/nu14061179

57 Jian C, Luukkonen P, Sädevirta S, *et al.* Impact of short-term overfeeding of saturated or unsaturated fat or sugars on the gut microbiota in relation to liver fat in obese and overweight adults. *Clin Nutr* 2021;**40**:207–16.

58 Tagliamonte S, Laiola M, Ferracane R, *et al.* Mediterranean diet consumption affects the endocannabinoid system in overweight and obese subjects: possible links with gut microbiome, insulin resistance and inflammation. *Eur J Nutr* 2021;**60**:3703–16.

59 Del Bo' C, Bernardi S, Cherubini A, *et al.* A polyphenol-rich dietary pattern improves intestinal permeability, evaluated as serum zonulin levels, in older subjects: The MaPLE randomised controlled trial. *Clin Nutr* 2021;**40**:3006–18.

60 Wei S, Brejnrod AD, Trivedi U, *et al.* Impact of intensive lifestyle intervention on gut microbiota composition in type 2 diabetes: a post-hoc analysis of a randomized clinical trial. *Gut Microbes* 2022;**14**:2005407.

61 Iversen KN, Dicksved J, Zoki C, *et al.* The Effects of High Fiber Rye, Compared to Refined Wheat, on Gut Microbiota Composition, Plasma Short Chain Fatty Acids, and Implications for Weight Loss and Metabolic Risk Factors (the RyeWeight Study). *Nutrients* 2022;**14**. doi:10.3390/nu14081669

62 Tindall AM, McLimans CJ, Petersen KS, *et al.* Walnuts and Vegetable Oils Containing Oleic Acid Differentially Affect the Gut Microbiota and Associations with Cardiovascular Risk Factors: Follow-up of a Randomized, Controlled, Feeding Trial in Adults at Risk for Cardiovascular Disease. *J Nutr* 2020;**150**:806–17.

63 Łagowska K, Drzymała-Czyż S. A low glycemic index, energy-restricted diet but not Lactobacillus rhamnosus supplementation changes fecal short-chain fatty acid and serum lipid concentrations in women with overweight or obesity and polycystic ovary syndrome. *Eur Rev Med Pharmacol Sci* 2022;**26**:917–26.

64 Sargeant JA, King JA, Yates T, *et al.* The effects of empagliflozin, dietary energy restriction, or both on appetite-regulatory gut peptides in individuals with type 2 diabetes and overweight or obesity: The SEESAW randomized, double-blind, placebo-controlled trial. *Diabetes Obes Metab* 2022;**24**:1509–21.

65 Xue Y, Cui L, Qi J, *et al.* The effect of dietary fiber (oat bran) supplement on blood pressure in patients with essential hypertension: A randomized controlled trial. *Nutr Metab Cardiovasc Dis* 2021;**31**:2458–70.

66 Ma Y, Sun Y, Sun L, *et al.* Effects of gut microbiota and fatty acid metabolism on dyslipidemia following weight-loss diets in women: Results from a randomized controlled trial. *Clin Nutr* 2021;**40**:5511–20.

67 Castonguay-Paradis S, Lacroix S, Rochefort G, *et al.* Dietary fatty acid intake and gut microbiota determine circulating endocannabinoidome signaling beyond the effect of body fat. *Sci Rep* 2020;**10**:15975.

68 Chen Y, Feng R, Yang X, *et al.* Yogurt improves insulin resistance and liver fat in obese women with nonalcoholic fatty liver disease and metabolic syndrome: a randomized controlled trial. *Am J Clin Nutr* 2019;**109**:1611–9.

69 Kaczmarczyk M, Szulińska M, Łoniewski I, *et al.* Treatment With Multi-Species Probiotics Changes the Functions, Not the Composition of Gut Microbiota in Postmenopausal Women With Obesity: A Randomized, Double-Blind, Placebo-Controlled Study. *Front Cell Infect Microbiol* 2022;**12**:815798.

70 Bellikci-Koyu E, Sarer-Yurekli BP, Akyon Y, *et al.* Effects of Regular Kefir Consumption on Gut Microbiota in Patients with Metabolic Syndrome: A Parallel-Group, Randomized, Controlled Study. *Nutrients* 2019;**11**. doi:10.3390/nu11092089

71 Hiel S, Gianfrancesco MA, Rodriguez J, *et al.* Link between gut microbiota and health outcomes in inulin - treated obese patients: Lessons from the Food4Gut multicenter randomized placebo-controlled trial. *Clin Nutr* 2020;**39**:3618–28.

72 Mitchell CM, Davy BM, Ponder MA, *et al.* Prebiotic Inulin Supplementation and Peripheral Insulin Sensitivity in adults at Elevated Risk for Type 2 Diabetes: A Pilot Randomized Controlled Trial. *Nutrients* 2021;**13**. doi:10.3390/nu13093235

73 Gutiérrez-Repiso C, Hernández-García C, García-Almeida JM, *et al.* Effect of Synbiotic Supplementation in a Very-Low-Calorie Ketogenic Diet on Weight Loss Achievement and Gut Microbiota: A Randomized Controlled Pilot Study. *Mol Nutr Food Res* 2019;**63**:e1900167.

74 Heianza Y, Sun D, Smith SR, *et al.* Changes in Gut Microbiota-Related Metabolites and Long-term Successful Weight Loss in Response to Weight-Loss Diets: The POUNDS Lost Trial. *Diabetes Care* 2018;**41**:413–9.

75 Karusheva Y, Koessler T, Strassburger K, *et al.* Short-term dietary reduction of branched-chain amino acids reduces meal-induced insulin secretion and modifies microbiome composition in type 2 diabetes: a randomized controlled crossover trial. *Am J Clin Nutr* 2019;**110**:1098–107.

76 Chong PL, Laight D, Aspinall RJ, *et al.* A randomised placebo controlled trial of VSL#3® probiotic on biomarkers of cardiovascular risk and liver injury in non-alcoholic fatty liver disease. *BMC Gastroenterol* 2021;**21**:144.

77 Stubbs BJ, Cox PJ, Evans RD, *et al.* A Ketone Ester Drink Lowers Human Ghrelin and Appetite. *Obesity* 2018;**26**:269–73.

78 Khalili L, Alipour B, Asghari Jafar-Abadi M, *et al.* The Effects of Lactobacillus casei on Glycemic Response, Serum Sirtuin1 and Fetuin-A Levels in Patients with Type 2 Diabetes Mellitus: A Randomized Controlled

Trial. *Iran Biomed J* 2019;**23**:68–77.

79 McMurdie PJ, Stoeva MK, Justice N, *et al.* Increased circulating butyrate and ursodeoxycholate during probiotic intervention in humans with type 2 diabetes. *BMC Microbiol* 2022;**22**:19.

80 Liu F, Li P, Chen M, *et al.* Fructooligosaccharide (FOS) and Galactooligosaccharide (GOS) Increase Bifidobacterium but Reduce Butyrate Producing Bacteria with Adverse Glycemic Metabolism in healthy young population. *Sci Rep* 2017;**7**:11789.

81 van der Beek CM, Canfora EE, Kip AM, *et al.* The prebiotic inulin improves substrate metabolism and promotes short-chain fatty acid production in overweight to obese men. *Metabolism* 2018;**87**:25–35.

82 Chambers ES, Byrne CS, Rugyendo A, *et al.* The effects of dietary supplementation with inulin and inulin-propionate ester on hepatic steatosis in adults with non-alcoholic fatty liver disease. *Diabetes Obes Metab* 2019;**21**:372–6.

83 Depommier C, Everard A, Druart C, *et al.* Serum metabolite profiling yields insights into health promoting effect of A. muciniphila in human volunteers with a metabolic syndrome. *Gut Microbes* 2021;**13**:1994270.

84 Sandberg J, Kovatcheva-Datchary P, Björck I, *et al.* Abundance of gut Prevotella at baseline and metabolic response to barley prebiotics. *Eur J Nutr* 2019;**58**:2365–76.

85 Van Meijel RLJ, Venema K, Canfora EE, *et al.* Mild intermittent hypoxia exposure alters gut microbiota composition in men with overweight and obesity. *Benef Microbes* 2022;**13**:355–63.

86 Johnstone AM, Kelly J, Ryan S, *et al.* Nondigestible Carbohydrates Affect Metabolic Health and Gut Microbiota in Overweight Adults after Weight Loss. *J Nutr* 2020;**150**:1859–70.

87 Brahe LK, Le Chatelier E, Prifti E, *et al.* Dietary modulation of the gut microbiota--a randomised controlled trial in obese postmenopausal women. *Br J Nutr* 2015;**114**:406–17.

88 Xu D, Pan D, Liu H, *et al.* Improvement in cardiometabolic risk markers following an oatmeal diet is associated with gut microbiota in mildly hypercholesterolemic individuals. *Food Res Int* 2022;**160**:111701.

89 Xiao S, Fei N, Pang X, *et al.* A gut microbiota-targeted dietary intervention for amelioration of chronic inflammation underlying metabolic syndrome. *FEMS Microbiol Ecol* 2014;**87**:357–67.

90 Sohn M, Na GY, Chu J, *et al.* Efficacy and Safety of Lactobacillus plantarum K50 on Lipids in Koreans With Obesity: A Randomized, Double-Blind Controlled Clinical Trial. *Front Endocrinol* 2021;**12**:790046.

91 Hasain Z, Raja Ali RA, Ahmad HF, *et al.* The Roles of Probiotics in the Gut Microbiota Composition and Metabolic Outcomes in Asymptomatic Post-Gestational Diabetes Women: A Randomized Controlled Trial. *Nutrients* 2022;**14**. doi:10.3390/nu14183878

92 Haji-Ghazi Tehrani L, Mousavi SN, Chiti H, *et al.* Effect of Atkins versus a low-fat diet on gut microbiota, and cardiometabolic markers in obese women following an energy-restricted diet: Randomized, crossover trial. *Nutr Metab Cardiovasc Dis* 2022;**32**:1734–41.

93 Hill EB, Chen L, Bailey MT, *et al.* Facilitating a high-quality dietary pattern induces shared microbial responses linking diet quality, blood pressure, and microbial sterol metabolism in caregiver-child dyads. *Gut Microbes* 2022;**14**:2150502.

94 Mo S-J, Lee K, Hong H-J, *et al.* Effects of Lactobacillus curvatus HY7601 and Lactobacillus plantarum KY1032 on Overweight and the Gut Microbiota in Humans: Randomized, Double-Blinded, Placebo-Controlled Clinical Trial. *Nutrients* 2022;**14**. doi:10.3390/nu14122484

95 Lydia A, Indra TA, Rizka A, *et al.* The effects of synbiotics on indoxyl sulphate level, constipation, and quality of life associated with constipation in chronic haemodialysis patients: a randomized controlled trial. *BMC*

Nephrol 2022;**23**:259.

96 Linkens AMA, van Best N, Niessen PM, *et al.* A 4-Week Diet Low or High in Advanced Glycation Endproducts Has Limited Impact on Gut Microbial Composition in Abdominally Obese Individuals: The deAGEing Trial. *Int J Mol Sci* 2022;**23**. doi:10.3390/ijms23105328

97 Benítez-Páez A, Hess AL, Krautbauer S, *et al.* Sex, Food, and the Gut Microbiota: Disparate Response to Caloric Restriction Diet with Fiber Supplementation in Women and Men. *Mol Nutr Food Res* 2021;**65**:e2000996.

98 Li J, Morrow C, McLain A, *et al.* Effects of a Low-Carbohydrate, High-Protein Diet on Gut Microbiome Composition in Insulin-Resistant Individuals With Chronic Spinal Cord Injury: Preliminary Results From a Randomized Controlled Trial. *Arch Phys Med Rehabil* 2022;**103**:1269–78.

99 Companys J, Calderón-Pérez L, Pla-Pagà L, *et al.* Effects of enriched seafood sticks (heat-inactivated B. animalis subsp. lactis CECT 8145, inulin, omega-3) on cardiometabolic risk factors and gut microbiota in abdominally obese subjects: randomized controlled trial. *Eur J Nutr* 2022;**61**:3597–611.

100 Zhang X, Zhao A, Sandhu AK, *et al.* Red Raspberry and Fructo-Oligosaccharide Supplementation, Metabolic Biomarkers, and the Gut Microbiota in Adults with Prediabetes: A Randomized Crossover Clinical Trial. *J Nutr* 2022;**152**:1438–49.

101 Sugino KY, Hernandez TL, Barbour LA, *et al.* A maternal higher-complex carbohydrate diet increases bifidobacteria and alters early life acquisition of the infant microbiome in women with gestational diabetes mellitus. *Front Endocrinol* 2022;**13**:921464.

102 Seethaler B, Nguyen NK, Basrai M, *et al.* Short-chain fatty acids are key mediators of the favorable effects of the Mediterranean diet on intestinal barrier integrity: data from the randomized controlled LIBRE trial. *Am J Clin Nutr* 2022;**116**:928–42.

103 Narmaki E, Borazjani M, Ataie-Jafari A, *et al.* The combined effects of probiotics and restricted calorie diet on the anthropometric indices, eating behavior, and hormone levels of obese women with food addiction: a randomized clinical trial. *Nutr Neurosci* 2022;**25**:963–75.

104 Kern T, Blond MB, Hansen TH, *et al.* Structured exercise alters the gut microbiota in humans with overweight and obesity-A randomized controlled trial. *Int J Obes* 2020;**44**:125–35.

105 Santos-Marcos JA, Haro C, Vega-Rojas A, *et al.* Sex Differences in the Gut Microbiota as Potential Determinants of Gender Predisposition to Disease. *Mol Nutr Food Res* 2019;**63**:e1800870.

106 Watanabe A, Tochio T, Kadota Y, *et al.* Supplementation of 1-Kestose Modulates the Gut Microbiota Composition to Ameliorate Glucose Metabolism in Obesity-Prone Hosts. *Nutrients* 2021;**13**. doi:10.3390/nu13092983

107 Roach LA, Meyer BJ, Fitton JH, *et al.* Improved Plasma Lipids, Anti-Inflammatory Activity, and Microbiome Shifts in Overweight Participants: Two Clinical Studies on Oral Supplementation with Algal Sulfated Polysaccharide. *Mar Drugs* 2022;**20**. doi:10.3390/md20080500

108 Cortés-Martín A, Iglesias-Aguirre CE, Meoro A, *et al.* Pharmacological Therapy Determines the Gut Microbiota Modulation by a Pomegranate Extract Nutraceutical in Metabolic Syndrome: A Randomized Clinical Trial. *Mol Nutr Food Res* 2021;**65**:e2001048.

109 Galié S, García-Gavilán J, Camacho-Barcía L, *et al.* Effects of the Mediterranean Diet or Nut Consumption on Gut Microbiota Composition and Fecal Metabolites and their Relationship with Cardiometabolic Risk Factors. *Mol Nutr Food Res* 2021;**65**:e2000982.

110 Danshiitsoodol N, Noda M, Kanno K, *et al.* Plant-Derived Lactobacillus paracasei IJH-SONE68 Improves the

Gut Microbiota Associated with Hepatic Disorders: A Randomized, Double-Blind, and Placebo-Controlled Clinical Trial. *Nutrients* 2022;**14**. doi:10.3390/nu14214492

111 Sun Y, Ling C, Liu L, *et al.* Effects of Whey Protein or Its Hydrolysate Supplements Combined with an Energy-Restricted Diet on Weight Loss: A Randomized Controlled Trial in Older Women. *Nutrients* 2022;**14**. doi:10.3390/nu14214540

112 Cicero AFG, Fogacci F, Bove M, *et al.* Impact of a short-term synbiotic supplementation on metabolic syndrome and systemic inflammation in elderly patients: a randomized placebo-controlled clinical trial. *Eur J Nutr* 2021;**60**:655–63.

113 Galié S, García-Gavilán J, Papandreou C, *et al.* Effects of Mediterranean Diet on plasma metabolites and their relationship with insulin resistance and gut microbiota composition in a crossover randomized clinical trial. *Clin Nutr* 2021;**40**:3798–806.

114 Li X, Yin J, Zhu Y, *et al.* Effects of Whole Milk Supplementation on Gut Microbiota and Cardiometabolic Biomarkers in Subjects with and without Lactose Malabsorption. *Nutrients* 2018;**10**. doi:10.3390/nu10101403

115 Moreno-Indias I, Sánchez-Alcoholado L, Pérez-Martínez P, *et al.* Red wine polyphenols modulate fecal microbiota and reduce markers of the metabolic syndrome in obese patients. *Food Funct* 2016;**7**:1775–87.

116 Vetrani C, Maukonen J, Bozzetto L, *et al.* Diets naturally rich in polyphenols and/or long-chain n-3 polyunsaturated fatty acids differently affect microbiota composition in high-cardiometabolic-risk individuals. *Acta Diabetol* 2020;**57**:853–60.

117 Karlsson C, Ahrné S, Molin G, *et al.* Probiotic therapy to men with incipient arteriosclerosis initiates increased bacterial diversity in colon: a randomized controlled trial. *Atherosclerosis* 2010;**208**:228–33.

118 Luoto R, Kalliomäki M, Laitinen K, *et al.* The impact of perinatal probiotic intervention on the development of overweight and obesity: follow-up study from birth to 10 years. *Int J Obes* 2010;**34**:1531–7.

119 Savard P, Lamarche B, Paradis M-E, *et al.* Impact of Bifidobacterium animalis subsp. lactis BB-12 and, Lactobacillus acidophilus LA-5-containing yoghurt, on fecal bacterial counts of healthy adults. *Int J Food Microbiol* 2011;**149**:50–7.

120 Fava F, Gitau R, Griffin BA, *et al.* The type and quantity of dietary fat and carbohydrate alter faecal microbiome and short-chain fatty acid excretion in a metabolic syndrome 'at-risk' population. *Int J Obes* 2013;**37**:216–23.

121 Queipo-Ortuño MI, Boto-Ordóñez M, Murri M, *et al.* Influence of red wine polyphenols and ethanol on the gut microbiota ecology and biochemical biomarkers. *Am J Clin Nutr* 2012;**95**:1323–34.

122 Tulipani S, Urpi-Sarda M, García-Villalba R, *et al.* Urolithins are the main urinary microbial-derived phenolic metabolites discriminating a moderate consumption of nuts in free-living subjects with diagnosed metabolic syndrome. *J Agric Food Chem* 2012;**60**:8930–40.

123 Leber B, Tripolt NJ, Blattl D, *et al.* The influence of probiotic supplementation on gut permeability in patients with metabolic syndrome: an open label, randomized pilot study. *Eur J Clin Nutr* 2012;**66**:1110–5.

124 Dewulf EM, Cani PD, Claus SP, *et al.* Insight into the prebiotic concept: lessons from an exploratory, double blind intervention study with inulin-type fructans in obese women. *Gut* 2013;**62**:1112–21.

125 Vulevic J, Juric A, Tzortzis G, *et al.* A mixture of trans-galactooligosaccharides reduces markers of metabolic syndrome and modulates the fecal microbiota and immune function of overweight adults. *J Nutr* 2013;**143**:324–31.

126 Puupponen-Pimiä R, Seppänen-Laakso T, Kankainen M, *et al.* Effects of ellagitannin-rich berries on blood lipids, gut microbiota, and urolithin production in human subjects with symptoms of metabolic syndrome. *Mol Nutr Food Res* 2013;**57**:2258–63.

127 Sharafedtinov KK, Plotnikova OA, Alexeeva RI, *et al.* Hypocaloric diet supplemented with probiotic cheese improves body mass index and blood pressure indices of obese hypertensive patients--a randomized double-blind placebo-controlled pilot study. *Nutr J* 2013;**12**:138.

128 Roager HM, Licht TR, Poulsen SK, *et al.* Microbial enterotypes, inferred by the prevotella-to-bacteroides ratio, remained stable during a 6-month randomized controlled diet intervention with the new nordic diet. *Appl Environ Microbiol* 2014;**80**:1142–9.

129 Lee SJ, Bose S, Seo J-G, *et al.* The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: a randomized double-blind controlled clinical trial. *Clin Nutr* 2014;**33**:973–81.

130 Campbell C, Grapov D, Fiehn O, *et al.* Improved metabolic health alters host metabolism in parallel with changes in systemic xeno-metabolites of gut origin. *PLoS One* 2014;**9**:e84260.

131 Rincón D, Vaquero J, Hernando A, *et al.* Oral probiotic VSL#3 attenuates the circulatory disturbances of patients with cirrhosis and ascites. *Liver Int* 2014;**34**:1504–12.

132 Alisi A, Bedogni G, Baviera G, *et al.* Randomised clinical trial: The beneficial effects of VSL#3 in obese children with non-alcoholic steatohepatitis. *Aliment Pharmacol Ther* 2014;**39**:1276–85.

133 Salazar N, Dewulf EM, Neyrinck AM, *et al.* Inulin-type fructans modulate intestinal Bifidobacterium species populations and decrease fecal short-chain fatty acids in obese women. *Clin Nutr* 2015;**34**:501–7.

134 Bjerg AT, Sørensen MB, Krych L, *et al.* The effect of Lactobacillus paracasei subsp. paracasei L. casei W8® on blood levels of triacylglycerol is independent of colonisation. *Benef Microbes* 2015;**6**:263–9.

135 Foerster J, Maskarinec G, Reichardt N, *et al.* The influence of whole grain products and red meat on intestinal microbiota composition in normal weight adults: a randomized crossover intervention trial. *PLoS One* 2014;**9**:e109606.

136 Ampatzoglou A, Atwal KK, Maidens CM, *et al.* Increased whole grain consumption does not affect blood biochemistry, body composition, or gut microbiology in healthy, low-habitual whole grain consumers. *J Nutr* 2015;**145**:215–21.

137 Han K, Bose S, Wang J-H, *et al.* Contrasting effects of fresh and fermented kimchi consumption on gut microbiota composition and gene expression related to metabolic syndrome in obese Korean women. *Mol Nutr Food Res* 2015;**59**:1004–8.

138 Damms-Machado A, Mitra S, Schollenberger AE, *et al.* Effects of surgical and dietary weight loss therapy for obesity on gut microbiota composition and nutrient absorption. *Biomed Res Int* 2015;**2015**:806248.

139 Miccheli A, Capuani G, Marini F, *et al.* Urinary (1)H-NMR-based metabolic profiling of children with NAFLD undergoing VSL#3 treatment. *Int J Obes* 2015;**39**:1118–25.

140 Simon M-C, Strassburger K, Nowotny B, *et al.* Intake of Lactobacillus reuteri improves incretin and insulin secretion in glucose-tolerant humans: a proof of concept. *Diabetes Care* 2015;**38**:1827–34.

141 Tripolt NJ, Leber B, Triebl A, *et al.* Effect of Lactobacillus casei Shirota supplementation on trimethylamine-N-oxide levels in patients with metabolic syndrome: An open-label, randomized study. *Atherosclerosis* 2015;**242**:141–4.

142 Rebello CJ, Burton J, Heiman M, *et al.* Gastrointestinal microbiome modulator improves glucose tolerance

in overweight and obese subjects: A randomized controlled pilot trial. *J Diabetes Complications* 2015;**29**:1272–6.

143 Haro C, Montes-Borrego M, Rangel-Zúñiga OA, *et al.* Two Healthy Diets Modulate Gut Microbial Community Improving Insulin Sensitivity in a Human Obese Population. *J Clin Endocrinol Metab* 2016;**101**:233–42.

144 Stadlbauer V, Leber B, Lemesch S, *et al.* Lactobacillus casei Shirota Supplementation Does Not Restore Gut Microbiota Composition and Gut Barrier in Metabolic Syndrome: A Randomized Pilot Study. *PLoS One* 2015;**10**:e0141399.

145 Martín-Peláez S, Mosele JI, Pizarro N, *et al.* Effect of virgin olive oil and thyme phenolic compounds on blood lipid profile: implications of human gut microbiota. *Eur J Nutr* 2017;**56**:119–31.

146 Vetrani C, Costabile G, Luongo D, *et al.* Effects of whole-grain cereal foods on plasma short chain fatty acid concentrations in individuals with the metabolic syndrome. *Nutrition* 2016;**32**:217–21.

147 Lambert JE, Parnell JA, Tunnicliffe JM, *et al.* Consuming yellow pea fiber reduces voluntary energy intake and body fat in overweight/obese adults in a 12-week randomized controlled trial. *Clin Nutr* 2017;**36**:126–33.

148 Firouzi S, Majid HA, Ismail A, *et al.* Effect of multi-strain probiotics (multi-strain microbial cell preparation) on glycemic control and other diabetes-related outcomes in people with type 2 diabetes: a randomized controlled trial. *Eur J Nutr* 2017;**56**:1535–50.

149 Balfegó M, Canivell S, Hanzu FA, *et al.* Effects of sardine-enriched diet on metabolic control, inflammation and gut microbiota in drug-naïve patients with type 2 diabetes: a pilot randomized trial. *Lipids Health Dis* 2016;**15**:78.

150 Ferolla SM, Couto CA, Costa-Silva L, *et al.* Beneficial Effect of Synbiotic Supplementation on Hepatic Steatosis and Anthropometric Parameters, But Not on Gut Permeability in a Population with Nonalcoholic Steatohepatitis. *Nutrients* 2016;**8**. doi:10.3390/nu8070397

151 Hald S, Schioldan AG, Moore ME, *et al.* Effects of Arabinoxylan and Resistant Starch on Intestinal Microbiota and Short-Chain Fatty Acids in Subjects with Metabolic Syndrome: A Randomised Crossover Study. *PLoS One* 2016;**11**:e0159223.

152 Tovar J, de Mello VD, Nilsson A, *et al.* Reduction in cardiometabolic risk factors by a multifunctional diet is mediated via several branches of metabolism as evidenced by nontargeted metabolite profiling approach. *Mol Nutr Food Res* 2017;**61**. doi:10.1002/mnfr.201600552

153 Murphy R, Tsai P, Jüllig M, *et al.* Differential Changes in Gut Microbiota After Gastric Bypass and Sleeve Gastrectomy Bariatric Surgery Vary According to Diabetes Remission. *Obes Surg* 2017;**27**:917–25.

154 Heinsen F-A, Fangmann D, Müller N, *et al.* Beneficial Effects of a Dietary Weight Loss Intervention on Human Gut Microbiome Diversity and Metabolism Are Not Sustained during Weight Maintenance. *Obes Facts* 2016;**9**:379–91.

155 Pedersen C, Gallagher E, Horton F, *et al.* Host-microbiome interactions in human type 2 diabetes following prebiotic fibre (galacto-oligosaccharide) intake. *Br J Nutr* 2016;**116**:1869–77.

156 Frugé AD, Ptacek T, Tsuruta Y, *et al.* Dietary Changes Impact the Gut Microbe Composition in Overweight and Obese Men with Prostate Cancer Undergoing Radical Prostatectomy. *J Acad Nutr Diet* 2018;**118**:714–23.e1.

157 Bergeron N, Williams PT, Lamendella R, *et al.* Diets high in resistant starch increase plasma levels of trimethylamine-N-oxide, a gut microbiome metabolite associated with CVD risk. *Br J Nutr* 2016;**116**:2020–

9.

158 Mobini R, Tremaroli V, Ståhlman M, *et al.* Metabolic effects of Lactobacillus reuteri DSM 17938 in people with type 2 diabetes: A randomized controlled trial. *Diabetes Obes Metab* 2017;**19**:579–89.

159 Karl JP, Meydani M, Barnett JB, *et al.* Substituting whole grains for refined grains in a 6-wk randomized trial favorably affects energy-balance metrics in healthy men and postmenopausal women. *Am J Clin Nutr* 2017;**105**:589–99.

160 Salden BN, Troost FJ, Wilms E, *et al.* Reinforcement of intestinal epithelial barrier by arabinoxylans in overweight and obese subjects: A randomized controlled trial: Arabinoxylans in gut barrier. *Clin Nutr* 2018;**37**:471–80.

161 Canfora EE, van der Beek CM, Hermes GDA, *et al.* Supplementation of Diet With Galacto-oligosaccharides Increases Bifidobacteria, but Not Insulin Sensitivity, in Obese Prediabetic Individuals. *Gastroenterology* 2017;**153**:87–97.e3.

162 Hernández-Alonso P, Cañueto D, Giardina S, *et al.* Effect of pistachio consumption on the modulation of urinary gut microbiota-related metabolites in prediabetic subjects. *J Nutr Biochem* 2017;**45**:48–53.

163 Nilsson A, Johansson-Boll E, Sandberg J, *et al.* Gut microbiota mediated benefits of barley kernel products on metabolism, gut hormones, and inflammatory markers as affected by co-ingestion of commercially available probiotics: a randomized controlled study in healthy subjects. *Clin Nutr ESPEN* 2016;**15**:49–56.

164 Reimer RA, Willis HJ, Tunnicliffe JM, *et al.* Inulin-type fructans and whey protein both modulate appetite but only fructans alter gut microbiota in adults with overweight/obesity: A randomized controlled trial. *Mol Nutr Food Res* 2017;**61**. doi:10.1002/mnfr.201700484

165 Bendtsen LQ, Blædel T, Holm JB, *et al.* High intake of dairy during energy restriction does not affect energy balance or the intestinal microflora compared with low dairy intake in overweight individuals in a randomized controlled trial. *Appl Physiol Nutr Metab* 2018;**43**:1–10.

166 Hjorth MF, Roager HM, Larsen TM, *et al.* Pre-treatment microbial Prevotella-to-Bacteroides ratio, determines body fat loss success during a 6-month randomized controlled diet intervention. *Int J Obes* 2018;**42**:580–3.

167 Beaumont M, Portune KJ, Steuer N, *et al.* Quantity and source of dietary protein influence metabolite production by gut microbiota and rectal mucosa gene expression: a randomized, parallel, double-blind trial in overweight humans. *Am J Clin Nutr* 2017;**106**:1005–19.

168 Haro C, García-Carpintero S, Rangel-Zúñiga OA, *et al.* Consumption of Two Healthy Dietary Patterns Restored Microbiota Dysbiosis in Obese Patients with Metabolic Dysfunction. *Mol Nutr Food Res* 2017;**61**. doi:10.1002/mnfr.201700300

169 Colica C, Avolio E, Bollero P, *et al.* Evidences of a New Psychobiotic Formulation on Body Composition and Anxiety. *Mediators Inflamm* 2017;**2017**:5650627.

170 Nabhani Z, Hezaveh SJG, Razmpoosh E, *et al.* The effects of synbiotic supplementation on insulin resistance/sensitivity, lipid profile and total antioxidant capacity in women with gestational diabetes mellitus: A randomized double blind placebo controlled clinical trial. *Diabetes Res Clin Pract* 2018;**138**:149–57.

171 Jones RB, Alderete TL, Martin AA, *et al.* Probiotic supplementation increases obesity with no detectable effects on liver fat or gut microbiota in obese Hispanic adolescents: a 16-week, randomized, placebo-controlled trial. *Pediatr Obes* 2018;**13**:705–14.

172 Loo RL, Zou X, Appel LJ, *et al.* Characterization of metabolic responses to healthy diets and association with

blood pressure: application to the Optimal Macronutrient Intake Trial for Heart Health (OmniHeart), a randomized controlled study. *Am J Clin Nutr* 2018;**107**:323–34.

173 Büsing F, Hägele FA, Nas A, *et al.* High intake of orange juice and cola differently affects metabolic risk in healthy subjects. *Clin Nutr* 2019;**38**:812–9.

174 González-Sarrías A, Romo-Vaquero M, García-Villalba R, *et al.* The Endotoxemia Marker Lipopolysaccharide-Binding Protein is Reduced in Overweight-Obese Subjects Consuming Pomegranate Extract by Modulating the Gut Microbiota: A Randomized Clinical Trial. *Mol Nutr Food Res* 2018;**62**:e1800160.

175 Rabiei S, Hedayati M, Rashidkhani B, *et al.* The Effects of Synbiotic Supplementation on Body Mass Index, Metabolic and Inflammatory Biomarkers, and Appetite in Patients with Metabolic Syndrome: A Triple-Blind Randomized Controlled Trial. *J Diet Suppl* 2019;**16**:294–306.

176 Holscher HD, Guetterman HM, Swanson KS, *et al.* Walnut Consumption Alters the Gastrointestinal Microbiota, Microbially Derived Secondary Bile Acids, and Health Markers in Healthy Adults: A Randomized Controlled Trial. *J Nutr* 2018;**148**:861–7.

177 Bomhof MR, Parnell JA, Ramay HR, *et al.* Histological improvement of non-alcoholic steatohepatitis with a prebiotic: a pilot clinical trial. *Eur J Nutr* 2019;**58**:1735–45.

178 Szulińska M, Łoniewski I, van Hemert S, *et al.* Dose-Dependent Effects of Multispecies Probiotic Supplementation on the Lipopolysaccharide (LPS) Level and Cardiometabolic Profile in Obese Postmenopausal Women: A 12-Week Randomized Clinical Trial. *Nutrients* 2018;**10**. doi:10.3390/nu10060773

179 Kassaian N, Feizi A, Aminorroaya A, *et al.* The effects of probiotics and synbiotic supplementation on glucose and insulin metabolism in adults with prediabetes: a double-blind randomized clinical trial. *Acta Diabetol* 2018;**55**:1019–28.

180 Wilson R, Willis J, Gearry RB, *et al.* SunGold Kiwifruit Supplementation of Individuals with Prediabetes Alters Gut Microbiota and Improves Vitamin C Status, Anthropometric and Clinical Markers. *Nutrients* 2018;**10**. doi:10.3390/nu10070895

181 Mano F, Ikeda K, Joo E, *et al.* The Effect of White Rice and White Bread as Staple Foods on Gut Microbiota and Host Metabolism. *Nutrients* 2018;**10**. doi:10.3390/nu10091323

182 Angiletta CJ, Griffin LE, Steele CN, *et al.* Impact of short-term flavanol supplementation on fasting plasma trimethylamine N-oxide concentrations in obese adults. *Food Funct* 2018;**9**:5350–61.

183 Velikonja A, Lipoglavšek L, Zorec M, *et al.* Alterations in gut microbiota composition and metabolic parameters after dietary intervention with barley beta glucans in patients with high risk for metabolic syndrome development. *Anaerobe* 2019;**55**:67–77.

184 Erickson ML, Malin SK, Wang Z, *et al.* Effects of Lifestyle Intervention on Plasma Trimethylamine N-Oxide in Obese Adults. *Nutrients* 2019;**11**. doi:10.3390/nu11010179

185 Malin SK, Kullman EL, Scelsi AR, *et al.* A Whole-Grain Diet Increases Glucose-Stimulated Insulin Secretion Independent of Gut Hormones in Adults at Risk for Type 2 Diabetes. *Mol Nutr Food Res* 2019;**63**:e1800967.

186 Kjølbæk L, Benítez-Páez A, Gómez Del Pulgar EM, *et al.* Arabinoxylan oligosaccharides and polyunsaturated fatty acid effects on gut microbiota and metabolic markers in overweight individuals with signs of metabolic syndrome: A randomized cross-over trial. *Clin Nutr* 2020;**39**:67–79.

187 Wan Y, Yuan J, Li J, *et al.* Unconjugated and secondary bile acid profiles in response to higher-fat, lower-carbohydrate diet and associated with related gut microbiota: A 6-month randomized controlled-feeding trial. *Clin Nutr* 2020;**39**:395–404.

188 Rezazadeh L, Gargari BP, Jafarabadi MA, *et al.* Effects of probiotic yogurt on glycemic indexes and endothelial dysfunction markers in patients with metabolic syndrome. *Nutrition* 2019;**62**:162–8.

189 Culpepper T, Rowe CC, Rusch CT, *et al.* Three probiotic strains exert different effects on plasma bile acid profiles in healthy obese adults: randomised, double-blind placebo-controlled crossover study. *Benef Microbes* 2019;**10**:497–509.

190 Awoyemi A, Trøseid M, Arnesen H, *et al.* Effects of dietary intervention and n-3 PUFA supplementation on markers of gut-related inflammation and their association with cardiovascular events in a high-risk population. *Atherosclerosis* 2019;**286**:53–9.

191 Frost F, Storck LJ, Kacprowski T, *et al.* A structured weight loss program increases gut microbiota phylogenetic diversity and reduces levels of Collinsella in obese type 2 diabetics: A pilot study. *PLoS One* 2019;**14**:e0219489.

192 Christensen L, Vuholm S, Roager HM, *et al.* Prevotella Abundance Predicts Weight Loss Success in Healthy, Overweight Adults Consuming a Whole-Grain Diet Ad Libitum: A Post Hoc Analysis of a 6-Wk Randomized Controlled Trial. *J Nutr* 2019;**149**:2174–81.

193 Hess AL, Benítez-Páez A, Blædel T, *et al.* The effect of inulin and resistant maltodextrin on weight loss during energy restriction: a randomised, placebo-controlled, double-blinded intervention. *Eur J Nutr* 2020;**59**:2507–24.

194 Horvath A, Leber B, Feldbacher N, *et al.* Effects of a multispecies synbiotic on glucose metabolism, lipid marker, gut microbiome composition, gut permeability, and quality of life in diabesity: a randomized, double-blind, placebo-controlled pilot study. *Eur J Nutr* 2020;**59**:2969–83.

195 Li L, Xiong Q, Zhao J, *et al.* Inulin-type fructan intervention restricts the increase in gut microbiome-generated indole in patients with peritoneal dialysis: a randomized crossover study. *Am J Clin Nutr* 2020;**111**:1087–99.

196 Burton KJ, Krüger R, Scherz V, *et al.* Trimethylamine-N-Oxide Postprandial Response in Plasma and Urine Is Lower After Fermented Compared to Non-Fermented Dairy Consumption in Healthy Adults. *Nutrients* 2020;**12**. doi:10.3390/nu12010234

197 Talebi S, Karimifar M, Heidari Z, *et al.* The effects of synbiotic supplementation on thyroid function and inflammation in hypothyroid patients: A randomized, double-blind, placebo-controlled trial. *Complement Ther Med* 2020;**48**:102234.

198 Eriksen AK, Brunius C, Mazidi M, *et al.* Effects of whole-grain wheat, rye, and lignan supplementation on cardiometabolic risk factors in men with metabolic syndrome: a randomized crossover trial. *Am J Clin Nutr* 2020;**111**:864–76.

199 Jamar G, Santamarina AB, Casagrande BP, *et al.* Prebiotic potencial of juçara berry on changes in gut bacteria and acetate of individuals with obesity. *Eur J Nutr* 2020;**59**:3767–78.

200 Mirzaeian S, Saraf-Bank S, Entezari MH, *et al.* Effects of synbiotic supplementation on microbiota-derived protein-bound uremic toxins, systemic inflammation, and biochemical parameters in patients on hemodialysis: A double-blind, placebo-controlled, randomized clinical trial. *Nutrition* 2020;**73**:110713.

201 Zhu C, Sawrey-Kubicek L, Bardagjy AS, *et al.* Whole egg consumption increases plasma choline and betaine without affecting TMAO levels or gut microbiome in overweight postmenopausal women. *Nutr Res* 2020;**78**:36–41.

202 Chen L, He FJ, Dong Y, *et al.* Modest Sodium Reduction Increases Circulating Short-Chain Fatty Acids in Untreated Hypertensives: A Randomized, Double-Blind, Placebo-Controlled Trial. *Hypertension* 2020;**76**:73–9.

203 Sanborn VE, Azcarate-Peril MA, Gunstad J. Lactobacillus rhamnosus GG and HbA1c in middle age and older adults without type 2 diabetes mellitus: A preliminary randomized study. *Diabetes Metab Syndr* 2020;**14**:907–9.

204 Kassaian N, Feizi A, Rostami S, *et al.* The effects of 6 mo of supplementation with probiotics and synbiotics on gut microbiota in the adults with prediabetes: A double blind randomized clinical trial. *Nutrition* 2020;**79-80**:110854.

205 Vitale M, Giacco R, Laiola M, *et al.* Acute and chronic improvement in postprandial glucose metabolism by a diet resembling the traditional Mediterranean dietary pattern: Can SCFAs play a role? *Clin Nutr* 2021;**40**:428–37.

206 Igwe EO, Roodenrys S, Probst YC, *et al.* Low anthocyanin plum nectar does not impact cognition, blood pressure and gut microbiota in healthy older adults: A randomized crossover trial. *Nutr Res* 2020;**82**:74–87.

207 Ramos-Romero S, Léniz A, Martínez-Maqueda D, *et al.* Inter-Individual Variability in Insulin Response after Grape Pomace Supplementation in Subjects at High Cardiometabolic Risk: Role of Microbiota and miRNA. *Mol Nutr Food Res* 2021;**65**:e2000113.

208 Le Barz M, Vors C, Combe E, *et al.* Milk polar lipids favorably alter circulating and intestinal ceramide and sphingomyelin species in postmenopausal women. *JCI Insight* 2021;**6**. doi:10.1172/jci.insight.146161

209 Biruete A, Cross T-WL, Allen JM, *et al.* Effect of Dietary Inulin Supplementation on the Gut Microbiota Composition and Derived Metabolites of Individuals Undergoing Hemodialysis: A Pilot Study. *J Ren Nutr* 2021;**31**:512–22.

210 Kavyani M, Saleh-Ghadimi S, Dehghan P, *et al.* Co-supplementation of camelina oil and a prebiotic is more effective for in improving cardiometabolic risk factors and mental health in patients with NAFLD: a randomized clinical trial. *Food Funct* 2021;**12**:8594–604.

211 Bel Lassen P, Belda E, Prifti E, *et al.* Protein supplementation during an energy-restricted diet induces visceral fat loss and gut microbiota amino acid metabolism activation: a randomized trial. *Sci Rep* 2021;**11**:15620.

212 Saleh-Ghadimi S, Dehghan P, Sarmadi B, *et al.* Improvement of sleep by resistant dextrin prebiotic in type 2 diabetic women coincides with attenuation of metabolic endotoxemia: involvement of gut-brain axis. *J Sci Food Agric* 2022;**102**:5229–37.

213 Wan J, An L, Ren Z, *et al.* Effects of galactooligosaccharides on maternal gut microbiota, glucose metabolism, lipid metabolism and inflammation in pregnancy: A randomized controlled pilot study. *Front Endocrinol* 2023;**14**:1034266.

214 Papadopoulou RT, Theodorou MR, Ieong CS, *et al.* The Acute Effect of Meal Timing on the Gut Microbiome and the Cardiometabolic Health of the Host: A Crossover Randomized Control Trial. *Ann Nutr Metab* 2020;**76**:322–33.

215 Polito R, Costabile G, Nigro E, *et al.* Nutritional factors influencing plasma adiponectin levels: results from a randomised controlled study with whole-grain cereals. *Int J Food Sci Nutr* 2020;**71**:509–15.